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Item 5 (c) (vii) of the provisional agenda*

Technical work: review of notifications of final regulatory action: mercury

Mercury: supporting documentation provided by the European Union

Note by the Secretariat

As is mentioned in the note by the Secretariat on mercury: notifications of final regulatory action (UNEP/FAO/RC/CRC.19/11), the annex to the present note sets out documentation provided by the European Union to support its notification of final regulatory action for mercury in the industrial category. The present note, including its annex, has not been formally edited.

* UNEP/FAO/RC/CRC.19/1/Rev.1.

Annex

Mercury: supporting documentation provided by the European Union

List of documents:

1. Committee for Risk Assessment (RAC), Committee for Socio-economic Analysis (SEAC). Opinion on an Annex XV dossier proposing restrictions on mercury in measuring devices. ECHA/RAC/RES-O-0000001363-81-02/F. ECHA/SEAC/ RES-O-0000001363-81-03/F. Compiled version prepared by the ECHA Secretariat of RAC's opinion (adopted 8 June 2011) and SEAC's opinion (adopted 15 September 2011). European Chemicals Agency.
2. Committee for Risk Assessment (RAC), Committee for Socio-economic Analysis (SEAC). Background document to the opinions on the Annex XV dossier proposing restrictions on Mercury in measuring devices. ECHA/RAC/ RES-O-0000001363-81-02/F. ECHA/SEAC/ RES-O-0000001363-81-03/S1. 15 September 2011. European Chemicals Agency.
3. Opinion of the Scientific Panel on Contaminants in the Food Chain on a request from the Commission related to mercury and methylmercury in food. Request N° EFSA-Q-2003-030. Adopted on 24 February 2004. The EFSA Journal (2004) 34, 1-14.
4. Mercury as undesirable substance in animal feed. Scientific opinion of the Panel on Contaminants in the Food Chain. Question N° EFSA-Q-2005-288. Adopted on 20 February 2008. The EFSA Journal (2008) 654, 1-76.
5. Scientific opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA Panel on Contaminants in the Food Chain (CONTAM). EFSA Journal 2012;10(12):2985.
6. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). The safety of dental amalgam and alternative dental restoration materials for patients and users. 2008.
7. Scientific Committee on Health and Environmental Risks (SCHER). Opinion on the environmental risks and indirect health effects of mercury from dental amalgam (update). 2014.
8. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Opinion on the safety of dental amalgam and alternative dental restoration materials for patients and users. 2015.
9. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Mercury sphygmomanometers in healthcare and the feasibility of alternatives. 2009.
10. Scientific Committee on Health and Environmental Risks (SCHER). Opinion on mercury in certain energy-saving light bulbs. 2010.
11. Communication from the Commission to the Council and the European Parliament. Community Strategy Concerning Mercury. SEC(2005) 101. Brussels, 28.01.2005. COM(2005) 20 final.
12. Communication from the Commission to the European Parliament and the Council on the review of the Community Strategy Concerning Mercury. Brussels, 7.12.2010. COM(2010) 723 final.
13. Proposal for a regulation of the European Parliament and of the Council on mercury, and repealing Regulation (EC) No 1102/2008. Brussels, 2.2.2016. COM(2016) 39 final. 2016/0023 (COD).
14. REGULATION (EU) 2017/852 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 17 May 2017 on mercury, and repealing Regulation (EC) No 1102/2008.

Committee for Risk Assessment (RAC)

Committee for Socio-economic Analysis (SEAC)

Opinion

on an Annex XV dossier proposing restrictions on

mercury in measuring devices

ECHA/RAC/RES-O-0000001363-81-02/F
ECHA/SEAC/ RES-O-0000001363-81-03/F

Compiled version prepared by the ECHA Secretariat of RAC's opinion (adopted 8 June 2011) and SEAC's opinion (adopted 15 September 2011)

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8 June 2011
RES-O-0000001363-81-02/F

15 September 2011
RES-O-0000001363-81-03/F

Opinion of the Committee for Risk Assessment
And
Opinion of the Committee for Socio-economic Analysis
on an Annex XV dossier proposing restrictions of the manufacture, placing on the market or use of a substance within the Community

Having regard to Regulation (EC) No 1907/2006 of the European Parliament and of the Council 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (the REACH Regulation), and in particular the definition of a restriction in Article 3(31) and Title VIII thereof, the Committee for Risk Assessment (RAC) has adopted an opinion in accordance with Article 70 of the REACH Regulation and the Committee for Socio-economic Analysis (SEAC) has adopted an opinion in accordance with Article 71 of the REACH Regulation on the proposal for restriction of

Chemical name(s):	***Mercury***
EC No.:	***231-106-7***
CAS No.:	***7439-97-6***

This document presents the opinions adopted by RAC and SEAC. The Background Document (BD), as a supportive document to both RAC and SEAC opinions, gives the detailed ground for the opinions.

PROCESS FOR ADOPTION OF THE OPINIONS

EUROPEAN CHEMICALS AGENCY (ECHA) has submitted a proposal for a restriction together with the justification and background information documented in an Annex XV dossier. The Annex XV report conforming to the requirements of Annex XV of the REACH Regulation was made publicly available at ***http://echa.europa.eu/consultations/restrictions/ongoing_consultations_en.asp*** on ***24 September 2010***. Interested parties were invited to submit comments and contributions by ***24 March 2011***.

ADOPTION OF THE OPINION

ADOPTION OF THE OPINION OF RAC:

Rapporteur, appointed by RAC: ***Frank JENSEN***
Co-rapporteur, appointed by RAC: ***Boguslaw BARANSKI***

The RAC opinion as to whether the suggested restrictions are appropriate in reducing the risk to human health and/or the environment has been reached in accordance with Article 70 of the REACH Regulation on ***08 June 2011***.

The opinion takes into account the comments of interested parties provided in accordance with Article 69(6) of the REACH Regulation.

The RAC opinion was adopted ***by consensus***.

ADOPTION OF THE OPINION OF SEAC

Rapporteur, appointed by the SEAC: ***Cees LUTTIKHUIZEN***
Co-rapporteur, appointed by the SEAC: ***Izabela RYDLEWSKA-LISZKOWSKA***

The draft opinion of SEAC

The draft opinion of SEAC on the suggested restriction has been agreed in accordance with Article 71(1) of the REACH Regulation on ***15 June 2011.***

The draft opinion takes into account the comments of and contributions from the interested parties provided in accordance with Article 69(6) of the REACH Regulation.

The draft opinion was published at ***http://echa.europa.eu/reach/restriction/restrictions_under_consideration_en.asp*** on ***17 June 2011.*** Interested parties were invited to submit comments on the draft opinion by ***16 August 2011***.

The opinion of SEAC

The opinion of the SEAC on the suggested restriction was adopted in accordance with Article 71(1) and (2) of the REACH Regulation on **15 September 2011.**

The opinion takes into account the comments of interested parties provided in accordance with Articles 69(6) and 71(1) of the REACH Regulation.

The opinion of SEAC was adopted ***by consensus***.

OPINION

THE OPINION OF RAC

RAC has formulated its opinion on the proposed restriction based on information related to the identified risk and to the identified options to reduce the risk as documented in the Annex XV report and submitted by interested parties as well as other available information as recorded in the Background Document. RAC considers that the proposed restriction on ***Mercury in measuring devices*** is the most appropriate Community wide measure to address the identified risks in terms of the effectiveness in reducing the risks provided that the scope and/or conditions are modified.

The conditions of the restriction proposed by RAC are:

Mercury, CAS 7439-97-6, EC 231-106-7

The following restrictions with derogations are proposed for mercury measuring devices in professional and industrial uses. They do not affect the existing restriction on mercury in measuring devices intended for sale to general public and on mercury in fever thermometers established in entry 18a of Annex XVII to the REACH Regulation.

1. Mercury containing barometers, hygrometers, manometers, sphygmomanometers, strain gauges to be used with plethysmographs, tensiometers, thermometers and other non-electrical thermometric applications shall not be placed on the market after [18 months of the entry into force]. This applies also to measuring devices placed on the market empty intended to be filled with mercury.

2. The restriction in paragraph 1 shall not apply to:

   (a) Sphygmomanometers to be used (i) in epidemiological studies which are on-going at entry into force; (ii) as reference standards in clinical validation studies of mercury-free sphygmomanometers.

   (b) Thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers until [5 years after the entry into force].

   (c) Mercury triple point cells that are used for the calibration of platinum resistance thermometers.

3. Mercury pycnometers and mercury metering devices for determination of the softening point shall not be placed on the market after [18 months of the entry into force].

4. The restrictions in paragraphs 1 and 3 shall not apply to measuring devices which are to be displayed in exhibitions for cultural and historical purposes.

THE OPINION OF SEAC

SEAC has formulated its opinion on the proposed restriction based on information related to socio-economic benefits and costs documented in the Annex XV report and comments submitted by interested parties as well as other available information as recorded in the Background Document. SEAC considers that the proposed restriction on ***Mercury in measuring devices*** is the most appropriate Community-wide measure to address the identified risks considering the proportionality of its socio-economic benefits to its socio-economic costs provided that the scope and conditions are modified.

The conditions of the restriction proposed by SEAC are:

Mercury, CAS 7439-97-6, EC 231-106-7

The following restrictions with derogations are proposed for mercury measuring devices in professional and industrial uses. They do not affect the existing restriction on mercury in measuring devices intended for sale to general public and on mercury in fever thermometers established in entry 18a of Annex XVII to the REACH Regulation.

1. Mercury containing barometers, hygrometers, manometers, sphygmomanometers, strain gauges to be used with plethysmographs, tensiometers, thermometers and other non-electrical thermometric applications shall not be placed on the market after [18 months of the entry into force]. This applies also to measuring devices placed on the market empty intended to be filled with mercury.
2. The restriction in paragraph 1 shall not apply to:
   (a) Sphygmomanometers to be used (i) in epidemiological studies which are on-going at entry into force; (ii) as reference standards in clinical validation studies of mercury-free sphygmomanometers.
   (b) Thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers until [5 years after the entry into force].
   (c) Mercury triple point cells that are used for the calibration of platinum resistance thermometers.
3. Mercury pycnometers and mercury metering devices for determination of the softening point shall not be placed on the market after [18 months of the entry into force].
4. The restrictions in paragraphs 1 and 3 shall not apply to:
   (a) Measuring devices more than 50 years old on 3 October 2007, or
   (b) Measuring devices which are to be displayed in public exhibitions for cultural and historical purposes.

JUSTIFICATION FOR THE OPINION OF RAC AND SEAC

The opinion covers restriction proposals for a number of mercury measuring devices[1], with the aim to reduce the amount of mercury in our society.

Restrictions without device specific derogations are proposed for the placing on the market of mercury containing barometers, hygrometers, manometers, tensiometers, strain gauges and of mercury using pycnometers and meters for the determination of the softening point.

Restrictions with limited derogations for the placing on the market are proposed for sphygmomanometers and thermometers, while no restrictions are proposed for mercury using porosimeters, mercury probes used for capacitance-voltage determinations and electrodes.

"Placing on the market" in these restrictions includes not only placing on the market for the first time, meaning the second-hand market is included. There is no proposal to restrict the use of mercury measuring devices that are already placed on the market.

Based on the information received during the public consultation on the Annex XV restriction report, RAC suggests that the proposed restriction would not apply to measuring devices which are to be displayed in exhibitions for cultural and historical purposes[2]. This derogation would replace the proposed derogation in the Annex XV restriction report for measuring devices that are more than 50 years old on 3 October 2007.

Identified hazard and risk

Justification for the opinion of RAC

Mercury is a very hazardous substance. Mercury is highly toxic to humans, ecosystems and wildlife, in particular when chemically converted to methylmercury. The nervous system and the developing brain are the most sensitive target organs.

Mercury is found both naturally and as an introduced contaminant in the environment. Anthropogenic emissions have widespread impacts on human and environmental health. Mercury is considered to be a global persistent pollutant; in the environment it cannot be broken down to any harmless form. Once emitted, mercury enters the complex biogeochemical cycle. After intensive use of mercury over many years mercury can be found in almost all environmental compartments, like the atmosphere, soil and water systems and in biota all over the world. The formation of methylmercury and subsequent biomagnification in food chains considerably increases risks posed by mercury causing, among others, chronic intoxications of people, although it is difficult to determine the proportion of mercury contaminating the environment, which is turned into methylmercury. Therefore it is necessary to reduce the risk of exposure to mercury for humans and the environment. The key, long term benefit of reducing mercury emissions will be decreased levels of mercury in the environment. This, in turn, will lead to lower levels of human exposure to mercury, including methylmercury in fish, with resultant health benefits. It will also reduce the impacts of mercury on soils and biodiversity.

According to the EU Community strategy concerning mercury most people in coastal areas of Mediterranean countries, and around 1-5% of the population in central and northern Europe, show bioindicators of exposure that are around internationally accepted safe levels for

[1] The term "mercury measuring devices" is used throughout this document to cover both, measuring devices containing mercury and measuring devices using mercury.
[2] SEAC specified in its opinion that this relates to public exhibitions.

methylmercury and large numbers among Mediterranean fishing communities and the Arctic population exceed them significantly.

Although the BD to this opinion underlines that mercury as an element is persistent and that methylmercury bioaccumulates, biomagnifies, and is highly toxic, it does not explicitly compare these properties of mercury with the PBT criteria of Annex XIII to REACH. However, the following comparison is made in the opinion document on phenylmercury compounds[3].

The inorganic form of mercury is not covered by Annex XIII. Elemental mercury is by definition persistent; as it is not removed from the environment through degradation processes and will always be potentially available for cycling into methylmercury (through complex processes under appropriate conditions, even at equilibrium there is a near constant level of methylmercury in sediment). Any increase in the environmental pool of inorganic mercury will provide an additional source of methylmercury, and this source will persist for many years. It is therefore not relevant to compare half-life data with the Annex XIII "P" criterion. Mercury cycling itself represents an equivalent level of concern for persistence (or even "very persistent"). Furthermore, rate of demethylation can be under anaerobic conditions lower than methylation.

The "B" criterion of Annex XIII is met by methylmercury as the bioconcentration factor (BCF) in fish can range from 8140 to 85 700 and is thus higher than the threshold value for bioaccumulative and very bioaccumulative. Methylmercury' biomagnification is very high with a typical increase of more than 1 log unit between trophic levels, and bioaccumulation factor BAF can reach values 10^7 times higher than the concentration measured in water (Hill et *al.*, 1996; Weiner *et al*., 2003).

The "T" criterion of Annex XIII is met by methylmercury which NOEC is 0.26 µg Hg /l which is 2 orders of magnitude below the threshold value of 10 µg/l. The classification of methylmercury and mercury for reproductive toxicity category 1B and 1A respectively also confirm this criterion.

Once released into the atmosphere, mercury can undergo long-range atmospheric transport, hence the atmosphere is the most important pathway for the worldwide dispersion and transport of mercury in the environment. The Arctic is believed to be a global sink of mercury due to a set of extraordinary circumstances occurring during Polar spring. Certain indigenous communities, for example in the Arctic, have been shown to be particularly vulnerable due to high levels of deposition and accumulation of methylmercury in their traditional foods (even though they use and emit virtually no mercury).

The global threat from mercury releases warrants action at local, national, regional and global level. There is now a world-wide common effort to reduce both demand and supply of mercury. In 2009, the UN Environment Governing Council agreed to take steps towards a global legally binding instrument to control uses and emissions of mercury. The Council of the European Union supports this step towards an international treaty.

The European Union has launched an EU mercury strategy in 2005. It contains 20 measures to reduce mercury emissions, cut supply and demand. Two of the measures are:

"Action 7. The Commission intends to propose in 2005 an amendment to Directive 76/769EEC to restrict the marketing for consumer use and healthcare of non-electrical or electronic measuring and control equipment containing mercury.

Action 8. The Commission will further study in the short term the few remaining products and applications in the EU that use small amounts of mercury. In the medium to longer term, any

[3] http://echa.europa.eu/reach/restriction/restrictions_under_consideration_en.asp

remaining uses may be subject to authorisation and consideration of substitution under the proposed REACH Regulation, once adopted".

The Strategy has resulted in restrictions on the placing on the market for the general public of measuring devices containing mercury. In this restriction (Annex XVII, entry 18a, of the REACH Regulation) there is a review clause which states: *"[The Commission] shall carry out a review of the availability of reliable safer alternatives that are technically and economically feasible."*

The current proposal of restriction of mercury in measuring devices and present Annex XV dossier is the result of this review clause.

RAC recognises this as unusual starting point for an opinion. Therefore the proposal and therefore also this opinion has focussed on the technical feasibility of the alternatives with their hazards, exposures and risks being compared with those of mercury in semi-quantitative and qualitative terms.

It is estimated that 3.5 to 7.6 tonnes of mercury is placed on the market in mercury containing measuring devices in 2010. These amounts are used to estimate the maximum potential for mercury emissions to the environment that might ultimately occur. This assumption is considered appropriate because of an estimated low separate collection rate of mercury waste and resulting inadequate waste treatment of a substantial part of the devices. This inappropriate waste collection leads in the long term to a relatively high share of mercury used in these devices being released to the environment.

For measuring equipment using mercury (porosimeters, mercury probes used for capacitance-voltage determinations and mercury electrodes used in voltammeters) the total use is 5-15 tonnes per year (mostly porosimeters 5-14 tonnes per year). It should be noted, that these figures are the amount of mercury the laboratories purchase and cannot be used to estimate maximum potential for emission as is the case for the measuring equipment containing mercury. To estimate emissions several additional factors need to be considered. These include number of measurements carried out, practices to purify and regenerated used mercury and the risk management measures and operational conditions applied to control the emissions and exposures.

The total mercury consumption in Europe was in 2007 estimated to be 320-530 tonnes. 160-190 tonnes of the total amount were used in the chlor-alkali production and 90-110 were used in dental amalgams. The amount used in mercury measuring devices thus equals about 4% of the total, while the restricted devices will be lower due to the large use in porosimeters.

Justification that action is required on a Community-wide basis

Justification for the opinion of RAC

RAC considers that it is justified that the proposed restriction needs to be on a Community-wide basis.

The mercury measuring devices containing mercury are used widespread across the EU countries. Emissions come from daily use and waste handling. Mercury is volatile at low temperature and can easily be transported over long distances both through air and biota.

The main reason to act on a Community-wide basis is the cross-boundary human health and environmental problem. Furthermore, the fact that the goods need to circulate freely within the EU stresses the importance of the Community-wide action, as some Member States have already national restrictions for mercury measuring devices. Thus, the use of mercury in these

devices needs to be controlled also at the EU level. In addition, acting at Community level strengthens the possibilities to address the adverse impacts of mercury at worldwide level.

Justification for the opinion of SEAC

The proposed Community-wide restrictions are in principle appropriate; comments on the proposal are elaborated below. The mercury measuring devices are produced in as well as imported to the European Union (EU). The proposed restrictions will cut off the supply of these mercury measuring devices to the market in the EU and therefore contribute to the reduction of the available amount of mercury in that market. The proposed restrictions would remove the potentially distorting effect that the current national restrictions may have, leading to a level playing field within the EU for producers and importers. In addition, acting at a Community level could strengthen the possibilities of policymakers to address the adverse impacts of mercury worldwide.

Justification that the suggested restriction is the most appropriate Community-wide measure

Justification for the opinion of RAC

Restriction of use of mercury in selected measuring devices is a part of EU strategy to reduce use of mercury, particularly it is a result of the action undertaken in response to a review clause built into the current entry 18a for mercury in Annex XVII to REACH.

RAC considers the proposed community wide restrictions to be necessary and appropriate. It reduces the risk of exposure to mercury for both man and the environment. Implementation of this restriction will considerably reduce the amount of mercury in measuring devices in professional and industrial uses being introduced on the EU market. The risks associated with alternative measuring devices without mercury are considered to be significantly lower than health and environmental risks posed by mercury in mercury measuring devices.

RAC is of the opinion that the proposed restriction will reduce effectively the amount of mercury being released into environment from mercury measuring devices, contribute to reduction of the level of environmental or occupational exposure to mercury of humans and environmental biota and it will increase a use of alternative measuring devices posing substantially smaller risk to humans and environment than measuring devices containing mercury.

Mercury measuring devices proposed to be restricted are small devices scattered in numerous workplaces of various types, and assuring an appropriate collection and management of wastes is difficult. The currently used risk management measures (RMM) applied on voluntary and mandatory basis were found not sufficiently effective in preventing continuous increase of mercury level in the environment and in the human, animal and plant tissues. Thus, the other risk management measures were not effective in controlling health and environmental risks posed by mercury.

Mercury measuring devices are not a major source of mercury release into the environment; however it has been demonstrated that there are alternative devices, which can replace the devices containing mercury and the use of which is associated with risks to human health and environment substantially smaller than risks caused by mercury.

Several existing pieces of legislation abate the risks arising from mercury in different stages of the life-cycle of measuring devices. However, none of the measures currently in place is

sufficient to remove the concern fully, although there is a difference between their observed effectiveness with regard to measuring devices containing mercury and measuring devices using mercury. No other EU legislation which may have the potential of reducing the emissions and risks posed by mercury was identified.

The originally proposed exemption for mercury-in-glass thermometers used by industry to measure temperatures above 200°C is proposed to be deleted. It was originally proposed due to economic reasons – these reasons have been investigated further and SEAC reached the conclusion that the exemption is no longer necessary. RAC approves this removal of the exemption because the technically feasible alternatives pose substantially lower environmental and human health risks.

RAC would like to highlight the need for other Community-wide measures to improve the collection rate of mercury measuring devices already on the market and to take adequate measures for proper waste handling. An effective collection system for these devices is needed and requires cooperation with the EU authorities for waste legislation.

RAC would also highlight the need to address the production of mercury measuring devices intended for export out of the Community, as exposure will still arise from this production until measures are taken to address production intended for export (like the Regulation (EC) No 1102/2008).

Another issue RAC would highlight is the necessity for addressing the use of mercury in porosimeters. The amount used 5-14 t/y is by far the biggest use in measuring equipment and the uncertainties regarding recycling/reuse are large. Consequently, RAC urges the Commission to look into this within a very short period of time and if appropriate propose new legislative measures e.g. a long transitional period to allow users to adapt to a ban.

Justification for the opinion of SEAC

In the justification of the most appropriate Community-wide measure below, SEAC considers the proposed restriction from a broad perspective, covering the European waste legislation and the EU mercury export ban Regulation. Following the overall assessment, justifications are given for the restriction proposal in general and for each specific measuring device in particular.

In principle, considering the available information, the suggested restrictions for measuring devices are at the moment the most appropriate Community-wide measures to prevent further emissions from devices, being placed on the market. The suggested restrictions will reduce the total amount of mercury coming from these measuring devices in the long term. The proposed restrictions for the placing on the market, however, only partly address the risks of mercury in measuring devices. Other EU legislation, also with the potential to reduce the identified risks, is not assessed in detail in the BD, because of the scope of the review clause in paragraph 4 of entry 18a ‘mercury’ in Annex XVII of the REACH Regulation. This review clause aims at phasing out of mercury in measuring devices specifically, whenever technically and economically feasible.

The suggested restrictions do not prevent that mercury could be released to the environment when the existing devices enter the waste stage at the end of their life-cycle. The BD gives a rough indication that only 20% of the measuring devices are correctly collected in accordance with the requirements set out in the hazardous waste legislation. This implies that the other 80% of the mercury measuring devices already on the market are most probably not correctly dealt with. This could for example lead to mercury emissions to air by incineration or leaking

to groundwater or soil in case of inadequately protected landfills or other environmental unsound disposal. So outside the scope of REACH there may be a need for other Community-wide measures, and - additional to the proposed restrictions - a proper collection system for these devices may also be necessary to avoid mercury emissions into society from these devices. Collection rates for these devices should therefore improve, though this may require cooperation with the EU authorities for waste legislation. SEAC observes that a number of the electronic alternatives are covered by the RoHS Directive, where the waste impact is regulated through the WEEE Directive. In the present recast of these directives there is a discussion about an obligation for Member States to collect at least 65% of these devices. This demonstrates the need to improve the collection rate of mercury measuring devices already on the market and to take adequate measures for proper waste management.

A consequence of the proposed restriction is that the devices already in use cannot be placed on the market again and at the end of their service-life they have to be disposed of as hazardous waste in accordance with the EC waste legislation. Enforceability at the waste stage is considered appropriate and feasible, because environmentally sound disposal of hazardous waste is a legal obligation for all European Member States.

The proposed restriction does not affect the use of the measuring devices that are already placed on the market. Those devices were bought at a time when there was no restriction and may not yet have reached the end of their service-lives. A premature phase out by restricting their use could easily lead to unjustified capital losses. These losses of the residual value of capital are naturally affected by the potential transitional period after the entry into force of a use ban. In addition to the losses of the residual value of capital, the users affected by such a ban would be facing higher annualised costs for a certain period of time. These impacts have been estimated only for sphygmomanometers. According to the BD, assuming a 5 year transitional period, would lead to a compliance cost of € 8 million (present value for 2011-2024), and affect around 200,000 existing sphygmomanometers (see Annex 3b, Chapter 5). Enforceability of a use ban is more complicated in practice because the devices are used in many different places and users will first have to be made aware of this restriction before they switch to alternative devices.

A possible distorting effect with respect to the aim of the proposed restriction to reduce and eliminate the use of mercury is the allowed production by manufacturers in the EU for exports as long as the EC Regulation 1102/2008 does not limit the export of these devices. Especially in the case of measuring devices where restrictions are proposed without any derogation, SEAC considers an export ban a logical building block to further reduce the amount of mercury in the global community. Assessment of the socio-economic impact of an export ban for these devices falls outside the scope of the restriction proposal and is therefore not elaborated in the BD. An export ban should, however, result in better enforceability of the proposed restriction as manufacturing for both the European market as well as for export would then be prohibited. Article 8(4) of the EC Regulation 1102/2008 requires the Commission to submit a report and possible review of this Regulation by 15 March 2013, with amongst others the need for an extension of the export ban to mercury containing measuring devices.

Nevertheless, SEAC observes that the proposed Community-wide restrictions without derogations for some devices or with limited derogations for other devices are appropriate. Also the general exemptions for devices, older than 50 years or for devices which are to be displayed in public exhibitions for cultural and historical purposes, are appropriate.

The risk management options per device are further elaborated in conjunction with their effectiveness in reducing the risks in the next section.

Effectiveness in reducing the identified risks, proportionality to the risks

Justification for the opinion of RAC

The main purpose of the proposed restrictions is to reduce the mercury pool in the society, thus avoiding emissions and exposures causing negative impacts on human health and environment. Because of the well known and recognised properties of mercury, a quantitative exposure assessment or risk characterisation was not carried out. Instead, the total estimated amount of mercury placed on the market in measuring devices containing mercury is used to estimate the maximum potential for mercury *emissions to the environment* that might ultimately occur. The proposed restriction is expected to reduce the amount of mercury placed on the EU market (in devices or to be used in measurements) by 60 tonnes for a 20 year period starting from 2015[4]. It can be mentioned that this volume reduction would also decrease direct *exposure of workers* in production, use and waste phase -with the exception of exposure related to remaining production for exports. Table 1 summarises the risk reduction capacity of the proposed restriction for each device. As described above, the amounts of mercury placed on market annually are used to estimate the maximum emissions potential. Both estimates for the representative year (2024) and for the total effect of the 20 years (i.e. 2015-2034) are presented.

Table 1: Estimated amount of mercury not placed on the market as a result of the proposed restriction in 2015-2034 as well as in 2024

Device	**2024 per annum kg**	**2015-2034 cumulative kg**
Sphygmomanometers*	1 900	39 000
Thermometers (including hygrometers)*	500	10 000
Barometers**	350	7 000
Manometers (including tensiometers)**	200	4 000
Strain gauges**	14	280
Pycnometers***	~0	~0
Metering devices***	~0	~0
Total	**2 964**	**60 280**

Notes: * Number of the mercury containing devices projected to decline by 5% per annum as described in the device specific annexes 3a and 5a
** Assuming no change in the trend
*** There does not seem to be remaining markets for these devices in the EU and thus, the estimated amount of mercury not placed on the market would be close to 0 kg

RAC agrees with the originally proposed restrictions except for:
1. The exemption for mercury-in-glass thermometers used in industry to measure temperatures above 200°C as technically sufficient alternatives with better environmental and human health properties already exist.
2. The wording of "Restriction on the placing on the market of plethysmographs designed to be used with mercury strain gauges". This should be rephrased as the existing plethysmographs can be used without mercury. So the intention should be to only restrict the mercury containing strain gauges which could be reflected this way: "Restriction on the placing on the market of mercury containing strain gauges".

[4] Considering the estimates for the amounts of mercury used in products and processes in EU for 2010 (see section B.4 figure 1), the proposed restriction accounts for 1.5 % of the total use. However, the measuring devices account for 4 %, as the suggested restriction does not cover all the mercury measuring devices.

According to Annexes 1-10, technically feasible alternatives are available for mercury barometers, hygrometers, manometers, sphygmomanometers, strain gauges, thermometers, pycnometers, and metering devices, with the exception of:
- sphygmomanometers that are used in on-going epidemiological studies or as reference standards in clinical validation studies of mercury-free sphygmomanometers;
- thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers; and
- mercury triple point cells that are used for the calibration of platinum resistance thermometers[5].

In addition, technical feasibility of alternatives could **not** be established for mercury porosimeters, mercury probes used for capacitance-voltage determinations and devices using mercury electrodes in voltammetry (see section 3.3 of Annex 7, annex 10 and Annex 6 respectively).

As shown in Annex C to the BD the alternatives to mercury used in measuring devices are of lower relative risk compared to mercury measuring devices. This is shown in table 2.

Table 2 Semi-quantitative comparison of risks related to mercury containing measuring devices and their alternatives

	Production	**Service-life**	**Waste stage**		
			Proper treatment	No proper treatment	
				Incineration	Landfill
Hg	3	3	3	4	4
Hg-free liquid	1-2*	1-2*	1-2**		
EEE	1-2***	1	1	2	2
mechanical	1	1	1****		

Notes 1 - negligible risk potential; 2 -low risk potential; 3 - moderate risk potential; 4 - high risk potential
Hg - mercury containing measuring devices; Hg-free - measuring devices with mercury-free fillings; EEE - electronic measuring devices; mechanical - mechanical measuring devices.
*Overall risk potential, depending on the properties and share of liquids replacing mercury containing measuring devices.
** Overall risk potential, depending on type of treatment (incineration or landfill),and the properties and share of liquids replacing mercury containing measuring devices. Waste not subject to separate collection requirements.
*** As a rather conservative estimate.
****Waste not subject to separate collection requirements.

Justification for the opinion of SEAC

This section includes a device specific assessment, elaborating the possible options for the proposed restrictions in conjunction with their effectiveness in reducing the risks and the economic feasibility of possible alternatives. In the second part SEAC gives its view on the proportionality to the risks.

[5] Triple point cells are not thermometers, but they might fall under the broader wording that is used in the proposed restriction ('*thermometers and other non-electrical thermometric applications containing mercury*'). For this reason they are discussed as well.

Measuring devices without or with limited derogations:

Barometers
For barometers two other restriction options are identified in Section 4.1.2 of Annex 1 to the BD:

- To restrict also the use of existing mercury containing barometers
- To derogate the placing on the market of new mercury containing barometers for calibration purposes.

SEAC considers a restriction of the use of existing mercury containing barometers not to be an appropriate Community-wide measure. General arguments not to restrict the uses given in the previous section are also valid for the specific option here not to restrict the use of existing barometers. SEAC considers furthermore that there is no need for a derogation of new mercury containing barometers for calibration purposes because experiences in several Member States show that there is no need for this derogation.

The alternatives are economically feasible as they are available to users in the same price range and electronic barometers are already taking over market shares. Furthermore, the impact of the proposed restriction on the increased production costs of industrial users is estimated to be relatively small.

Manometers and tensiometers
For manometers and tensiometers no other Community-wide measures or restriction options have been identified. There are alternatives for all applications and the available evidence indicates that they are cheaper than mercury manometers and tensiometers, suggesting that the alternatives are both technically and economically feasible. SEAC hence agrees with the proposal for restrictions.

Strain gauges
Only one option was assessed, namely a ban on the placing on the market of plethysmographs designed to be used with mercury strain gauges. As a result of the public consultation, a restriction on the placing on the market of mercury strain gauges (instead of on placing on the market of plethysmographs designed to be used with mercury strain gauges) is preferred because the same plethysmographs can also be used with mercury-free strain gauges.

Considering the high investment cost for the plethysmograph itself (~ € 20,000), the additional annualised cost per gauge (~ € 12) by using the alternative indium-gallium strain gauges to the overall cost of measurements is considered negligible. SEAC concludes that economically feasible alternatives are available and already used to replace mercury strain gauges.

Pycnometers
Only one restriction option was considered, noting that this option will consolidate the current situation. There is evidence that replacement by available alternatives is already taking place. SEAC hence agrees with the proposed restriction.

Mercury metering device for the softening point determination
Only one restriction option was considered, noting that this option will consolidate the current situation. The alternatives, available from the same producer as mercury metering devices, are preferred by users and there is no evidence that economic feasibility is problematic. SEAC agrees with the proposed restriction.

Sphygmomanometers
The BD identifies two options, namely a restriction on the placing on the market (with limited derogations), and a restriction on use. Both options were assessed for their economic feasibility. The BD notes that a use ban provides opportunities for a more effective implementation of national collection campaigns. However, due to practical difficulties (enforceability) and potentially low risk reduction capacity a use ban is not proposed. Furthermore, the general remarks above about not restricting the use of devices are also valid here.

The compliance costs for the first option (restriction on the placing on the market) are calculated to be € 3.2 million per annum (or present value for 2015-2034 € 29 million), which results in an estimated cost-effectiveness of this measure of € 1,300 per kg Hg. Given the uncertainties in the calculations a sensitivity analysis was carried out in Annex 3b of the BD. The high cost scenario resulted in an estimated cost-effectiveness indication of € 3,000 per kg Hg, whereas the low cost scenario resulted in - € 2,400 per kg Hg. A negative cost implies a cost saving or benefit. It is concluded that the proposed restriction on sphygmomanometers is justified.

The second option (restriction on the use) has also been assessed in the BD. The present value compliance costs (for 2011-2024) for this option are estimated to be around € 8 million. Both the compliance costs as the risk reduction capacity are highly dependent on the proposed transitional period.

SEAC notes that the two derogations for use of sphygmomanometers (i) in on-going epidemiological studies and (ii) as reference standard for validation of mercury-free devices are without a time-limit. To SEAC's opinion this seems to be acceptable for the following reasons: (i) the derogation for on-going epidemiological studies is time-limited by nature, as it is covering only studies that are on-going at the entry into force, and (ii) it has not been possible to determine the time needed to develop (and recognise) a mercury-free alternative as a reference standard for clinical validation of existing and future mercury-free blood-pressure measuring devices.

The proposed restriction with limited derogations for sphygmomanometers is the most appropriate Community-wide measure. Also for sphygmomanometers entering the waste stage an effective collection system could contribute to the reduction of mercury releases into the environment.

Thermometers
There are five options assessed in the BD:
1a. Restriction of all laboratory thermometers.
1b. Restriction of laboratory thermometers with a time-limited derogation for some uses.
2a. Restriction of all industrial mercury thermometers.
2b. Restriction of industrial thermometers with a derogation for mercury-in-glass thermometers for temperature measurements above 200°C.
2c. As 2b, including a derogation for mercury dial thermometers.

Table A5a-11 in the BD summarizes the risk reduction capacities and the costs associated with the implementation of the different restriction options. The proposed restriction in the original Annex XV report was a combination of the options 1b and 2b. Taking into account additional advantages of electronic thermometers such as automatic reading and data generation, SEAC concludes that the restriction but without the derogation, that is based on options 1b and 2a, is justified. The public consultation did not bring up any evidence to the contrary.

It is concluded that technically feasible alternatives are available for all applications, with the exception of:

A) thermometers used for testing according to analysis standards that prescribe mercury thermometers, because some time is needed to amend those standards; and
B) mercury triple point cells because mercury is needed as a reference point in the 1990 International Temperature Scale.

The proposed derogations for these applications are justified. For the so-called laboratory thermometers intended to perform tests according to standards, the proposed derogation is time-limited.

All technically feasible alternatives are also economically feasible alternatives. The annualised costs of electronic alternatives for all lab thermometers, industrial dial thermometers, industrial thermometers measuring temperatures below 200°C, and thermometers for measuring ambient temperature and other meteorological measurements are either equal, lower or marginally higher than those for the mercury-containing thermometers. Calculations in the BD demonstrate the economic feasibility of alternatives for industrial thermometers for temperature measurements above 200°C. The annualised cost of alternatives for industry thermometers measuring temperature above 200°C is per device estimated to be around € 13 higher than the annualised cost of a corresponding mercury thermometer, including potential labour time savings (see Table A5b-25 of the BD). The additional annualised costs are estimated to be a relatively small percentage of the industrial users' total costs for purchases of goods and services and are expected to contribute only marginally to the final product cost. Furthermore, the alternatives have additional benefits over the mercury-containing devices which are not considered in the above estimate related to lower spill cleanup costs. In addition, the alternatives have already taken over the market for industrial thermometers and the majority of users are no longer heavy users of mercury-containing devices.

The compliance costs for the proposed restriction for thermometers are calculated to be € 9 million per annum (or present value for 2015-2034 € 97 million), which results in an estimated cost-effectiveness of this measure of € 19,200 per kg Hg. However, there are large uncertainties in these calculations and several one parameter sensitivity analyses are carried out in the Annex 5b of the BD for the different thermometer segments. The results of these sensitivity analyses vary between cost savings and costs of several hundred thousand Euros per kg Hg.

Based on the quantitative and qualitative information on effectiveness (including estimates on compliance costs, cost effectiveness and benefits), practicality and monitorability of the restriction options, it is concluded that the proposed restriction on thermometers is justified.

<u>Measuring devices for which no restriction has been proposed:</u>

Porosimeters

There are four options identified to reduce the risks related to the use of mercury in porosimeters:

1. The 1st option (with 3 sub-options) aims at reducing the amount of mercury used in porosimeters.
2. The 2nd option is the promotion of better waste handling.
3. The 3rd option (including 2 sub-options) is the promotion of appropriate handling of mercury in the use phase.
4. A further assessment of the technical feasibility of alternatives.

Due to the high uncertainty in the technical feasibility of alternatives the placing on the market of porosimeters is proposed not to be restricted. Although porosimeters significantly contribute to the amount of mercury used in devices, action on a Community-wide basis for these devices is at present not justified. SEAC urges the Commission to consider this issue at the short term and, if appropriate, to propose additional legislative measures e.g. a certain transitional period for industry to develop technical alternatives and to allow users to adapt to a ban.

Mercury electrodes used in voltammetry
Only one restriction option was considered: a restriction on the placing on the market of mercury to be used as mercury electrodes in voltammetry. The assessment concluded not to restrict this application; the reason for not restricting is in the evidence that feasible technical alternatives do not exist. SEAC agrees with the proposal.

Mercury probes used for capacitance-voltage determinations
Only one restriction option was considered: a restriction on the placing on the market of mercury probes used for capacitance-voltage determinations. The assessment concluded not to restrict this application; the reason for not restricting is in the evidence that none of the alternatives are both technically and economically feasible. SEAC agrees with the proposal.

Proportionality

The available information about the costs and benefits of the proposed restrictions included in the BD is limited and surrounded by considerable uncertainty. The BD presents the estimated cost-effectiveness of the proposed restrictions in Table 12. The overall cost-effectiveness is estimated to be € 4,100 per kg Hg, but of course there are variations between the different measuring devices.

Appendix 2 of the BD provides a literature review of studies estimating the compliance costs of different policy measures to reduce mercury from different sources, and the human health benefits of reduced mercury emissions, as well as the restoration costs. It includes in Table 1 e.g. cost information of replacing mercury containing items in the US/Minnesota between US$ 20 and 2000 (€ 17 and 1,745) per kg Hg, which comes closest to replacing the existing mercury measuring devices addressed here in the context of REACH.

Table 2 in Appendix 2 is furthermore considering the health benefits from reduced mercury exposure. In this approach uncertainty margins between € 4,926 and 17,683 per kg Hg are found for the avoided damage costs due to reduced mercury exposure, also based on scant empirical evidence from the US. These benefit estimates relate to emissions (to air) and are not directly comparable with the cost-effectiveness of reducing the amount of mercury placed on the market that is estimated in the BD. Furthermore, the values relate to human health impacts, thus omitting the values of impacts that affect the environment as such. Nevertheless, it is illustrative to compare the value ranges for the costs and benefits and to note that the lower end benefit estimate (€ 4,926) is still almost a factor three higher than the higher end cost estimate for replacing mercury items in US/Minnesota (€ 1,745). The lower bound of the benefit estimate refers to the cost of illness for persistent IQ deficits in children, which is scientifically considered most robust and credible. The upper bound refers to the estimated additional health damage costs related to premature male mortality rates due to the cardiovascular effects of eating mercury contaminated fish and is considered much less certain. The estimated benefits exclude however potential environmental benefits. Even if mercury placed on the market in measuring devices is not necessarily released into the environment, at least not immediately, the rate of collection of mercury measuring devices

after their service-life is low and significant amounts may therefore enter the environment in the long term.

Comparing the estimated costs of the proposed restrictions in Table 12 of the BD with the estimated benefits in Table 2 in Appendix 2 of the BD, the weighted average compliance costs of the proposed restrictions for mercury measuring devices (€ 4,100 per kg Hg) are lower than the lower bound of the benefit estimate, justifying an overall restriction. However, the costs vary across measuring devices. The costs of replacing sphygmomanometers can be justified compared to the expected health benefits and are hence considered proportionate to the reduced risk. The costs of replacing strain gauges (€ 9,600 per kg Hg) are almost a factor two higher than the lower bound benefit estimate, but fall well inside the range of € 4,926 and € 17,683 per kg Hg for reduced mercury exposure. The costs of thermometers and hygrometers are a factor two higher than the costs of strain gauges and a little bit higher than the upper bound of the benefit estimate, making it harder to justify the proposed restriction for this category of mercury containing measuring devices.

However, there is evidence of the economic feasibility of substitution of mercury measuring devices such as pycnometers, manometers, sphygmomanometers, tensiometers, hygrometers and thermometers with non-mercury measurement devices in existing markets. Hence, the proposed restriction is further justified for these measurement devices as the mercury measuring devices have to some extent been replaced already or are in the process of being substituted. In the case of mercury barometers, the cost information collected for the BD suggests that cheaper and hence economically feasible alternatives are available, even though the mercury measuring devices have not yet been fully replaced by the non-mercury alternatives. Similar indications are found for laboratory and industrial thermometers, further strengthening the economic proportionality argument, although the evidence of cheaper and more preferred alternatives is not as clear-cut in all cases here. For strain gauges there are indications that alternatives are economically feasible and for mercury pycnometers and mercury metering devices for the softening point determination there does not seem to be a remaining market in the EU.

In summary SEAC notes that the process of replacing mercury measuring devices by mercury free alternatives is already taking place. This trend demonstrates the economic feasibility of the proposed restrictions. Although the costs and benefits are surrounded with uncertainties, SEAC concludes that the proposed restrictions are considered proportionate to the risk.

Practicality, incl. enforceability

Justification for the opinion of RAC

Bans of other mercury containing measuring equipment for the use of consumers have been in place without problems. Likewise bans on other articles are a part of the Annex XVII of the REACH Regulation. Enforceability will depend on the final legal text proposed by the Commission, but as other similar bans are in place the enforceability is regarded as easy to reach.

Justification for the opinion of SEAC

With the deletion of the derogation for industrial mercury-in-glass thermometers above 200°C, the concern of a potential loophole of the restriction on industrial thermometers has been addressed.

Testing

Various analytical methods for mercury are available and well established. In the measuring devices, mercury is enclosed in a kind of container as the functional and separable part of the article. A specific sampling method is likely not needed. In most cases, a visual inspection as suggested in the BD will be sufficient. Indeed, most mercury measuring devices have a glass column filled with liquid mercury. As explained in section 4.2.1.2 of Annex 5a, also Gallium has a silvery appearance, but the capillary would have a concave instead of convex meniscus as observed with mercury in a glass capillary. The sole exception is mercury dial thermometers that have a mercury filled metal bulb. In this case, a simple identification by a non-destructive analytical method (XRF) can be used. The new entry does not introduce a limit value.

Enforceability

The Forum warned of potential difficulties with the verification of the compliance with some derogations of the proposed entry, e.g. evidence of the use of a sphygmomanometer in epidemiological studies which are on-going at entry into force, or the age of measuring devices being more than 50 years. A consequence of the latter one might be that the market for used devices could be difficult to control. As the proposed restriction is also worded to cover measuring devices placed on the market intended to be filled with mercury, the Forum expressed its reservations with regard to the possibilities to prove the intention to fill empty measuring devices with mercury. The intention to fill empty measuring devices with mercury could probably be based on information in catalogues, order books or operating manuals. To a certain extent this meets the comments from the Forum. The Forum was not consulted on the derogation for devices to be displayed in exhibitions for cultural and historical purposes, as this derogation was introduced to the proposed restriction only after receiving the second Forum advice and it was not found inevitable.

Monitorability

Justification for the opinion of RAC

In addition to national reporting of enforcement success, notifications of any violation of the restrictions could be reported and could in that way be used to monitor the results of the implementation of the proposed restriction.

Justification for the opinion of SEAC

SEAC welcomes the advice from the Forum regarding the monitorability of the proposed restrictions by market surveillance. Order books, financial administrations, operating manuals or catalogues of suppliers enable inspectorates to monitor the placing on the market of restricted measuring devices. The Forum underlines in its advice a preference to close the markets for export outside the EU as well. This is supportive to the opinion of SEAC regarding EC Regulation 1102/2008.

BASIS FOR THE OPINION

The Background Document, provided as a supportive document, gives the detailed grounds for the opinions.

Basis for the opinion of RAC

The main change introduced in restriction(s) as suggested in this opinion compared to the restrictions proposed in the Annex XV restriction dossier submitted by ***ECHA*** is the deletion of the proposed exemption for mercury in glass thermometers used by industry to measure temperatures above 200°C. The basis for this change is the availability of technically feasible alternatives, which pose substantially lower environmental and human health risks. In addition, based on the information received during the public consultation, RAC suggests that the proposed restriction would not apply to measuring devices which are to be displayed in exhibitions for cultural and historical purposes, replacing the proposed derogation in the Annex XV restriction report for measuring devices that are more than 50 years old on 3 October 2007.

Basis for the opinion of SEAC

The main changes compared to the original restriction proposal by ***ECHA*** are that:

i. the restriction on placing on the market of plethysmographs designed to be used with mercury strain gauges was replaced with a restriction on the placing on the market of mercury strain gauges,
ii. the derogation for industrial thermometers for temperature measurements above 200°C was removed, and
iii. a derogation for measuring devices which are to be displayed in public exhibitions for cultural and historical purposes was added.

The basis for these changes is new information submitted through the public consultation.

European Chemicals Agency

Committee for Risk Assessment (RAC)
Committee for Socio-economic Analysis (SEAC)

Background document
to the opinions on the Annex XV dossier
proposing restrictions on
Mercury in measuring devices

ECHA/RAC/ RES-O-0000001363-81-02/F
ECHA/SEAC/ RES-O-0000001363-81-03/S1

Mercury
EC number: 231-106-7
CAS number: 7439-97-6

This Background Document (BD) shall be regarded as further reference material to the opinions of the Committees for Risk Assessment and Socio-economic Analysis. It contains further details and assessment in addition/beyond the justifications provided in the opinions including, where relevant, information that has been received during the opinion making process and may be used to better understand the opinions and their justifications. The BD is a supporting document based on the Annex XV restriction report submitted by MS, and updated to support the opinions of the Committees.

15 September 2011

Preface

The existing restriction in Entry 18a of Annex XVII to the REACH Regulation on mercury in measuring devices includes a review clause. According to the clause, the Commission was to carry out a review of the availability of reliable safer alternatives that are technically and economically feasible for mercury containing measuring devices and where such alternatives are available present, if appropriate, a proposal to extent the existing restriction. The Commission sent its review report to ECHA on 20 November 2009 and requested ECHA to prepare a corresponding Annex XV restriction report.

This Background Document (BD) concerns the industrial and professional uses of mercury in measuring devices as the existing entry in Annex XVII already restricts the placing on the market of mercury containing measuring devices for general public. The following measuring devices are covered:

- Barometers
- Manometers (including tensiometers)
- Metering devices for the determination of softening point
- Mercury electrodes (used in voltammetry)
- Mercury probes used for capacitance-voltage determinations
- Porosimeters
- Pycnometers
- Sphygmomanometers
- Strain gauges (used with plethysmographs)
- Thermometers (including hygrometers)

Barometers, manometers, sphygmomanometers and strain gauges are used to measure pressure and thermometers temperature. Porosimeters, pycnometers and metering devices for determination of softening point measure different parameters related to the structure and porosity of a sample. Mercury electrodes are used with specific devices like polarographs, for instance to determine trace elements in the environment and in biological fluids. Mercury probes are used to measure several parameters related to the purity of the material such as permittivity, doping, oxide charge and dielectric strength.

Barometers, manometers, sphygmomanometers, strain gauges and thermometers contain mercury as an integral part of the device whereas metering devices (for determination of softening point), mercury probes (for capacitance-voltage determinations), polarographs (using mercury electrodes), porosimeters and pycnometers use mercury during the measurement. This difference has an effect on the assessment of the devices as will be described later in this report. The devices included in the BD are also significantly different with regard to other factors, such as number of devices in the EU, the amount of mercury involved, the type of users (private practitioners, laboratories and research institutions, meteorological stations, airfields, ships, different industries etc), and reasons for the continued use.

The main focus of this document is on the assessment of the technical and economic feasibility of alternatives for the mercury devices. This emphasis on possibilities to transfer to alternatives stems from the review clause in the existing restriction.

Furthermore, extensive amount of work has already been carried out on the hazard properties, fate, emissions of and exposures to mercury at international, EU and national levels and there is a wide agreement on the human health and the environmental concerns related to mercury and on the need for further actions where technically and economically possible. Based on this, the hazard profile is discussed only briefly. Furthermore, a qualitative approach is taken to the emission and exposure assessment. The approach taken to describe the hazard, emissions and exposure in this report is presented and justified in Section B.2. Based on this approach taken, Part B of the BD deviates from the standard format for an Annex XV restriction report, as published by ECHA (2009).

Furthermore, the number and different nature of the devices covered in this BD have led to the development of device specific annexes that discuss the following information:

- Technical description of the device
- Description of release and exposure
- Available information on the alternatives (Part C)
- Justification why the proposed restriction is the most appropriate Community-wide measure (Part E).

Consequently, Part E in the main document is in practise a summary of the proposed restrictions and provides a short justification for proposed actions / non-actions on different devices while Part C in the main document is reduced to a general introduction.

The main information source used for the assessments of the technical and economic feasibility of alternatives to mercury measuring devices is Lassen et al. (2008). This report called "*Options for reducing mercury use in products and applications, and the fate of mercury already circulating in society*" was commissioned by the European Commission (DG Environment). Lassen et al. (2008) and other information sources have an extensive amount of data on mercury in measuring devices, but still there were some data gaps for the remaining specific uses. Therefore, ECHA complemented this information by commissioning a consultant for the preparation of this restriction report. The results from the additional work are referred to as Lassen et al. (2010) in this report and can be found as Appendix 3. In addition, ECHA staff carried out literature and internet searches. These are reported in the relevant sections as well as in Appendix 2. To keep the workload proportionate, the efforts were targeted to gather data that could support the conclusion as to whether technically and economically feasible alternatives exist.

Content

A. Proposal

A.1 Proposed restriction(s)

A.1.1 The identity of the substance(s)

- Substance name: Mercury
- IUPAC name: Mercury
- EC number: 231-106-7
- CAS number: 7439-97-6
- Index number: 080-001-00-0

A.1.2 Scope and conditions of restriction(s)

For transparency reasons the original scope and conditions of the restriction as presented by the ECHA as dossier submitter in the original Annex XV restriction report is presented below. The opinions of RAC and SEAC are presented below in Chapter A.1.2.2.

Original Annex XV restriction report

Based on the justifications summarised in Section A.2 and discussed in the report, the following restrictions with derogations are suggested for mercury measuring devices in professional and industrial uses[1]:

1. Barometers, hygrometers, manometers, sphygmomanometers, tensiometers, thermometers and other non-electrical thermometric applications containing mercury shall not be placed on the market. This applies also to measuring devices placed on the market empty intended to be filled with mercury.

   It is suggested that the placing on the market of devices containing mercury for the following uses are derogated from the restriction described above:

   (a) Sphygmomanometers that are used (i) in long-term, epidemiological studies which are on-going at entry into force; (ii) as reference standards in clinical validation studies of mercury-free sphygmomanometers.

   (b) Mercury-in-glass thermometers used in industrial applications for temperature measurements above 200°C as demonstrated by the reading scale.

   (c) Thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers. It is suggested that this derogation will be valid until five years after the date of the adoption of this restriction.

[1] These suggested restrictions and related derogations concern only professional and industrial uses of the devices. They do not affect the existing restriction on mercury in measuring devices intended for sale to general public and on mercury in fever thermometers established in entry 18a of Annex XVII to the REACH Regulation.

(d) Mercury triple point cells that are used for the calibration of platinum resistance thermometers.

2. Plethysmographs designed to be used with mercury strain gauges, mercury pycnometers and mercury metering devices for determination of the softening point shall not be placed on the market.

It is suggested that the restrictions mentioned under paragraphs 1 and 2 will apply 18 months after the adoption of the respective Commission proposal.
Furthermore, it is suggested that these restrictions would not apply to measuring devices mentioned above that are more than 50 years old.

Opinion of RAC and opinion of SEAC

The following opinion of RAC and opinion SEAC are identical excluding the derogation in paragraph 4. In addition to the derogation proposed by RAC for measuring devices which are to be displayed in exhibitions for cultural and historical purposes, SEAC proposes to have derogation for measuring devices more than 50 years old on 3 October 2007. This derogation is consistent with the existing entry 18a of Annex XVII to the REACH Regulation on mercury in measuring devices intended for sale to general public and on mercury in fever thermometers. Furthermore, based on a comment received in the public consultation on the draft opinion of SEAC, SEAC proposes to clarify the scope of the derogation for measuring devices which are to be displayed in exhibitions for cultural and historical purposes by adding the word **public** to the derogation.

Opinion of RAC:

The following restrictions with derogations are proposed for mercury measuring devices in professional and industrial uses. They do not affect the existing restriction on mercury in measuring devices intended for sale to general public and on mercury in fever thermometers established in entry 18a of Annex XVII to the REACH Regulation.

3. Mercury containing barometers, hygrometers, manometers, sphygmomanometers, strain gauges to be used with plethysmographs, tensiometers, thermometers and other non-electrical thermometric applications shall not be placed on the market after [18 months of the entry into force]. This applies also to measuring devices placed on the market empty intended to be filled with mercury.
4. The restriction in paragraph 1 shall not apply to:

   (a) Sphygmomanometers to be used (i) in epidemiological studies which are on-going at entry into force; (ii) as reference standards in clinical validation studies of mercury-free sphygmomanometers.

   (b) Thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers until [5 years after the entry into force].

(c) Mercury triple point cells that are used for the calibration of platinum resistance thermometers.

5. Mercury pycnometers and mercury metering devices for determination of the softening point shall not be placed on the market after [18 months of the entry into force].
6. The restrictions in paragraphs 1 and 3 shall not apply to measuring devices which are to be displayed in exhibitions for cultural and historical purposes.

Opinion of SEAC:

The following restrictions with derogations are proposed for mercury measuring devices in professional and industrial uses. They do not affect the existing restriction on mercury in measuring devices intended for sale to general public and on mercury in fever thermometers established in entry 18a of Annex XVII to the REACH Regulation.

1. Mercury containing barometers, hygrometers, manometers, sphygmomanometers, strain gauges to be used with plethysmographs, tensiometers, thermometers and other non-electrical thermometric applications shall not be placed on the market after [18 months of the entry into force]. This applies also to measuring devices placed on the market empty intended to be filled with mercury.
2. The restriction in paragraph 1 shall not apply to:
   (a) Sphygmomanometers to be used (i) in epidemiological studies which are on-going at entry into force; (ii) as reference standards in clinical validation studies of mercury-free sphygmomanometers.
   (b) Thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers until [5 years after the entry into force].
   (c) Mercury triple point cells that are used for the calibration of platinum resistance thermometers.
3. Mercury pycnometers and mercury metering devices for determination of the softening point shall not be placed on the market after [18 months of the entry into force].
4. The restrictions in paragraphs 1 and 3 shall not apply to:
   (a) Measuring devices more than 50 years old on 3 October 2007, or
   (b) Measuring devices which are to be displayed in public exhibitions for cultural and historical purposes.

A.2 Summary of the justification

Identified hazard and risk

Mercury and its compounds are highly toxic to humans, ecosystems and wildlife, with amongst others serious chronic irreversible adverse neurotoxic and neurodevelop-mental effects.

The RAC opinion includes a PBT assessment for mercury-methylmercury concluding and equivalent level of concern in terms of persistency, due to mercury cycling and methylation *versus* demethylation rates under anaerobic conditions, as well as the clear potential for bioaccumulation and toxicity identyfied for methylmercury.

It is estimated that 3.5 to 7.6 tonnes of mercury is placed on the market in mercury containing measuring devices in 2010 (see Table 1). These amounts are used to describe the maximum potential for mercury emissions to the environment that might ultimately occur. This is considered appropriate for the purpose of this BD as the low separate collection rate and resulting inadequate waste treatment of a substantial part of the devices, leads in the long term to a relatively high share of mercury used in these devices being released to the environment.

Table 1: The amount of mercury estimated to be placed on the market in the EU in mercury containing measuring devices in 2010

Measuring device containing mercury	**Amount of Hg placed on the market in the EU in 2010 (t/y)**
Barometers	0.1-0.5
Manometers (including tensiometers)	0.04-0.4
Sphygmomanometers	2.6-5.1
Strain gauges (used with plethysmographs)	0.014
Thermometers (including hygrometers)	0.7-1.6
Total	**3.5-7.6**

Source: Lassen et al. (2008) as updated in device specific annexes 1 – 5.

In addition, around 5-15 tonnes of mercury is supplied annually to be used with porosimeters, pycnometers, devices using mercury electrodes in voltammetry, mercury probes used for capacitance-voltage determinations and metering devices for determining the softening point (see Table 2).

The annual amounts presented (in Tables 1 and 2) are not comparable. The figures in Table 2 are the amount of mercury the laboratories purchase and cannot be used to estimate maximum potential for emission as is the case in Table 1. To estimate

emissions several additional factors need to be considered. These include number of measurements carried out, practices to purify and regenerate used mercury and the risk management measures and operational conditions applied to control the emissions and exposures. Furthermore, available information indicates that the hazardous waste legislation requirements are generally complied with when handling the mercury contaminated waste generated during these measurements.

Table 2: The amount of mercury estimated to be purchased in the EU to be used with measuring devices in 2010

Measuring device using mercury	**Amount of Hg purchased to be used for measurements (t/y)**
Mercury electrodes (used in voltammetry)	0.1-0.5
Mercury probes used for capacitance-voltage determinations	0.001-0.005
Metering devices for the softening point determination	not available
Porosimeters	5-14
Pycnometers	not available
Total	**5-15**

Source: Lassen et al. (2008), device specific annexes 6-10

Once released to the environment, mercury persists in the environment, where it circulates between air, water, sediments, soil and biota in various forms. Mercury can be transformed to methylmercury, the most toxic form, which biomagnifies especially in the aquatic food chain, making populations and wildlife with a high intake of fish and seafood particularly vulnerable.

Several existing pieces of legislation abate the risks arising from mercury in different stages of the life-cycle of measuring devices. However, none of the measures currently in place is sufficient to remove the concern fully, although there is a difference between their observed effectiveness with regard to measuring devices containing mercury and measuring devices using mercury.

The emissions from mercury measuring devices, although relatively small, contribute to the overall emissions of mercury to the environment and thereby also to the exposure of species and of humans via the environment. Therefore, measuring devices containing or using mercury are of concern.

Justification that action is required on a Community-wide basis

The main reason to act on a Community-wide basis is the cross boundary human health and environmental problem related to mercury. Furthermore, the fact that the goods need to circulate freely within the EU stresses the importance of the Community-wide action. Thus, the use of mercury in these devices needs to be

controlled at the EU level. In addition, acting at Community level strengthens the possibilities to address the adverse impacts of mercury at worldwide level.

Justification that the proposed restriction is the most appropriate Community-wide measure

Tables 3 and 4 summarise the justifications for the proposed restriction as well as the justification for not proposing any regulatory action for each device. The main purpose of the proposed restrictions is to reduce the mercury pool in the society, thus avoiding negative impacts on human health and environment. Nevertheless, based on the review clause, the justification is focused on the technical and economic feasibility of the alternatives.

Table 3: Proposed restrictions and summary of justification for measuring devices containing mercury

Measuring device containing mercury	Proposed restriction	Summary of justification
Barometers	Restriction on the placing on the market of mercury barometers.	Technically and economically feasible alternatives are available.
Manometers (including tensiometers)	Restriction on the placing on the market of mercury manometers and tensiometers.	Technically and economically feasible alternatives are available.
Sphygmomanometers	Restriction on the placing on the market of mercury sphygmomanometers with limited derogations.	Technically and economically feasible alternatives are available in most applications.
Strain gauges (used with plethysmographs)	Restriction on the placing on the market of mercury strain gauges to be used with plethysmographs.	Technically and economically feasible alternatives are available.
Thermometers (including hygrometers)	Restriction on the placing on the market of mercury thermometers with derogations for i) thermometers to perform specific analytical tests according to established standards and ii) mercury triple point cells that are used for the calibration of platinum resistance thermometers	Technically feasible alternatives are available for majority of applications. Reasons for derogations: i) some current standards refer to mercury thermometers and time is needed to revise them ii) mercury is one of the reference points needed in the International Temperature Scale (ITS-90)

Table 4: Proposed restrictions and summary of justification for measuring devices using mercury

Measuring device using mercury	**Proposed restriction**	**Summary of justification**
Mercury electrodes (used in voltammetry)	No restriction proposed	Technically feasible alternatives are not available in all applications. In addition, two main alternatives seem not to be economically feasible.
Mercury probes used for capacitance-voltage determinations	No restriction proposed	Technically and economically feasible alternatives are not available.
Metering devices for the softening point determination	Restriction on the placing on the market of mercury metering devices for the softening point determination	Technically feasible alternatives are available and in use. The alternatives also seem to be economically feasible.
Porosimeters	No restriction proposed	High uncertainties in the technical feasibility of the alternatives. Consequently the economic feasibility was not assessed in detail.
Pycnometers	Restriction on the placing on the market of mercury pycnometers.	Technically feasible alternatives are available and in use. The alternatives also seem to be economically feasible.

B. Information on hazard and risk

B.1 Name and other identifiers of the substance

Name of a substance: Mercury
EC Number: 231-106-7
CAS Number: 7439-97-6
Molecular weight: 200.59
The classification and labelling of mercury is provided in Appendix 1.

B.2 Scope and approach

Scope
The existing restriction in Entry 18a of Annex XVII to the REACH Regulation for mercury in measuring devices includes a review clause[2]. According to that clause, the Commission was to carry out a review of the availability of reliable safer alternatives that are technically and economically feasible for mercury containing measuring devices and where such alternatives are available to present, if appropriate, a proposal to extend the existing restriction. The Commission services have collected a significant amount of new information from stakeholders on measuring devices and have received the SCENIHR opinion on the safety, availability and quality of alternative methods for blood pressure measurements (SCENIHR, 2009). The Commission has sent ECHA its review report (see Appendix 5) and requested the European Chemicals Agency to prepare an Annex XV dossier as foreseen by Article 69 of REACH.

Export
Regulation (EC) No 1102/2008[3] bans the export of metallic mercury and certain mercury compounds from 15 March 2011. Furthermore, Article 8(1)(a) of this Regulation calls for examining the need to extend the export ban to products containing mercury naming in particular thermometers, barometers and sphygmomanometers. For reasons of legal consistency it has not been considered whether there is a need to ban the export of mercury in measuring devices in the framework of the REACH Regulation in the course of preparing the restriction report. Consequently, the BD did not further address the need or possibilities to limit export of mercury in measuring devices. Since the submission of the report on the 15th of

[2] Paragraph 4 of Entry 18a of Annex XVII of the REACH Regulation as amended by Commission Regulation (EC) No 552/2009
"By 3 October 2009 the Commission shall carry out a review of the availability of reliable safer alternatives that are technically and economically feasible for mercury containing sphygmomanometers and other measuring devices in healthcare and in other professional and industrial uses. On the basis of this review or as soon as new information on reliable safer alternatives for sphygmomanometers and other measuring devices containing mercury becomes available, the Commission shall, if appropriate, present a legislative proposal to extend the restrictions in paragraph 1 to sphygmomanometers and other measuring devices in healthcare and in other professional and industrial uses, so that mercury in measuring devices is phased out whenever technically and economically feasible."
[3] Regulation (EC) No 1102/2008 on the banning of exports of metallic mercury and certain mercury compounds and mixtures and the safe storage of metallic mercury, OJ L 304, 14.11.2008, p.75.

June 2010, a stakeholders meeting was held in Brussels by the Commission (DG ENV) on the 18th of June 2010 on the review of the Community Strategy Concerning Mercury. In part, this meeting was also an information exchange as required by Article 8 of Regulation (EC) No 1102/2008. A new Communication on the review of the Community Strategy Concerning Mercury was adopted by the Commission on 7/12/2010.[4] According to Article 8(4) of Regulation (EC) No 1102/2008, the Commission has to submit to the European Parliament and the Council a report by 15 March 2013, if appropriate accompanied by a proposal for a revision of Regulation (EC) No 1102/2008, which shall reflect and evaluate the outcome of amongst others the information exchange required by Article 8(1).

Electrical and electronic equipment

Several mercury containing measuring devices are dependent on electric currents in order to work properly, and thus fall under the definition of 'electrical and electronic equipment' in the RoHS Directive[5]. For reasons explained in Appendix 4, they are not covered by this BD. This is in line with recital 1 of the Directive 2007/51/EC that introduced the restriction on mercury in measuring devices, now subject to revision and reads: "*The Commission communication of 28 January 2005 on the Community strategy concerning mercury, which considered all uses of mercury, concluded that it would be appropriate to introduce Community-level marketing restrictions on certain* ***non-electrical or non-electronic*** *measuring and control equipment containing mercury, which is the main mercury product group not covered by Community action so far*." (emphasis added).

Exemption for scientific research and development

According to article 67(1) of the REACH Regulation, restrictions "*shall not apply to the manufacture, placing on the market or use of a substance in scientific research and development*". Article 3(23) defines scientific research and development (SRD) as "*any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year*". Based on this definition the SRD exemption may also cover any analysis, e.g., those carried out for quality control or environmental monitoring purposes, provided that the conditions set out in Article 3(23) are met.

With regard to these conditions, Article 3(23) explicitly limits activities covered by the SRD exemption to those "*carried out under controlled conditions in a volume less than 1 tonne per year*". Based on this explicit requirement, analytical activities that are not run under controlled conditions and substances that are used for research purposes in quantity of more than 1 tonne per year, cannot benefit from the exemption.

The SRD exemption would apply in all the cases where the above conditions are satisfied, and where the substance is used directly in analysis, on its own or in a

[4] The text of the new Communication is available on:
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2010:0723:FIN:EN:PDF

[5] 'electrical and electronic equipment' or 'EEE' means equipment which is dependent on electric currents or electromagnetic fields in order to work properly and equipment for the generation, transfer and measurement of such currents and fields falling under the categories set out in Annex IA to Directive 2002/96/EC (WEEE) and designed for use with a voltage rating not exceeding 1 000 volts for alternating current and 1 500 volts for direct current (Article 3(a) of Directive 2002/95/EC).

preparation, including in conjunction with analytical equipment, such as measuring devices using mercury (metering devices for determination of softening point, polarographs using mercury electrodes, porosimeters and pycnometers).

Contrary to substances used directly for analytical purposes, on their own or in preparation (or in conjunction with measuring devices), substances forming an integral part of an analytical device cannot benefit from the SRD exemption in so far as it is not the substance which is directly used in the analysis but the article. In these cases, the main purpose of the substance is not directly related to the analytical operation but to another function, even though sometimes a crucial function. This is the case of mercury in measuring devices, which forms an integral part of the device but is not used and delivered as such during the analytical process (e.g., barometers, manometers, sphygmomanometers, strain gauges and thermometers).

In summary, this BD covers placing on the market and use of mercury for non-electrical or non-electronic measuring devices in professional and industrial uses. The need for marketing or use restrictions for other uses of metallic mercury or other mercury compounds is not within the scope of this BD.

Background

Several international governance bodies have undertaken action to address the global human health and environmental concerns related to emissions of and exposure to mercury. The existing restriction on mercury in measuring devices, and the current restriction proposal to extend this restriction, is part of this overall action.

United Nations

The UNEP mercury programme has been established and strengthened by a series of Governing Council decisions. In February 2003, the UNEP Governing Council decided that "*national, regional and global actions, both immediate and long-term, should be initiated as soon as possible to protect human health and the environment through measures that will reduce or eliminate releases of mercury and its compounds to the environment*", and urged "*all countries to adopt goals and take national actions, as appropriate, with the objective of identifying exposed populations and ecosystems, and reducing anthropogenic mercury releases that impact human health and the environment*" (UNEP, 2003).

In February 2009 the UNEP Governing Council adopted a decision, where it recalled the findings of the 2002 global mercury assessment that mercury is a substance of global concern due to its long-range atmospheric transport, its persistence in the environment once anthropogenically introduced, its ability to bioaccumulate in ecosystems and its significant negative effects on human health and the environment. The Governing Council further requested to continue and enhance, as part of the international action on mercury, the existing work in reducing mercury use in products and processes and raising awareness of mercury free-alternatives.

The organisation of activities concerning mercury at the United Nations level is described in the following quotes:

"The UNEP mercury programme has been established and strengthened by a series of Governing Council decisions since decision 21/5 in 2001. The UNEP mercury programme delivers activities on mercury through the UNEP Global Mercury Partnership, and will also support the negotiations of an internationally legal instrument for control of mercury." (UNEP, 2010)

"The overall goal of the UNEP Global Mercury Partnership is to protect human health and the global environment from the release of mercury and its compounds by minimizing and, where feasible, ultimately eliminating global, anthropogenic mercury releases to air, water and land." (UNEP, 2010)

One of the Partnership Areas focuses specifically on products containing mercury, also covering measuring devices:
"*The goal of the Mercury-Containing Products Partnership Area is to phase out and eventually eliminate mercury in products and to eliminate releases during manufacturing and other industrial processes via environmentally sound production, transportation, storage, and disposal procedures. Key product areas identified under this partnership area include: batteries, dental amalgams, measuring and control (largely medical sector), electric and electronic switches, fluorescent lamps, cosmetics*." (UNEP, 2010)

The UNEP Governing Council agreed to elaborate a legally binding instrument on mercury and gave a mandate to an intergovernmental negotiating committee (INC) to prepare this (UNEP, 2010). Two sessions of this committee have been held: INC-1 in Stockholm, Sweden, in June 2010 and INC-2 in Chiba, Japan, in January 2011.

<u>European Community</u>
In the EU, mercury has been under different policy actions. The Community Strategy Concerning Mercury (COM(2005) 20 final) has 20 action points with the aim to reduce mercury levels in the environment and human exposure, especially from methylmercury in fish.

In October 2007, the Commission adopted a restriction for mercury in all fever thermometers and in other measuring devices intended for sale to the general public (Directive 2007/51/EC, current Entry 18a of Annex XVII to REACH). This restriction established that as soon as new information on reliable safer alternatives for sphygmomanometers and other measuring devices becomes available, the Commission shall consider extending the restriction.

<u>Other regional and global actions</u>
In addition to the described actions on the UN and EU-level, several other regional and global initiatives are active in identifying sources of mercury emissions and exposures, monitoring concentrations of mercury in the environment, defining protection objectives and recommending measures to address the mercury problem. Examples are the UNECE Convention on Long Range Transboundary Air Pollution (CLRTAP); the OSPAR Convention for the Protection of the Marine Environment of the North-East Atlantic; the Helsinki Convention on the Protection of the Marine Environment of the Baltic Sea Area; the UNEP Mediterranean Action Plan (MAP); the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal; the Rotterdam Convention on the Prior Informed Consent

(PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade; The Arctic Council Action Plan to Eliminate Pollution of the Arctic (working groups ACAP and AMAP); and Nordic Co-operation.
Also, without going into the details, it is noted that there are restrictions and other legal measures on individual country or state level, such as for instance national restrictions of some EU-countries (see section B.5), the Mercury Export Ban Act in the US[6], and the ban for mercury added products in Canada[7].

Approach
As mentioned above, Entry 18a of Annex XVII requests the Commission to present a legislative proposal to extend the restrictions where reliable safer alternative substances or technologies that are technically and economically feasible are available for mercury containing sphygmomanometers and other measuring devices in healthcare and in other professional and industrial uses. Based on this entry, the Commission prepared a review report on the technical and economic feasibility of alternatives (see Appendix 5) and requested ECHA "*to evaluate new scientific evidence concerning the availability of reliable safer alternatives that are technically and economically feasible for mercury-containing sphygmomanometers and other measuring devices in healthcare and in other professional and industrial uses*", and to present the outcome in an Annex XV restriction report.

Therefore, the focus of the BD is on the technical and economic feasibility of the alternatives, while the hazards and exposure are described in general and qualitative terms.

The risks related to the use of mercury measuring devices cannot be assessed in isolation, and further restrictions related to these devices has to be seen as one of the means in the Community Strategy Concerning Mercury to reduce the overall mercury emissions.

Hazard
The hazardous properties and risks of mercury and methylmercury have been extensively studied and described in different scientific reports and have been acknowledged at high policy levels. A systematic literature survey would be unlikely to deliver new information that would change the consensus at the EU and international level on this hazard profile and the need for reduction of the mercury pool in the society. Hence, since a comprehensive description of the hazardous properties of mercury would mean duplicating the extensive work already carried out and agreed upon and taking into account the fact that the focus of the dossier is on the technical and economic feasibility of alternatives, the hazard assessment in this BD is brief and qualitative, and the technical dossier (IUCLID 5 –file) does not contain robust study summaries.

Exposure
Annex XV of REACH calls for the assessment of risks in accordance with the relevant parts of Annex I. Mercury as an element is persistent and has extremely

[6] http://www.epa.gov/mercury/regs.htm#laws
[7] http://www.gazette.gc.ca/rp-pr/p1/2011/2011-02-26/html/reg4-eng.html#41

complex processes of bioaccumulation and biomagnification that involve complicated biogeochemical cycles and ecological interactions (see section B.3 and UNEP, 2002). Therefore, it is not possible to carry out a quantitative exposure estimation with sufficient reliability, and a qualitative characterisation of risks in accordance with section 6.5 of Annex I to REACH is considered appropriate.

Since release estimates would not serve a quantitative exposure assessment or risk characterisation and would have to be expressed in exceedingly broad ranges to take into account all accumulated uncertainties[8], no quantitative release estimates are made either. The focus of the exposure assessment is on the minimisation of mercury emissions to the environment, which is also supported by the objectives in the Community Strategy Concerning Mercury to '*reduce mercury emissions'* and '*reduce the entry into circulation of mercury in society by cutting demand*' and the decision of the UNEP GC to '*reduce or eliminate releases of mercury and its compounds to the environment*' (UNEP, 2003).

As described above the main focus of this BD is on the technical and economical feasibility of the alternatives. The estimated amounts of mercury placed on the market in different devices are used to illustrate the risk reduction capacity of the restriction options. Where available, the risk reduction capacity is expressed as amount of mercury (kg Hg) which would not be placed on the market per year. This is then used when assessing the proportionality of the restriction options. Where technical or economic feasibility of alternatives cannot be established and consequently restrictions are not proposed in this BD the estimated amounts together with other considerations can be used to describe the remaining concern related to mercury included in or used with measuring devices.

Measuring devices covered by this BD can be divided to two categories i) devices containing mercury as an integral part of the device (barometers, manometers, sphygmomanometers, strain gauges and thermometers) and ii) devices using mercury during the measurements (porosimeters, pycnometers, mercury electrodes used in voltammetry, mercury probes used for capacitance-voltage determinations and metering devices). This difference is crucial for the description of releases and emissions in this BD as explained below and in Section B.4.

Release from measuring device containing mercury

The total estimated amount of mercury placed on the market in measuring devices containing mercury is used to describe the maximum potential for mercury emissions to the environment that might ultimately occur.

[8] See section B.4 and the ECHA Guidance on information requirements and chemical safety assessment, Chapter R.18 (ECHA, 2010) that mentions the following with respect to the use or release estimates for mercury: "*Note: Release estimates based on the release factors for mercury, lead and cadmium should not be used for exposure quantification and/or quantitative risk characterisation. A qualitative assessment is more appropriate here. Such qualitative assessment is needed to take into account the uncertainties around the environmental behaviour of the metal (for mercury) and/or the hazard profile of the substances related to human health (carcinogenic and reproductive toxicity with regard to cadmium and lead).*"

This estimation is obviously not to be confused with a quantitative estimate of actual emissions which would require in particular detailed information on the current waste management practices and emissions resulting from the waste stage (see section B.4.1). Mercury is an integral part of these devices and they normally operate without a need to handle mercury[9]. Mercury is disposed of together with the devices at the end of their service life. Therefore, the emission estimation related to measuring devices containing mercury concentrates on the release of mercury to the environment during the waste stage. Also the existing restriction covering mercury containing devices focused on the waste stage as described in recital 2 of Directive 2007/51/EEC which states: '*(2) There would be benefits for the environment and, in the long term, for human health, through* ***preventing mercury from entering the waste stream****, if restrictions on the marketing of measuring devices containing mercury were introduced.* (emphasis added).

In addition to the amounts placed on the market also the dispersiveness of use, proportion of proper waste collection and disposal, was well as other factors described in the BD (including also occupational exposure during production and service-life of the devices), are taken into account when illustrating the emissions and exposures related to different devices.

Release from measuring devices using mercury

The situation is more complex for devices using mercury during the measurements. The amount of mercury placed on the market cannot be used for these devices as a proxy for maximum potential for emissions in a similar way as it is used for mercury containing devices. The annual amount of mercury purchased by the laboratories to be used in the measurements is given to illustrate the volumes involved. However, for reasons given in section B.4.2 this amount alone does not describe the potential releases and exposures related to the measuring devices using mercury. Further parameters and qualitative descriptions are used to give a more complete picture.

Technical and economic feasibility of the alternatives

The technical and economic feasibility of alternatives is assessed in the device specific annexes based on the available information and the information collected in the stakeholder and public consultations. For technical feasibility, the argumentation is based on a qualitative description of the devices and their technical properties. For economic feasibility quantitative information is presented if available, including both investment and recurrent costs. When the annualised costs of alternatives are estimated to be lower than the annualised costs of the mercury device, it is straightforward to conclude that alternatives are economically feasible. When the annualised costs of alternatives are estimated to be higher, additional argumentation on the feasibility is provided. These comprise the relevance of i) the additional cost of mercury-free devices compared to the total costs of measurement (including the working time needed to measure) or ii) the additional cost of mercury-free devices compared to the total cost of purchases of goods and services by the user.

[9] With the exception of filling devices with mercury prior to their first use and during maintenance (e.g. of sphygmomanometers, barometers and manometers).

Proportionality

The total amount of mercury placed on the market in the measuring devices is used to assess the proportionality of the restriction options. The cost-effectiveness (€/kg Hg) of avoiding mercury is calculated for different devices by dividing the cost of using an alternative device by the amount of mercury that is avoided (for details, see Annexes 3b and 5b). A literature review on the compliance costs of other policies to reduce mercury and the human health benefits of reduced mercury emissions, as well as restoration costs in the EU and elsewhere is provided in Appendix 2. These costs give an order of magnitude comparison with the cost-effectiveness of the reduction of mercury in measuring devices estimated in this BD.

Summary

In summary, the approach to describe hazard in brief and to focus the exposure assessment on the minimisation of emissions was deemed warranted considering:

- that this BD supports the extension of the existing restriction on mercury in measuring devices where technically and economically feasible alternatives are available;
- the common understanding on the hazardous properties of mercury and its transformation products; and
- it would not be possible to perform a reliable quantitative estimation of releases, and especially of the resulting exposure levels.

Information sources for hazard and risk

The hazard and fate of mercury and its compounds are described in numerous peer-reviewed reports. The following reports were considered key documents:

- *'Global Mercury Assessment'*, published by UNEP in 2002 (and UNEP 2008a and b);
- '*Methylmercury'* (WHO, 1990) ;
- '*Risks to Health and the Environment Related to the Use of Mercury Products*' prepared for the Commission by RPA in 2002.

It is noted that references used and cited in these key documents are not explicitly referred to in this BD.

For the qualitative description of potential releases and exposure, amounts of mercury included in or used with the measuring devices are mainly taken from Lassen et al. (2008). Additional information on release and exposure situations for porosimeters is gathered during the preparation of this dossier (Lassen et al., 2010 in Appendix 3).

B.3 General description of hazard and fate

Fate

Elemental mercury (Hg(0)) is a shiny, silver-white metal that is a liquid at room temperature. At room temperature some of the metallic mercury will evaporate and form mercury vapours. Mercury vapours are colourless and odourless.

After release, mercury persists in the environment, where it circulates between air, water, sediments, soil and biota in various forms (UNEP, 2002).

Elemental mercury vapour is transported on a hemispherical/global scale making mercury emissions a global concern. Elemental mercury in the atmosphere can undergo transformation into inorganic mercury forms[10], providing a significant pathway for deposition of emitted elemental mercury. Mercury vapour has an atmospheric residence time that is between 0.4 and 3 years (WHO, 1990). Emitted mercury vapour is converted to soluble forms, these soluble forms have residence times of a few weeks (WHO, 1990). Soluble forms of mercury are deposited by rain into soil and water.

Mercury in soil is mostly bound to bulk organic matter and is susceptible to wash out in runoff only when attached to suspended soil or humus. Mercury has a long retention time in soil and as a result, the mercury accumulated in soil may continue to be released to surface waters and other media for long periods of time, possibly hundreds of years.

Various chemical reactions can return mercury to the elemental form which can be readily re-emitted. Thus, mercury that has been deposited can be re-emitted and continue travelling through the atmosphere from source regions to receptor regions in a series of 'hops' (so called grasshopper effect). Mercury may be accumulated in polar regions, where colder conditions may be less favourable to re-emissions (UNEP, 2008b).

A portion of the inorganic mercury is methylated (particularly within sediments) to methylmercury, which enters the water column (RPA, 2002). Methylmercury is by far the most common organic mercury compound in the environment (UNEP, 2002). The rate of mercury methylation depends on factors such as the activity of mercury methylating bacteria (e.g. sulphate reducers), concentration of bioavailable mercury (UNEP, 2002). These factors in turn are influenced by parameters such as temperature, pH, redox potential and the presence of inorganic and organic complexing agents (UNEP, 2002). Chemical methylation of mercury is also possible, and biotic demethylation occurs as well (UNEP, 2002). Methylation and demethylation processes are in fact determining the actual methylmercury concentrations in the environment (UNEP, 2002).

[10] Oxidation states +I and +II

Although all forms of mercury can accumulate to some degree, methylmercury is absorbed and accumulates to a greater extent than other forms (UNEP, 2002)[11]. Marine and freshwater fish, as well as marine mammals, bioaccumulate[12] methylmercury in their muscle tissue (UNEP, 2008). Fish bind methylmercury strongly, and elimination of methylmercury from fish is very slow, which causes fish to accumulate methylmercury over time (UNEP, 2002).

Moreover, methylmercury biomagnifies[13] throughout the many aquatic trophic levels (UNEP, 2002). The highest levels in the aquatic food web are found in fish that are apical predators of older age (such as king mackerel, pike, shark, swordfish, walleye, barracuda, large tuna, scabbard, and marlin) and fish-consuming mammals such as seals and toothed whales (UNEP, 2008a). Other fish-eating species, such as seabirds, but also humans are situated at top level of the trophic chain through eating (predator) fish and other seafood (UNEP, 2002).[14]

On a global scale, the Arctic region and its species has been in focus because of the tendency of mercury to be transported over a long-range. However, the impacts of mercury are by no means restricted to the Arctic region. The same food web characteristics and similar dependence on mercury contaminated food sources are found in specific ecosystems and human communities in many countries around the world, particularly where a fish diet is predominant. (UNEP, 2002)

The bioaccumulation factor[15] for methylmercury in edible freshwater and saltwater fish and marine mammals can mount to many thousands (UNEP, 2002), and can even be well above one million (SCHER, 2008). In other words, low concentrations in the environment can still lead to high dietary exposure. Much is known about mercury bioaccumulation and biomagnification, but because of the complexity of the processes involved, the extent of mercury biomagnification in fish is not easily predicted (UNEP, 2002).

[11] Inorganic mercury can also be taken up, but generally at a lower rate and with lower efficiency compared to methylmercury (UNEP, 2002).

[12] Bioaccumulation refers to uptake from all environmental sources including water, food and sediment. UNEP (2002) gives the following description: "The term bioaccumulation refers to the net accumulation over time of metals within an organism from both biotic (other organisms) and abiotic (soil, air, and water) sources."

[13] Biomagnification refers to accumulation via the food chain. UNEP (2002) gives the following description: "The term biomagnification refers to the progressive build up of some heavy metals (and some other persistent substances) by successive trophic levels – meaning that it relates to the concentration ratio in a tissue of a predator organism as compared to that in its prey (AMAP, 1998)."

[14] In EU the maximum levels for mercury in fishery products, in muscle meat of fish and in crustacae are given in the Commission Regulation (EC) No 1881/2006, amended No 629/2008. In addition, the Joint FAO/WHO Expert Committee on Food Additives (JECFA), established a provisional tolerable weekly intake (PTWI) of 1.6μg/kg bw, and the US National Research Council (NRC) established an intake limit of 0.7μg/kg bw (EFSA, 2004). According to EFSA, estimated intakes of mercury in Europe varied by country, depending on the amount and the type of fish consumed. The mean intakes in some countries exceeded the NRC-limit, and high intakes may also exceed the JECFA-limit (EFSA, 2004). Several EU Member States have issued advice to vulnerable populations to avoide or limit the frequency of intake of certain fish species (COM, 2008). The Commission advises that women who might become pregnant, woman who are pregnant or women who are breastfeeding, as well as young children, should not eat more than 100g per week of large predatory fish, such as swordfish, shark, marlin and pike (COM, 2008).

[15] The overall bioaccumulation factor is the ratio between the concentration in the organisms and the concentration in water (SCHER, 2008).

Hazard

Each form of mercury has its own toxicological profile, although, in general terms, the organic mercury compounds have the highest toxicity, followed by elemental mercury and inorganic mercury compounds. The focus is on the description of the hazards of methylmercury, since it is the most toxic form and, as described earlier, is of highest concern since it biomagnifies in food webs (UNEP, 2008). Elemental mercury is described in brief since mercury in measuring devices might result in direct human exposure to elemental mercury. Inorganic mercury compounds are not described here, since they are of less relevance.

Methylmercury

Humans
Methylmercury is highly toxic especially to the nervous system. Methylmercury toxicity has been demonstrated at low exposure levels (EFSA, 2004). In adults, the first effects at the lowest doses are non-specific symptoms, such as paresthesia, malaise and blurred vision. This may progress to cerebellar ataxia (clumsiness or unsteadiness), dysarthria (speech disorder), constriction of the visual fields and loss of hearing. With increasing exposure there are signs such as construction of the visual field, deafness, dysarthria and ataxia, and ultimately leading to coma and death (UNEP, 2002).

Methylmercury exhibits severe neurodevelopmental effects. It passes both the placental barrier and the blood-brain barrier. The developing nervous system in unborn and newborn children is the most sensitive target organ. The effects can take place even at exposure levels where the mother remains healthy or suffers only minor symptoms due to mercury exposure. At lower exposure levels, the effects may only become apparent later during the development as psychomotor and mental impairment and persistent pathological reflexes. In infants exposed to high levels of methylmercury during mothers' pregnancy, the clinical picture can be indistinguishable from cerebral palsy caused by other factors, the main pattern being microcephaly, hyperreflexia and gross motor and mental impairment, and in rare cases, blindness or deafness (UNEP, 2002). Some studies suggest even small increases in methylmercury exposures may cause adverse effects on the cardiovascular system, thereby leading to increased mortality (UNEP, 2002).

The examples of mercury poisoning in Japan and Iraq have shown on a population scale the severe neurological effects of methylmercury to humans. At first the poisoning in Minamata, Japan, was regarded as an epidemiological disease of unidentified causes (Minamata Disease), first seen in abnormal behaviour in animals, and in 1956 reported first in humans. In 1959 the cause was officially recognized as being methylmercury foodpoisoning. The methylmercury originated from discharged mercury containing wastewater from an acetaldehyde production factory into Minamata bay. According to the National Institute for Minamata Disease, there are 2955 legally recognized patients. (National Institute for Minamata Disease, 2010).

In Iraq, the poisoning incidents in 1956 and 1959-1960 and in 1971-1972 were due to the consumption of seed grain that had been treated with fungicides containing methyl- and ethylmercury. After the incident in 1971-1972 it was reported severe

damage to the central nervous system in infants prenatally exposed to methylmercury (WHO, 1990 and UNEP, 2002). In adults the symptom was paresthesia and in more severe cases ataxia, blurred vision, slurred speech and hearing difficulties (UNEP, 2002).

In addition there are number of other epidemiological studies with pregnant women having marine diets and their children which provide some supporting evidence to the previous findings related to the neurological effects (WHO, 2007).

Environment
As in humans, mercury exposure of animals may result in severe neurological effects. These effects were clearly seen in the Minamata poisoning, where birds experienced severe difficulties in flying, and domestic animals, especially cats, showed signs of severe neurological intoxication. (UNEP, 2002)

In birds, methylmercury has been associated with eggshell thinning in the 1950's and 1960's. Methylmercury was used as a fungicidal seed dressing, and severe poisoning of wildlife was observed in Scandinavia and North America. Populations of pheasants and other seed-eating birds, as well as birds of prey were drastically reduced and in some areas nearly disappeared. Adverse effects of mercury on reproduction can occur at egg concentrations as low as 0.05 to 2.0 mg/kg (wet weight). UNEP (2002), reported eggs of certain Canadian species to be in this range, and concentrations in the eggs of several other Canadian species were said to continue to increase and are approaching these levels (UNEP, 2002).

To adult fish, direct exposure to methylmercury from the surrounding water is generally not a serious concern. However evidence suggests that mercury exposure to early life stages of some fish can affect growth, development and hormonal status at levels within a factor of 10 of levels encountered in “pristine” lakes. Effects from indirect exposure via dietary uptake and maternal transfer of methylmercury to eggs and developing embryos might be of concern (UNEP, 2002).

Mercury is toxic to micro-organisms and has long been used to inhibit the growth of bacteria in laboratory experiments. Evidence suggests that mercury is responsible for a reduction of micro-biological activity vital to the terrestrial food chain in soils over large parts of Europe – and potentially in many other places in the world with similar soil characteristics (UNEP, 2002).

<u>Elemental mercury</u>
Elemental mercury is very toxic to humans via inhalation. About 80 percent of inhaled vapours are absorbed by the lung tissues. This vapour easily penetrates the blood-brain barrier and is a well documented neurotoxicant causing neurological and behavioural disorders in humans when inhaled. Specific symptoms include tremors, emotional lability, insomnia, memory loss, neuromuscular changes, and headaches. Intestinal absorption of elemental mercury is low.

The EU harmonised classification and labelling of mercury is described in Appendix 1.

B.4 General qualitative description of potential release and exposure

More than 60 different applications for mercury have been identified in the EU. Lassen et al. (2008) estimated that in 2007 between 320 and 530 tonnes of mercury was used in industrial processes and products in the EU27+2. The biggest annual tonnages are used in chlor-alkali production and in dental amalgams representing 47 % and 27 % of the total amount of mercury used in the EU for all applications. The demand of mercury for chlor-alkali production is steadily declining as a result of a phase-out of the mercury-cell process[16]. The Figure 1 presents the shares of each application areas, including measuring devices, from the total annual use of mercury in products and industrial processes in the EU. For measuring devices the estimated share is currently 4 %. This does not correspond to the estimate for the risk reduction capacity of the proposed restriction (see general part E), as not all the measuring devices are covered by the proposal. The proposed restrictions represent around 1.5 % of the annual use.

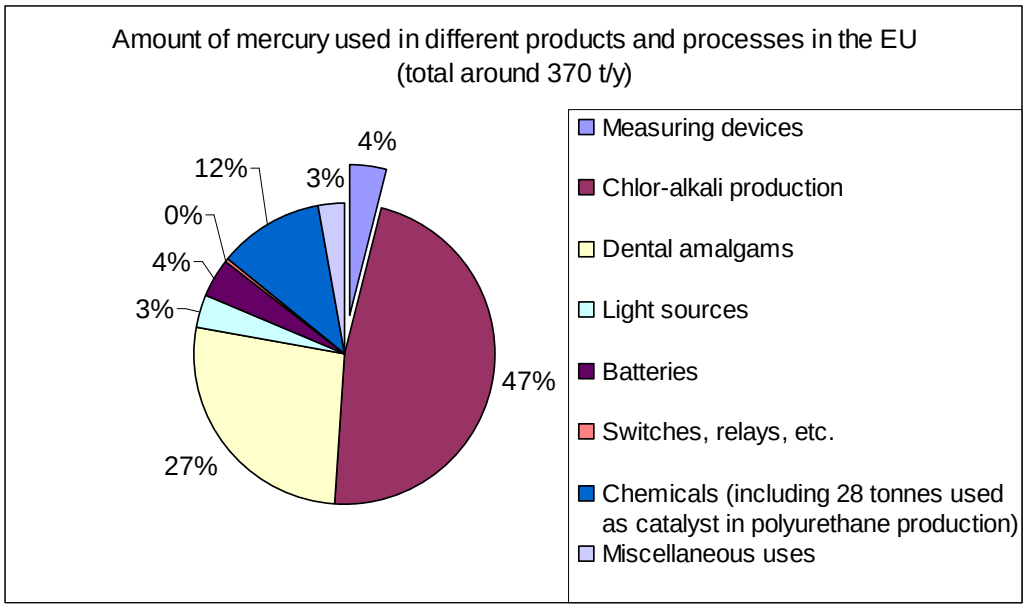

Figure 1: The amount of mercury used in products and industrial processes in the EU annually. Source: Figures based on Lassen et al. (2008) and device specific Annexes for measuring devices[17].

[16] The OSPAR Decision 90/3 of 14 June 1990 on reducing atmospheric emissions from existing chlor-alkali plants recommended that "*existing mercury cell chlor-alkali plants be phased out as soon as practicable. The objective is that they should be phased out completely by 2010*". Euro Chlor and its members state that they continue implementing a voluntary agreement on the gradual conversion to membrane technology. According to Eurochlor, the final phase out for the chlor-alkali production should be completed by 2020. (http://www.eurochlor.org/news/detail/index.asp?id=272) The chlor-alkali industry is also covered by the IPPC Directive, which requires installations to have permit conditions based on best available techniques (BAT). The mercury-cell process is not considered to be BAT for the chlor-alkali sector.

[17] The estimates for the measuring devices have been updated based on the information gathered in the stakeholder consultation.

To put the amounts of mercury used in products in a wider perspective, this paragraph gives an overview of the order of magnitude of emissions from anthropogenic and natural sources occurring in Europe and globally. It is estimated that around 1930 tonnes of mercury was released to the atmosphere from anthropogenic sources globally in 2005. Around 45% of this volume stems from the burning of fossil fuels. Europe is responsible for 150 tonnes, i.e. 8% of the global emissions. Emissions from natural sources (including releases from volcanoes and geothermal activity, wildfires and weathering of rocks and soils) are situated between 900 and 2300 tonnes for the year 2005. In addition, 900-2500 tonnes of mercury is estimated to return to the atmosphere as re-emissions. (UNEP, 2008b)

The following subsections describe the potential mercury releases and exposure during the life-cycle of mercury containing measuring devices and devices using mercury. Details for specific devices are given in Annexes 1 to 10.

B.4.1 Mercury emissions from measuring devices containing mercury

The amount of mercury placed on the market in the EU in different measuring devices containing mercury is estimated to be between 3.5 and 7.6 tonnes in 2010. Device specific figures are summarised in Table 5. The service-life of the measuring devices containing mercury is usually longer than 1 year, and consequently the accumulated pool of mercury in measuring devices in use is higher than the amount placed on the market annually. The estimates on the accumulated pool are also presented in Table 5. The estimate for accumulated pool considers the average life-time of the device and also possible trend in the number of devices placed on the market before 2010.

Table 5: The amount of mercury estimated to be placed on the market in the EU in mercury containing measuring devices in 2010

Measuring device containing mercury	**Amount of Hg placed on the market in the EU in 2010 (t/y)**	**The estimated accumulated pool of Hg in the devices in 2010 (t)**
Barometers	0.1-0.5	3
Manometers (including tensiometers)	0.04-0.4	4
Sphygmomanometers	2.6-5.1	39
Strain gauges (used with plethysmographs)	0.014	0.014
Thermometers (including hygrometers)	0.7-1.6	88
Total	**3.5-7.6**	**134**

Source: Lassen et al. (2008)[18] as updated in device specific Annexes 1 – 5[19].

[18] Lassen et al. (2008) estimated the amount of mercury placed on the EU market in measuring devices containing mercury to be between 7 and 17 tonnes in 2007 (this amount included also devices for consumer use). Of this amount, 3 – 8 tonnes per year are covered by the existing restriction on the placing on the market of mercury containing measuring devices for sale to general public and placing on the market of fever thermometers and therefore not anymore available on the EU market (the

Mercury emissions to the environment and direct human exposure may occur during all life-cycle stages of mercury containing measuring devices, but in particular emissions to the environment from the waste stage are of concern. Figure 2 shows the life cycle of mercury containing devices and indicates the relative size of mercury losses from different life cycle stages. The size of the arrows illustrates the importance of emissions in the different stages.

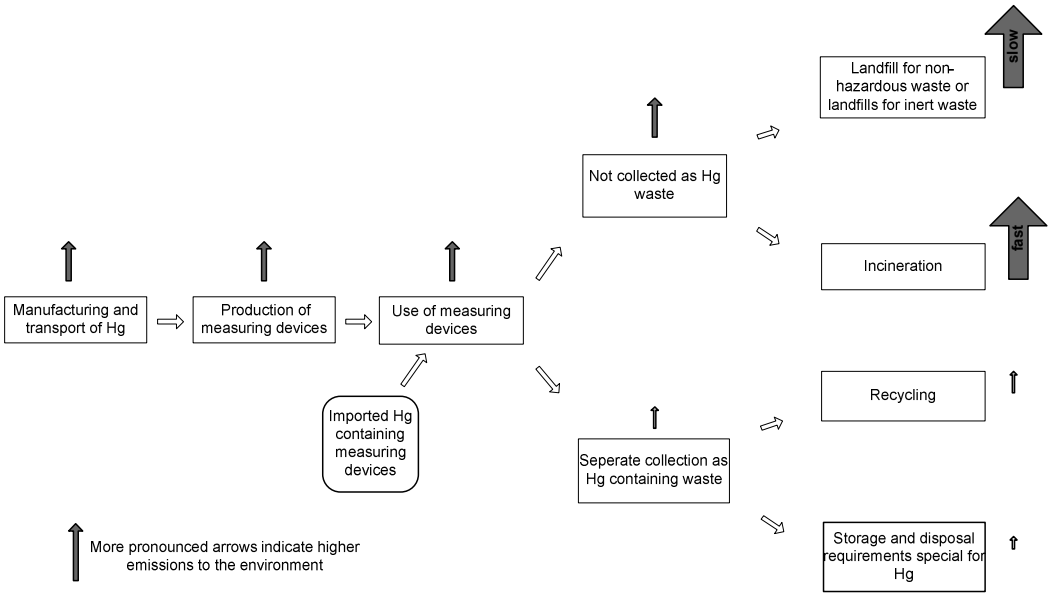

Figure 2 Scheme of the life-cycle of mercury in measuring devices

Production of measuring devices

In the production phase of mercury containing devices occupational exposure and emissions to the environment may occur during the handling of mercury, filling of the devices, breakage of devices, and the handling of mercury contaminated waste.
To prevent occupational exposure via air –the most important route of exposure for workers, a Community-wide IOELV has been adopted (see section B.5). However, the IOELV might not be effective in preventing or reducing exposure from accidental breakage, spillage of mercury, and leakage.
In addition, emissions to the environment (to air and water, direct or indirect via waste disposal) arising from the production of measuring devices does not seem to be

measures in entry 18a of Annex XVII of REACH apply since 3 April 2009). Based on these figures the amount of mercury placed on the market in mercury containing measuring devices not covered by the existing restriction is roughly estimated to have been between 4 and 9 tonnes per year in 2007.

[19] The estimates for some of the measuring devices have been updated based on the information gathered in the stakeholder consultation (see Part G and Appendix 3 for information on stakeholder consultation).

covered by Community legislation specifically setting limits on mercury emissions to air or water (see section B.5).

Service-life of measuring devices

During the service-life of the devices emissions of and exposure to mercury may occur during professional and industrial uses of mercury containing measuring devices, including maintenance, filling devices with mercury (e.g. sphygmomanometers, barometers and manometers) and breakage of devices. Exposure of workers (professional and industrial users)[20] occurs mainly via air, and emission to the environment include direct or indirect (via waste disposal) emissions to air and water. Existing occupational health and environmental legislation (see section B.5) is not considered to be effective in preventing or reducing emissions or exposure related to professional and industrial use of mercury containing measuring devices.

Waste stage of measuring devices

Mercury containing measuring devices are legally required to be collected separately from other (hazardous and non-hazardous) waste streams at the end of their service life (see also section on waste legislation in B.5).

Typically, after separate collection, the mercury containing waste has to undergo pretreatment (which can consist of sorting out, breaking of glass devices, etc). Subsequently the mercury can be separated from the other waste material and concentrated by vacuum distillation. The off gases can be treated with dust filters and activated carbon filters. The dust and the contaminated carbon from the gas treatment can be returned into the process used to isolate the mercury from the other parts of the devices (BREF Waste Treatments Industries, 2006). The resulting mercury can be refined and used as a secondary material or disposed of in compliance with amongst others the very specific rules for mercury waste storage in Regulation No 1102/2008.

Proper separate collection of mercury containing devices is a way to reduce emissions, but is challenging and costly, especially for devices where discarding is not very regular (e.g. as a result of a long life-time) and where devices are geographically widely spread. Promoting and organising collection is very dependant on priorities in individual Member States (Lassen et al., 2008). As a rough figure[21], collection

[20] For illustrative purposes, in the Netherlands 72 cases of human exposure to mercury have been reported to the National Poisons Information Centre in 2009, and 50 cases in 2010 (until 21 October). About one third of the cases concerns the breakage of fever thermometers. The remaining part concerns several applications like other thermometers, barometers and lamps (pers. comm.).

[21] For (amongst others) the following reasons it is very difficult to obtain good information on rates of separate collection of mercury measuring devices.
According to the list of wastes (LoW), established by Commission Decision 2000/532/EC, mercury containing measuring devices fall under code "20 01 21* fluorescent tubes and other mercury-containing waste" (the asterisk points to classification as hazardous waste). Within this code, the mass of measuring devices is overshadowed by the mass of fluorescent tubes. Moreover, waste statistics reporting by Member States is done according to 'aggregated' waste categories. Fluorescent tubes and other mercury-containing waste is added together with 6 other entries under code 08.43.1 (Other

efficiencies of mercury in measuring devices in accordance with requirements set out in the hazardous waste legislation are estimated to be as low as approximately 20%. Collection efficiencies above 50% should in general not be expected (Lassen et al., 2008).

If not collected and treated in accordance with hazardous waste legislation, mercury containing waste is fed to landfill or incineration, which results in higher emissions compared to treatment according to hazardous waste legislation as described above. So called 'secondary techniques' for the abatement of mercury emissions from installations for incineration and landfills are briefly described in Box 1.

The low separate collection rate and resulting inappropriate waste treatment of a substantial part of measuring devices, leads in the long term to a relatively high share of mercury in measuring devices being released to the environment. Figure 2 represents the possible routes of mercury release to environment from measuring devices.

In principle it would be possible to make release estimates for the incinerated and landfilled waste fraction by estimating the mass flows going to the different fractions and by applying release factors to those estimates. However, the mercury volumes placed on the EU market in measuring devices and the fraction that is not specifically treated as mercury containing hazardous waste are rather uncertain. Also, it is unknown what fractions are incinerated and what fractions are landfilled. In addition, the reported release factors[22] are very variable and entailed with high uncertainty, and no good models exist to predict the releases from landfills[23].

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discarded machines and equipment components, Hazardous), and it seems even that the actual reporting is only required on the level of "08 Discarded equipment, hazardous".
In addition, uncertainty on the quantity and mercury content of devices brought on the market in the past and uncertainty on when they are discarded (life times of devices) further complicates estimating the rate of separate collection (needed to compare with the estimated amount of separately collected mercury waste measuring devices).
Questionnaires were sent out to Member States as part of the study by Lassen et al. (2008), to obtain information on the individual waste codes (which is as explained not generally available). Only a few Member States submitted detailed waste data, and only 3 Member States submitted information on waste of mercury in measuring and control equipment.

[22] Kindbom and Munthe (2007) assumed a release factor of 0.5 to air for mercury in measuring devices that are incinerated in municipal solid waste **incineration**. A tenfold lower default release factor of 0.05 is suggested for municipal solid waste incineration in the draft ECHA Guidance on information requirements and chemical safety assessment, Chapter R.18 (ECHA, 2010). The guidance however also notes that metals are not destroyed and could be emitted to a rather high extent to air, even if flue gas is cleaned.
Kindbom and Munthe (2007) assumed an emission factor of 0.05 to air for the 1st year for mercury measuring devices in **landfills**, and a factor of 0.001 for the 9 consecutive years. Emissions for the years after were not estimated, but assumed to be very low as the waste will be covered with more layers. It is not clear whether the authors take into account emissions through flaming of gasses. The draft ECHA Guidance on information requirements and chemical safety assessment, Chapter R.18 (ECHA, 2010) does not report a specific release factor for mercury.

[23] The ECHA Guidance on information requirements and chemical safety assessment, Chapter R.18 (ECHA, 2010) mentions in this respect the following: "*Since no good models exist to predict the releases from landfills, the registrant should demonstrate control of risk based on a qualitative argumentation as to why the substance is unlikely to be released under landfill conditions. This argumentation may be based on volatility, water solubility, degradability and adsorption behaviour.*"

To sufficiently remove all these uncertainties, very extensive surveys on the market for all mercury devices, and on the compliance rate with the hazardous waste legislation in all Member States and on country-specific waste management practises would have to be carried out, without guarantee of success.

In other words, the release estimates would have to be expressed in exceedingly broad ranges to take into account all the accumulated uncertainty. Since such estimates would not serve any quantitative exposure assessment or risk characterisation[24], it was not judged useful to attempt to quantify emissions entailed with such high uncertainty, whereas the actual aim is to minimise exposure and emissions. The total estimated amount of mercury included in the measuring devices (see Table 5) was considered to be more useful to describe what emissions to the environment might ultimately occur, and therefore in what follows only a qualitative description of releases and risk management measures is given.

It is assumed that releases from waste incineration and landfills will at least be significant, and mercury measuring devices ending up in incineration are assumed to contribute to peaks that overload flue-gas cleaning system capacities for mercury removal (see also Box 1).

Virtually all handling of mercury can lead to emissions[25]. To some limited extent this will also be the case during the management of properly collected mercury containing measuring devices according to the hazardous waste requirements (see section B.5). However due to all the provisions and requirements for treatment of hazardous waste, these emissions are in magnitude incomparable to the emissions that may occur when mercury containing measuring devices go to installations for incineration or disposal of non-hazardous waste.

Box 1 Abatement of mercury emissions

Waste incineration
(source: BREF Waste Incineration, 2006)

There is a direct linear relationship between the amount of mercury in the *raw* flue-gases and the amount of mercury in the waste. Typical concentrations for municipal waste incineration plants are 0.05 – 0.5 mg/m³ in crude flue-gas. There are two ways to satisfy the mercury emission limit of 0.05 mg/m^3 in the waste incineration Directive (Directive 2000/76/EC). The most important means is limiting the input of mercury in the installation by proper collection, the other being an efficient mercury removal.

[24] As described in section B.2, it is not possible to carry out a quantitative exposure estimation for mercury with sufficient reliability because of the properties of mercury.

[25] As also indicated in Figure 2, mercury can be released to air during all waste handling operations (collection, transport, and temporary storage) prior to disposal or recovery operations; during dumping, spreading, compacting and burial of waste in landfills; from landfill gas vents and from the surface of landfills; during pretreatment prior to incineration; through exhaust of waste incineration; and to a limited extent also during recovery and permanent storage operations. In addition to the emissions to air, mercury is released to soil and (ground)water via leachate from landfills.

The majority of installations need special gas cleaning measures in order to meet the mercury emission limit value for air (but note that continuous monitoring of mercury emission levels is not required by Directive 2000/76/EC). Especially when the waste stream contains significant amounts of metallic mercury emissions are more difficult to control, since removal of metallic mercury is more challenging compared to ionic mercury. The precise abatement performance and technique required will depend on the levels and distribution of mercury in the waste. Under certain conditions such as a high input rate of mercury, the removal capacity limits of a flue gas cleaning systems may be exceeded, leading to temporarily elevated mercury emissions. Some short-term high loads have been noted in municipal solid waste. These are generally associated with the presence of batteries, electrical switches, thermometers, laboratory wastes, etc.

At high enough chlorine content, mercury in the crude flue gas will be increasingly in the ionic form which can be deposited in wet scrubbers. Volatile mercury compounds, such as $HgCl_2$, will condense when flue-gas is cooled, and dissolve in the scrubber effluent. To maintain scrubbing efficiency and prevent clogging in the wet scrubber system, a portion of the scrubber liquor must be removed from the circuit as waste water. This waste water must be subjected to special treatment (neutralisation, precipitation of heavy metals), before discharge or use internally.

Many waste streams contain relatively high amounts of mercury in metallic form, and therefore generally require adsorption by the use of carbon based reagents to achieve the emission levels, or alternatively by transformation into ionic mercury by adding oxidants that are subsequently deposited in the wet scrubber. Injected activated carbon is filtered from the gas flow using bag filters, and when saturated, the used activated carbon is often landfilled as hazardous waste. However, saturated active carbon is sometimes burnt in the incinerator in order to further remove dioxins (PCDD/F), what might lead to re-circulation of metallic mercury.

Landfill

According to recital 8 of Directive 1999/31/EC on the landfill of waste, both the quantity and hazardous nature of waste intended for landfill should be reduced where appropriate. This can only be achieved by proper collection. Mercury measuring devices that end up in landfills will result in emissions to air, soil and water.

Certain general requirements for landfills in respect to location, water control, leachate management, bottom and surface sealing and stability can to a certain extent limit the release rate for mercury emissions from landfills. Due to its properties it is nevertheless likely that in the course of time the mercury will be slowly emitted to the environment.

B.4.2 Mercury emissions from measuring devices using mercury

Around 5-15 tonnes of mercury is annually purchased by laboratories to be used with porosimeters, pycnometers, devices using mercury electrodes in voltammetry and metering devices for determining the softening point. These devices do not contain mercury, but mercury is used during the measurements and consequently the devices need to be refilled with mercury regularly. The estimated amount of mercury purchased for the use with measuring devices is presented in Table 6. It is stressed that these amounts are not comparable to the amounts placed on the market in mercury containing measuring devices (Table 5). Below, it is explained how the amounts in Table 6 as well as other parameters, are used to describe the mercury cycle related to these measurements.

Table 6: The amount of mercury estimated to be purchased in the EU to be used with measuring devices in 2010

Measuring devices using mercury	**Amount of Hg purchased to be used in the measurement (t/y)**
Mercury electrodes (used in voltammetry)	0.1-0.5
Metering devices for the softening point determination	not available
Mercury probes used for capacitance-voltage determinations	0.001-0.005
Porosimeters	5-14
Pycnometers	not available
Total	**5-15**

Source: Lassen et al. (2008), device specific Annexes 6-10[26]

The devices described in this section use mercury as 'an analytical chemical' for their functioning. They have to be filled with mercury regularly and mercury is not an integral part of these measuring devices. Without rigorous risk management measures and use conditions, mercury emissions and exposure of workers and environment occur when carrying out measurements with porosimeters and similar devices, when handling the used mercury (including its regeneration or purification for reuse) and as a result of handling of mercury contaminated waste. Therefore, risk management measures and operational conditions recommended by the producers of the devices and reported to be used by the laboratories performing the measurements are used to qualitatively describe the minimisation of releases.

There is no single parameter to describe the potential release and exposure from the measuring devices using mercury. Therefore, several parameters are used in device specific annexes. The amount of mercury purchased by the users is used to describe

[26] The estimates for some of the measuring devices have been updated based on the information gathered in the stakeholder consultation, and consequently may differ from what is reported e.g. in the Lassen et al. (20008).

the flow of mercury between the users and the suppliers of mercury (including companies offering regeneration or purification services).

As the same mercury can be used several times (after in-house or outsourced regeneration or purification) the amount of mercury used annually in the measurements is reported to describe the magnitude of the mercury involved in the use phase of devices. The available information suggests that the emissions to the environment during the use phase are likely to be low. The same applies to exposure of workers. It is stressed that the laboratories concerned will have to ensure that the newly established occupational exposure limit value for mercury and the requirements of hazardous waste legislation will be complied with (see section B.5).

The amount of mercury containing waste disposed of annually is estimated where possible. These amounts are considerably lower than the amount purchased by the users. This is because the purchased amount includes also mercury purified and regenerated by specialised companies and resold to the users. The available information (see Annex 7, and Lassen et al. 2010), suggests that compliance with the hazardous waste legislation is considerably higher for devices using mercury than for devices containing mercury. The main reason for this difference in compliance would be that handling of mercury and mercury waste is part of normal use of porosimeters and other similar devices. Consequently the standard operation procedures of laboratories performing measurements with these devices should cover treatment of mercury containing wastes.

It is stressed that the main focus of this BD is on the assessment of technical and economic feasibility of alternatives. The potential releases and exposures are described primarily to illustrate the risk reduction capacity of the restriction options. Although the releases and exposures related to the use of mercury with these four types of measuring devices appear to be relatively low, it is stressed that the objective expressed in the Community mercury strategy to reduce the entry into circulation of mercury into society still applies. Consequently the use of mercury with the remaining measuring devices should be phased out as soon as technically and economically feasible alternatives are available.

B.5 Summary of existing legal requirements and their effectiveness

Several existing pieces of legislation aim to reduce or control risks arising from chemicals in their different life-cycle phases. In the following sections the effectiveness of this legislation to specifically address the concerns with mercury in measuring devices is assessed.

Waste legislation

Mercury-containing measuring devices are classified as dangerous according to the European List of Waste (Commission Decision 2000/532/EC)[27], and should be handled according to the rules under Directive 91/689/EEC on hazardous waste (the directive was repealed by the Waste Framework Directive 2008/98/EC with effect

[27] Code "20 01 21* fluorescent tubes and other mercury-containing waste"

from 12 December 2010). These rules in both the old and new framework, relate to amongst others a ban for mixing hazardous waste with other waste streams and record keeping and permit requirements for waste treatment establishments.

Landfill of mercury containing waste has to be dealt with according to the requirements for the 'hazardous waste' class in Directive 1999/31/EC on the landfill of waste, and according to the acceptance criteria for landfills in Decision 2003/33/EC. Some specific rules for mercury waste are laid down in Regulation No 1102/2008. The Regulation contains rules on the safe storage of metallic mercury. Until special requirements and acceptance criteria are adopted under a Comitology procedure, only temporary above-ground storage is permitted. The concern is that eventually mercury in landfills may slowly be remobilised over time (UNEP, 2008b). These concerns for remobilisation are in particular related to the indefinite persistence of mercury, but also to the liquid status of mercury, high vapour pressure, and solubility in water. Storage in salt mines, and storage in deep underground, hard rock formations are under assessment as options for final disposal.

Mercury in measuring devices that are not collected separately and are received in landfills for non-hazardous waste or for inert waste, will not be sufficiently contained. Certain general requirements for landfills in respect to location, water control, leachate management, bottom and surface sealing and stability do exist, and can to a certain extent abate mercury emissions from these landfills, although it is likely that eventually a significant proportion of the mercury slowly will be emitted - if not all in the course of time.

Similarly, mercury in measuring devices that are not collected properly and are incinerated, will lead to significant emissions. Nevertheless, according to the waste incineration Directive (Directive 2000/76/EC) both hazardous as non-hazardous waste incineration has to satisfy an air emission limit value of 0.05 Hg mg/m^3 [28], and an emission limit value for mercury and its compounds in discharges of waste water of 0,03 mg/l (from the cleaning of exhaust gases). However, in contrast to continuous monitoring of dust, HCl, SO_2, CO, C_xH_y, NO_x, and HF, the waste incineration Directive only requires a minimum of two measurements each year for mercury compounds. Local authorities can require more frequent measurements, and in some Member States, such as Austria and Germany, continuous monitoring is required.

Despite these legal provisions, in particular because of low separate collection rates of mercury containing measuring devices, significant emissions occur in the waste phase from all mercury containing measuring devices covered by this BD. The problems with regard to these emissions are described more in detail in the section B.4. It can be concluded that the risk management measures provided for in the waste legislation do not sufficiently address the concerns with mercury arising from the waste phase of mercury containing measuring devices. The efforts needed from the enforcement authorities to ensure that the existing requirements in the waste legislation are complied to are difficult to estimate and would vary between the Member States. However, taking into account the relatively high awareness with regard to the environmental and human health risks related to mercury (compared to many other hazardous wastes) and the fact that the requirements have been in place for a

[28] Average value over the sample period of a minimum of 30 minutes and a maximum of 8 hours

relatively long time it does not seem plausible to rely only on better enforcement of waste legislation to address the issue of placing new mercury measuring devices on the market.

With regard to measuring devices using mercury, the available information indicates that the hazardous waste legislation requirements are generally complied with to a substantially higher extent (see Annex 7 and Appendix 3).

Occupational health legislation

Several pieces of occupational health legislation are in place to manage the risks of the use of mercury in the working environment during the production of measuring devices containing mercury, filling of devices by the users, professional use of mercury with devices such as porosimeters, and during the treatment of mercury contaminated waste.

An 8-hour TWA for mercury and divalent inorganic mercury compounds of 0.02 mg/m^3 is included in the 3rd list of IOELVs[29] under the Chemical Agents at Work Directive (Directive 98/24/EC). Several Member States had already established national exposure limits before the Community-wide IOELV had been adopted (e.g., BE, IE, LT and UK). The IOELV will have to be implemented in all Member States by 18 December 2011 at the latest. The relevant biological monitoring techniques that complement the IOELV should be taken into account by MSs during health surveillance.

Finally, the Young People at Work Directive 94/33/EEC and the Pregnant Workers Directive 92/85/EEC apply to work with mercury (Repr. Cat. 2). They are targeted towards protection of vulnerable populations.

Although occupational health legislation has a crucial role to play in avoiding occupational exposure from mercury in general, measures such as IOELVs are not effective in preventing or reducing exposure resulting from certain events related to the measuring devices containing mercury, such as accidental breakage, spillage or leakage. With regard to measuring devices using mercury, based on available information, there are no reasons to assume that the newly established occupational exposure limits for mercury would be insufficient to protect workers.

Legislation controlling emissions to the environment during production

Production of mercury containing measuring devices does not seem to be covered by Community legislation specifically setting limits on mercury emissions to air or water. Production does not seem to be covered by the IPPC Directive (Directive 2008/1/EC) or the Council Directive 84/156/EEC on limit values and quality objectives for mercury discharges by sectors other than the chlor-alkali electrolysis industry.

[29] List of Indicative Occupational Exposure Limit Values established by the Commission Directive 2009/161/EU of 17 December 2009

Medical devices directive

Sphygmomanometers and strain gauges fall under the scope of the medical devices directive (Directive 93/42/EEC concerning medical devices). The directive foresees that devices must meet a series of "essential requirements", such as for example a requirement to be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the device. However the existence of these requirements has not prevented that breakage and leakage still occurs in real-life, with emission, exposure and costs associated with cleaning the spills as consequences.

National restrictions

Denmark, The Netherlands, Norway and Sweden have national restrictions on mercury in measuring devices. The following provides an overview of the information received from these Member States and Norway. An effort is made to summarise the elements of importance for mercury in measuring devices. For the full description of the restrictions, the national legislation should be consulted. The metering devices for the softening point determination are not mentioned in the national restrictions.

Denmark

Denmark prohibits import, sale and export of mercury and mercury-containing products. The Danish restriction entered into force in 1994, was expanded in 1998 and 2003, was prolonged in 2008, and subsequently has been amended to take into account the entries 18 and 18a of Annex XVII to the REACH regulation. The legislation foresees a possibility for the Danish EPA to allow derogations, but according to information received from the Danish EPA this possibility has never been put to practise. The legislation foresees a list of exemptions to the general ban that are relevant to mercury measuring devices.

Thermometers for special applications, i.e. calibration of other thermometers and analysis equipment are exempted. According to the Danish EPA, in practise this can be translated to an exemption of thermometers for laboratory use. Manometers for calibration of other pressure gauges, barometers for calibration of other barometers, products for research, products for teaching, and products for the repair of existing mercury-containing equipment are exempted as well. Also an exemption is foreseen for 'mercury-containing chemicals for special applications'. According to the Danish EPA, mercury-intrusion porosimetry would, depending on the actual use, fall under one of the exemptions to the restriction.

The Danish EPA reported not to have experienced any particular problems introducing the national restriction.

The Netherlands

The Netherlands restrict production and import of mercury containing products since 1 January 2000. Possession of a product containing mercury or use for trading (2nd hand market) or production purposes is restricted since 1 January 2003 (unless it was already in use before that date). The restriction is not applicable to antiques (>100 years old).
The restriction does not apply to pycnometers or porosimeters, a McLeod compression manometer meant for measuring absolute pressures lower than 20kPa, thermometers exclusively intended to perform specific analytical tests according to established standards, equipment for the calibration of platinum resistance thermometers using the triple point of mercury (the Netherlands would have only one such device).

Norway

The sale of mercury thermometers is prohibited in Norway since 1 October 1998. Thermometers for professional use for meteorological, hydrological and oceanographical measurements and for control measurements and calibrations in laboratories were exempted until 1 January 2001.

Since 1 January 2008 there is a prohibition to manufacture, import, export and sell compounds and articles containing mercury. It is also prohibited to use compounds containing mercury. The restrictions do not apply to analysis and research purposes, but mercury thermometers for analysis and research purposes are specified not to be exempted from the prohibition, and polarographs are said to be exempted for analysis and research purposes only until 31 December 2010. According to information received from the Norwegian Climate and Pollution Agency (Klif), mercury used with porosimeters would fall under 'analysis and research', and thus is not restricted in Norway. Import and sales are however forbidden. Suppliers have to apply for an exemption in order to place mercury on the market for analysis and research.

Exemptions can be granted to the prohibitions. The most common cases with exemptions to buy mercury thermometers are for the following:

- Analyses according to ASTM[30] in cases where mercury thermometers are specified;
- Calibration thermometers (where very high precision is essential);
- Maximum thermometers to be placed inside older autoclaves (without thermo-couples). The applicants claim that data loggers cannot stand the high temperatures.

According to Klif, Norway has received only very few such applications during the last few years, less than ten a year. All ASTM standards referred to concerned testing of oil products (pour point, flash point open cup and closed cup, and possibly also cloud point were thought to be amongst these standards).

[30] ASTM International is one of the main standardisation organisations, see also section 3.3 of Annex 5a.

Sweden

Sweden prohibits the placing on the market, use and export of mercury and chemical compounds and mixtures containing mercury. It is prohibited to place on the market or to export goods containing mercury. The Swedish Chemicals Agency (KemI) may issue regulations to derogate from the general restriction, and in addition can grant exemptions in individual cases. The original version of the restriction dates from 1991. In what follows is described how the Swedish mercury restriction affects individual mercury measuring devices (based on information received from KemI).

Thermometers
In Sweden, the production, sale and export of mercury thermometers is restricted since 1993. The granted exemptions concerning mercury containing thermometers are:

- Use for flash point determination according to standard method ASTM D93 (granted in 2006, expired);
- Import of two thermometers ASTM D97, which were then exported to be used according to 2381 Cloudpoint (granted in 2007, expired);
- Export of 10 thermometers to be used for flash point determination according to dir. 67/548/EEG (granted in 2007, expired);
- Export of thermometers to be used for flash point determination according to dir. 67/548/EEG (granted in 2007, will expire 30 June-2011).

KemI is not aware of any other problems to replace mercury containing thermometers and is not aware of particularly high costs when replacing them.

Porosimeters
The Swedish restriction applies to mercury containing devices as well as devices that make use of mercury. Until end of year 1995 there was an exemption to import, to manufacture and to place porosimeters on the market. According to an investigation made by a consultant 2004, commissioned by KemI, feasible alternative technology for pore sizes exceeding 2000 Å (0.2 μm) was not available at that time. There are further two exemptions granted in 2006 for two porosimeters sold to a company and to a university respectively. The intended uses were pore sizes exceeding 1000 Å mainly for research and development.

Strain gauges
The translation of the current exemption for strain gauges (2007) reads:

> "*The applicant may manufacture and sell up to 150 mercury containing strain gauges each year and these must be used in already existing equipment*
>
> *- to measure blood flow in a muscle within clinical routine activities up to 2010-12-31*
>
> *- for other uses within clinical routine activities up to 2009-12-31*
>
> *- for research and development up to 2012-12-31 given that the project started prior to 2007-12-31. If the research concerns blood flow in a muscle the project may start not later than 2010-12-31.*
>
> *- to validate mercury free alternatives up to 2010-12-31.*
>
> *The applicant has the duty to keep records on the uses.*"

Manometers
KemI reports that there have not been any applications for exemptions to the restriction from 2005 up to now. As far as they are aware of, there have been no applications for exemption before 2005 either.

B.6 Summary of hazard and risk

Mercury and its compounds are highly toxic to humans, ecosystems and wildlife, with amongst others serious chronic irreversible adverse neurotoxic and neurodevelop-mental effects.

The RAC opinion includes a PBT assessment for mercury-methylmercury concluding and equivalent level of concern in terms of persistency, due to mercury cycling and methylation *versus* demethylation rates under anaerobic conditions, as well as the clear potential for bioaccumulation and toxicity identyfied for methylmercury.

It is estimated that 3.5 to 7.6 tonnes of mercury is placed on the market in mercury containing measuring devices in 2010 (see Table 7). These amounts are used to describe the maximum potential for mercury emissions to the environment that might ultimately occur. This is considered appropriate for the purpose of this BD as the low separate collection rate and resulting inadequate waste treatment of a substantial part of the devices, leads in the long term to a relatively high share of mercury used in these devices being released to the environment. Although not the primary concern, it is worth mentioning that direct exposure of workers can occur during production, professional/industrial use of the devices and during waste management operations.

Table 7: The amount of mercury estimated to be placed on the market in the EU in mercury containing measuring devices in 2010

Measuring device containing mercury	**Amount of Hg placed on the market in the EU in 2010 (t/y)**
Barometers	0.1-0.5
Manometers (including tensiometers)	0.04-0.4
Sphygmomanometers	2.6-5.1
Strain gauges (used with plethysmographs)	0.014
Thermometers (including hygrometers)	0.7-1.6
Total	**3.5-7.6**

Source: Lassen et al. (2008) as updated in device specific annexes 1 – 5.

In addition around 5-15 tonnes of mercury is supplied annually to be used with porosimeters, pycnometers, devices using mercury electrodes in voltammetry and metering devices for determining the softening point (see Table 8).

The annual amounts presented (in Tables 7 and 8) are not comparable. The figures in Table 8 are the amount of mercury the laboratories purchase and cannot be used to estimate maximum potential for emission as is the case in Table 7. To estimate

emissions several additional factors need to be considered. These include number of measurements carried out, practices to purify and regenerated used mercury and the risk management measures and operational conditions applied to control the emissions and exposures. Furthermore, the available information indicates that the hazardous waste legislation requirements are generally complied with when handling the mercury contaminated waste generated during these measurements.

Table 8: The amount of mercury estimated to be purchased in the EU to be used with measuring devices in 2010

Measuring device using mercury	**Amount of Hg purchased to be used for measurements (t/y)**
Mercury electrodes (used in voltammetry)	0.1-0.5
Metering devices for the softening point determination	not available
Mercury probes used for capacitance-voltage determinations	0.001-0.005
Porosimeters	5-14
Pycnometers	not available
Total	**5-15**

Source: Lassen et al. (2008), device specific annexes 6-10

Once released to the environment, mercury persists in the environment, where it circulates between air, water, sediments, soil and biota in various forms. Mercury can be transformed to methylmercury, the most toxic form, which biomagnifies especially in the aquatic food chain, making populations and wildlife with a high intake of fish and seafood particularly vulnerable.

Several existing pieces of legislation abate the risks arising from mercury in different stages of the life-cycle of measuring devices. However, none of the measures currently in place is sufficient to remove the concern fully, although there is a difference between their observed effectiveness with regard to measuring devices containing mercury and measuring devices using mercury.

The emissions from mercury measuring devices, although relatively small, contribute to the overall emissions of mercury to the environment and thereby also to the exposure of species and of humans via the environment. Therefore, measuring devices containing or using mercury are of concern.

C. Available information on the alternatives

As explained in the Preface, a deviation from the reporting format is made to improve the flow and readability of the text as several different measuring devices are assessed in this BD. In this general part C, information on risks related to alternatives that is relevant for all devices is reported. In addition, information on technical and economic feasibility from the Annexes 1-10 is summarised.

It is reminded that the emphasis lays on the identification of potential alternative substances and techniques, and their technical and economic feasibility.

C.1 Identification of potential alternative substances and techniques

Potential alternatives have been identified for all devices and are described in Annexes 1-10.

C.2 Human health and environment risks related to alternatives

C.2.1. Measuring devices containing mercury -Comparison of risks posed by mercury devices and their alternatives

In the following, a semi-quantitative comparison of the risks of alternatives compared to measuring devices containing mercury is made for each stage in the life-cycle. The potential for risk is described with semi-quantitative indicator scores ranging from 1 to 4.[31]

Alternative liquids

Alternative liquids used in thermometers are ethanol (ethyl alcohol), methanol, pentane, pentanol, toluene, kerosene, creosote, petroleum, i-amyl benzoate (isoamyl benzoate or isopentyl benzoate), and 'citrus-extract-based solvents' (see section 3.1 of Annex 5a). The market share of these alternatives is unknown, and this information seems not to be readily available. From a product catalogue it appears that the choice of liquid depends in the case of thermometers amongst others on the lower and upper limits of temperature measurement and that many liquids are to a certain extent interchangeable (see section 3.1 of Annex 5a).

For barometers 'a red silicone fluid' is used, but other liquids might be used as well. Alternative liquids in use for manometers are most commonly water or alcohols.

There might be some direct human exposures and release to the environment arising from the *production phase* of organic liquid filled thermometers, barometers, and manometers, from filling barometers or manometers by the end-users, or from the *use phase* (breakage). Since many of the liquids are volatile, such exposure would be

[31] 1 = negligible risk potential; 2 = low risk potential; 3 = moderate risk potential; and 4 = high risk potential.

similar to mercury in terms of route of exposure and exposure levels, but would for most liquids be in comparison insignificant on the basis of intrinsic properties (e.g. ethanol). Most liquids could thus be scored 1. For creosote (classified as carcinogen cat. 1B according to Annex VI to the CLP Regulation), and possibly some other alternative liquids it suffices to say that the risks might in the worst case be of a comparable order to mercury (both creosote and mercury could be scored 3). Note that creosote seems only to be used as an alternative liquid in thermometers, and represents only a fraction of the alternatives used to replace mercury thermometers. On the whole, replacing mercury containing measuring devices with the spectrum of alternatives, clearly results in a reduction of risk. Overall, the production and use phase of the alternatives is scored as a range of 1-2, in order to reflect that the risk potential will depend on the share of each liquid that replaces mercury (the score of 2 would be conservative, acknowledging that the share of ethanol and other alcohols are many times higher than creosote).

As described in section B.4, the main risk of the use of mercury in measuring devices is related to the *waste phase* and the persistency of mercury as an element. There is no legal requirement to separately collect devices with alternative liquids, and thus these devices will go to either municipal waste incineration or landfill. In contrast to mercury devices, the share of devices filled with organic liquids that is incinerated does not cause risks to the environment (the organic substances are entirely oxidised). Thus, a score of 1 could be attributed for the share of liquids that are incinerated.

When diverted to landfill, substances such as ethanol and pentane are not considered to pose environmental risks in the waste phase since they are readily biodegradable (EU RAR n-pentane, 2003) (EC JRC, 2000a). Also, pentanol quickly degrades (EC JRC, 2000b). Such substances are given a score of 1. Substances such as kerosene, creosote and petroleum, might degrade slower when landfilled or released to the environment (to air or as leachate), but still much faster than mercury (which is an element). These specific substances could be accorded a scoring of 3. In order to reflect the dependence on the share of each liquid that replaces mercury, an overall score of 1-2 could be attributed to landfilling of the alternatives.

The use of water as an alternative liquid in manometers poses no risks (score 1 for all life-cycle stages).

One of the several alternatives to mercury strain gauges are strain gauges containing gallium-indium alloys. Annex 4 describes the comparably low to negligible risks related to the use of gallium and indium in strain gauges for plethysmography[32].

[32] Gallium is also used in some thermometers, but as explained in Annex 5a, these thermometers are currently only used for niche-applications. Gallium thermometers are not considered a direct replacement of mercury thermometers for economical reasons, and it seems likely so also for technical reasons (such as precision and wetting of glass).

Electronic alternatives

Background

Electronic alternatives (electronic thermometers, sphygmomanometers, barometers, manometers and strain gauges) to mercury measuring devices would contribute with a very small fraction to the overall volume of Waste Electrical and Electronic Equipment (WEEE)[33]. All WEEE or 'e-waste' can contain small amounts of heavy metals, flame retardants, phthalates, and other substances with hazardous properties. Especially the very large volumes of e-waste in society makes the presence of these small amounts of hazardous substances significant, and causes e-waste to be of concern to the environment and human health.

RoHS[34] and WEEE[35] Directives are a pair of legislation working in synergy, essentially to overcome emissions from hazardous substances present in e-waste.

The RoHS Directive restricts currently the presence of lead, mercury, cadmium, hexavalent chromium, polybrominated biphenyls (PBB) and polybrominated diphenyl ethers (PBDE) in new electrical and electronic equipment put on the market[36]. However, it currently does not (yet) cover the categories 'monitoring and control instruments'[37] and 'medical devices'[38]. The proposed RoHS recast[39] includes the above mentioned currently omitted category in its scope, and consequently also electronic alternatives to mercury measuring devices would be covered by the RoHS Directive in the future. The European Parliament voted in the first reading on 3 February 2011 and the council reached Political Agreement on 14 March 2011. Both support inclusion of the two categories in the scope of RoHS.

The WEEE Directive provides for the creation of collection schemes, thus preventing electronic waste ending up in unsorted municipal waste. The collection requirements are applicable to the categories 'monitoring and control instruments' and 'medical devices'.

[33] A small fraction of the category 'monitoring and control instruments', which itself is estimated to be 0.2% of the 8.3 - 9.1 million tonnes e-waste produced in 2005 (http://ec.europa.eu/environment/waste/weee/pdf/final_rep_unu.pdf)

[34] Directive 2002/95/EC on the restriction of the use of certain hazardous substances in electrical and electronic equipment (RoHS).

[35] Directive 2002/96/EC on waste electrical and electronic equipment (WEEE).

[36] The concentration limit for the restriction is 0.1% by weight, with the exception of cadmium where a 0.01% by weight in homogeneous materials shall be tolerated.

[37] Directive 2002/96/EC mentions under 'monitoring and control instruments': smoke detectors; heating regulators; thermostats; measuring, weighing or adjusting appliances for household or as laboratory equipment; and other monitoring and control instruments used in industrial installations (e.g. in control panels).

[38] Directive 2002/96/EC mentions under 'medical devices': radiotherapy equipment; cardiology; dialysis; pulmonary ventilators; nuclear medicine; laboratory equipment for in-vitro diagnosis; analysers; freezers; fertilization tests; and other appliances for detecting, preventing, monitoring, treating, alleviating illness, injury or disability.

[39] Proposal for a Directive of the European Parliament and of the Council on the restriction of the use of certain hazardous substances in electrical and electronic equipment (recast), COM(2008) 809 final.

Comparison of exposure and release between mercury containing devices and their alternatives

It is difficult to make an assessment of the risk potential of the production of electronic alternatives. Both in the production of mercury containing measuring devices and the electronic alternatives, occupational health legislation has to be complied with. Production of semi-conductor parts of electronic alternatives occurs under 'clean room' conditions, however environmental releases might occur. In the production of plastics, substances might be used, potentially in less controlled conditions than in the semi-conductor industry. It can be concluded that during production of both mercury containing measuring devices and their electronic alternatives, exposure of workers and release to the environment can occur. Notably, mercury devices such as manometers and barometers have to be filled with mercury by the customer before use, which entails occupational exposure of a concern that is not comparable to exposures or releases during the production of electronic alternatives. A scoring of 1-2 is attributed to the production stage of electronic alternatives and 3 to mercury devices.

Importantly, during the service-life of the mercury measuring devices, breakage of devices and normal maintenance leads to release to the environment and exposure of workers to the highly toxic and volatile elemental mercury. No comparable exposure or release exists during the service-life of electronic alternatives, and thus professional exposure and environmental releases are comparably negligible. The scoring of the service-life is therefore 1 for the electronic alternatives, and 3 for mercury devices.

Similarly to mercury measuring devices, the main concern of electronic goods are risks related to the waste stage. At the end of service-life, both electronic alternatives and mercury devices legally have to be collected separately, and for both compliance with the legal requirement is poor[40]. Poor compliance has an important detrimental effect on the level of control in the subsequent waste treatment, and the principal risks arise from the fractions that are not collected separately.

There are however a number of important differences between electronic alternatives and mercury devices to be noted:

- Amounts
  Most importantly, the amounts of hazardous substances per electronic alternative are comparably negligible to mercury containing measuring devices where the mercury content is several gram per device or much higher. This consideration is important in each life-cycle step.
- Collection, transport and pre-treatment
  In the course of collection, transport and pre-treatment[41] of mercury measuring devices and the resulting breakage, some mercury will be released to the air.

[40] According to the Commission "*only one third of electrical and electronic waste in the European Union is reported as separately collected and appropriately treated. A part of the other two thirds is potentially still going to landfills and to sub-standard treatment sites in or outside the European Union.*" (DG ENV website http://ec.europa.eu/environment/waste/weee/index_en.htm, retrieved on 26 August 2010.). Concerning the collection of mercury devices, see part B.4.

[41] Pre-treatment is understood as mixing, shredding, and sorting activities that are typically carried out on municipal wastes before it is landfilled or incinerated.

No similar releases of hazardous substances exist during such activities carried out with waste electronic alternatives.

For these reasons, a score of 1 can be attributed to the share of electronic alternatives that are collected separately and are subsequently treated properly, whereas mercury devices that are collected separately would be attributed a score of 3.

For both mercury devices and their alternatives, the fractions that are *not* collected separately, can go to landfills for non-hazardous waste or incineration plants for non-hazardous waste. Again, there are a number of important differences to be noted:

- Landfill
  As a result of landfill activities (spreading, compacting, etc.) and the destructive pre-treatment (see previous indent) most devices will be present in broken state in the landfill, thus allowing a large volume of uncontained liquid mercury per device to evaporate or leach out of landfills. In contrast, the small amounts of hazardous substances present per waste electronic alternative device are generally not liquid or volatile, are bound in the matrix of the device, or otherwise relatively well contained, and are thus released and leaching out only very slowly. A score of 2 is attributed to landfill of electronic alternatives, and a score of 4 to mercury devices.
- Incineration
  During incineration in plants for non-hazardous waste, from both mercury devices as from their electronic alternatives emission to air and water occurs. Here again, the quantities of hazardous substances emitted from the waste electronic alternatives is low in comparison with mercury devices. A score of 2 is attributed to incineration of electronic alternatives, and a score of 4 to mercury devices.

Mechanical alternatives

Mechanical alternatives (aneroid sphygmomanometers, aneroid barometers, aneroid manometers and bi-metal dial thermometers) have a composition similar to any other everyday article. According to product catalogues, materials used for these articles are plastics (PC, Polyamide, TP-Elastomer, PMMA, etc.), metals (stainless steel, galvanized steel, aluminium, anodized aluminium, brass, nickel-plated metal, copper-beryllium-alloy, bronze, NiFe-alloy, etc.), coatings, glass, silicone, and other common materials (Ludwig Schneider, 2010; Omega, 2010; Trerice, 2010; WIKA, 2010; Palmer Wahl, 2010; Jumo, 2010; ARMATURENBAU, 2010; Wittich & Visser, 2010; HEINE Optotechnik, 2010). As a consequence, and especially in comparison with mercury containing measuring devices, there are no known notable risks related to these devices (score 1 for all life-cycle stages).

Table 9 gives an overview of the potential for risk by means of semi-quantitative indicator scores. The overview makes clear that the risks of every alternative type is lower than mercury containing measuring devices in all life-cycle stages.

Table 9 Semi-quantitative comparison of risks related to mercury containing measuring devices and their alternatives

	Production	Service-life	Waste stage		
			Proper treatment	No proper treatment	
				Incineration	Landfill
Hg	3	3	3	4	4
Hg-free liquid	1-2*	1-2*	1-2**		
EEE	1-2***	1	1	2	2
mechanical	1	1	1****		

1 = negligible risk potential; 2 = low risk potential; 3 = moderate risk potential; 4 = high risk potential
Hg = mercury containing measuring devices; Hg-free = measuring devices with mercury-free fillings; EEE = electronic measuring devices; mechanical = mechanical measuring devices.
* Overall risk potential, depending on the properties and share of liquids replacing mercury containing measuring devices.
** Overall risk potential, depending on type of treatment (incineration or landfill),and the properties and share of liquids replacing mercury containing measuring devices. Waste not subject to separate collection requirements.
*** As a rather conservative estimate.
**** Waste not subject to separate collection requirements

C.2.2 Measuring devices using mercury

Gas pycnometers use an inert gas such as helium or nitrogen to measure the replacement volume. The alternative methods to mercury metering devices for the softening point determination use water or glycerol, mechanical and/or electronic parts. No significant risks have been identified related to the use of these alternatives.

There are several potential alternative methods to mercury porosimetry, mercury probes and to mercury electrodes used in voltammetry. Since technical feasibility could not be established, the risks of all potential techniques have not been assessed in great detail. Some alternative methods make use of liquids (such as water, hexane, gallium and indium) or gas (such as nitrogen, argon, krypton and CO_2). Use of some other methods, such as X-Ray Tomography, might present a higher risk than methods using gas or liquids.

More information on alternatives can be found in Annexes 6 to 10.

C.3 Technical feasibility of alternatives

According to Annexes 1-10, technically feasible alternatives are available for mercury barometers, manometers, sphygmomanometers, strain gauges, thermometers, pycnometers, and metering devices, with the exception of:

- sphygmomanometers that are used in on-going epidemiological studies or as reference standards in clinical validation studies of mercury-free sphygmomanometers;
- thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers; and

- mercury triple point cells that are used for the calibration of platinum resistance thermometers[42].

In addition, technical feasibility of alternatives could **not** be established for mercury porosimeters and devices using mercury electrodes in voltammetry (see section 3.3 of Annex 7 and Annex 6 respectively). For mercury probes used for capacitance-voltage determinations, none of the alternatives are both technically and economically feasible.

C.4 Economic feasibility

According to Annexes 1-10, economically feasible alternatives are available for mercury barometers, manometers, sphygmomanometers, strain gauges, thermometers, pycnometers and metering devices.

For mercury porosimeters and devices using mercury electrodes in voltammetry, the technical feasibility of alternatives could not be established and thus the economic feasibility was not fully assessed. For mercury probes used for capacitance-voltage determinations, none of the alternatives are both technically and economically feasible.

[42] Triple point cells are not thermometers, but they might fall under the broader wording that is used in the proposed restriction ('*thermometers and other non-electrical thermometric applications containing mercury*'). For this reason they are discussed as well.

D. Justification for action on a Community-wide basis

As stated in part B of this report the need to consider the extension of the current restriction on mercury in measuring devices at Community level was already established in Directive 2007/51/EC.

D.1 Considerations related to human health and environmental risks

As explained in section B, the hazard properties of mercury and its transformation products are widely recognized. It is difficult for any Member State to act alone to effectively protect its environment or its population from mercury exposure, because the human health and environmental problem related to mercury is cross boundary. This is also well recognised by the Community mercury strategy and by the activities of UNEP and regional organisations.

As reported in Section B.4 mercury measuring devices are used throughout the EU, although some Member States have already established national restrictions (see section B.5). Consequently, the mercury emissions originating from the entire life cycle of measuring devices, and in particular their waste stage, take place in most of the Member States, even though the amount of emissions in different parts of the EU varies depending on the amounts of devices used and disposed of, and on the waste management practices.

Therefore, the risks need to be controlled on a Community-wide basis.

D.2 Considerations related to internal market

The proposed restrictions cover devices that are extensively traded among and used in all Member States most of which have not established national restrictions. The devices containing mercury are both produced in and imported to the EU as reported in Annexes 1 to 10. The justification to act on a Community-wide basis stems from the fact that the goods need to circulate freely within the EU. The proposed restriction would remove the potentially distorting effect that current national restrictions may have on the free circulation of goods. The second justification is that regulating mercury through Community-wide action ensures that the producers of the devices in different Member States are treated in an equitable manner. Furthermore, acting at Community level would ensure a ‘level playing field’ among all producers and importers of the devices.

D.3 Other considerations

The Community is currently promoting measures at international level[43] that aim to address human health and environmental problems relating to mercury (see section B.2). Mercury is both a regional and a worldwide problem. Therefore, acting at Community level strengthens the Community's and its Member States' possibilities to cooperate constructively with other countries and relevant institutions.

D.4 Summary

The main reason to act on a Community-wide basis is the cross-boundary human health and environmental problem. Furthermore, the fact that the goods need to circulate freely within the EU stresses the importance of the Community-wide action, as some Member States have national restrictions for mercury measuring devices. Thus, the use of mercury in these devices needs to be controlled also at the EU level. In addition, acting at Community level strengthens the possibilities of policymakers to address the adverse impacts of mercury at worldwide level.

[43] For instance, the Community is active in the United Nation's Environment Programme's Mercury Programme (see http://www.chem.unep.ch/mercury/).

E. Justification why the proposed restriction is the most appropriate Community-wide measure

As explained in the Preface, a deviation from the reporting format is made to improve the flow of the restriction report as several different measuring devices are assessed in one report. In this general part E, a summary of the justifications why the proposed restrictions are the most appropriate Community-wide measure is reported. It starts with an overview of the assessment of the proposed restrictions against their effectiveness, practicality and monitorability. This is followed by device specific summaries for the proposed restrictions as well as summaries for justifications for not proposing restrictions for certain devices. Finally, the justification for derogations and conditions common for all devices are provided.

The details of the assessment are provided in device specific Annexes 1 to 10.

Summary of the assessment of the proposed restrictions

While the major part of the assessment of the options and reasons for proposals can be found in the device specific annexes, some common issues and a summary are discussed below.[44]

The main purpose of the proposed restrictions is to reduce the mercury pool in the society, thus avoiding emissions and exposures causing negative impacts on human health and environment. While the main benefits of these restriction proposals result from the prevention of mercury from entering the waste stream, the proposed restrictions on the placing on the market would also result in additional other benefits related to reduction of possible exposure of workers during production and use of the devices. There may be also some further co-benefits (e.g. during waste handling).

Based on the review clause in the existing restriction on mercury in measuring devices, the justification for proposing further restrictions focuses on the technical and economic feasibility of the alternatives. The costs of avoiding mercury in euros per kilogramme (€/kg Hg) are presented to assess and conclude on the proportionality of the restriction options, when data exist to allow such estimation. For the purposes of this restriction report a literature review has been carried out of the compliance and other costs, as well as human health benefits of regulating mercury. This review has been used to support the assessment of the proportionality of restriction options. For details, see Appendix 2.

[44] Note that it has not been considered appropriate to make a distinction between professional and industrial users for assessing possible restrictions on mercury measuring devices in this report. Nevertheless, the typical groups of users are described in the device specific annexes.

Assessment of effectiveness

For the reasons mentioned in section B.2, a quantitative exposure assessment or risk characterisation was not carried out in this BD. Instead, the total estimated amount of mercury placed on the market in measuring devices containing mercury is used to describe the maximum potential for mercury *emissions to the environment* that might ultimately occur. The proposed restriction is estimated to reduce the amount of mercury placed on the EU market (in devices or to be used in measurements) by 60 tonnes for a 20 year period starting from 2015[45]. It can be mentioned that this volume reduction would also decrease direct *exposure of workers* in production, use and waste phase -with the exception of exposure related to remaining production for exports.

It is recognised that the time when the restriction becomes effective depends on the decision making process and the transitional periods after the decision is taken by the Commission. For the purpose of the risk reduction capacity and cost calculations of this report it is assumed that the restrictions would apply from the beginning of 2015.

The temporal scope of the analysis was selected in the following manner. Taking into account the uncertainties related to the available data and the assumed declining trend in the number of mercury devices placed on the market, 20 years scope is regarded appropriate. As the average lifetime of mercury containing devices is around 10 years in most applications, the restriction would have its full effect 10 years after adoption, i.e. in 2024, when all the existing mercury containing devices would be replaced. Thus, year 2024 was selected as a representative year to illustrate annualised impacts.

Table 10 gives details of the amount of mercury that is estimated not to be placed on the market in the EU as a result of the proposed restriction. Both the representative year (2024) and the total effect of the 20 years (i.e. 2015-2034) are presented.

Table 10: Estimated amount of mercury not placed on the market as a result of the proposed restriction in 2015-2034 as well as in 2024

Device	2024 per annum kg	2015-2034 cumulative kg
Sphygmomanometers*	1 900	39 000
Thermometers (including hygrometers)*	500	10 000
Barometers**	350	7 000
Manometers (including tensiometers)**	200	4 000
Strain gauges**	14	280
Pycnometers***	~0	~0
Metering devices***	~0	~0
Total	**2 964**	**60 280**

Source: Derived from Annexes 1-10

Notes: * Number of the mercury containing devices projected to decline by 5% per annum as described in the device specific annexes 3a and 5a

[45] Considering the estimates for the amounts of mercury used in products and processes in EU for 2010 (see section B.4 figure 1), the proposed restriction accounts for 1.5 % of the total use. However, the measuring devices account for 4 %, as the suggested restriction does not cover all the mercury measuring devices.

** Assuming no change in the trend

*** There does not seem to be remaining markets for these devices in the EU and thus, the estimated amount of mercury not placed on the market would be close to 0 kg.

The compliance costs of the proposed restrictions are estimated to be €13.3 million in 2024, or cumulatively €129 million for 2015-2034 (Table 11). The compliance costs for barometers, manometers, metering devices, pycnometers and strain gauges are not (fully) quantified. Nevertheless, in the case of barometers and manometers the qualitative evidence strongly suggests that the alternatives to mercury devices cost the same as mercury devices. In other words, the additional cost is about €0 in this case. For metering devices and pycnometers no information was available on the costs of alternatives. However, there does not seem to be remaining markets for these devices in the EU and thus, costs would be close to €0.

Table 11: Estimated compliance costs of the proposed restriction in 2015-2034 as well as in 2024

Device	2024 per annum € million	2015-2034 cumulative € million
Sphygmomanometers	3.2	29
Thermometers *	9.0	97.4
Barometers	0	0
Manometers (including tensiometers)	0	0
Strain gauges	0.13	2.6
Pycnometers**	~0	~0
Metering devices**	~0	~0
Total	**12.3**	**129**

Source: Annexes 1-10

Note: * Labour time savings when using electronic alternatives are included in this figure, see Annex 5a and 5b.

** There does not seem to be remaining markets for these devices in the EU and thus, costs would be close to €0

As the environmental and human health impacts are not quantified, no further comparison between the benefits and costs of the proposal is possible. However, it was possible to quantify the reduction in the amount of mercury placed on the market in the EU as a result of the proposed restrictions. Based on these estimates the cost-effectiveness of the proposed restrictions is estimated. These are given in Table 12. Overall the cost-effectiveness of the proposed restriction is estimated to be €4,100/kg Hg but naturally there are variations between the different measuring devices.

Table 12: Estimated cost-effectiveness of the proposed restrictions

Device	Cost-effectiveness (€/kg)
Sphygmomanometers	1,300
Thermometers*	19,200**
Barometers	0
Manometers (including tensiometers)	0
Strain gauges	9,600
Pycnometers***	not available
Metering devices***	not available
Total*	**4,100**

Source: Annexes 1-10

Note: * Weighted average (kg of mercury used as the weight) excluding hygrometers
** Labour time savings when using electronic alternatives for industrial thermometers measuring temperatures above 200ºC are included in this figure, see Annex 5a and 5b.
*** There does not seem to be remaining markets for these devices in the EU

Assessment of practicality

All the device specific restriction proposals concern the placing on the market of the mercury included in or used with the measuring devices. No use or other conditions are proposed, even though for some devices they are assessed to some extent. In general, no problems related to the implementability and manageability of the proposed restriction were identified.

The enforcement of the placing on the market of the mercury measuring devices can be assessed mainly by inspecting producers, and by verifying if importers and distributors still supply mercury measuring devices.
However, enforceability of the proposed derogations in the restriction for thermometers might be more problematic (see Annex 5a).

Adding a concentration limit to the restriction proposal for devices containing mercury is not considered necessary since it is clear in the context of the restriction that metallic mercury or alloys of metallic mercury are used in closed columns. It is clearly not the purpose that enforcement authorities would verify if a device would contain in e.g. its plastic or glass parts a certain concentration below a threshold. As explained in the Annexes 1-5, visual inspection suffices to determine if mercury is used as a liquid in the column. The sole exception to this would be mercury dial thermometers that have a mercury filled metal bulb. In the latter case a non-destructive analytical method named X-ray fluorescence (XRF) can be used. See also the First Advice of the Forum on the enforceability of the proposed restriction on mercury measuring devices, adopted 19 November 2010. For the reasons mentioned above, it could even be considered confusing for the actors to introduce a concentration limit, and thus would reduce the clarity of the restriction proposal.

Assessment of monitorability

The monitoring of the restriction for all the devices will be done through enforcement and no additional monitoring is envisaged. Therefore, the monitorability of the

restriction options for different measuring devices is not discussed further in the device specific Annexes. The current monitoring of environmental concentrations of mercury or methylmercury does not give information on the effectiveness of the existing restriction for mercury measuring devices and it is not feasible to target the monitoring to provide such information. This is because of the share of mercury measuring devices is only about 4% of the total amount of the mercury used in the EU. The share of measuring devices of the emissions caused by the intentional use in the EU is not known. Furthermore, there are mercury releases from other sources than intentional use in articles and processes (e.g. power plants).

Other community-wide measures than restriction

Other community-wide measures are not assessed in detail in the device specific annexes. This approach is taken as the review clause in the existing restriction asks for extension of the current restriction where technically and economically feasible alternatives are available.

Mercury is already covered by several pieces of Community legislation. On the basis of assessment described in Section B.5 (and B.4), the current legislation and in particular waste legislation is not sufficient to address the concerns related to placing on the market of *new* measuring devices containing mercury. In other words, action under waste legislation is considered not to be the most appropriate risk management option to address the concerns with placing on the market of *new* mercury measuring devices. Moreover, it should be noted that restriction is an important waste prevention instrument, thus satisfying the top priority in the waste hierarchy[46].

It is acknowledged that low separate collection of existing devices is of concern. Action to improve the separate collection rate of the *existing* mercury measuring devices in society that have reached the end of their service life could be undertaken as a separate and additional measure to the proposed restriction. Analysis of the possibilities for and appropriateness of such action is not in the remits of this BD, but can be considered by the Commission and Member States in the appropriate fora under e.g. the framework of waste legislation and the Community Strategy Concerning Mercury.

Based on available information, as described for instance in Box 1 of Annex 7 (Porosimeters) and in Appendix 3, with regard to measuring devices using mercury hazardous waste requirements appear to be complied with to a substantially higher extent. In addition, there are no indications that the newly established occupational exposure limits for mercury would be insufficient to protect the workers. Restriction options 2 and 3 in Annex 7 (Porosimeters) discuss the needs and possibilities to strengthen the compliance with the existing obligations under waste and occupational health legislation by introducing conditions in Annex XVII of REACH. However, such conditions are not proposed due to reasons given in Annex 7.

[46] 'prevention' means measures taken before a substance, material or product has become waste, that reduce: (a) the quantity of waste, including through the re-use of products or the extension of the life span of products; (b) the adverse impacts of the generated waste on the environment and human health; or (c) the content of harmful substances in materials and products (Dir 2008/98/EC).

The proposed restrictions and summary of the device specific justifications

Measuring devices containing mercury

- *Barometers*

Proposal: Restriction on the placing on the market of mercury barometers.

Justification: Technically feasible alternatives are available and electronic alternatives already dominate the market. The alternatives are available at approximately the same price as mercury barometers. Consequently restricting the placing on the market of mercury barometers would not introduce additional costs (cost-effectiveness is around €0 per kg Hg not placed on the market).

- *Manometers (including tensiometers)*

Proposal: Restriction on the placing on the market of mercury manometers and tensiometers.

Justification: Technically feasible alternatives are available and in use. The alternatives are available at approximately the same price as mercury manometers. Consequently restricting the placing on the market of mercury barometers would not introduce additional costs (cost-effectiveness is around €0 per kg Hg not placed on the market).

- *Sphygmomanometers*

Proposal: Restriction on the placing on the market of mercury sphygmomanometers with limited derogations for (i) on-going epidemiological studies and (ii) using mercury sphygmomanometers as reference standards in clinical validation studies of mercury-free sphygmomanometers.

Justification: Technically feasible alternatives are available with very limited exemptions based on the opinion of SCENIHR. Based on the assessment of compliance costs (in Annex 3b), the alternatives are also regarded as economically feasible. The cost of avoiding mercury (around €1300/kg Hg) is considered to be proportional.

- *Strain gauges (used with plethysmographs)*

Proposal: Restriction on the placing on the market of mercury strain gauges to be used with plethysmographs.

Justification: Technically feasible alternatives for mercury strain gauges used with plethysmographs are available. The alternatives are also economically feasible.

- *Thermometers (including hygrometers)*

Proposal: Restriction on the placing on the market of mercury thermometers and other non-electrical thermometric applications containing mercury with derogations for i) thermometers to perform specific analytical tests according to standards that require the use of a mercury thermometer (time-limited); and ii) mercury triple point cells that are used for the calibration of platinum resistance thermometers.

Justification: Technically feasible alternatives are available for all applications, with the exception of: thermometers used for testing according to analysis standards that prescribe mercury thermometers, because some time is needed to amend those standards; and mercury triple point cells because mercury is needed as a reference point in the 1990 International Temperature Scale. Economically feasible alternatives are available for all applications.

Measuring devices using mercury

- *Mercury electrodes (used in voltammetry)*

Proposal: No restriction.

Justification: Technically feasible alternatives are not available in all applications. The technical limitations are related, for instance, to mobility and sensitivity of the alternative devices and to the parameters measured. In addition, two main alternatives seem not to be economically feasible due to higher price and recurrent costs and requirements on the laboratory infrastructure.

- *Metering devices for determination of softening point*

Proposal: Restriction on the placing on the market of metering devices for determination of softening point.

Justification: Technically feasible alternatives are available and they seem to dominate the market. No information has been found indicating that the alternatives would be economically infeasible.

- *Porosimeters*

Proposal: No restriction.

Justification: Technical feasibility of the alternatives could not be established under the framework of this report. The alternatives may not be feasible for the users as they do not measure exactly the same parameters. The comparability of the measurement results is difficult to be assessed. In addition the applicability of the alternatives is limited in terms of pore sizes covered and the type of sample (e.g. applicable only to hydrophobic samples). Assessment of technical feasibility is complicated by the fact that porosimeters are used in several application areas which all have their own technical features. As the technical feasibility could not be established, the economical feasibility was not assessed in details. In addition, waste management of mercury and mercury contaminated samples and other materials is part of the normal operation of the laboratories performing measurements with these devices. The reported practices in laboratories appear to support the view that the waste handling of mercury used in the measurements would be conducted in accordance to the requirements of the hazardous waste legislation (see Annex 7 and Appendix 3).

- *Pycnometers*

Proposal: Restriction on the placing on the market of mercury pycnometers.

Justification: Technically feasible alternatives are available and they seem to dominate the market. No information has been found indicating that the alternatives would be economically infeasible.

- *Mercury probes used for capacitance-voltage determinations*

Proposal: No restriction

Justification: None of the alternatives for mercury probes used in capacitance-voltage or current-voltage measurements are both technically and economically feasible. This is mainly because in most of the cases the replacement of a mercury probe used for capacitance-voltage determinations would require several other measuring devices.

Justification for derogations and conditions common for all devices

Justification to propose a transitional period of 18 months

The actors need some time to adapt after a regulation has entered into force. The reasons are technical, economic, practical and regulatory.

Examples of technical adaptation are: when measuring devices change, industry, laboratories and their customers may need to adapt the processes where the measurement takes place. In some cases the products using measuring devices need to be changed, too.

Examples of reasons for adaptation due to economic reasons are: it would seem economically disproportionate if manufacturers, importers, wholesale and retail sellers could suddenly not place on the market their existing stocks of devices. These considerations are particularly important due to the fact that many operators in measuring device market are small and medium sized companies.

Examples for practical reasons for a transitional period are: responsible authorities may need to make arrangements to be able to enforce the new restrictions. It takes some time for them to inform each other as well as the suppliers and customers in all markets about the change in legislation. This is also a specific issue for importers who need to inform non-EU suppliers about the change in EU regulation.

Theoretically, the length of the transitional period could be different for different devices. However, for reasons of clarity to enforcers and to the actors who have to comply with the restrictions, there is a merit of having one single transitional period, unless there are good grounds to do otherwise.

For some devices like barometers, manometers, pycnometers and metering devices where the alternatives already dominate the market, a shorter transitional period could be justified. However, as only relatively small amounts of mercury, if any, is currently placed on the EU market in these devices, an earlier date would not reduce the mercury placed on the market considerably. Therefore, risk reduction capacity would not be significantly higher (due to low tonnages) and it is regarded to be more valuable to have a more coherent entry with the same transitional period for all the devices.

For the above reasons a transitional period of 18 months is considered reasonable for the market operators and administration to adapt to the requirements of the proposed restriction. A shorter period could imply implementation problems and there seems to be no need for a longer one, apart from the issue relating to the use of mercury thermometers prescribed by analysis standards. In this latter case a transitional period of 5 years is suggested.

Derogations for devices with cultural and historical value

In addition to device specific derogations, a general derogation for placing on the market of old devices (more than 50 years old) was proposed by the dossier submitter. This derogation is similar to the one in the existing restriction on consumer devices (Entry 18a).

The derogation is meant to allow a general selling and buying of old, historically valuable mercury containing devices which can be regarded as antiques or cultural goods. The negative impact of this derogation on the risk reduction capacity is insignificant. As the continued use of the existing devices is proposed to be allowed, the derogation would simply allow a very limited number of old devices to be placed on the market, if needed.

The same date as in the equivalent derogation in the existing restriction (more than 50 years old on 3 October 2007, paragraph 3 a) in entry 18a of Annex XVII of REACH)

is proposed to be used. Setting the same date for all devices keeps the entry simpler and clearer, and thus easier to comply with and more enforceable.

However, based on information received during the public consultation, a need for an additional derogation for measuring devices which are to be displayed in exhibitions for cultural and historical purposes was identified. Some of the devices for which restrictions are proposed may not fulfil the prerequisite of being 50 years old, but nevertheless have historical or cultural value. For instance technical museums should be able to obtain or lend professional and industrial measuring devices to be displayed in the exhibitions. This would not be possible without additional derogation as placing on the market also covers the second hand market, and placing on the market of devices free of charge.

In the opinion of RAC, the general derogation for old measuring devices (more than 50 years old) was replaced by the derogation for measuring devices which are to be displayed in exhibitions for cultural and historical purposes. However, in the opinion of SEAC, both derogations are proposed. Furthermore, based on a comment received in the public consultation on the draft opinion of SEAC, SEAC proposes to clarify the scope of the derogation for measuring devices which are to be displayed in exhibitions for cultural and historical purposes by adding the word **public** to the derogation.

Justification for not proposing a review clause

During the preparation of this report it has been considered whether a review clause would be helpful for mercury devices for which a restriction had not been proposed. Such review clause could be focussed on the availability of technically and economically feasible alternatives for mercury devices and it could promote the development of the alternative devices, substances and methods. However, it was recognised that it is difficult to estimate the impact of such a review clause.

A Member State or ECHA can propose a re-examination of an existing restriction in accordance with Article 69(5) of REACH when this is deemed necessary.

In conclusion, for reasons of legislative coherence and clarity, a review clause was not proposed in this restriction report.

F. Socio-economic assessment

F.1 Human health and environmental impacts

For the reasons explained in Part B, the risk reduction capacity of the proposed restriction has been described by using as a proxy the amount of mercury placed on the market in the EU included in or to be used with the measuring devices. These amounts have been described in the device specific annexes. It is important to note that the specific human health or environmental impacts of introducing a restriction could not be quantified. Furthermore it was not considered proportionate to even aim at such quantification given the reasons explained in the Part B.4. As human health and environmental impacts could not be quantified, it is also not possible to monetise these impacts.

The proposed restriction is estimated to reduce the amount of mercury placed on the EU market (in devices or to be used in measurements) by 60 tonnes between 2015 and 2034. Table 10 in Part E gives details. It is evident that not placing 60 tonnes of mercury on the market has a positive impact on the environment and human health. These effects have been discussed in the Part B.3.

F.2 Economic impacts

Apart from the assessment the economic feasibility of alternatives and for some devices assessing the compliance costs, no additional economic impacts from introducing the proposed restrictions have been assessed. Detailed compliance cost assessments for sphygmomanometers and thermometers can be found in Annexes 3b and 5b.

The administrative costs related to the proposed restrictions have been qualitatively reflected in device specific annexes, where this has been possible and regarded proportional. In general administrative costs both to authorities and market operators concerned are assumed to be low.

The compliance costs of the proposed restrictions are estimated to be €12.3 million in 2024, or cumulatively €129 million for 2015-2034. Table 11 in Part E gives details. Furthermore Table 12 gives the average cost-effectiveness of replacing mercury devices with mercury-free ones. Overall the proposed restrictions would cost about €4,100 per kg Hg on the average. Note that this average has been calculated using kilograms as weights. A simple, unweighted average would have given misleading information about the economic impact.

Based on a literature review, Appendix 2 presents the compliance costs, human health benefits and restoration costs of reduced mercury emissions to better understand the estimated compliance costs in relation to other actions and policies to reduce mercury.

F.3 Social impacts

Restricting the placing on the market of mercury measuring devices affects the employment of those who are currently producing them. Table 13 presents the number of identified producers of each measuring device in and outside the EU, number of employees in production of mercury devices in the EU and the share of production in the EU to internal markets. Unfortunately, the number of employees producing mercury measuring devices is not known for all devices, as such information is not easy to collect.

Table 13: Number of producers of mercury measuring devices in EU in 2007

Measuring device	Number of identified producers in the EU	Number of identified producers outside the EU	Number of employees in production of mercury devices in the EU	Share of production in the EU to internal markets
Barometers*)	1 (possibly a couple)	Unknown	2-20	not available
Devices using mercury electrodes	1	1 (Switzerland)	not available	not available
Manometers (incl. tensiometers)	2**)	Unknown	not available	not available
Mercury porosimeters	0	4 (USA)	0	not applicable
Mercury probes***)	0	2 (USA)	not available	not available
Mercury pycnometers	0	1 (USA)	0	not applicable
Metering devices*)	1	Unknown	not available	not available
Sphygmomanometers*)	4	Unknown	30-50	15%
Strain gauges (used with plethysmographs)	1	1 (USA)	not available	100%
Thermometers (incl. hygrometers) *)	11	Unknown	1000-1500	50%

Source: Lassen et al. (2008), Lassen et al. (2010), see Appendix 3

Notes: *) Manufacturers are known to produce also mercury free devices

**) The production of mercury tensiometers may be discontinued in the EU (Lassen et al., 2008)

***) The mercury probes used for capacitance-voltage determinations were recognized as a mercury measuring device based on the information received in the last day of the public consultation on the Annex XV restriction report. The two producers in the USA were identified by ECHA via internet search.

All identified producers of mercury barometers, metering devices (for determination of softening point), sphygmomanometers and thermometers in EU produce also the

mercury-free alternatives. Mercury porosimeters and pycnometers are not produced in the EU. For manometers and barometers, the markets of mercury containing devices are very small compared to mercury-free alternatives.

Given that the restriction proposal does not cover restriction of exports of measuring devices, and given that exports are not restricted by Regulation (EC) No 1102/2008 (see also part B.2), European companies will be allowed to continue producing mercury containing measuring devices for exports. Since in addition most producers of mercury devices are also producing or placing on the market mercury-free alternatives, the social impacts of the proposed restriction would be minimal.

In conclusion, the proposed restriction is estimated to have either no or very small social impacts, in particular on the employees in companies as well as on the aggregate employment of companies producing measuring devices. For the users of the restricted mercury containing measuring devices, no negative social impacts have been identified.

F.4 Wider economic impacts

Specific care has been taken to ensure that the proposed restriction on mercury containing measuring devices is compatible with the international trade rules under the World Trade Organisation. This has been done by adhering to the following principles.

Restricting the placing on the market of mercury measuring devices means that the non-EU producers will no longer be able to export them into the EU. However, these producers can export the alternatives to mercury containing devices into the EU. Thus, the competitiveness of the EU measuring device producers is not affected to the detriment of their competitors outside the EU. In sum, devices containing mercury produced in as well as imported to the EU are regulated exactly in the same manner.

F.5 Distributional impacts

Mercury containing measuring devices are used in laboratories, small and large industry installations, hospitals as well as private practitioners. Thus, regulating the placing on the market of new devices will affect both small or micro (also self-employed) enterprises[47] as well as big companies. Nevertheless, as mercury-free devices cost normally around the same as the mercury device and as the use of existing devices until the end of their service-life is allowed, the impacts on users (including SME's) is small. Therefore any distributional impact would also be small.

Most of the companies producing mercury containing measuring devices are small or medium sized, i.e. are categorised as SME companies (Lassen et al., 2008). As the restriction treats all of these in the same manner all across the EU and as no

[47] In "micro" entreprises, there are less than 10 staff, in "small" entreprises there are less than 50 staff.

economies of scale exist in the production of measuring devices, no specific SME related impacts have been identified.

It is not known to what extent the mercury containing measuring devices are used more in the new Member States compared to the EU15. In some Member States (see Section B.5) there have been national measures to move away from the mercury measuring devices. Thus, these Member States have already partly replaced the mercury devices so it is possible that this restriction proposal would induce relatively speaking slightly higher implementation costs to new Member States. It should also be considered that some devices may be used more in relative terms in the EU15 compared to new Member States. This is due to for instance economic structure. Thus the distributional impacts in terms of costs across different Member States are estimated to be minor.

F.6 Main assumptions used and decisions made during analysis

Throughout the analysis a 4% discount rate has been used as this is in line with ECHA (2008) and the Commission (2008a). The time period of the analysis is 20 years (between 2015-2034) as this represents a period during which most of the direct impacts of the restriction will occur. Results are also presented as annualised using the year 2024 as a representative year, when most of the proposed restrictions would be in full effect.

The causal chain from production or use of mercury devices to health impacts has been explained in Part B. Given that the health and environmental impacts of the proposed restriction have not been estimated (see Section B.2), the methodology used in SEA has been that of cost-effectiveness. As a proxy for effectiveness of risk reduction, the amount of mercury included in the measuring devices sold annually in EU has been used. For the measuring devices using mercury similar assumption has not been needed for two reasons:

- There seems not to markets for mercury pycnometers and mercury metering devices anymore, and consequently no compliance costs.
- For porosimeters and mercury electrodes no compliance cost calculations were conducted as the technical feasibility could not be established.
- For mercury probes no compliance cost calculations were conducted due to strong qualitative evidence supporting that none of the alternatives (or set of alternatives) are both technically and economically feasible.

G. Stakeholder consultation

Public consultation on the Annex XV restriction report (September 2010 - March 2011)

After submission of the original Annex XV restriction report, ECHA organised a public consultation on the restriction report. During the consultation, comments were received from 28 stakeholders, representing individuals, industry, NGO's and Member States. The comments received, as well as the responses from the dossier submitter (ECHA) and from the rapportteurs of the Committees for Risk Assessment and Socio-economic Analysis will be made available on the ECHA website. Furthermore, the Background Document was updated based on the received comments.

Public consultation on the draft opinion of SEAC (June 2011 - August 2011)

ECHA organised a public consultation on the draft opinion of SEAC on mercury in measuring devices. During the consultation, comments were received from 5 stakeholders. The comments received, as well as the responses from the rapporteurs of SEAC are available on the ECHA website. Based on one of the comments the derogation for historically and culturally valuable measuring devices was further defined by adding a word "public" to the derogation.

The redrafted derogation (addition in bold) reads:

*The restrictions in paragraphs 1 and 3 shall not apply to measuring devices which are to be displayed in **public** exhibitions for cultural and historical purposes.*

Furthermore, based on another comment received on thermometers, a footnote 81 in the Annex 5a (Thermometers) to this BD was added related to the reaction time of electronic alternatives.

Stakeholder consultation during the preparation of the restriction report (beginning of 2010)

In December 2009, ECHA contracted Cowi consulting company, together with ENTEC and IOM to carry out a focussed stakeholder consultation on mercury measuring devices (Lassen et al. 2010, see Appendix 3). The consultation took place between January and May 2010. The objective was mainly to collect input data to assess the proportionality of the restriction options and for socioeconomic analysis – in particular on costs of alternatives as well as technical and economic feasibility of replacement.

In this consultation questionnaires tailored to each equipment type were sent to identified producers. An example of the questionnaire is available in Appendix 3 of this BD. In some cases more detailed information was requested through follow-up questions. Based on (Lassen et al., 2008) it was deemed that the contacted producers represent the majority of producers in the EU. Still, in segments where import from countries outside the EU takes place, it was not always possible to consult the non-EU

producers. It was considered unnecessary to consult the producers of barometers due to earlier work giving already an adequate information basis.

In addition to work by Lassen et al (2010), during January-April 2010, ECHA consulted those Member States that were identified to have national bans for mercury measuring devices. The data are reported in Section B.5. Other Member States were not approached when preparing this report. Nevertheless, Commission has consulted Member States in summer 2008.

Commission's consultation (summer 2008)

The review by Commission (see Appendix 5), describes the consultation of Member states and stakeholders as follows:

> "In summer 2008, DG-Enterprise & Industry has launched a consultation with Member States and other interested stakeholders. More specifically, questionnaires were prepared and circulated to the Members of the Commission Experts Working Group on Limitation of Chemicals (LWG) and to the Experts Working Group on Medical Devices (MDEG) asking them to provide input concerning:
>
> - the availability of alternatives to mercury-containing sphygmomanometers in the Member States and whether these are adequately validated and calibrated;
> - essential uses of mercury-containing sphygmomanometers that are required in Member States (e.g. treatment of special medical conditions);
> - other mercury-containing measuring devices used for research and in industrial uses and the availability of alternatives for such devices.
>
> In addition, the Commission sent the questionnaires to interested NGOs, industry trade associations, and scientific organisations requesting them to submit any information (reports of relevant studies/clinical trials etc.) which would be helpful for the purposes of the review."

Other consultations (before 2010)

In addition to the stakeholder consultation carried out in the framework of preparing this B.D. and to the review of Commission (see Appendix 5), a lot of information on mercury containing measuring devices had been collected by the Commission and stakeholders in recent years. During the preparation of these reports stakeholders have also been consulted. The following reports have been used as a main source when preparing the original restriction report and this Background Document:

- Lassen et al. (2008), published by DG ENV: Options for reducing mercury use in products and applications, and the fate of mercury already circulating in society
- Concorde (2009) published by EEB: Turning up the pressure: Phasing out mercury sphygmomanometers for professional use
- SCENIHR (2009) opinion on Mercury Sphygmomanometers in Healthcare and the Feasibility of Alternatives.

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Device specific Annexes

Annex 1: Barometers

Content

1. Technical description of mercury barometers

Mercury barometers are instruments used to measure atmospheric pressure by measuring the changes in the height of the mercury column. A mercury barometer is typically a glass tube filled with mercury. One end of the tube is sealed while the other end of the tube is submerged in a container filled with mercury. Large barometers for professional use (e.g. laboratory use) may contain up to 1.1 kg of mercury according to the Lassen et al. (2008). Typically the more precise equipment has wider columns and consequently more mercury.

As the placing on the market mercury barometers for the general public has been restricted in the EU from 3 October 2009 (Entry 18a in Annex XV of the REACH Regulation), the remaining uses are industrial and professional applications including weather stations, meteorological departments, airports and airfields, wind tunnels, oil refineries, engine manufacturing, sporting sites, offshore installations (e.g. windmill parks) and on ships. According to one supplier small local airfields may still use their old mercury-containing equipment, as the automatic reading of the meter is not essential (Lassen, C. and Maag, J., 2006).

2. Description of release and exposure

Based on the approach described in Part B of the main document, the estimations on i) the total amount of mercury accumulated in devices in the EU and ii) the amount of mercury placed on the market annually in the EU are used to describe the potential release and exposure during the waste phase of the devices (see Table A1-1). Furthermore, to get a more comprehensive picture, the annual amounts iii) used in the production of devices, iv) imported into the EU and v) exported from the EU are given to illustrate the potential for direct exposure of workers during the production and service-life of the devices. However, it is stressed that this report does not further assess the potential concerns related to workers as explained in Part B. If quantitative estimates are not available, a qualitative description is given.

Table A1-1: Amounts of mercury accumulated, used in production, placed on the market and imported and exported in barometers in 2010

Mercury	Estimated amounts
Pool accumulated in barometers (in industrial and professional use) in the EU	~ 3 t Hg Assuming 10 years lifetime for a barometer (Lassen et al., 2008) and no trend in number of devices placed on the market, results in 3 tonnes of Hg accumulated in barometers in industrial and professional applications.
Placed on the market in barometers in the EU	0.1-0.5 t Hg/y (Lassen et al., 2008)
Used in production of barometers in the EU	No data available to quantify. At least one (possibly few) producers of Hg barometers in the EU (Lassen et al., 2008).
Imported into the EU in barometers	No data available.
Exported from the EU in barometers	The producers of barometers also export devices. Up to 40 kg of Hg is exported from the UK annually in barometers. (Lassen et al., 2008)

Box 1: General qualitative description of potential release and exposure

Production phase

According to Lassen et al. (2008) there is at least one (possibly few) producer of mercury barometers in the EU. Nevertheless, there is no data available to quantify the amount of mercury used in the production. The producers also export mercury barometers outside the EU, for example up to 40 kg mercury per year is exported from the UK in barometers. It is estimated that in the EU around 2-20 persons are full-time employed in the production of mercury barometers for both the EU and non-EU markets. The only identified producer of mercury barometers is a SME size enterprise. (Lassen et al., 2008)

There is no data available on emissions and exposure during the production phase, but it is assumed that some emissions may occur during the production of these devices due to the volatile properties of mercury.

Service-life

There is no reliable information on the number of mercury barometers in industrial and professional use and thus on the related accumulated amount of mercury in the barometers. However, according to Lassen et al. (2008) the professional barometer market in the EU is estimated to use 0.1-0.5 tonnes of mercury per year. Assuming an average service-life of 10 years for barometers, and having no trend in the number of devices placed on the market, results in accumulated stock of around 3 tonnes. Nevertheless, according to Lassen et al. (2008) the market is estimated to be decreasing.

In the UK, the professional barometer market is estimated to use less than 10 kg mercury per year (Collin 2008 as cited in Lassen et al., 2008). The users are scientific, medical and special test laboratories, airfields as well as some educational institutes. Some scientific mercury barometers are used for calibration of other barometers such as aneroid and electronic types.

According to WMO (2008) the main risks to workers occur in laboratories where mercury barometers are frequently emptied or filled. Emissions might occur in meteorological stations if mercury is not cleaned up immediately after spillages or when the device is broken. However, WMO (2008) gives detailed instructions on how to clean up mercury spillages. Some companies in the EU are specialised in restoration of mercury barometers and some information on maintenance can be found on their websites:

http://www.bafra.org.uk/html_pages/articles_mercurialbarometer.html
http://www.quicksilver-barometers.co.uk/
http://www.czajkowski-furniture.co.uk/barometer-restoration-and-conservation.htm

Waste phase

The amount of mercury to be disposed of as waste each year corresponds to the amount of mercury placed on the market in barometers 10 years earlier (assuming 10 years service-life). As the mercury barometer market is estimated to be declining (Lassen et al., 2008), the amount of mercury disposed of in barometers (in industrial and professional use) is assumed to be higher than annual amount of mercury placed on the market in the same year.

There is no specific information on how mercury barometers and the mercury content are collected and handled. However, WMO (2008) instructs the weather stations on how the collected mercury can be either disposed or recovered with a reference to contact local authorities and/or suppliers. Based on this, it is assumed that the collection rate might be somewhat higher for mercury in barometers than the roughly estimated average collection rate of 20 % as hazardous waste for mercury containing measuring devices as stated in Lassen et al. (2008).

3. Available information on alternatives (Part C)

3.1 Identification of potential alternatives

Several barometers have been identified by Lassen et al. (2008) as alternatives for mercury containing barometers. These include electronic barometers (e.g. aneroid displacement transducers and electronic resistance or capacitance barometers), aneroid mechanical barometers and mercury free liquid barometers.

3.2 Human health and environment risks related to alternatives

• *Electronic alternatives*
As described in general part C, the human health and environmental risks related to the use of electronic alternatives are insignificant in comparison with the potential emission and exposure associated with the amount of mercury in barometers.

• *Aneroid mechanical barometers*
Materials used for these articles are everyday materials such as plastics and stainless steel. There are no indications of risks to human health or the environment related to the use of bi-metal dial thermometers (see also description on mechanical alternatives in general part C).

• *Mercury free liquid barometers*
The filling liquids commonly used are mineral oils and coloured silicon-based fluids.
A barometer 'Eco-celli" is marketed as mercury free, "not hazardous" and 'environmentally safe', with a "red silicon-based fluid" and a gas filled in a U-shaped tube (Dingens Barometers & Clocks, 2011). The same company has introduced another mercury free liquid barometer; 'Innovacelli' which is also marketed as 'the barometer does not contain mercury or any other toxic agents'. Although the exact properties of the fluid are unknown, there are no known notable risks related to these devices and especially in comparison with mercury containing measuring devices, the risk associated with mercury free liquid barometers is considered to be negligible.

Overall the human health and environmental risks related to the alternative devices seems to be negligible compared to the risks of mercury containing devices.

3.3 Technical feasibility of alternatives

Lassen et al. (2008) state that: 'No specific applications for which mercury barometers cannot be replaced have been identified.' The reasons for using the mercury barometers seem to be that users are used to this barometer and that it is easy to recognise when the equipment is not functioning correctly.
Based on the available information, technically feasible alternatives to mercury barometers exist for all applications.

3.3.1 Electronic barometers

Barometers having an electronic read-out (with equivalent accuracy and stability) have many advantages compared to mercury barometers. These can be operated also remotely while mercury containing barometers need to be observed by people at the place of measurement. The ratio of purely automatic weather stations to observer-staffed weather stations increases steadily. (WMO, 2008)

Electronic barometers are already widely used by professionals in the EU. They use transducers which transform the sensor response into a pressure-related electrical quantity in the form of either analogue or digital signals. Many electronic barometers have automatic data logging. Such devices have currently the highest market share in the EU. Electronic barometers are marketed for different kind of professional applications like weather stations, aviation, laboratories and industrial pressure measurements. The electronic barometers are regarded as precise as the mercury barometers. (Lassen et al., 2008). The electronic barometers are used also for calibration of other barometers (personal communication with Lassen, 2010).

The following kind of electronic barometers are used:

i) A cylindrical resonator barometer (or vibrating cylinder air-pressure transducer) is designed to measure absolute air pressure using the vibrating element principle. It provides a frequency output from which pressure is computed and it can be read by a computer. For example, in Denmark, this type of barometer is normally used for calibration of other barometers.

ii) An aneroid displacement transducer contains a sensor with electrical properties (resistance or capacitance) that changes as the atmospheric pressure changes. In Denmark these barometers are today used e.g. by weather stations, ships, airports.

iii) A modern version of the pressure transducer using piezoelectric transducer (digital piezoresistive barometer) determines two resonance frequencies of the piezoelectric element. By calculating a linear function of these frequencies and with an appropriate set of variables obtained after calibration, a pressure is calculated by a microprocessor which is independent of the temperature of the sensor.

iv) Bourdon tube barometers consist of a sensor element that changes its shape under the influence of pressure changes and a transducer that transforms the changes into a form directly usable by the observer. Precise and stable digital instruments with quartz Bourbon tubes are used as working standard reference barometers in calibration laboratories (WMO, 2008).

According to a producer of mercury barometer for the professional market, electronic barometers can replace mercury containing barometers for all applications (Lassen et al., 2008*)*. According to the WMO (2008) mercury barometers are, in general, regarded as having good long-term stability and accuracy, but are now losing favour to equally accurate electronic barometers, which are easier to read.

The WMO (2008) guide specifies that electronic barometers should be calibrated about once a year. According to the guide this calibration is done more frequently than for mercury barometers.

3.3.2 Aneroid mechanical barometer

The mechanical aneroid barometer consists of an evacuated metal diaphragm linked mechanically to an indicating needle. These barometers have been used for 200 years and are considered just as accurate as the traditional mercury barometer. According to WMO (2008) the greatest advantages of conventional aneroid barometers over mercury barometers are their compactness and portability, which make them especially practical at sea or in the field.

3.3.3 Mercury-free liquid barometer

According to a producer in the EU, a mercury-free liquid barometer is a U-shaped glass tube filled with a red silicone fluid and gas. The principle to measure air pressure is based on the compressibility of gasses instead of the weight of liquid mercury. There is one producer of this type of barometer, and it is marketed for use in schools and hospitals. Adjacent to the barometer tube is a thermometer filled with blue coloured methanol (methyl-alcohol).

3.4 Economic feasibility

According to Lassen et al. (2008) the price of the mercury barometers varies from €100 to 1000 and non-electronic alternatives are available at the same price range. However, the prices are difficult to compare as some of them are affected by the decorative purpose of the given barometers. Even for professional users the barometers are sometimes regarded as a piece of furniture (personal communication with Lassen, 2010).

Electronic precision barometers based on vibrating element sensors are available at higher prices. However, these have many additional features (e.g. measuring more parameters than only air pressure) that explain the cost difference. Therefore, it is difficult to compare directly the price of an electronic precision barometer with the price of a mercury containing device. (Lassen et al., 2008)

Mercury-free liquid barometers are between 30 and 50 % cheaper than the comparable mercury containing barometers (Lassen et al., 2008). In spite of the cheaper price of mercury-free barometers, some users might be in favour of using the mercury containing barometer because of the tradition. E.g. it is easier to see if the mercury barometer functions correctly (Lassen et al., 2008).

Lassen et al. (2008) roughly estimated that changing to alternatives would not increase the costs to the users. This is supported by Gallican et al. (2003) who concluded that the aneroid and electronic barometers are cost-competitive and acceptable alternatives to the mercury barometers.

It is estimated that a waste treatment cost for mercury sphygmomanometers is €30 compared to the €2 for electronic alternative (Concorde, 2009). As industrial mercury

barometers may contain more mercury than sphygmomanometers, the corresponding cost difference between mercury and mercury free barometers can be assumed to be the same or more. There are no mercury barometer specific estimates on waste treatment costs available.

Based on the information described above, alternatives are regarded as economically feasible.

4. Justification why the proposed restriction is the most appropriate Community-wide measure (Part E)

4.1 Identification and description of potential risk management options

4.1.1 Risks to be addressed – the baseline

As described in section B.2, the total estimated amount of mercury placed on the market in measuring devices containing mercury is used to describe the maximum potential for mercury emissions to the environment that might ultimately occur. The amount of mercury placed on the market in barometers for industrial and professional use is estimated to be 0.1-0.5 t per year in the EU. It is estimated that the amount of mercury barometers used by professionals is decreasing (WMO, 2008).

Although not the primary concern, it is worth mentioning that direct exposure of workers can occur during production, professional/industrial use of the devices and during waste management operations.

4.1.2 Options for restrictions

The following options for restriction were identified:

1) restriction on the placing on the market of new mercury containing barometers,
2) restriction on the placing on the market of new mercury containing barometers and the use of existing mercury containing barometers, and
3) restriction on the placing on the market of new mercury containing barometers with a derogation for calibration.

Only the option 1 has been taken for further assessment for the following reasons.

The banning of the use of existing mercury barometers is not assessed further based on the following reasons; It is estimated that the number of mercury barometers used

by professionals has already been decreasing. In addition it is assumed that the collection rate for these specialised uses is higher than what has been assumed for instance for sphygmomanometers. Considering the relatively low risk reduction capacity and the costs related to replacing the barometer before the end of the service life, the use ban is not considered to be proportionate. In addition the enforcement of the use ban would require resources and might be in practice difficult to carry out in effective way.

Denmark has in its national ban a derogation for calibration purposes and the Danish Meteorological Institute has as a national reference a mercury containing barometer However, it has not been used in recent years and it seems that it has not been maintained either (Personal communication with Lassen, 2010). In the Netherlands, Sweden and Norway no derogation for the use of mercury barometers for calibration exists in their national bans. Therefore it can be concluded that there seems to be no need to introduce an exemption for calibration in this restriction proposal. The average life time of barometers is 10 years (Lassen et al., 2008) which gives flexibility to use existing mercury barometers for calibration purposes during this period.

4.2 Assessment of risk management options

4.2.1 Restriction of the placing on the market barometers

4.2.1.1 Effectiveness

Risk reduction capacity

The risk reduction achieved by introducing the restriction will be an annual reduction of metallic mercury entering the EU society of approximately 0.1-0.5 tonnes per year. According to Lassen et al. (2008) there are only one or few producers of mercury barometers in the EU. This volume is a measure for reduction of the maximum potential for mercury emissions to the environment that might ultimately occur. In addition, it can be mentioned that the volume also reduces direct exposure of workers in production, use and waste phase, with the exception of exposure related to remaining production for exports.

Emissions related to the use and waste phase of devices already on the market will not be affected by the proposed restriction.

It is assumed that compared to mercury devices the alternatives do not pose significant environmental or human health risks.

Proportionality

Technical feasibility

As stated in section 3.3 technically feasible alternatives are available (Lassen et al., 2008 and WMO, 2008). Electronic barometers dominate already the market for professional use in the EU.

Economic feasibility

Based on the information given in Section 3.4, it is concluded that the costs to the users would not increase if mercury barometers are replaced by alternatives. In some cases the costs are not comparable as for example electronic barometers have features like automatic data logging, the possibility to measure many parameters at the same time etc. that are different compared with the mercury barometer and might for these reasons result in higher prices. It depends on the case whether these additional features are of relevance (and of economic value).

In the EU at least one (possibly few) producer of mercury barometers exist. During the stakeholder consultation of the existing restriction of the placing on the market mercury barometers for sale to the general public, two producers[48] of mercury barometers were opposed to the proposal. Their claim was that if a restriction is introduced it would lead to a negative impact on their future business. However, the current EU markets are only for professional use. This is minor compared what the markets used to be before the placing on the market of mercury barometers to households was restricted[49]. Thus, the impact to the producers to further restrict the markets of mercury barometers is estimated to be small.

According to WMO (2008) the calibration of electronic barometers will need to be done more frequently than for mercury barometers, thus potentially increasing the cost to National Meteorological Services, particularly those with extensive barometer networks. However, as the trend has been to move away from mercury barometers these costs of calibration are not considered to cause major impacts among users, in particular since certain new features have been gained with this change.

Based on the information above, it is estimated that restricting the placing on the market of mercury barometers would not introduce compliance costs (i.e. the cost-effectiveness ~€0 per kg Hg not placed on the market).

Given that the additional costs of using mercury free barometers are ~€0, it is evident that these costs are proportionate to the risks related to mercury. To better understand the estimated compliance costs in relation to other actions and policies to reduce mercury, one can compare the cost effectiveness of the proposed restriction (~€0/kg Hg) with the policy options reviewed in Appendix 2.

[48] Five producers were identified, but only one produce mercury barometers for industrial and professional use

[49] Total mercury consumption in barometers in 2007 was estimated to be 2-5 tonnes Hg/year of which 0.1-0.5 tonnes was for professional use (Lassen et al., 2008). From 3 October 2009, the placing on the market of mercury barometers has been prohibited in the EU.

4.2.1.2 Practicality

Implementability and manageability

Technically feasible alternatives are available and it is estimated that the costs to the users would not increase significantly. As it is not proposed to restrict the current use, the mercury barometers may be used until the end of their service life.

Enforceability

The compliance with the restriction on the placing on the market of mercury barometers can be verified by following the fairly limited number of producers (one to few), importers and distributors of these devices.

4.3 The proposed restriction and summary of the justifications

Proposal:

Restriction on the placing on the market of mercury containing barometers after 18 months of entry into force of the amendment of Annex XVII.[50]

Summary of justification:

The main purpose of the proposed restrictions is to reduce the mercury pool in the society, thus avoiding negative impacts on human health and environment. Technically and economically feasible alternatives to mercury containing barometers are available and electronic barometers already dominate the market in the EU.

[50] The scope of the current entry related to barometers in the Annex XVII will become wider.

Annex 2: Manometers and tensiometers

Content

1. Technical description of manometers and tensiometers

Manometers are instruments for measuring pressure. The mercury containing manometers measure the difference in gas pressure between the measured environment and a reference.

Manometers usually consist of a U-shaped glass or plastic tube containing a liquid (usually water, alcohol or mercury). The surface of the liquid in one end of the tube moves proportionally with changes in pressure on the liquid in the other end. When pressure is applied, the liquid level in one arm rises, while the level in the other drops. A set of calibrated markings beside one of the arms permits a pressure reading to be taken, usually in inches or millimetres.

The column (U-tube) may be either vertical or inclined from the vertical to elongate the scale and further amplify the liquid movement. The inclined-tube manometer is used for smaller pressure measurements or where greater accuracy is required. One limb of the inclined tube manometer forms into a reservoir and the other is inclined at a known angle. Their accuracy relies less on the reader's skills, are more sensitive but unless the inclined limb is relatively long they cannot be used over a wide range of pressures. Inclined tube manometers cannot be read remotely and it is usually used with gases.

Manometers have a variety of laboratory, industrial and specific applications such as visual monitoring of air and gas pressure for compressors, vacuum equipment and special tank applications such as medical gas cylinders, fire extinguishers, etc. In addition, mercury manometers are used for calibration purposes.

Tensiometers are designed to measure the surface tension of liquids, to determine the soil moisture tension and for measuring the tension in a wire, fibre or beam (answers.com, 2010). The mercury containing tensiometers are devices used for measuring the suction or negative pressure of soil water (soil water potential). The reason why tensiometers are covered with manometers in this report is that the only part of tensiometer potentially containing mercury is the manometer. However, some alternatives for mercury tensiometers are based on totally different methods of measuring the soil moisture, and consequently these alternatives are not related to alternatives for manometers.

A mercury tensiometer comprises of capillary tubing linking to the mercury manometer. The capillary tubes have at the other ends, inserted in the soil, porous cups, normally constructed from ceramic.

Tensiometers are mainly used for research applications, in the scientific study of soils and plants, or in agriculture for planning the irrigation scheduling (Lassen et al., 2008, Smajstrla & Harrison, 2002).

2. Description of release and exposure

Based on the approach described in the Part B of the main document, the estimations on i) the total amount of mercury accumulated in devices in the EU and ii) the amount of mercury placed on the market annually in the EU are used to describe the potential release and exposure during the waste phase of the devices (Table A2-1). Furthermore, to get a more comprehensive picture, the annual amounts iii) used in the production of devices, iv) imported into the EU and v) exported from the EU are given to illustrate the potential for direct exposure of workers during the production and service-life of the devices. However, it is stressed that this report does not further assess the potential concerns related to workers as explained in Part B. If quantitative estimates are not available, a qualitative description is given.

Table A2-1: Amounts of mercury accumulated, used in production, placed on the market and imported and exported in manometers (including tensiometers) in 2010.

Mercury	Estimated amounts
Pool accumulated in manometers in the EU	~ 4 t Hg Assuming 20 years lifetime for a manometer and no trend in number of devices placed on the market, results in 4 tonnes of Hg accumulated in manometers.
Placed on the market in manometers in the EU	0.04-0.4 t Hg/y (Lassen et al., 2008)
Used in production of manometers in the EU	No data available to quantify. At least one producer of Hg manometers and one of Hg tensiometers[51] in the EU (Lassen et al., 2008).
Imported into the EU in manometers	No data available.
Exported from the EU in manometers	No data available.

Box 1: General qualitative description of potential release and exposure

Production phase

Only one producer of mercury manometers and one producer of mercury tensiometers have been identified in the EU and the production of tensiometers was discontinued in 2008. (Lassen et al., 2008)

As the manometers and tensiometers are supplied without mercury due to weight and transport costs (the customers fill them in with mercury before use), there are no

[51] According to Lassen et al. (2008), the production of tensiometers may be discontinued.

mercury emissions during the production phase.

Use phase

There is no reliable information on the number of mercury manometers in use and thus on the related accumulated amount of mercury in the manometers. However, around 10-15 tensiometers are estimated to be sold per year in the EU (Lassen et al., 2008). According to Lassen et al. (2008) the professional manometer and tensiometers market in the EU is estimated to use 0.04-0.4 tonnes of mercury per year. Assuming an average service-life of 20 years for manometers and tensiometers, and having no trend in the number of devices placed on the market, results in accumulated stock of around 4 tonnes.

In Denmark, before the Danish ban, the mercury use was estimated at 4-8 kg per year (Lassen et al., 2010).

The mercury content of a U-tube manometer may vary but it is estimated that normally a manometer contains 70-140g mercury. Nevertheless, special manometers may contain up to 10 kg of mercury e.g. mercury manometer used as reference instrument in Denmark. It contains a 6 m mercury column with up to 5-10 kg of mercury. It is read with a laser and data are processed electronically.

The mercury manometers and tensiometers are shipped without mercury and filled with mercury by the user. Thus the risks related to use phase may be more relevant for manometers and tensiometers than other devices filled during the production. In addition, some mercury may be released in case of breakage e.g. over pressuring the manometer can result in the mercury being blown out of the tube and contaminating the surroundings. Nevertheless, risks related to waste phase are regarded to be most relevant for manometers.

Waste phase

The appropriate collection of mercury manometers and the handling of these devices in accordance with hazardous waste legislation are crucial for the potential releases of mercury to the environment. According Lassen et al. (2008) around 20 % of mercury in measuring devices is collected as hazardous waste. This indicates that emissions during the waste phase are likely to occur.

3. Available information on alternatives (Part C)

3.1 Identification of potential alternative techniques

Different types of alternatives have been identified for mercury manometers: Liquid filled in tube manometers, elastic pressure sensors and electronic manometers (or

digital manometers). The mercury manometers contained by the tensiometers are commonly replaced by elastic pressure sensors or electronic manometers. In addition, the moisture soil measurement can be carried out by quantitative methods like gravimetric soil sampling, neutron scatter, or dielectric constant methods (Morris, 2006).

Liquid filled in tube manometers are built on the same principle as the mercury ones, but they use other liquids, like water (most common used after the mercury) or alcohols. The pressure is expressed as depth of the fluid used. The density of the fluid can vary (diferencesbetween.net, 2011).

Mechanical alternatives / Elastic pressure sensors contain elements that flex, stretch, or temporarily deforms when a pressure is applied. They initially convert pressure into a displacement which is then read on a scale. The following two types of elastic pressure sensors have been identified:

> *Bourdon tube manometers* consist of a tube of elliptical or oval cross section. A common design is the C-shaped tube sealed at one end and connected to a pointer. When increased pressure is applied to the open end, it deflects outwards proportionate with the pressure. This motion is transferred through a link to gear train connected to an indicating needle. Bourdon gauges are normally connected to gas cylinders to give an indication of the quantity of gas in the cylinders.
>
> *Pressure gauges with diaphragms* contain a two sided flexible membrane with a known pressure. One side is an enclosed capsule containing air or other fluid at a predetermined pressure. The other side can be either opened or screwed into the system to be measured. The diagram is attached to a meter measuring how much the membrane bends when an outside pressure is applied. The pressure is expressed as the amount of force per unit (diferencesbetween.net, 2010). They are either:
> - Mechanical pressure gauges are measuring devices containing a needle (pointer) attached to the diaphragm and rotating throughout a graduated dial.
> - Electric resistance strain gauges uses a long strip of an electric resistor that resists the flow of electricity attached to the diaphragm. The bending diaphragm stretches out the resistor, increasing the resistance. The high variations of the diaphragm increase the resistance and drop the electric current. The outside pressure is determined by measuring the current.

Electronic manometers make use of transducers which transform the sensor response into a pressure-related electrical quantity in the form of either analogue or digital signals. They measure the pressure by use of pressure transducers, e.g. piezoelectric or capacitance pressure transducers which are connected via an analogue to digital converter to a display or data logger.

Other devices than manometers are available to measure both absolute & gauge pressure and for the calibration of high accuracy barometers and Air Data Test Sets. The modern devices like model DPG10A from Chamois (Chamois, 2010) combine the metrological performance of pressure balance (a combination of pistons and weights) with the convenience of digital instrumentation.

Other alternative methods (than tensiometers) for the soil moisture measurement

The gravimetric method is a direct technique for determining the water content of soils. It involves weighing soil samples, drying them to a constant value of mass at 105°C, and using the difference in weight to calculate the amount of water in soil. For the soil moisture measurements of high value crops, large farms and scientific research purposes there are other techniques available: *neutron scatter*, *di-electric constant methods*, *time-domain reflectometry (TDR)*, *frequency domain reflectometry (FDR)*, and *infrared thermometry*.

3.2 Human health and environment risks related to alternatives

Liquid filled in tube manometers

The risk associated with the use of alternative liquids in manometers, such as water or alcohols, is considered to be negligible.

Mechanical alternatives / Elastic pressure sensors

Materials used for mechanical systems such as Bourdon tube manometers and pressure gauges with diaphragms are everyday materials such as plastics and stainless steel. There are no indications of risks to human health or the environment related to these mechanical system (see also description on mechanical alternatives in general part C).

Electronic alternatives

As described in general part C, the human health and environmental risks related to the use of electronic alternatives are insignificant in comparison with the potential emission and exposure associated with the amount of mercury in manometers.

Tensiometers

When the soil moisture is measured by other quantitative methods than by mercury tensiometers, like gravimetric soil sampling, neutron scatter, or dielectric constant methods, the associated risks vary as the techniques are based on totally different principles. The apparatus needed by these methods could contain other hazardous substances or they can be given by the high electrical power used or due to radioactive sources contained. However, these alternatives are not considered as direct substitutes for mercury tensiometers (see reasons in section 3.3), and the related risks are not considered further.

Overall the human health and environmental risks related to the alternative devices seems to negligible compared to the risks of mercury containing devices.

3.3 Technical feasibility of alternatives

According to a European producer of mercury manometers, there is no application for which mercury manometers cannot be replaced by other devices (Giussani 2008 as cited in Lassen et al., 2008).

According to a report from 2004 (Kemi, 2004), a special type of pressure measurement is required in the polyethylene manufacturing industry where a precision measurement is made at high temperature. The polyethylene product is evaluated by this pressure measurement, which is an important quality-assurance parameter. Alternatives have been tested but none of them have given the required result. Nevertheless, Swedish Chemicals Agency (Kemi) reports that there have not been any applications for exemptions to their national restriction for mercury barometers from 2005 up to now. As far as they are aware of, there have been no applications for exemption before 2005 either. Based on this information, technically feasible alternatives are available in this application.

Liquid filled in tube manometers

Any fluid can be used in manometers instead of mercury, but the mercury has the advantages of high density and low vapour pressure. For low pressure differences well above the vapour pressure of water, water is commonly used (and "inches of water" is a common pressure unit).

Mechanical alternatives / Elastic pressure sensors

Bourdon tube manometers

Bourdon tube manometers are more robust than mercury manometers and more suitable for measuring higher pressures. They are today sold for applications, where U-tube manometers with mercury were previously used (Lassen and Maag, 2006).

Pressure gauges with diaphragm elements

Pressure gauges with diaphragm are considered just as accurate as the traditional mercury manometer. For low-pressure applications metallic diaphragms and bellows are used (hydraulicspneumatics.com, 2010). Diaphragm elements are often used in gauges to indicate absolute pressure. A variety of options and accessories are available to enhance life and operation of gauges.

Electronic manometers (or digital manometers)

Electronic manometers are already widely used by professionals and there is increasing market for them. They have many advantages compared to mercury manometer as they require less servicing and maintenance and far less expertise and can thus be used by less experienced users. Compared with electronic manometers, the mercury manometers are more difficult to handle. Electronic manometers are also more precise than a mercury manometer if properly calibrated. They can be used for automatic and remote control.

For the heating and sanitations sectors, a type of small hand-held electronic manometers is available from many suppliers. They may serve similar purposes as the mercury manometers and are more user-friendly.

Other devices than manometers are also available on the market mainly for calibration uses and for absolute and gauge pressure measurements. They are modern devices containing pressure balances and digital parts. This combination results in high accuracy measurements.

Other alternative methods for (tensiometers) the soil moisture measurement

The gravimetric method is regarded to be too time consuming, labor-intensive, requiring sample equipment, weighing scale and an oven to be used for day-to day management decisions, this highly accurate and low-cost method is often used to calibrate other tools and indirect methods, such as neutron probe or di-electric constant methods. The spatial variability of soils and their water content implies a large number of samples. Other identified available techniques, like *neutron scatter*, *di-electric constant methods*, *time-domain reflectometry (TDR)*, *frequency domain reflectometry (FDR)*, and *infrared thermometry*, are generally more expensive, providing more features and not comparable to the more narrowed use of tensiometers.

3.4 Economic feasibility

According to Lassen and Maag (2006), the price of a U-tube mercury manometer is around 108 €. All the other prices quoted below are based on internet search conducted in February 2010 by ECHA and are meant to be indicative only.

Alternatives can replace the mercury manometer in all applications and, even more, they are usually cheaper than the corresponding mercury manometer. Liquid filled in tube manometers are built on the same principle as the mercury ones and their prices are on the range of €16 to 20. The market prices of bourdon tube manometers are also typically lower than the price of the mercury one and they are more robust and more suitable for measuring higher pressures (Lassen and Maag 2006). Prices for them range from €54 to 122. Prices for pressure gauges range from €30 to 76, depending on the used material. Finally, the electronic manometers have many advantages over the mercury ones, and there is increasing market for them. However, the price of electronic manometers is about 3-4 times higher for similar pressure range. As the

electronic manometers have the advantage of automatic measurements they cannot be directly compared to mercury manometers (Lassen and Maag 2006). The internet search suggested a price range from €110 to 350 for electronic manometers.

Since there is no application for which mercury manometers cannot be replaced by other devices and because alternatives are usually available at approximately the same price as that of a mercury manometer (see e.g. Lassen et al., 2008) there is no need for further compliance cost analysis to show that these devices are economically feasible options.

Two technically feasible devices, electronic tensiometers and bourden tube tensiometers, are already replacing the mercury tensiometers in all applications. According to Lassen et al. (2008) the prices of alternatives are below or equal to the prices of mercury tensiometers in the case of electronic devices and slightly higher for the tensiometers containing mechanical bourdon manometers. There is no evidence suggesting that there would be differences in recurrent costs between mercury and mercury-free tensiometers.

It is estimated that a waste treatment cost for mercury sphygmomanometers is €30 compared to the €2 for electronic alternative and €1 for mechanical alternative (Concorde, 2009). As mercury manometers contain around the same amount or more mercury than sphygmomanometers, the corresponding cost difference between mercury and mercury free manometers can be estimated to be the same or more. There are no manometer specific estimates on waste treatment costs available.

4. Justification why the proposed restriction is the most appropriate Community-wide measure (Part E)

4.1. Identification and description of potential risk management options

4.1.1 Risk to be addressed – the baseline

As described in section B.2, the total estimated amount of mercury placed on the market in measuring devices containing mercury is used to describe the maximum potential for mercury emissions to the environment that might ultimately occur. The maximum emission potential is estimated to be 0.04-0.4 tonnes per year in the EU including tensiometers (Lassen et al., 2008).

No response was received from the producers of manometers and tensiometers during the stakeholders consultation to assess the trend in the number (or the current number) of mercury manometers supplied annually to the EU markets.

Although not the primary concern, it is worth mentioning that direct exposure of workers can occur during production (but note that manometers are usually sold without mercury and are filled by the users), professional/industrial use of the devices and during waste management operations.

4.1.2 Options for restrictions

Since there is no application for which mercury manometers and tensiometers cannot be replaced by mercury-free alternatives already available, the only assessed restriction option is the restriction on the placing on the market of new mercury manometers and tensiometers for professional use. An exemption for mercury manometers which are to be displayed in exhibitions for cultural and historical purposes is proposed. In addition, SEAC proposes a derogation for devices that were more than 50 years old on 3 October 2007. These exemptions are to allow the placing on the market of historically and culturally valuable devices.

4.2 Assessment of risk management option: Restriction of the placing on the market of mercury manometers and tensiometers

4.2.1 Effectiveness

Risk reduction capacity

The maximum risk reduction achieved by introducing the restriction will be an annual reduction of metallic mercury entering the EU society of approximately 0.04-0.4 tonnes per year. This volume is a measure for reduction of the maximum potential for mercury emissions to the environment that might ultimately occur. In addition, it can be mentioned that the volume also reduces direct exposure of workers in use and waste phase.

The emissions resulting from the use and waste phase of the mercury manometers already in use will not be affected.

Proportionality

Technical feasibility

Based on the information from Lassen et al. (2008) technically feasible alternatives are available and in use.

Economic feasibility

The alternatives are usually cheaper than mercury manometers. Electronic manometers are an exception being 3-4 times more expensive but also offering automatic measurement. Given that technically equivalent alternatives are cheaper, it is estimated that restricting the placing on the market of mercury manometers and tensiometers would not introduce additional costs. In other words the compliance costs of the restriction would be ~€0 (i.e. cost-effectiveness ~€0 per kg Hg not placed on the market).

Given that the additional costs of using mercury free manometers and tensiometers are ~€0, it is evident that these costs are proportionate to the risks related to mercury. To better understand the estimated compliance costs in relation to other actions and

policies to reduce mercury, one can compare the cost effectiveness of the proposed restriction (~€0/kg Hg) with the policy options reviewed in Appendix 2

4.2.2 Practicality

Implementability and manageability

The technical feasible alternatives are already in use and it is not expected to have changes in the costs affecting the users. As it is not proposed to restrict the current use, the mercury manometers may be used until the end of the service life.

Enforceability

The compliance with restriction on placing on the market of mercury manometers can be verified by following the fairly limited number of producers, importers and distributors of these equipments.

4.3 The proposed restriction(s) and summary of the justifications

Proposal:

Restriction on the placing on the market of mercury manometers and tensiometers after 18 months of entry into force of the amendment of Annex XVII.

Summary of justification:

The main purpose of the proposed restrictions is to reduce the mercury pool in the society, thus avoiding negative impacts on human health and environment. Technically and economically feasible alternatives to mercury containing manometers (including tensiometers) are available and in use. The alternatives are available at approximately the same price as mercury manometers.

Annex 3a: Sphygmomanometers

Content

1. Technical description of sphygmomanometers

Mercury sphygmomanometers are devices used to measure blood pressure. They include a mercury manometer, an upper arm cuff, and a hand inflation bulb with a pressure control valve and require the use of a stethoscope. The method relies on the auscultatory technique, in which a clinician determines systolic and diastolic blood pressures (SBP and DBP) by listening (auscultating) for sounds that characterise different stages of blood flow during cuff deflation (Korotkoff sounds). Placing on the market of mercury sphygmomanometers intended for sale to the general public is already restricted by the existing restriction entry 18a in the Annex XVII of REACH Regulation. Thus, this report covers only professional uses.

2. Description of release and exposure

Based on the approach described in the Part B of the main document, the estimations on i) the total amount of mercury accumulated in devices in the EU and ii) the amount of mercury placed on the market annually in the EU are used to describe the potential release and exposure during the waste phase of the devices. (Table A3a-1). Furthermore, to get a more comprehensive picture, the annual amounts iii) used in the production of devices, iv) imported into the EU and v) exported from the EU are given to illustrate the potential for direct exposure of workers during the production and service-life of the devices. However, it is stressed that this report does not further assess the potential concerns related to workers as explained in Part B.

Table A3a-1: Amounts of mercury accumulated, used in production, placed on the market and imported and exported in sphygmomanometers in 2010

Mercury	Estimated amounts
Pool accumulated in sphygmomanometers in the EU	~ 26-51 t Hg
Placed on the market in sphygmomanometers in the EU	~ 2.6-5.1 t Hg/y
Used in production of sphygmomanometers in the EU	~ 6-9 t Hg/y (Based on EEB, 2009).
Imported into the EU in sphygmomanometers	~ 2-4 t Hg/y (Based on EEB, 2009)
Exported from the EU in sphygmomanometers	~ 5-8 t Hg/y (EEB, 2009), i.e. 85 % of production (Lassen et al., 2008)

Box 1: General qualitative description of potential release and exposure

Production phase

In addition to releases from the use and waste phase of sphygmomanometers, as described below, some emissions to the environment and exposure of workers occur

in the production phase of mercury sphygmomanometers. It is estimated that around 6-9 tonnes of mercury is used annually in the production of sphygmomanometers in the EU. Around 5-8 tonnes of that is exported from the EU in sphygmomanometers. (EEB, 2009) According to Lassen et al. (2008) the production of mercury sphygmomanometers employ 30-50 persons in the EU.

Considering that the waste phase is seen as the main problem, and considering that having quantitative information on emissions would not impact the conclusions on the feasibility of alternatives, no further efforts were made to obtain such information.

Service-life

The current pool of mercury in sphygmomanometers in society is roughly estimated to be between 26 and 51 tonnes[52].

Mercury-containing measuring devices are used by private practitioners as well as in hospitals. The amount of mercury in each single place of use is small (around 85 g per device) and the use is geographically wide spread.

In the event of breakage or leaks occurring during the use of sphygmomanometers, workers and patients may be exposed (Lassen et al. (2008) and EEB (2009)). Cleaning up of spills is not likely to happen in an appropriate way, and proper ventilation of the room might be forgotten. In addition breakage and leakage can result in releases to the environment.

Waste phase of sphygmomanometers

The amount of mercury in sphygmomanometers placed on the market in the EU in 2010 is estimated to be between 2.6 and 5.1 tonnes. This amount is in the range estimated by Lassen et al. (2008) of 3-6 tonnes per year. This indicates also the amount of mercury disposed with sphygmomanometers annually. However, due to the assumed declining trend in the number of mercury sphygmomanometers placed on the market per year after 2010, also the amount of mercury disposed with these devices is declining (Lassen et al., 2010). Lassen et al. (2008) estimated the collection rate as hazardous waste for all the mercury containing measuring devices of 20%.

In particular the waste phase (separate collection of mercury sphygmomanometers and the handling of these devices in accordance with hazardous waste legislation) is crucial for the potential releases of mercury to the environment. The appropriate collection of sphygmomanometers at the end of their service life as hazardous waste has been reported to be poor in hospitals. A survey by the European Environmental Bureau (EEB) in 8 countries (Czech Republic, France, Germany, Greece, Hungary, Italy, Spain and United Kingdom) revealed that only half of the 37 interviewees

[52] Lassen et al. (2008) estimated that around 30 000 to 60 000 mercury sphygmomanometers are placed on the market annually in the EU 27. Assuming that there was no trend in number of devices sold annually between 2000 and 2010, and assuming a lifetime of 10 years for mercury sphygmomanometers gives an estimate of 300 000 to 600 000 mercury sphygmomanometers accumulated in the society in 2010. Assuming that one mercury sphygmomanometer contains in average 85 g of mercury gives an estimate of 26 to 51 tonnes of mercury accumulated in the society in sphygmomanometers.

(senior administrators, administrators, doctors, nursing directors, nurses, biomedical and technical specialists and other staff) were aware that mercury waste has to be collected separately to other waste streams. Some interviewees said that infectious hospital waste and hazardous waste streams were collected in the same bins. Even 30% of the interviewees stated that cleaning staff would discard mercury waste with the normal waste (Concorde East/West 2009). This relatively strong picture might need to be moderated bearing in mind the small sample size (n=37). Nevertheless the survey gives an indication that the awareness on how to dispose off mercury is poor, and that collection rates for mercury-containing measuring devices are low.

The sphygmomanometer waste ends-up partly in hospital waste for incineration, partly in municipal waste, and partly in hazardous waste. There is no information on how well the private practitioners take care of the separate collection and correct disposal of the mercury devices. However, it is not likely that the situation would be better than in hospitals. Overall this matches the general collection estimates for mercury-containing measuring devices in the report from Lassen et al. (2008) (estimated collection rate as hazardous waste of 20%).

3. Available information on alternatives (Part C)

The opinion of SCENIHR (2009) is the main basis for the information in this section and it provides more detailed information on mercury sphygmomanometers and mercury-free alternatives.

3.1 Identification of potential alternative techniques

There are several types of mercury-free alternatives on the market for blood pressure measurement to address the full range of functions required by the health care sector. These alternatives are based on either auscultatory or oscillometric techniques. There are also devices on the market utilising both techniques. Different types of sphygmomanometers in use can be categorised for instance in terms of inflation method, manometer type, need for using a stethoscope, blood pressure measurement frequency, placement of the pressure cuff, need for electrical current, etc.

The following categorisation into alternative devices is used in Sections 3.3 and 3.4 when assessing the technical and economic feasibility:

- Sphygmomanometers based on auscultatory technique
    - Non-automated aneroid sphygmomanometers (e.g. shock-resistant aneroid)
    - Non-automated electronic sphygmomanometers
    - Automated auscultatory sphygmomanometers

- Sphygmomanometers based on oscillometric techniques
    - Semiautomatic oscillometric sphygmomanometers
    - Automated oscillometric sphygmomanometers

3.2 Human health and environment risks related to alternatives

Mechanical alternatives

Materials used for mechanical systems (non-automated aneroid sphygmomanometers) are everyday materials such as plastics and stainless steel. There are no indications of risks to human health or the environment related to these mechanical system (see also description on mechanical alternatives in general part C).

Electronic alternatives

As described in general part C, the human health and environmental risks related to the use of electronic alternatives (non-automated electronic sphygmomanometers, automated auscultatory sphygmomanometers, and oscillometric sphygmomanometers) are insignificant in comparison with the potential emission and exposure associated with the amount of mercury in manometers.

Thus, in general, the human health and environmental risks are insignificant in comparison with the potential emission and exposure associated with the amount of mercury in sphygmomanometers. The accuracy and reliability of the blood pressure measurements with alternative devices is assessed and documented in Section 3.3 (technical feasibility of alternatives) below.

3.3 Technical feasibility of alternatives

3.3.1 Sphygmomanometers based on auscultatory technique

The auscultation method is based on the observation of the recurrence of the blood flow in the occluded artery (by using a cuff) of the upper arm by listening to the sounds when the occlusion is completely removed (by dilation of the cuff) and normal blood flow is restored. All the mercury containing sphygmomanometers are based on the auscultatory method.

Clinically validated, auscultatory mercury-free devices are equivalent to mercury sphygmomanometers, and are thus suitable also for specific groups of patients, including patients with arrhythmias, diabetes, pre-eclampsia and the elderly (SCENIHR 2009).

Compared to the mercury sphygmomanometers, the validated manual mercury-free sphygmomanometers allow, in some cases, obtaining a faster reading. In addition, the use of them obviously avoids all hazards and costs generated by the mercury. All manual mercury-free devices are prone to the problems related to the auscultatory technique, like observer bias and terminal digit preference, a phenomenon whereby an observer rounds off a measurement to a digit of his or her choosing. In this respect there is no difference to mercury-containing devices. (Concorde East/West, 2009)

Non-automated aneroid sphygmomanometers (e.g. shock-resistant aneroid)

The aneroid sphygmomanometers for manual reading work in a similar way as the mercury sphygmomanometers, but they contain an aneroid gauge that replaces the mercury manometer. Their accuracy and reliability vary with the design and quality of device. The aneroid sphygmomanometers have been in use for about 100 years and when used properly, and a proper maintenance protocol is followed, give accurate results.

The aneroid devices may be susceptible to calibration drift without this being apparent to the user. In general, aneroid sphygmomanometers should be calibrated according to the manufacturer's recommendation, or at least annually (IAG, 2005). According to Concorde (2009), the recommended calibration frequency by the British Hypertension Society (BHS) for aneroid shock-resistant sphygmomanometers is once a year, compared to the mercury devices typically needing calibration once every two years. Better designs to deal with this problem have recently appeared, after producers introduced a new concept with a resulting more shock resistant sphygmomanometer and a 5-year calibration warranty.

For the clinical use, several aneroid sphygmomanometers are validated by the British Hypertension Society (BHS 2008).

Non-automated electronic sphygmomanometers

The manual electronic sphygmomanometers work in a similar way to the mercury sphygmomanometers, but combine an electronic manometer (electrical transducer instead of mercury) with a digital display (numerical, circular/linear/bar graph) for manual reading. Validated manual electronic sphygmomanometers are available and provide the same accuracy as mercury devices. According to Concorde (2009), the BHS recommends electronic auscultatory sphygmomanometers to be calibrated once in three years.

Automated auscultatory sphygmomanometers

The automated auscultatory devices were designed in the 1970's to replace the observer and stethoscope with a microphone and some analogue electronics. These devices automatically display each detected Korotkov sound. Automated auscultatory sphygmomanometers are still used to replace oscillometric devices for patients with an irregular heart beat. The reliability of automated auscultatory devices depends on the correct placement of the microphone.

3.3.2 Sphygmomanometers based on oscillometric techniques

Oscillometric sphygmomanometers measure changes in artery pulsation during cuff inflation/deflation and then use software containing algorithms to calculate the systolic and diastolic values. As oscillometric devices operate on the bases of a

different principle, they have not been considered as one-to-one alternatives for mercury sphygmomanometers.

Oscillometric devices have many advantages, and there is an increasing market for them. They require less servicing and maintenance than mercury sphygmomanometers, although they need to undergo regular checks. They also require far less expertise and can be used by patients themselves, thus removing the white-coat effect and offer more reproducible blood measurements. Oscillometric devices can also be used by patients with infirmities such as arthritis and deafness. They have also been reported to be more predictive of cardiovascular events.

Despite the above mentioned advantages of oscillometric devices, the auscultatory blood pressure measurements are necessary for some specific clinical conditions including arrhythmia, pre-eclampsia and certain vascular diseases. Thus, calibrated manual devices should be available in all clinical areas in case they are needed to check any non-auscultatory blood pressure measurements on individual patients.

Semi-automatic oscillometric sphygmomanometers

Semi-automatic devices based on the oscillometric technique include an electronic monitor with a pressure sensor, a digital display, an upper arm cuff and a hand-operated inflation bulb. The semi-automatic electronic devices are today standard for home/self assessment and also widely used by general medical practitioners.

According to SCENIHR (2009) opinion, some validated semi-automated sphygmomanometers based on oscillometry are available and partly replacing the mercury sphygmomanometers, even though they are not regarded as technically equivalent alternatives. They can be used by hospitals and general practitioners in most clinical conditions, but they are not suitable for measuring blood pressure of patients with pre-eclampsia, arrhythmias such as fibrillation, and for reasons that are not always apparent, probably influenced by arterial wall properties and pulse pressure (SCENIHR, 2009).

Automated oscillometric sphygmomanometers

Automated blood pressure devices for hospital use are more advanced equipment, which often combines the measurements of blood pressure with monitoring of temperature, heart rate and blood oxygen level. An accurate automated sphygmomanometer capable of providing printouts of systolic and diastolic blood pressure, together with heart rate and the time and date of measurement, should eliminate errors of interpretation, abolish observer bias and terminal digit preference. The devices for both 24-hour measurements and blood pressure measurements at home are more reproducible and predict cardiovascular events more precisely than blood pressure measurements in the clinic. The price of this equipment is typically on the order of 10 times the price of a mercury sphygmomanometer, but these advanced devices cannot be directly compared to mercury sphygmomanometers, as they have many more features.

3.3.3 Opinion of SCENIHR

SCENIHR (2009) recognised in its opinion that technically feasible alternatives exist, and that the mercury sphygmomanometers are gradually disappearing from clinical use. Clinically validated, auscultatory mercury-free devices are equivalent to mercury sphygmomanometers, and are thus suitable also for specific groups of patients, including patients with arrhythmias, diabetes, pre-eclampsia and the elderly (SCENIHR, 2009).

Mercury-free blood pressure measuring devices (when clinically validated) are generally reliable substitutes for mercury-containing sphygmomanometers in clinical practice. SCENIHR (2009) identified only two minor applications, where mercury containing measuring devices would still be needed.

- "For on-going, long-term, epidemiological studies currently using mercury sphygmomanometers it is advisable not to change the method of measurement. Therefore it will be necessary to keep mercury sphygmomanometers available in order to compare them with the alternatives in these studies." (SCENIHR 2009)

- "It is recommended that mercury sphygmomanometers remain available as a reference standard for clinical validation of existing and future mercury-free blood-pressure measurement devices. Therefore, the mercury sphygmomanometer should remain available as a reference standard until an alternative device is developed and recognised as such." (SCENIHR 2009)

3.4 Economic feasibility

Different models of sphygmomanometers even within each category (e.g. shock-resistant aneroid) vary in terms of quality and properties and there is correspondingly a large price range. In addition the way sphygmomanometers are used (and misused) varies greatly among different users (e.g. the level of maintenance and frequency of calibration ranges from none at all to precisely following the producer's recommendations). Thus, it is difficult to estimate how well the assumptions made when assessing the economic feasibility (including compliance costs in Annex 3b) of "representative" devices reflects the reality.

Two technically feasible devices based on auscultatory method, i.e. shock-resistant aneroid and (non-automated) electronic sphygmomanometers, are assessed against their economic feasibility. They can replace the mercury sphygmomanometer in all clinical conditions. The main results concerning economic feasibility are given in table A3a-2. It should be noted that the annualised costs of devices are highly sensitive to assumptions regarding the average lifetime and calibration frequencies. A detailed analysis including input data is available in Annex 3b.

Table A3a-2: Average prices of representative sphygmomanometers (ex factory, without VAT)

	Sphygmomanometer			
	Auscultatory			Oscillometric
	Mercury containing	Shock-resistant aneroid	Electronic	Semi-automatic
Investment cost (price of the device)	€40	€40	€110	€40
Average lifetime	10 years	5 years	10 years	not available
Annualised recurrent cost (including e.g. calibration and waste treatment costs)	€9	€16	€9	not available
Annualised cost per device (including investment and recurrent costs)	€14	€25	€22	not available

Source: Lassen et al. (2010), for oscillometric device Lassen et al. (2008)

Semi-automatic oscillometric devices are also reported to replace mercury sphygmomanometers. According to Lassen et al. (2008) they are available at approximately the same price as that of a mercury or shock-resistant aneroid sphygmomanometer. While these devices seem to be economically feasible they have not been analysed further neither in Annex 3b nor in section E. This is justified as the results of the analysis would not differ much from compliance cost calculations of shock resistant aneroid sphygmomanometers, which are analysed in detail.

The annualised cost of alternatives is estimated to be around €10 higher than the annualised cost of mercury sphygmomanometer. However, as the labour cost of using sphygmomanometer is much higher than the price of the equipment the overall impact on health care costs is insignificant[53]. Thus the alternatives are considered to be economically feasible for the users.

[53] Assuming that EU average cost of a 20 minute visit to a health care provider is (with overhead) €50 one can estimate that the cost of a blood pressure measurement (of 2 minutes) is about €5 in labour cost while the additional equipment cost is about €0.025 per measurement (€10 euros per annum divided by an assumed average blood pressure measurements of 400 per year). Comparing with the labour cost of measuring blood pressure, the additional cost is about 0,5%.

4. Justification why the proposed restriction is the most appropriate Community-wide measure (Part E)

4.1 Identification and description of potential risk management options

4.1.1 Risk to be addressed – the baseline

As described in section B.2, the total estimated amount of mercury placed on the market in measuring devices containing mercury is used to describe the maximum potential for mercury emissions to the environment that might ultimately occur. The amount of mercury in sphygmomanometers placed on the market in the EU is estimated to be around 4 tonnes in the EU in 2010 (see section 2). Based on information from producers of sphygmomanometers (Lassen et al., 2010) it is estimated that without additional legislative action the European market of mercury sphygmomanometers will decline by about 5% annually, i.e. from 45,000 in 2010 to about 28,000 in 2020.

The pool of mercury in sphygmomanometers in use in the EU is estimated to be around 40 tonnes in 2010 as described in the Chapter 2. The above mentioned declining trend in the placing on the market the mercury sphygmomanometers has an effect on the pool in the future.

Lassen et al. (2008) estimated that only 20% of the mercury in measuring devices, including sphygmomanometers, is collected as hazardous waste. It is difficult to estimate the future trend of collection and the share of proper waste management. However, there is no indication that the collection rate would improve without new targeted action in the future.

Although not the primary concern, it is worth mentioning that direct exposure of workers can occur during production, professional use of the sphygmomanometers and during waste management operations.

4.1.2 Options for restrictions

Based on the tentative screening of possible restriction options, two options to reduce the risk from mercury containing sphygmomanometers in the EU have been assessed more in detail. They are 1) Restriction on the placing on the market and 2) Restriction on the use of mercury sphygmomanometers. The option 2 should be regarded as a possible additional element to option 1 and its impacts are not assessed independently. Both options include derogations for specific applications of mercury sphygmomanometers based on the opinion of SCENIHR (2009). In addition, both options have a derogation to allow the placing on the market of historically and culturally valuable sphygmomanometers (see Part E of the main document for details).

1) Restriction on the placing on the market with limited derogations:

Restriction of placing on the market mercury containing sphygmomanometers after 18 months of entry into force with derogations for

a. on-going (at the time of entry into force) epidemiological studies
b. validation of new mercury-free devices

2) Restriction of use of mercury containing sphygmomanometers in addition to option 1:

Restriction of use of mercury containing sphygmomanometers after 6.5 (i.e. 5 years after ban on placing on the market) years of entry into force with derogations for

a. on-going (in the time of entry into force) epidemiological studies
b. validation of new mercury-free devices

In addition to these two restriction options which are further assessed in this report, the following additional aspects were considered, but for reasons explained below not retained for further assessment:

Conditions to prevent non-compliance were considered in conjunction with restriction options 1 and 2. Since the use of mercury containing sphygmomanometers for validation purposes and for epidemiological studies would not be restricted, mercury-containing devices would still be available on the market, and might be bought and used (illegally) for restricted uses. To prevent this kind of non-compliance, suppliers of mercury sphygmomanometers could be required to keep a list of their customers and their uses. Such a list could be used by enforcement authorities when checking the compliance with the restriction. Another possibility to prevent non-compliance, would be to require suppliers to inform the end-user about the allowed uses. These conditions were not considered further. The reason was that the administrative burden was considered rather high and not to be proportionate to the relatively small risk of some professional end-users buying mercury containing sphygmomanometers for a restricted use.

4.2 Assessment of risk management options (sphygmomanometers)

4.2.1 Option 1: Restricting the placing on the market of mercury sphygmomanometers

4.2.1.1 Effectiveness

Risk reduction capacity

The risk reduction achieved by introducing the restriction is described as an annual reduction of metallic mercury used in the EU. That is 3.8 tonnes in 2010 and declining 5 % annually. E.g. in 2015 risk reduction capacity is 3.0 tonnes and in 2024 1.9 tonnes of avoided mercury. This volume is a measure for reduction of the

maximum potential for mercury emissions to the environment that might ultimately occur. In addition, it can be mentioned that the volume also reduces direct exposure of workers in production, use and waste phase -with the exception of exposure related to remaining production for exports.

Emissions related to the use and waste phase of devices already on the market will not be affected.

The number of new devices required for epidemiological studies and for validation of new mercury-free alternatives is expected to be very low, probably much less than 100 sphygmomanometers per year. Consequently, these derogations would result in very low volumes of 'new' mercury.

The risk associated with the alternative aneroid and electronic devices is considered to be insignificant in comparison with the potential emission and exposure associated with the amount of mercury in mercury-containing sphygmomanometers (see section C.1.2).

Proportionality

The proposed restriction is targeted to reduce the mercury pool in the society by gradually substituting mercury-containing sphygmomanometers with technically and economically feasible mercury-free alternatives. The proposed derogations for epidemiological studies and for validation of new mercury-free alternatives have been designed to ensure that the proposed restriction is proportionate.

Technical feasibility

The technical feasibility of alternatives is discussed more in detail in Chapter C.1.3.1. The SCENIHR (2009) opinion established that technically feasible alternatives are already available on the market and have a considerable market share. Two technically feasible alternatives have been identified. The alternatives are based on the auscultatory technique: i) shock resistant aneroid sphygmomanometer and ii) electronic sphygmomanometer. In addition, some oscillometric semi-automatic or automatic devices can replace mercury devices in most of the applications.

SCENIHR (2009) identified two applications where the use of mercury-containing sphygmomanometers would still be necessary because they considered that in these applications technically feasible alternatives do not exist. Based on the evidence given by SCENIHR, it is proposed that derogations apply for the following two applications:

> (1) use of mercury containing sphygmomanometers as a reference standard for clinical validation studies of existing and future non-mercury-containing sphygmomanometers ; and
> (2) use of mercury containing sphygmomanometers for on-going, epidemiological studies currently using mercury sphygmomanometers.

Economic feasibility (including the costs)

In section C.1.3.1 the economic feasibility of alternatives was described. In this section the compliance and administrative costs are summarised. More detailed information on compliance costs including the values used in calculations can be found in Annex 3b. Two alternatives using auscultatory technique are assessed against their economic feasibility. These are i) shock-resistant aneroid and ii) electronic sphygmomanometer with manual reading.

A third alternative – based on oscillometric technique – has also been analysed to some extent in Chapter C, as it is according to SCENIHR (2009) replacing mercury-containing sphygmomanometer by some users. In this compliance costs analysis the oscillometric devices are not separately addressed. The reason is that even if some proportion of mercury containing devices were replaced by sphygmomanometers based on oscillometric method the related costs would be quite similar to the costs of shock-resistant aneroid devices.

The overall costs for an end-user of a sphygmomanometer consist of the investment (price of the device) and recurrent costs. Recurrent costs related to sphygmomanometers are caused for instance by calibrating, waste handling, batteries, spill response and training. As the available estimates for spill response and training have more uncertainty than other parameters, they are not considered in the "central" case. The central case can be regarded as the best estimate. Nevertheless, the effect of spill response is taken into account in the sensitivity analysis. Compliance cost calculations for sphygmomanometers are highly sensitive to the cost and frequency of calibration.

The table A3a-3 presents the main outcomes of the compliance cost analysis. Taking into account the uncertainties, the additional annualised cost per device is estimated to be between €25 and -€23, negative value representing cost savings. This means that substituting the mercury sphygmomanometer with mercury-free alternative would either decrease or increase the annualised cost of the user. In the central case estimate the additional annualised cost would be around €11 per device.

Table A3a-3: Summary of compliance costs of avoiding mercury in sphygmomanometers and cost effectiveness

	Central case	Sensitivity analysis Scenario 1 "high costs"	Sensitivity analysis Scenario 2 "low costs"
Annualised cost of mercury sphygmomanometer per device	€14	€9	€35
Annualised cost of alternative[54] per device	€25	€34	€12
Additional annualised cost of alternative[1] per device	€11	€25	-€23
Compliance costs (present value 2015-2034 in the EU)	€29 million	€120 million	-€44 million
Compliance costs (in 2024 in the EU)	€3.2 million	€12 million	-€4.2 million
Cost per kg of mercury avoided	€1300	€3000	-€2400

Source: Annex 3b

Based on the results on additional costs per device, it is estimated that the annual cost for reducing 1 kg of mercury in the production of sphygmomanometers is around €1300 per kg of mercury avoided. For sensitivity, two other estimates have been calculated. In the "high cost" scenario the cost per kg of mercury avoided would be €3000. However, the "low cost" scenario actually results €2400 savings for each kg of mercury avoided. This saving is due to lower recurrent costs for operating electronic sphygmomanometers than for mercury containing devices.

To better understand the compliance costs in relation to other actions and policies to reduce mercury, one can compare the cost effectiveness of the proposed restriction (€1,313/kg Hg) with the policy options reviewed in Appendix 2.

Administrative costs

The restriction of placing on the market of sphygmomanometers has not been analysed with regard to administrative costs. The reasons are explained in sections E.2.1.2 (practicality) and E.2.1.3 (monitorability). In summary, the administrative costs are assumed to be so low that no specific analysis was carried out.

[54] A representative device which takes into account the replacement ratio between aneroid and electric sphygmomanometers, i.e. in base case 80 % replaces the hg sphygmomanometer with aneroid and 20 % with electronic device, in Scenario 1 0/100% and in Scenario 2 95/5%.

4.2.1.2 Practicality

Implementability and manageability

According to the SCENIHR (2009) opinion and as discussed in Section C, technically feasible alternatives for mercury containing sphygmomanometers are already readily available in the EU. In Section 3.4 above and Annex 3b it is demonstrated that these alternatives are also economically feasible. As the production of mercury containing sphygmomanometers may continue for export, and the import of the devices is also allowed for derogated uses, the availability of mercury sphygmomanometers for derogated uses is covered. In summary, the necessary technology and economically feasible alternatives are already available on the market and the transitional period of 18 months would allow the retailers to handle the existing stock within the timeframe set in the restriction.

The proposed restriction and derogations are simple and therefore easy to understand for the actors. As the number of devices needed for derogated uses is marginal, the mercury containing sphygmomanometers should not to be advertised in the EU markets anymore. This will contribute to a better awareness on the restriction among the users of sphygmomanometers.

Enforceability

The compliance with the restriction on placing on the market of mercury containing sphygmomanometers can be verified by following the fairly limited number of producers, importers and distributors of these equipments.

As a result of the restriction, the number of mercury containing sphygmomanometers will decrease dramatically over time. The restriction on the placing on the market of mercury containing devices may also raise, at least temporarily, the awareness of the users of the devices on the need for special care during the use and disposal of the devices. Therefore, the restriction may help in the implementation and enforcement of waste legislation.

4.2.1.4 Overall assessment of restriction option 1

The amount of mercury introduced to the European market is estimated to reduce by 3.0-1.2 tonnes per annum between 2015 and 2034. The range is due to the declining trend in the number of mercury sphygmomanometers sold annually. The continued use of existing devices until the end of their service-life, taking into account the uncertainties related to their proper disposal, will continue to cause some emissions and exposure. The technical feasibility of alternatives is demonstrated by SCENIHR (2009) and the specific derogations for epidemiological studies and validation purposes were suggested. The cost of reducing the use of mercury in sphygmomanometers is estimated to be between -€2400 (i.e. saving) and €3000 with a central estimate of €1300 per kg of mercury. These costs are considered to be proportionate to the risk reduction capacity. To better understand the estimated compliance costs in relation to other actions and policies to reduce mercury, one can compare the cost effectiveness of the proposed restriction (€1300/kg Hg) with the policy options reviewed in Appendix 2.

4.2.2 Option 2: Restricting the use of sphygmomanometers

Restricting the use of existing sphygmomanometers is an additional element to restricting the placing on the market of the new devices. A transitional period of five years for a use ban after entry into force of restriction on placing on the market (Option 1) is proposed, i.e. the ban on the use would become effective 6.5 years after entry into force. This will allow the use of newly purchased equipment for a reasonable time and would give sufficient time to users to replace their devices. When assessing the effectiveness and practicality of this additional element, all results reported above for restriction on the placing on the market would apply as well.

4.2.2.1 Effectiveness

Risk reduction capacity

A use ban is a chance for implementing more effective national collection campaigns, and a possibility to bring the message of proper collection of the mercury containing devices across. In this way a higher proportion of the devices in use could be collected in compliance with waste legislation. Thus, mercury emissions will be reduced (but not avoided) from the waste phase. The risk reduction capacity would be limited in comparison with a restriction on the placing on the market of new devices, since the volume concerns mercury in devices that are already on the market, no emissions can be avoided during the production and only very little emissions would be avoided in the use phase as a result of the earlier retirement of the devices. The risk reduction that can be associated to a use ban is a potential for a higher separate collection rate of the existing devices, and associated reduced (but not avoided) emissions in the waste phase. The impacts of a use ban and potential accompanying efforts for improving separate collection are difficult to assess and depend on the efforts taken by Member States to raise awareness on the use ban and to promote proper waste collection. In addition restricting the use of mercury containing sphygmomanometers could reduce the emission and exposure during the use and maintenance of the devices already on the market.

In addition, if the use of the devices is not restricted the awareness of proper waste handling of mercury sphygmomanometers among the few users still left after 10 or 20 years, will probably get worse. This may lead to more emissions to environment from the waste phase.

It can be estimated that the use ban after 6.5 years of the entry into force would affect approximately 200,000 mercury sphygmomanometers[55], i.e. 17 tonnes of mercury. The affected sphygmomanometers would be collected on average 2.5 years before the end of the service-life. Hence, the risk reduction capacity is dependent on the proposed transitional period.

[55] It can be assumed that banning the use after 5 years of the ban on placing on the market would have an effect on 200 000 mercury sphygmomanometers, as devices bought during five last years before the ban on placing on the market (between 2011-2015) would need to be replaced before end of their service-life.

Proportionality

Technical feasibility

Technical feasibility and availability of mercury-free sphygmomanometers is the same as for restriction option 1.

Achieving the risk reductions requires that Member States raise awareness on the use restriction and on proper disposal of sphygmomanometers. This can be achieved by different means, for instance by using the routine information channels and campaigns on proper collection and handling of hazardous waste. More targeted information campaigns could include the use of associations of medical professionals (websites, special magazines, events etc) or sending information letters to hospitals and private practitioners.

It might be sufficient to use and promote the use of existing hazardous waste collection points and treatment facilities. There can of course be national or local voluntary action to appoint temporary additional collection points. The suppliers of sphygmomanometers could also agree to voluntarily take back mercury-containing devices when new devices are bought.

Economic feasibility (including the costs)

Compliance costs
If the use of mercury containing sphygmomanometers were banned 5 years after the restriction for placing on the market becomes effective, it would truncate the service-life of around 200,000 existing devices. This will cause two kinds of additional costs for users. Before the use ban would become effective, it increases the annualised cost by reducing the life-time of the device (i.e. introducing a loss of residual value of the capital). After that it increases the annualised costs of the users as alternative devices are assessed to be more expensive in the central case. The additional present value compliance cost (for 2011-2024) is estimated to be around €8 million, i.e. approximately 26 % of the compliance costs of banning the placing on the market (present value for 2015-2034). To simplify the analysis, these calculations are based on the assumption that all the mercury sphygmomanometers are replaced by aneroid devices. The compliance costs are highly dependent on the proposed transitional period, just like the risk reduction capacity. For details, see Annex 3b.

Administrative costs
As the existing waste collection system can be used to collect sphygmomanometers no significant costs arising from the collection are foreseen. In fact the collection of existing devices can introduce cost savings related to enforcement of waste legislation and to keeping up the awareness and systems for collection of mercury sphygmomanometers.

Costs related to possible information campaign depends on the efforts taken by Member States. As an example, the cost of contacting all the doctors in the EU by

sending letters is roughly estimated to be between €300,000-600,000[56]. The high awareness on the use restriction does not automatically translate to a high compliance. More intensive enforcement with additional inspections can be a way to promote the compliance, but will also introduce additional costs.

Total costs

The compliance costs of replacing 200 000 mercury sphygmomanometer before the end of their service-life are estimated to be around €8,000,000 (present value 2011-2024) and possible administrative costs between €300,000-600,000. Based on this, it is estimated that the cost of bringing forward the collection would be around €500 per kg of mercury. This cost is related to existing mercury sphygmomanometers and to bringing forward the disposal. This cost-effectiveness figure cannot be compared with cost-effectiveness as calculated in Restriction option 1.

4.2.2.2 Practicality

Implementability and manageability

Technically feasible alternatives available and the slightly increased costs for users due to earlier replacement of devices do not significantly affect the users.

As the mercury sphygmomanometers are widely used by general practitioners, achieving high awareness on requirements demands information campaigns. Without these campaigns the desired compliance and reduction in risk is not likely to be achieved. Due to high number of users, the efforts needed from Member States to raise the awareness to an adequate level can become significant. Member States may also use professional organisations to reach the practitioners. In addition, manufacturers and sellers of sphygmomanometers will promote the awareness on the legal requirements quite effectively, as they gain from the early replacement of mercury devices.

Enforceability

Mercury containing sphygmomanometers are widely used by general practitioners. Additional efforts needed to ensure high compliance may be significant, even if awareness is regarded to be at adequate level. In practice the enforcement of users may be limited due to dispersive use of sphygmomanometers.

[56] According to Eurostat, there is approximately 1.5 million doctors in the EU. Hospitals can be contacted with one letter, and it is assumed that 60-80% of doctors would be reached through hospitals. In addition, the staff time to prepare the letters is estimated to be 4-8 hours per Member State, i.e. 108-216 hours. Assuming an hourly expense of €30, the preparation of the letters would cost between €3240-6480 in total. Sending a letter can be estimated to cost €1 per letter.

4.2.2.4 Overall assessment of restriction option 2

Restricting the use of existing mercury containing sphygmomanometer is not suggested due to practical difficulties mainly in enforceability. After adequate awareness among users is achieved, the authorities would need to ensure high compliance. This could be done through enforcement. The risk reduction capacity is difficult to assess, but if a real improvement in waste handling is achieved, it could reduce the emissions from the waste phase significantly. The cost of bringing forward the collection of some mercury sphygmomanometers is estimated to be around €500 per kg of mercury. However, separate collection of devices entering the waste stage could also contribute to minimizing emissions of mercury and could therefore be considered as a complementary measure.

4.3 The proposed restriction(s) and summary of the justifications

Proposal:

The placing on the market of mercury containing sphygmomanometers after 18 months of entry into force of the amendment of Annex XVII with derogations to devices that are used (i) in epidemiological studies which are on-going on entry into force; (ii) as reference standards in clinical validation studies of mercury-free sphygmomanometers.

Summary of justification:

The main purpose of the proposed restrictions is to reduce the mercury pool in the society, thus avoiding negative impacts on human health and environment. Technically feasible alternatives to mercury containing sphygmomanometers are available with very limited exemptions as justified in the opinion of SCENIHR. Based on the assessment of compliance costs (in Annex 3b), the alternatives are also regarded as economically feasible. The cost-effectiveness (around €1300/kg) to avoid mercury is regarded as proportionate.

Annex 3b: Compliance cost calculations for Sphygmomanometers

Content

1. Introduction

This BD presents the compliance costs calculations of substituting mercury-containing sphygmomanometers with mercury-free alternatives after their service-life (restriction option 1 in the Annex XV restriction report). In addition, the additional cost impacts arising from the possible replacement of the existing stock of mercury containing sphygmomanometers (restriction option 2) is covered with limited efforts in Chapter 5. Two alternative devices (shock-resistant aneroid and electronic) are covered in the analysis due to their technical properties, which are quite similar to mercury-containing sphygmomanometer (e.g. manual reading as for mercury-containing sphygmomanometer). The technical feasibility of these alternatives has been assessed and verified by the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR 2009) and is not further discussed in this paper. Compliance costs are also calculated for this scenario, where both alternatives will gain a specific proportion of the markets.

2. Defining the temporal scope and choosing a representative year

The temporal scope of the analysis is established from the time when restriction is assumed to become effective in 2015 to 2034[57]. Taking into account the uncertainties related to available data and the assumed declining trend in the number of mercury sphygmomanometers 20 years scope is regarded sufficient. As the average lifetime of a mercury containing sphygmomanometer is estimated to be 10 years, the restriction would have its full effect in 2024, when all the existing mercury containing devices would be replaced.

The costs are reported in two ways:

1. In the cumulative approach the present values of costs are calculated for 2015-2034.
2. In the representative year approach the annualised costs, using the year 2024 as a representative year, are calculated.

3. Input data

The main sources of data used in the analysis are Lassen et al. (2008)[58], Concorde (2009)[59] and Lassen et al. (2010)[60]. The Table 1 below presents the input data used in

[57] This temporal scope is chosen for illustrative purposes. In reality the time when the restriction becomes effective (2015 in this analysis) depends on the speed of the decision making process and the transitional periods after entry into force.

[58] Options for reducing mercury use in products and applications, and the fate of mercury already circulating in society published by DG Environment. Available at http://ec.europa.eu/environment/chemicals/mercury/pdf/study_report2008.pdf

the analysis. The prices of devices (investment costs) are factory gate prices excluding VAT, but for other costs (recurrent costs) it is not known if the VAT is included or not.

In addition to data used for central case, the Table A3b-1 presents the values for parameters used in sensitivity analysis (scenarios 1 and 2). The sensitivity analysis with results is presented in Chapter 7.

4. Changes in the characteristics of the good

The value related to changes in characteristics of the good is not assessed in this analysis due to lack of data on end-users needs and perceptions. The technical feasibility of alternatives has been assessed and verified by Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). The fact that end-users have not replaced the mercury sphygmomanometers with possibly more economical alternatives (resulting in cost savings calculated in Scenario 2), may indicate that certain characteristics of mercury devices are more valuable than perceived in this analysis. This might also be due to asymmetric (incorrect) information among practitioners on quality of alternative devices.

[59] Turning up the Pressure: Phasing out Mercury Sphygmomanometers for Professional Use published by European Environmental Bureau. Available at http://www.eeb.org/publication/2009/SphygReport_EEB_Final-A5_11Jun2009.pdf

[60] Appendix 3 of the restriction report

Table A3b-1: Input data used in the analysis

Parameter	Device	Central case	Scenario 1: High costs	Scenario 2: Low costs
Discount rate		4%	4%	4%
Mercury devices sold per year 2010		45000	45000	45000
Annual decrease in number of devices sold		5%	0%	10%
Mercury per device (kg)		0.085	0.085	0.085
Average lifetime (years)	Mercury	10	10	**9**
	Shock-resistant aneroid	5	**4**	**6**
	Electronic	10	**6**	**15**
Investment cost (price of device)	Mercury	€ 40	€ 40	€ 40
	Shock-resistant aneroid	€ 40	€ 40	€ 40
	Electronic	€ 110	€ 110	**€ 90**[61]
Calibration costs (per calibration)	Mercury	€ 15	**€ 30**	**€ 30**
	Shock-resistant aneroid	€ 20	**€ 30**	**€ 30**
	Electronic	€ 20	**€ 40**	**€ 40**
Calibration frequency (once in *x* years)	Mercury	2	**5**	2
	Shock-resistant aneroid	1	1	**5**
	Electronic	3	3	**4**
Batteries (per year)	Mercury	€ 0	€ 0	€ 0
	Shock-resistant aneroid	€ 0	€ 0	€ 0
	Electronic	€ 3	**€ 4**	**€ 2**
Waste treatment (per device) [62]	Mercury	€ 30	**€ 10**	**€ 40**
	Shock-resistant aneroid	€ 1	**€ 2**	€ 1
	Electronic	€ 2	**€ 4**	**€ 1**
Spill response (per year)	Mercury	€ 0	€ 0	**€ 12**
	Shock-resistant aneroid	€ 0	€ 0	€ 0
	Electronic	€ 0	€ 0	€ 0
Replacement ratio[63]		75/25	**100/0**	**95/5**

[61] To cover the possible trend of the price of the electronic sphygmomanometer, it is simply assumed in Scenario 2 that the price would be 90 € throughout the analysis (2015-2034). This has approximately the same effect on compliance costs as 2 % annual decrease in the price.

[62] It is not known if the estimate considers that not all the users dispose of the mercury sphygmomanometers in accordance of the hazardous waste legislation.

[63] The ratio of replacement of the mercury containing sphygmomanometers by aneroid or electronic alternatives.

5. Cost calculations

The calculations have been carried out in Excel sheets using NPV (for present value) and PMT (for annualised cost) worksheet functions. All values used in this analysis refer to year 2010 price level, i.e. the prices are "real" as the effect of inflation has not been included in the analysis. Throughout the analysis a 4% discount rate is used and the expenditures are assumed to occur in the beginning of each year, i.e. 1 of January.

Calculating investment costs

In the central case it is assumed that prices of mercury-containing and alternative devices do not change between 2015 and 2034. In reality, there could be change in the prices in favour of electronic sphygmomanometers due to relatively new technology used in the device. This assumption is included in the Scenario 2 presented in Chapter 7. Table A3b-2 presents the calculation of investment costs of mercury-containing sphygmomanometer and two alternative devices.

Table A3b-2: Annualised investment costs per device (in 2010 price level)

	Investment costs (€) per device		
Year	Baseline: Mercury sphygmomanometer	Alternative 1: Shock resistant aneroid sphygmomanometer	Alternative 2: Electronic sphygmomanometer
1	40	40	110
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
6	0		0
7	0		0
8	0		0
9	0		0
10	0		0
Annualised	**5**	**9**	**14**
Additional annualised		**4**	**9**

The prices of the mercury and shock-resistant aneroid devices are estimated to be €40, and electric device €110. Due to shorter lifetime of the Alternative 1 compared to mercury-containing device, the additional annualised investment cost is estimated to be €4 per device. For Alternative 2 additional annualised investment cost is estimated to be €9 per device.

Calculating recurrent costs

The recurrent costs of sphygmomanometers consist mainly of calibrating costs. In addition there are costs related to batteries for electronic device, waste handling, spill response and training but some of these costs are not considered in the central case

analysis for the reason explained below. The devices are bought calibrated, i.e. the first calibration takes place at the earliest one year after the investment. The table A3b-3 presents the calculations of recurrent costs for different devices.

Table A3b-3: Annualised recurrent costs per device (in 2010 price level)

	Recurrent costs (€) per device		
Year	Baseline: Mercury sphygmomanometer	Alternative 1: Shock resistant aneroid sphygmomanometer	Alternative 2: Electronic sphygmomanometer
1	0	0	0
2	0	20	3
3	15	20	3
4	0	20	23
5	15	20	3
6	0	1	3
7	15	0	23
8	0	0	3
9	15	0	3
10	0	0	23
11	30	0	2
Annualised	**9**	**16**	**9**
Additional annualised		**8**[64]	**0**

The values of different parameters of recurrent costs are listed in table A3b-1 in Chapter 3. The additional annualised recurrent cost per device is estimated to be €8 for alternative 1 and €0 for alternative 2 compared to the baseline.

According to Concorde (2009) the annualised spill response cost per device is estimated to be €12 for the mercury containing sphygmomanometer and zero for alternatives (as there is no fear of mercury spill). The cost includes estimates on cost of spill kit, person-hours, spill area closure and cost of downtime, waste disposal etc. In addition it is assumed that there is a spill from 3 % of the mercury containing sphygmomanometers annually. The annualised training costs per device are estimated to be €5 for mercury containing, €2 for aneroid and €3 for electronic device. These parameters (spill response and training) are not considered in the base case analysis due to limited information on the assumptions behind the estimates. It is also difficult to assess if these actions take a place in the reality. Nevertheless, the spill response estimate is included in the Scenario 2 in sensitivity analysis. Taking into account these estimates changes the total recurrent costs in favour for alternatives.

Total costs and compliance costs

The following calculations (central case) are made assuming 5% annual decrease in the number of mercury-containing sphygmomanometers sold per year in the next 20 years, i.e. approximately 30 000 devices in 2020 compared to 45 000 in 2010. This

[64] The result may not seem to be correct (as 16-9=7) because of the rounding is used

reduction in using mercury-containing devices is at least partly due to increase in awareness of harmful properties of mercury. Table A3b-4 presents the calculations of total costs of mercury-containing sphygmomanometer and the two alternative devices.

Table A3b-4: Annualised total costs per device (in 2010 price level)

Year	Total costs (€) per device		
	Baseline: Mercury sphygmomanometer	Alternative 1: Shock resistant aneroid sphygmomanometer	Alternative 2: Electronic sphygmomanometer
1	40	40	110
2	0	20	3
3	15	20	3
4	0	20	23
5	15	20	3
6	0	1	3
7	15	0	23
8	0	0	3
9	15	0	3
10	0	0	23
11	30	0	2
Annualised	**14**	**25**	**22**
Additional annualised[65]		**12**	**9**

The additional annualised cost per device is estimated to be €12 for alternative 1 and €9 for alternative 2 compared to the mercury-containing device. These results can be derived from Tables 1 and 2 as sums of additional investment and recurrent costs.

In reality some of the users would replace the mercury sphygmomanometer with shock-resistant aneroid, some with electronic devices and some with alternatives not covered in this analysis due to their technical properties. According to SCENIHR (2009), in addition to sphygmomanometers covered in this analysis, also validated oscillometric devices are currently replacing mercury containing sphygmomanometers. Nevertheless, as the price of oscillometric device is approximately the same as aneroid shock-resistant sphygmomanometer, and there are no reasons to assume significant difference in recurrent costs, there is no need to assess them separately. Based on information from industry (Lassen et al., 2010) we assume in the central case that 75% of the mercury devices would be replaced with the shock-resistant aneroid sphygmomanometer and 25% with electronic one.

Table A3b-5 presents the compliance costs from replacing the mercury sphygmomanometer with shock-resistant or electronic alternative or with combination (75/25) of those as described above.

[65] The result may not seem to be correct (as 16-9=7) because of the rounding is used

Table A3b-5: Annualised and present value compliance costs for alternatives 1, 2 and the combination of alternatives (in 2010 price level)

	Compliance costs (€)		
	Alternative 1: Shock resistant aneroid sphygmomanometer	Alternative 2: Electronic sphygmomanometer	Alternatives 1+2
2015	421102	310914	393555
2016	822152	607023	768370
2017	1204104	889032	1125336
2018	1567869	1157612	1465304
2019	1914311	1413402	1789083
2020	2244255	1657011	2097444
2021	2558488	1889021	2391121
2022	2857758	2109982	2670814
2023	3142777	2320421	2937188
2024	3414223	2520839	3190877
2025	3251641	2400799	3038930
2026	3096801	2286475	2894219
2027	2949334	2177596	2756399
2028	2808890	2073901	2625142
2029	2675133	1975143	2500136
2030	2547746	1881089	2381081
2031	2426424	1791513	2267697
2032	2310880	1706203	2159711
2033	2200839	1624955	2056868
2034	2096037	1547577	1958922
Replacement ratio	**75%**	**25%**	
Compliance cost (present value 2015-2034)	**31,348,553**	**23,145,723**	**29,297,845**
Annualised compliance cost (2024)	**3,414,223**	**2,520,839**	**3,190,877**

The present value compliance costs for 2015-2034 are estimated to be between €23 million and €31 million and annualised compliance costs (2024) between €2.5 million and €3.4 million depending on the replacement ratio.

Costs related to banning the use of mercury containing sphygmomanometers

The compliance costs of banning the use of existing mercury containing sphygmomanometers are sensitive on the length of the possible transitional period between entry into force of the restriction and time when it becomes effective. The following compliance costs in Table A3b-6 are calculated based on assumption that no new mercury containing devices would be purchased after 2015, as there would be

a ban on placing on the market, and that the use ban would become effective in 2020. For simplicity, it is assumed that all the mercury sphygmomanometers would be replaced by the aneroid alternative. As the annualised cost per devise for the mercury sphygmomanometers with only 5 years lifetime is lower than for alternatives (with central case assumptions), it is assumed that the use ban would not effect the demand of mercury devices before 2015.

Table A3b-6: Compliance costs of banning the use of mercury containing sphygmomanometers after 5 five year transitional period (in 2010 price level)

Year	Type of effect	Compliance cost (€)
2011	Higher annualised cost per sphygmomanometer due to reduced lifetime of mercury sphygmomanometer (loss of residual value of capital)	57,373
2012		114,027
2013		244,279
2014		381,662
2015		627,956
2016		627,956
2017		627,956
2018		627,956
2019		627,956
2020	Additional costs due to higher annualised costs of aneroid sphygmomanometer compared to mercury device	2,326,856
2021		1,815,004
2022		1,327,525
2023		863,260
2024		421,102
Compliance cost (present value 2011-2024)		**7,732,792**
Cost effectiveness (€ per kg)		**467**

The use ban results in two kinds of effects for the users. Before 2020, when the use ban would be effective, it increases the annualised cost by reducing the life-time of the device i.e. introducing a loss of residual value of the capital. As the lifetime of a mercury containing sphygmomanometer is assumed to be 10 years, the use ban would cut down the service-life of devices bought between 2011 and 2015. Between 2015 and 2019, the annual cost would remain the same, as the number of users (devices) that would be affected in each year (with higher annualised cost) remains the same. This is because no new mercury measuring devices would be allowed to be placed on the market anymore. After 2020 the use ban introduces an increase in the annualised costs of the users, as alternative devices are calculated to be more expensive (central case). This cost impact is similar to cost impacts in restriction option 1 in the restriction report (ban on placing on the market). As the last mercury devices are assumed to be purchased in the beginning on 2015, the last compliance costs take place in 2024, i.e. after the 10 years lifetime.

Introducing the use ban (in 2020) in addition to a ban for placing on the market (in 2015) for mercury sphygmomanometers would introduce an additional compliance cost of around €8 million which means approximately 26 % increase in compliance costs. Assuming 8 years transitional period instead of 5 would introduce compliance costs of around €1.5 million, but at the same time reduce the risk reduction capacity from 17 tonnes of mercury to 6 tonnes.

6. Cost effectiveness

Table A3b-7 presents the costs of reducing the consumption of mercury by one kg when banning the placing on the market of mercury sphygmomanometers. The calculation is based on the annualised compliance costs and on assumption that one mercury sphygmomanometer contains 85 g of mercury. The cost effectiveness is calculated using the following formula:

$$C - E = \Delta C_i \times y \times \frac{1}{m}, \qquad (1)$$

where

$C - E$ = cost effectiveness (€/kg),
ΔC_i = additional annualised cost per device (€/year),
i = the device (Alternative 1 or Alternative 2)
y = lifetime of mercury-containing sphygmomanometer (years) and
m = mercury content per device (kg).

Table A3b-7: Cost effectiveness of replacing the mercury sphygmomanometers (in 2010 price level

	Central case	Scenario 1: High costs	Scenario 2: Low costs
Cost of reducing 1 kg of mercury consumption (€/kg)	**1,313**	3,014	-2,379

In the central case the cost of reducing 1 kg consumption of mercury in production of sphygmomanometer is estimated to be €1300. With parameters used for sensitivity analysis the cost is estimated to be between €3000 and – €2400 (cost savings) per kg.

One of the assumptions, the number of mercury-containing devices sold per year, does not have effect on cost-efficiency of action as both benefits (reduction in mercury consumption) and costs (compliance costs) will be affected by the same ratio. This is partly due to limited scope of our analysis (taking only into account the costs faced by end-users) which is not including e.g. regulatory costs. Nevertheless, the effect of annual number of mercury devices sold on cost-efficiency is assumed to be insignificant.

7. Assumptions and sensitivity analysis

One main assumption used in the analysis is the number of mercury-containing sphygmomanometers sold per year, which is assumed to decrease approximately 5 % annually 2015 and 2034 (45 000 devices sold in 2010) without regulation in central case. The other main assumption is that prices of devices are assumed to be stable between 2015 and 2034.

The assumptions, as well as the input data presented in Chapter 3, include more or less uncertainty especially as a quite long time horizon is adopted and the uncertainty tends to increase over a time.

To address the issue of uncertainty two scenarios are considered: a "high costs" with assumptions increasing the compliance costs (Scenario 1) and "low costs" in favour of banning mercury-containing devices (Scenario 2). Table A3b-8 gives the present value (2015-2034) and annualised (2024) compliance costs for the two scenarios. The values used in sensitivity analysis can be found in the Table A3b-1 in Chapter 3. The values in bold differ from the central case calculations and are chosen for sensitivity analysis as they are estimated to include significant uncertainty or possible trends before 2034.

Table A3b-8: Results of sensitivity analysis presented as annualised and present value compliance costs for the combination of alternatives (in 2010 price level)

	Central case	Scenario 1: High costs	Scenario 2: Low costs
Compliance cost (present value 2015-2034) (€)	72,295,288	116,054,281	-43,600,611
Annualised compliance cost (2024) (€)	6,903,029	11,529,562	-4,234,129

The annualised and present value compliance costs of Scenarios 1 and 2 can be regarded as lower and upper limit estimates with reasonable values for key parameters. Thus, the present value compliance costs are estimated to be between €116 million cost and €44 million savings.

8. Summary

The compliance costs of banning the placing on the market of mercury sphygmomanometers with mercury-free alternatives are estimated to be around €70 million (present value 2015-2034) or around €7 million (annualised in 2024). However, due to uncertainties in the data, high and low cost scenarios are analysed and they suggest present value compliance costs between €116 million and €44 million savings. This results in cost-effectiveness estimate between €3000 and –€2400 (cost savings) per kg of mercury avoided.

In addition, compliance costs for banning the use of mercury sphygmomanometers currently in use in 2020 (present value 2011-2024) is estimated to be around €8 million.

Annex 4: Strain gauges (used with plethysmographs)

Content

1. Technical description of strain gauges

Strain gauges are used for blood pressure and for pure blood flow measurements in body parts using a technique called strain gauge plethysmography[66] (measuring how limbs change in size at different pressures). They consist of a fine rubber tube filled with mercury which is placed around the body part in which the blood pressure or blood flow is measured. The method is used for instance for diagnosing certain kinds of arteriosclerosis. According to the Northeast Waste Management Officials' Association a standard mercury strain gauge contains approximately 1.25 grams of elemental mercury (NEWMOA 2010). The service-life of the mercury tube itself is around 1 year (Kemi 2005).

2. Description of release and exposure

Based on the approach described in Part B of the main document, the estimations on i) the total amount of mercury accumulated in devices in the EU and ii) the amount of mercury placed on the market annually in the EU are used to describe the potential release and exposure during the waste phase of the devices (see Table A4-1). Furthermore, to get a more comprehensive picture, the annual amounts iii) used in the production of devices, iv) imported into the EU and v) exported from the EU are given to illustrate the potential for direct exposure of workers during the production and service-life of the devices. However, it is stressed that this report does not further assess the potential concerns related to workers as explained in Part B. If quantitative estimates are not available, a qualitative description is given.

Table A4-1: Amounts of mercury accumulated, used in production, placed on the market, imported and exported in strain gauges in 2010

Mercury	Estimated amounts
Pool accumulated in strain gauges in the EU	~14 kg Hg
Placed on the market in strain gauges in the EU	~14 kg Hg/y
Used in production of strain gauges in the EU	0.015 kg in Sweden (Kemi, 2007)
Imported into the EU in strain gauges	<14 kg Hg/y
Exported from the EU in strain gauges	0 kg (One identified producer in Sweden producing less than 150 mercury strain gauges annually for Swedish markets)

[66] Mercury strain gauges are always used with a separate device, namely plethysmograph. No measurements with strain gauges are possible without the device.

Box 1: General qualitative description of potential release and exposure

Production, use and waste phase of mercury strain gauges

Kemi (2005) estimates that in Sweden no more than 200 mercury strain gauges are needed annually. When extrapolated to the whole EU27 (based on the population of Sweden which is approximately 1.8% of the population of EU27), it would suggest that only around 14 kg of mercury is used in mercury strain gauges sold annually in the EU27 (in around 11,000 strain gauges). This is also more or less the stock of mercury in strain gauges in the EU as the average service-life of a gauge is estimated to be 1 year (Kemi 2005). In Sweden the placing on the market of mercury strain gauges has been prohibited for many years, with only limited exemptions (KemI, 2007). Therefore, the estimate of 14 kg for the whole EU may be a significant underestimate. Nevertheless, there is no data available from the other Member States.

Some emissions to the environment and exposure of workers may occur in the production phase of mercury strain gauges. However, there is only one identified producer in the EU using only around 20 g of mercury annually.

The average lifetime of a mercury strain gauge is around 1 year (Kemi 2005). The relatively short service-life might be caused by the aging of the silicon tube (Kemi 2007). In addition the aging of the strain gauge causes the copper to dissolve in the mercury and thus the pressure in the gauge will go down and it cannot be used anymore (NEWMOA 2010). According to information received via public consultation, a producer of mercury strain gauges encourages the user to return the mercury strain gauges to the producer for collection and recycling (D.E. Hokanson, Inc., 2011).

As the rubber tubes are quite strong, the strain gauges are not susceptible to brake and emissions occurring during the service-life are estimated to be low. As the strain gauges are mainly used by hospitals, the level of proper waste handling may be similar to the situation with sphygmomanometers at hospitals. As described in Annex 3a (Sphygmomanometers), there are reported problems related to waste handling of sphygmomanometers used in hospitals.

3. Available information on alternatives (Part C)

3.1 Identification of potential alternatives

Several kinds of mercury-free alternatives exist for mercury strain gauges. Some of the alternatives can be used with the same plethysmographs as mercury strain gauges, but some of them are based on a different method. The mercury-free alternatives include:

- Strain gauges with indium-gallium
- Photo cell
- Laser-Doppler techniques
- Ultrasound-Doppler
- Ultrasound
- Filtrass

The strain gauges with indium-gallium are marketed for the same purposes as mercury strain gauges and they function based on the same technique. For these reasons indium gallium strain gauges are considered the main alternatives for mercury gauges, and technical and economic aspects of other alternatives are considered only when the technical and economic feasibility of indium gallium strain gauge is questionable.

The photo-cell technique registers changes in tissue colour at different pressures and can be used with the same plethysmographs.

The laser-Doppler technique measures the velocity of red blood cells to determine the blood flow in different pressures and is meant for big vessels. The Ultrasound-Doppler is based on the same technique but meant for small measurement volumes. Both photo cell and Doppler techniques are typically used for measurements in fingers and toes. (Kemi 2005)

Filtrass is a type of plehtysmographic method, but it does not use strain gauges.

3.2 Human health and environmental risks related to alternatives

The following paragraphs report some available information on indium and gallium. Indium-gallium strain gauges are considered the most direct alternative for mercury strain gauges as they rely on the same principles and use the same method, and they can be used with the existing plethysmographs for the same applications as the mercury strain gauges. Consequently, risks related to other identified alternatives than indium-gallium strain gauges are not further discussed here, although as described in section C.2.1 of the main report, the risks related to electronic alternatives are several orders of magnitude lower than the use of mercury containing devices.

4

Classification and labelling

Gallium and indium have no harmonised classification under Regulation (EC) No 1272/2008. A screening of C&L notifications received by ECHA revealed that most of the C&L notifications indicate for both gallium and indium skin and eye irritation hazard category 2. Some of the notifications also indicate aquatic chronic hazard category 4, STOT Single exposure hazard category 3, and in addition for indium STOT Repeated Exposure hazard category 1 and Flammable Solid hazard category 2. In US gallium is classified and labelled as corrosive (U.S.DOT-hazard level 8) (Repetto, G. and Paso, A.d. 2001).

Gallium

No registrations on Gallium were received by ECHA by 3 January 2011.

According to a company, properties of gallium have not been fully investigated, but it is reported to cause skin, eye and respiratory tract irritation, and may cause bone marrow abnormalities with damage to blood forming tissues (ACI Alloys, 2010). Administration of gallium to humans has caused metallic taste, skin rashes, and bone marrow depression. Ingestion (which is an irrelevant exposure route) may cause gastrointestinal irritation with nausea, vomiting and diarrhea (ACI Alloys, 2010). However, since gallium has a very low vapour pressure (1 Pa at 1037°C, in comparison to mercury which reaches 1 Pa at 42°C, Wikipedia 2010a, Wikipedia 2011), inhalation is not considered a relevant route of exposure, at least not in comparison to mercury. No information has been readily available concerning ecotoxicological properties of mercury.

Some information is available on mutagenic properties of the gallium nitrate and gallium arsenide (the latter is used in the semi-conductor industry). Gallium nitrate is undergoing research as a possible mutagen for its capacity of altering several cellular defence mechanisms involved in carcinogenesis. If bound to plasma transferrin concentrates at sites of accelerated cellular proliferation. (IARC Monographs, 2006, Repetto, G. and Paso, A.d. 2001). Gallium nitrate and chlorate have proven anticancer activity (Collery et al., 2002). However, as indicated above, oral and inhalation routes are not considered relevant routes of exposure when compared to mercury exposure from the same type of applications, and no information is available on the possible absorption rates of metallic gallium, and the subsequent oxidation rates from gallium to ionic gallium.

Indium

No registrations on Indium were received by ECHA by 3 January 2011.

There is less information available on the toxicological properties of indium than gallium. It seems that it has not been tested for its ability to cause cancer in animals. The probable carcinogenic properties of indium are linked to alterations in the synthesis and maintenance of enzyme systems that metabolize organic carcinogens (Repetto, G. and Paso, A.d. 2001).

4

Indium-gallium alloy

A comparative study performed by Chandler et al in 1994 revealed that indium-gallium alloy may be suitable substitute for mercury in dentistry amalgam, as their ion revealed not significant toxicity (Chandler et al, 1994). No further information on hazardous properties or risk related to indium-gallium alloy is available.

In addition, some information is available on galinstan, which is an alloy consisting of indium, gallium and tin. Compared with the high vapour pressure of mercury at room temperature (16.3×10^{-6} Pa (at 20°C)), galinstan has a significantly lower vapour pressure ($<10^{-6}$ Pa (at 500°C)) (Surmann, 2005). Therefore, the occurrence of galinstan vapours from accidental spills, waste (landfills) and its emission in the air is unlikely. Consequently, the direct exposure of workers is likely to be low.

Conclusion

As presented above, mercury has a more severe classification than gallium or indium. In addition, based on the information on gallium and on Galinstan (alloy of gallium, indium, and tin), the indium-gallium alloy seems to have significantly lower vapour pressure than mercury. This leads to lower emissions and exposure by lower evaporation rate. Furthermore, there is no information on fate or ecotoxicological properties. Thus, considering the clear evidence on the hazardous properties and risk of mercury, and acknowledging the scarce data on gallium and indium, the risk potential of the indium-gallium strain gauges can be considered to be lower, potentially by several orders of magnitude. Consequently, the transfer from mercury strain gauges to indium-gallium strain gauges is considered to reduce the overall risk to the environment and human health.

3.3 Technical feasibility of alternatives

According to Kemi (2005) the mercury-free alternatives are replacing mercury containing strain-gauges. The reasons why mercury containing strain gauges were still used in 2005 are both technical and economic.

Different alternatives can be used for different measurements and applications (Kemi 2007). As the indium gallium strain gauges function based on the same method as mercury strain gauges they are considered the main alternatives.

According to the information received in the public consultation, it seems that indium-gallium strain gauges are not suitable for measurements when the length of the tube is below 6cm. This is related to much lower resistance of the indium gallium compared to the mercury. However, according to Kemi (2005) there is no need for mercury plethysmographs for toe and finger examinations as they can use laser-Doppler or ultrasound equipments.

According to Kemi (2005) the mercury strain gauges were still needed in 2005 in research of absolute blood flow in arms and legs due to the huge amount or reference material available. It was also reported that mercury equipment is still in use for the

diagnosis and monitoring of critical limb ischemia and monitoring certain kinds of arteriosclerosis. However, Kemi (2005) estimated that within 4 to 5 years (i.e. by 2010) mercury-free plethysmographic equipment will be validated for all areas where mercury strain gauges are used.

As described in Section B.5 the current Swedish ban from 2007 has time limited exemptions (that can be prolonged) for strain gauges that reads:

> "*The applicant may manufacture and sell up to 150 mercury containing strain gauges each year and these must be used in already existing equipment*
>
> *- to measure blood flow in a muscle within clinical routine activities up to 2010-12-31*
>
> *- for other uses within clinical routine activities up to 2009-12-31*
>
> *- for research and development up to 2012-12-31 given that the project started prior to 2007-12-31. If the research concerns blood flow in a muscle the project may start not later than 2010-12-31.*
>
> *- to validate mercury free alternatives up to 2010-12-31.*
>
> *The applicant has the duty to keep records on the uses.*"

Only the exemption for ongoing scientific research and development projects is still valid in the beginning of 2011. However, according to the information received in the public consultation, only two years would be needed to validate the mercury-free alternatives for all application areas, i.e. until end of 2012. The proposed restriction with the additional time needed for the decision making and the 18 months transitional period will not apply before that.

3.4 Economic feasibility of the alternatives

According to a website of a supplier of strain gauges, a mercury strain gauge costs around €70 without VAT[67]. The most direct alternative indium gallium strain gauge costs around €82 without VAT[68], i.e. the additional annualised cost is €12 assuming average service life of 1 year for both mercury and indium gallium tube. (PMS instruments, 2011)

In other words, the indium gallium strain gauges are around 17% more expensive than mercury strain gauges. A producer of the strain gauges (Hokanson, 2011) estimated the price difference to be around 30%.

The tube functions with complex electronic equipment (plethysmograph) that cost more than €20,000. As the service-life for the electronic equipment is 10-15 years, the hospitals hesitate to invest in new equipment unless the old one breaks down (Kemi, 2005). However, according to the information received in the public consultation, indium-gallium strain gauges can be used also with existing plethysmographs and consequently, there is no need to replace existing devices.

Considering the additional annualised cost of around €12 and considering the relatively high investment cost of more than €20,000 of the plethysmographs

[67] £595.2 per set of 8 mercury gauges including VAT at 20%
[68] £691.2 per set of 8 indium gallium gauges including VAT at 20%

(dominating the cost per measurement), the indium gallium strain gauges are considered economically feasible alternatives for the users.

There is no data available to estimate the compliance costs related to using laser-Doppler and photocell techniques for measurements where short strain gauges are needed. However, considering that the photocells can be used with the same existing plethysmographs as mercury strain gauges (Kemi 2007), and considering the fact that this is only one specific application area, this impact is considered small.

4. Justification why the proposed restriction is the most appropriate Community-wide measure (PART E)

4.1 Identification and description of potential risk management options

4.1.1 Risk to be addressed – the baseline

As described in section B.2, the total estimated amount of mercury placed on the market in measuring devices containing mercury is used to describe the maximum potential for mercury emissions to the environment that might ultimately occur. For strain gauges this is roughly estimated to be 14 kg/y (in around 10,000 gauges). This is also the amount of mercury included in the strain gauges sold annually in the EU, as the lifetime is estimated to be 1 year. There are no data available to assess the trend of using mercury strain gauges but given the overall tendency to reduce mercury, it would seem appropriate to assume that the trend is declining.

Although not the primary concern, it is worth mentioning that some direct exposure of workers can occur during production, professional use of the strain gauges and during waste management operations.

4.1.2 Options for restrictions

Only one option to reduce the risks related to use of mercury in strain gauges is assessed further in the BD:

1. Ban on placing on the market of mercury strain gauges for plethysmographs after 18 months of the entry into force.

In the original Annex XV restriction report two additional restriction options were considered. These options were considered as it was not possible to conclude that indium gallium strain gauges could be used with existing plethysmographs. During the public consultation it became evident that also existing plethysmographs can use the indium gallium strain gauges. Thus, these additional options are not presented in this BD.

4.2 Assessment of risk management options

Restricting the placing on the market of mercury strain gauges to be used with plethysmographs after 18 months of the entry into force

The risk reduction capacity of the proposed restriction is around 14 kg per year. This is the maximum potential for mercury emissions to the environment that might ultimately occur. For 2014-2025, this is around 280 kg. In addition, it can be mentioned that the volume also reduces direct exposure of workers in use and waste phase.

Technically feasible alternatives exist for all the applications. The proposed restriction is estimated to introduce additional cost of €12 per strain gauge to the users of these devices. However considering the high investment cost of the plethysmographs itself (<€20,000), the additional cost introduced by indium-gallium strain gauges to the overall cost of the measurement is small and the alternatives are consider economically feasible.

Assuming no trend in the number of devices placed on the market annually (i.e. 11,000), gives a compliance cost of €132,000 per year. Between 2015-2024, this is around €2.6 million.

Based on the additional cost of €12 per device and assuming 1.25 g of mercury per strain gauge, it can be estimated that the proposed restriction would cost around €9,600 per kg of mercury not placed on the market. This estimate does not consider e.g. the possible differences in the waste handling fees of the devices.

With this restriction, it will be possible to reduce a relatively small amount of mercury (14 kg per year) from the market. It would not be worth the effort to regulate strain gauges alone as the administrative costs related to setting up a restriction would be relatively high. Given that a restriction needs to be set on many other devices, there is no significant additional administrative cost related to restricting the mercury strain gauges.

4.3 The proposed restriction(s) and summary of the justification

As described above, mercury strain gauges are used in plethysmographs.

Proposal:
Restriction on the placing on the market of mercury strain gauges to be used with plethysmogrpahs after 18 months of entry into force of the amendment of Annex XVII.

Summary of justification:

4

The main purpose of the proposed restrictions is to reduce the mercury pool in the society, thus avoiding negative impacts on human health and environment. Technically and economically feasible alternatives to mercury strain gauges are available for all applications.

Annex 5a: Thermometers[69]

Contents

[69] Including psychrometers (hygrometers) and other applications of mercury as a thermometric liquid.

1. Technical description of mercury thermometers

Mercury thermometers can be used for manual reading of all temperature measurements in the interval from the freezing point of mercury, -39°C, up to about 800°C, with an accuracy up to 0.01°C for high-precision laboratory thermometers (Lassen et al., 2008). Mercury-thallium thermometers can be used down to -58°C. Amongst the advantages of mercury as a thermometric liquid are cited that it does not age, does not cause wetting of the glass surface[70], and has a good expansion linearity over a wide temperature range (Ludwig Schneider, 2010).

Five types of mercury thermometers are identified and assessed in this restriction report:

- Mercury-in-glass thermometers
- Six's thermometer (maximum minimum thermometer)
- Maximum thermometers
- Mercury dial thermometers
- Mercury psychrometer (hygrometer)

In addition, mercury heat indicators, mercury triple point cells and possible other non-electrical thermometric applications are assessed. Hydrometers are sometimes specifically mentioned to have a mercury thermometer inside. They are not assessed separately since they are only one of the many applications of thermometers.

Mercury tilt switches in thermostats and mercury thermoregulators (also designated contact thermometer or accustat) are not in the scope of this restriction report, since they are dependent on electric currents in order to work properly, and therefore fall under the definition of 'electrical and electronic equipment' in the RoHS Directive (see section B.2 and Appendix 4).

Psychrometers (hygrometers) are based on thermometers and, therefore, they are covered in this mercury thermometer section of the restriction report.

Mercury-in-glass thermometers

Mercury-in-glass thermometers consist of mercury encased in a thin glass tube that rises and falls (expands and contracts) with temperature.

The amount of mercury in thermometers can vary significantly according to the application and design. Lassen et al. (2008) reported the mercury content of thermometers used for laboratories and in industry settings to range from 1 to 20 g, with an average content of 3-4 g. This is consistent with a producer, who reported a typical content of 3.5 g/piece (Lassen et al., 2010).

[70] Non-wetting of glass is a colloquial term pointing to the very low adhesive properties of mercury to glass compared to the strong cohesive forces in liquid mercury, causing very low capillary action and a convex meniscus of mercury in a glass tube (water in a glass tube for example has a concave meniscus and high capillary action).

Thermometers used in laboratories contain typically around 14 g of mercury (Lassen and Maag, 2006). In Lassen et al. (2010), producers reported a typical mercury content of 3, 4 and 11 g per laboratory thermometer.

In laboratories precision is often of importance. Precision laboratory thermometers typically have reading scales varying from 1 to 0.1°C. High-precision laboratory thermometers are used for determining ice point and boiling point, for calorimetry, and for other purposes, and have reading scales down to 0.01°C. In industrial settings a resolution of 0.1°C is generally not necessary (Lassen et al., 2010). This is confirmed by information in a catalogue of engine thermometers from two producers. Both usually have a reading scale less precise than 1°C, and only a few models have a 0.5°C scale (Ludwig Schneider, 2010 and Palmer Wahl, 2010).

Six's thermometers (maximum minimum thermometer)

Six's thermometer is a mercury-in-glass thermometer with a U-shaped tube that can be used to indicate minimum and maximum temperature during a given period of time. It is a less expensive, but generally less accurate, way to measure minimum and maximum temperature, compared to the standard combination of a separate mercury containing maximum thermometer and a spirit filled minimum thermometer (Finklin and Fischer, 1990). Alcohol is used as thermometric liquid, while the mercury serves merely as an indicator. This type of thermometer is still used to measure the extremes of temperature at a certain location, where great precision is not essential (Finklin and Fischer, 1990), for instance for professional gardening.

Maximum thermometers

Maximum thermometers are used for reading maximum temperatures in meteorology (daily temperatures), and industrial processes (Lassen et al., 2010), such as sterilisation (Amarell, 2010). A capillary constriction prevents the mercury column to flow back after cooling. The column has to be shaken back after every measurement. Maximum thermometers are provided by several producers, with a resolution down to 0.1°C (Lassen et al., 2010).

Mercury dial thermometers

Mercury dial thermometers consist of a mercury filled metal bulb connected to a dial (a bourdon coil and a needle for reading the temperature). They are applied mostly in the process industry and for marine applications. This group of thermometers has only a very limited remaining market.

For remote measurement, to e.g. control of large engines or combustion processes, thermometers consisting of a sensor and a mercury filled capillary connecting the sensor to the dial are used. Lassen et al. (2008) reported that these capillaries might be up to 40 m, and according to a consulted product catalogue even up to 76 m long (Palmer Wahl 2010).

The mercury content of mercury dial thermometers ranges from about 5 to 200 g (Lassen et al., 2008).

Mercury psychrometer (hygrometer)

A mercury psychrometer is a type of hygrometer used in the measurement of relative humidity and consists of two mercury thermometers, one with a dry bulb and one with a wet bulb. Evaporation from the wet bulb lowers the temperature. The temperature difference between the wet and the dry bulb provides the basis for calculating the relative humidity. Unless mentioned otherwise, mercury psychrometers are considered to be comprised in the word "thermometer" for the sake of simplicity.

Other non-electrical thermometric applications

Producer AGA Rangemaster Limited informed ECHA that it uses '*mercury heat indicators*' in its AGA cookers. The heat indicator provides a guide to the user that the cooker has sufficient heat stored by means of an indicator band. The device does not give an actual temperature reading. The visual indication of the stored heat allows adjustment of a separate thermostat that regulates the desired amount of stored heat. Once set, the ovens then operate at fixed temperatures. The heat indicators carry approximately 1.8 g of mercury and the EU annual market is around 2500 cookers containing such a device. This results in approximately 4.5 kg of mercury used for these high temperature applications, which is negligible in comparison with the use of mercury for thermometers. The producer believes the device is not used in other similar equipment or products. Nevertheless other non-electrical thermometric applications of mercury might exist. (AGA Rangemaster, pers. comm., 2010)

Equipment for the calibration of platinum resistance thermometers using the *triple point of mercury* is prescribed in the 1990 International Temperature Scale (ITS-90). ITS–90 uses numerous defined points, all of which are based on various thermodynamic equilibrium states of fourteen pure chemical elements and one compound (water) (Wikipedia, 2010e). One of those elements is mercury (mercury triple point cell). Three types of mercury triple point cells described by Strouse and Lippiatt (2001) contain 2,6 to 3,4 kg of mercury. However there are thought to be only a very limited amount in certain dedicated calibration laboratories. According to Lassen et al. (2008), the use of mercury for these applications is estimated to be negligible. As far as is known, at least the Nederlands Meetinstituut (Nmi - Dutch Measuring Institute) would have such a device (see also Peruzzi et al., 2007). Mercury triple point cells would amongst others be produced by the National Physical Laboratory in the UK (Lassen et al., 2010).

2. Description of release and exposure

In addition to the general restriction to place mercury measuring devices on the market for sale to the general public (including thermometers), specifically, the placing on the market of mercury-in-glass thermometers as a fever thermometer is

restricted for all uses (i.e. including professional use) by Entry 18a of Annex XVII as of 3 April 2009. To date, mercury-in-glass thermometers can still be placed on the market for the industrial and professional uses including as ambient temperature thermometers, laboratory thermometers and as thermometers for combustion and industrial processes. Thus the description of release concentrates on these types of thermometers.

Based on the approach described in the section B of the main document, the estimations of i) total amount of mercury accumulated in devices in EU and ii) the amount of mercury placed on the market annually in the EU are used to describe the potential release and exposure during the waste phase of the devices. (Table A5a-1). Furthermore, to get a more comprehensive picture, the annual amounts iii) used in the production of devices, iv) imported into EU and v) exported from EU are given to illustrate the potential for direct exposure of workers during the production and service-life of the devices. However, it is stressed that this report does not further assess the potential concerns related to workers as explained in Part B. If quantitative estimates are not available, a qualitative description is given.

Table A5a-1: Amounts of mercury accumulated, used in production, placed on the market, imported and exported in thermometers in the EU in 2010

Mercury	Estimated amounts
Pool accumulated in thermometers	90 tonnes *
Placed on the market in thermometers	0.7-1.6 tonnes per year **
Used in the production of thermometers	1.0-1.5 tonnes per year **
Imported in thermometers	0.2-0.8 *
Exported in thermometers	0.5-0.8 *

Sources: * calculated from Lassen et al. (2008), see Box 1. **Lassen et al. (2008).

Box 1: General qualitative description of potential release and exposure

Production phase

It is estimated that the EU use of mercury for thermometer production is somewhere in the order of 1.0-1.5 t/y, of which around 50% is destined for the EU market (Lassen et al., 2008). The volume also includes mercury included in thermometers that are present in hydrometers. About 1000-1500 employees are involved in the EU production of mercury thermometers (Lassen et al., 2008).

In addition to releases from the waste phase of thermometers, some emission to the environment and exposure of workers may occur in the production phase of thermometers.

Service life

Mercury thermometers have a vast application area. Such areas include chemical and other process industries; laboratories in industry; research and education; machines and engines; climate and refrigeration equipment; storehouses; museums; food sector (conservation and preparation); meteorology. Mercury is present in thermometers in small amounts and the use of thermometers can be characterised as being geographically very dispersed.

Roughly around half of the mercury used in thermometers for the EU market is for

laboratory use, the other half for industrial and marine applications (Lassen et al., 2008). Lassen et al. (2008) estimated that around 0.6-1.2t/y is used in mercury-in-glass thermometers for the EU market, 0.1-0.3 t/y in mercury dial thermometers, and 0.01-0.1 t/y in psychrometers, which gives a total use of mercury in thermometers for the EU market of around 0.7-1.6t/y. The remaining (professional) uses of mercury room thermometers and other meteorological applications might not be included in this estimate, but are thought to be relatively small. It has not been possible to obtain information on the volumes for these applications during the preparations and consultations carried out for this report.

The following gives a general qualitative description of potential release and exposure from the pool of thermometers that were brought on the market in the past and are currently still in use.

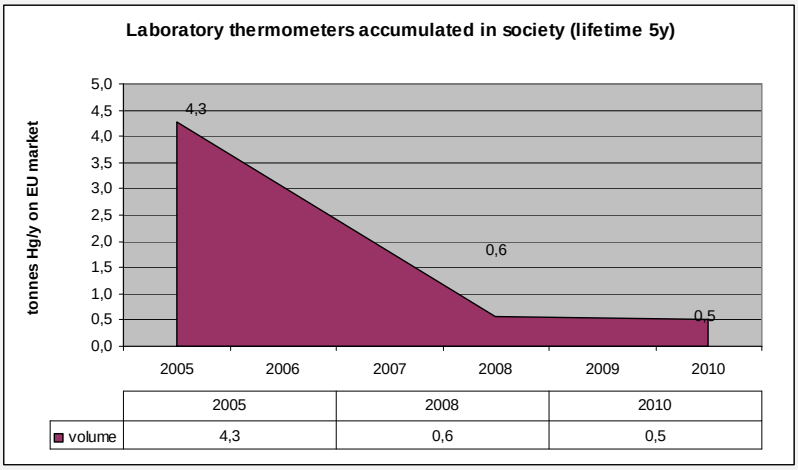
Based on estimates reported by Lassen et al. (2008), the volume of mercury that is included in non-fever thermometers[71] for the EU market in 1995 was estimated to be 28t/y (out of 55 t/y in measuring devices).

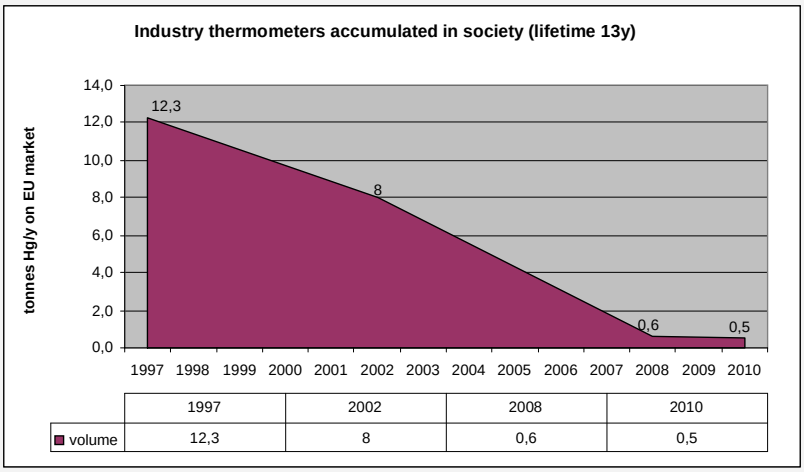
In 2002, the amount of mercury placed on the market in mercury containing measuring devices was estimated to be 33 t/y (EU 15+3). If the same proportions are applied to this figure as for the 1995 estimate, around 17t/y would have been placed on the market in non-fever thermometers. From 2008 onwards, the mean estimate of 0.7-1.6t/y is used for non-fever thermometers based on the estimations made by Lassen et al. (2008). Based on these figures, and assuming linearity between the above data points, the volume of mercury accumulated in industry thermometers is estimated to be 78 tonnes (lifetime of 13y[72]), in laboratory thermometers roughly 8 tonnes (lifetime of 5y), totalling to around **90 tonnes** in 2010 of mercury accumulated in non-fever thermometers. This is considerably more than the estimated volume of 40-100 tonnes for all measuring devices by Lassen et al. (2008). Lassen et al. (2008) used in the calculations a lifetime of thermometers of 5 years for all thermometers. If similarly a lifetime of 5 years would be used for industry thermometers in the above calculations, the estimated pool of mercury circulating in society would be 34 tonnes in 2010.

In addition to emissions from the waste phase (see below), mercury in glass thermometers for laboratory and industrial use easily break which results in emissions to the environment as well as direct human exposure (Lassen and Maag, 2006).

[71] Lassen et al. use the term 'medical thermometers' in stead of 'fever thermometers'. It is assumed that they are interchangeable in this context, since the authors write for example that 'mercury use in medical thermometers is now banned in the EU'.

[72] See assumptions for lifetimes in Annex 5b (Compliance cost calculations for thermometers).





Waste stage

As described in section B.4 of the main document, the waste phase is crucial for the potential releases of mercury to the environment (whether the mercury thermometers are collected separately from other waste streams and whether the separately collected devices are handled in accordance with hazardous waste legislation).

Partly the thermometer waste ends-up with unsorted municipal waste, another part is collected as hazardous waste. Lassen et al. (2008) estimated that only 20% of mercury containing measuring devices would be collected as hazardous waste. There does not seem to be evidence showing that this estimate would not be valid for thermometers, but it has to be noted that the figure is entailed with high uncertainty.

3. Available information on alternatives (Part C)

3.1 Identification of potential alternative substances and techniques

Alternatives are available for all applications of mercury-containing thermometers (Lassen and Maag, 2006). The following alternatives are described in this section:

- Mercury-free liquid-in-glass thermometers
- Gas or liquid dial thermometers
- Bi-metal dial thermometers
- Electronic thermometers
- Infrared thermometers

Mercury-free liquid-in-glass thermometers

The mercury-free liquid-in-glass thermometer is the most common replacement of the mercury thermometer at temperatures up to 250°C (Lassen et al., 2008). These thermometers are similar to mercury-in-glass thermometers, but use a different thermometric liquid.

The liquids typically used in mercury-free liquid-in-glass thermometers are organic liquids such as ethanol (ethyl alcohol), methanol, pentane, pentanol, toluene (toluol), kerosene, creosote, petroleum, i-amyl benzoate (isoamyl benzoate or isopentyl benzoate), and 'citrus-extract-based solvents' are reported to be used (Lassen et al., 2008) (Ludwig Schneider, 2010) (Amarell, 2005). To make the liquid more visible usually a red or blue dye is added. Product catalogues also refer to a blue-colored, organic, spirit fill (Trerice, 2010), or "eco-friendly, green filling, thermometer liquid and colour biodegradable", "red/blue special liquid" (Amarell, 2005), "non-toxic, mercury-free Blue Liquid" (Palmer Wahl, 2010).

The market share of these alternatives is unknown, and this information is not readily available. From a product catalogue it appears that the choice of liquid depends amongst others on the range of temperature measurement the liquid allows (Ludwig Schneider, 2010), and thus the market share is thought to be in part steered by the needs of measurement. Liquids are at least from the point of view of measurement range, to a certain extent interchangeable, for instance creosote and i-amyl benzoate[73] seem to have nearly the same measurement range (-40°C untill +210°C and -40°C untill +220°C respectively) (Ludwig Schneider, 2010).

Apart from organic liquids, also gallium or gallium alloys are used. Gallium has a very high liquid range, and compared to mercury has a low vapour pressure at high temperatures. Gallium alloy thermometers can be used in temperature ranges from 0 to 1200°C (Ludwig Schneider, 2010). Unlike mercury, liquid gallium metal is wetting. Wetting action of gallium-alloys can be overcome by covering the glass with a layer of gallium(III) oxide (Wikipedia, 2010a). Gallium is also used in Galinstan, an alloy of gallium, indium and tin, that is used in medical thermometers (Geratherm,

[73] CAS nr. 94-46-2, the substance has no harmonised classification.

2010). One company markets a maximum-thermometer for laboratory appliances with gallium filling for measurements up to 750°C (Amarell, 2010).

It is important to note that gallium thermometers are marketed for temperature measurements higher than 800°C, and/or for their exceptionally large measurement range (0-1200°C) (Appendix 3; Ludwig Schneider, 2010; Amarell, 2010). For these reasons, other technical reasons (precision and wetting of glass), and economic reasons (see Appendix 3), gallium is not considered to be a direct alternative to mercury in thermometers. In conclusion, gallium thermometers are normally used where mercury or other liquids would not be used.

Liquid-in-glass lab thermometers with a resolution up to 0.1°C and psychrometers with alcohol filling with a reading scale of 0.2°C exist in the market (Ludwig Schneider, 2010). A liquid-in-glass lab thermometer with organic filling, PerformaTherm™, has a resolution of 0.1°C and satisfies ASTM[74] standards (Lassen et al. 2008, and Lassen et al. 2010). Industry thermometers with "red/blue/green special liquid" fillings up to 360°C and a scale of 2°C exist on in the EU market (Amarell, 2005).

Liquid-in-glass thermometers are not only an alternative to mercury thermometers. They also complement mercury thermometers outside their measurement range (-58°C to +800°C). For low temperature, for example ethanol can be used, which has a melting point of -114°C (EC JRC, 2000a). For high temperature measurements, gallium fillings can be used. In addition, minimum thermometers are normally liquid-in-glass thermometers with organic filling (WMO, 2008). A producer markets meteorological precision minimum thermometers with alcohol filling, having a scale of 0.2 or 0.5°C depending on the needs (Ludwig Schneider, 2010).

Gas or liquid dial thermometers

Gas or liquid dial thermometers are similar to the mercury dial thermometers, but are filled with gas or liquid instead of mercury. Examples of such liquids are 'inert gas (non-toxic)', xylol (xylene), silicon oil, 'non-toxic, odorless, organic, and non-flammable liquid' (Trerice, 2010) (WIKA, 2010) (Palmer Wahl, 2010).

A producer offers capillary lengths up to 5 m for liquid filled remote systems, with liquid fillings both in "remote" and "rigid" (i.e. not remote) systems that can be used up to 500°F (260°C) (Palmer Wahl, 2010). The models in this catalogue have the same resolution whether they are actuated with mercury or with another liquid. According to Lassen and Maag (2006), such thermometers are available for measurements up to +600°C, which is confirmed by a product catalogue of WIKA, that offers "Gas Actuated Thermometers" within the ranges of -60°C to +600°C, scale spacing from 1 to 10°C according to the model, and capillary lengths according to user specifications.

Gas or liquid dial thermometers are direct replacements of mercury dial thermometers for temperature measurements from the lowest range up to +600°C. The resolution

[74] ASTM International (American Society for Testing and Materials) is one of the largest voluntary standards development organizations.

seems not to be affected (see above), but is anyhow not an important characteristic for the industrial applications where dial thermometers are used (Lassen et al., 2010).

Bi-metal dial thermometers

A bi-metal dial thermometer uses a bimetallic strip wrapped into the form of a coil. One end of the coil is fixed to the housing of the device and the other drives an indicating needle. The bimetallic strip converts a temperature change into mechanical displacement. The strip consists of two layers of different metals which expand at different rates as they are heated. The different expansions force the flat strip to bend if heated. (Wikipedia, 2010c)

Bi-metal thermometers are available for measuring temperatures in the range from about -70°C to 600°C (Lassen et al., 2008). Bi-metal thermometers have reading scales varying according to the model from 1 to 5 °C according to consulted product catalogues (WIKA, 2010) (Ludwig Schneider, 2010).

The dial thermometers have typically replaced mercury-in-glass thermometers for the temperature range above 250°C, e.g. for measuring the temperature of exhaust gases of diesel engines (Lassen et al., 2008), and are considered as replacements of mercury dial thermometers (Lassen et al., 2010). It is assumed that the authors refer to gas or liquid dial thermometers, as well as bi-metal dial thermometers.

Electronic thermometers

Electronic thermometers are also designated ‘digital thermometers’. The working of this group of alternatives is based on the thermoelectric effect, which is the conversion of temperature differences to electric voltage. The three main types – thermocouples; platinum resistance thermometers and thermistors – are described below. Electronic thermometers can be connected to a data logger via an analogue-to-digital converter.

Electronic thermometers are generally more accurate than mercury-containing thermometers, if properly calibrated (Lassen et al., 2008). Ripple and Strouse (2005) mention as advantages of electronic thermometers (platinum resistance thermometers, thermistors and thermocouples) possibly smaller measurement uncertainties, the ease of automation, the independence of the reading from the visual judgement of the user, and the absence of mercury. As disadvantages the need for a power source and somewhat higher initial costs are mentioned. Also higher calibration frequency, and thus higher recurrent costs could be mentioned as a disadvantage (see section 3.4 and Annex 5b). In addition mercury-in-glass and liquid-in-glass thermometers used below 150°C can be calibrated using the ice-point only, whereas platinum resistance thermometers (PRTs) and thermistors usually require a minimum of three calibration points.

Electrical thermometers with a digital display and/or automatic data logging make up an increasing part of the thermometer market. They are used throughout industry for

automatic temperature measurements, and use in laboratories is reported to represent an increasing part of the market in Denmark[75] (Lassen et al., 2008).

According to the World Meteorological Organisation electrical thermometers are in widespread use in meteorology. Their main virtue there is said to lie in remote indication, recording, storage, or transmission of temperature data. For soil temperature measurement, mercury thermometers are even regarded as unsuitable in comparison with electrical thermometers. (WMO, 2008)

Electronic thermometers approved by international insurance companies are marketed for refrigerated containers (Lassen and Maag, 2006).

1) Thermocouples
A thermocouple is made of two dissimilar metals joined so that a potential difference generated between the points of contact is a measure of the temperature. Thermocouples have a wide range from -270°C to 1800°C (MicroDAQ, 2010) and fast response time (under a second in some cases according to Burns Engineering, 2010).

Certain combinations of alloys have different sensitivities, and resulted in industry standard types such as K, S, R, E, J, and N thermocouples. Type K (chromel–alumel) is the most common general purpose thermocouple. Selection of the thermocouple type is driven by cost, availability, convenience, melting point, chemical properties, stability, and output (Wikipedia, 2010b).

2) Platinum resistance thermometers (PRTs)
An platinum resistance thermometer is a resistance temperature detector (RTD) that uses platinum for its element. Their function is based on the principle that electrical resistance of the metal changes in a predictable way depending on the rise or fall in temperature. The temperature range is -260 to 850°C (MicroDAQ, 2010).

The Pt100 sensor has a resistance of 100 ohms at 0°C and is by far the most common type of RTD sensor. The Pt500 sensor has a resistance of 500 ohms at 0°C and the Pt1000 has 1000 ohms resistance at 0°C (Omega, 2010). These thermometers are very accurate, and are used by laboratories accredited for calibration (Lassen et al., 2008). They are for example widely used for monitoring the temperature of foodstuffs during transport (Lassen et al., 2008). A very high precision system has a resolution of 0.001°C and a temperature range of -200 to +400°C. This device is marketed for process monitoring and production control in the chemical, pharmaceutical and food industries, as well as for research and development (Ludwig Schneider, 2010). On the internet the device is indicated to cost €980 (without VAT)

[75] Note that laboratory use is exempted from the Danish restriction of mercury thermometers, see section B.5

(Labnewsletter.com, 2010). The temperature sensor is available separately, and is provided with a DKD calibration certificate[76].

ASTM E1137 (Standard Specification for Industrial Platinum Resistance Thermometers) is a standard establishing physical, performance, and testing requirements, as well as resistance-temperature relationship and tolerances for metal-sheathed industrial platinum resistance thermometers (PRT) suitable for direct immersion temperature measurement (ASTM, 2010)

3) Thermistors
Thermistors also rely on the known variation of electrical resistance with temperature of a specially constructed resistor to convert temperature into a measurable electrical property, but unlike the above described PRTs the material used in a thermistor is generally a ceramic or polymer, in stead of metals (Wikipedia, 2010d). Thermistors have stabilities approaching a few thousandths of a degree Celsius per year, and are highly sensitive (approximately 4% change in resistance per degree Celsius). The typical temperature range is -80 to 150°C (MicroDAQ, 2010). However, the usable temperature range is limited to not more than 100°C for a single thermistor, and the maximum temperature of use is 110°C (Ripple and Strouse, 2005).

Infrared thermometers

Apart from the previously described electronic thermometers, infrared thermometers can be used to measure temperature in applications where conventional sensors cannot be employed. Infrared thermometers appear to have replaced mercury pyrometers (Lassen et al., 2008). An infrared thermometer is a non-contact temperature measurement device. The most basic design consists of a lens to focus the infrared (IR) energy on to a detector (thermocouple), which converts the energy to an electrical signal that can be displayed in units of temperature (Omega, 2010).

3.2 Human health and environment risks related to alternatives

In this section the human health and environment risks related to alternatives are described.

Mercury-free liquid-in-glass thermometers

For reasons explained in general part C, the risks as a result of organic liquids (such as alcohol, pentane, pentanol, toluene, kerosene, creosote, petroleum, i-amyl benzoate, and citrus-extract-based solvents) used in liquid-in-glass thermometers are

[76] The DKD Calibration Certificate documents officially the traceability of measuring results to national and international standards as required by the standards DIN EN ISO 9001 and ISO/IEC 17 025 for the monitoring of measuring instruments

in general considered to be low or insignificant, especially compared to the risks of mercury.

Gallium is also used in some thermometers, but as explained in section 3.1, these thermometers are not to be seen as direct replacements of mercury thermometers. However for the sake of completeness some considerations are given here shortly. Since gallium has a very low vapour pressure, exposure through inhalation is not considered relevant for thermometer users, and minimal during the production phase. Some cases of skin irritation might occur, but overall there are no indications that there would be considerable risks associated with gallium filled thermometers. See also Annex 4 for a description of the intrinsic properties of gallium.

Gas or liquid dial thermometers

Substances used in gas or liquid dial thermometers such as 'inert gas (non-toxic)', xylol (xylene), silicon oil, 'non-toxic, odourless, organic, and non-flammable liquid' are not considered to pose any considerable risks in comparison with mercury actuated systems.

Electronic thermometers

As described in general part C, the human health and environmental risks related to the use of electronic alternatives are insignificant in comparison with the potential emission and exposure associated with the amount of mercury in thermometers.

Bi-metal dial thermometers

Materials used for these articles are amongst others plastic, stainless steel, aluminium, anodized aluminium, galvanized steel, brass, nickeled metal, coatings, glass, silicone (Ludwig Schneider, 2010; Omega, 2010; Trerice, 2010). There are no indications of risks to human health or the environment related to the use of bi-metal dial thermometers (see also description on mechanical alternatives in general part C).

3.3 Technical feasibility of alternatives

An overview of the technical feasible alternatives to mercury thermometers is given in Table A5a-2. Alternatives exist for all applications of mercury-containing thermometers (Lassen and Maag, 2006). It is generally accepted that alternatives exist to all uses of mercury dial thermometers and mercury-in-glass thermometers at measuring resolution of 1°C and below 200°C (Lassen et al., 2008). Indeed, none of the producers of the thermometers consulted in the course of preparing this restriction report have indicated that mercury thermometers for measuring temperatures below 200°C at a resolution > 0.5 °C would be an essential use (Lassen et al., 2010).

Liquid-in-glass thermometers are in general fully suitable -and are the most common- replacement for all uses that do not require an accuracy better than 0.1°C, as long as the temperature measurements are below the 250°C range (Lassen et al., 2008) (Lassen et al., 2010). The maximum temperature of 105°C, response time, and separation of the liquid, have been mentioned as obstacles for the wide-spread use of the liquid-in-glass thermometer PerformaTherm™ (Lassen et al., 2008) (Lassen et al., 2010). Consulted companies have not given explicit technical reasons why gallium thermometers would not be technically feasible alternatives (Lassen et al., 2010).

Mercury dial thermometers used in the industry and marine applications can be replaced by gas or liquid dial thermometers or by bi-metal coil thermometers for all purposes. The producer Brannan (UK) claimed that mercury dial thermometers do not need to use mercury as an actuating medium, since alternatives exist (Lassen et al., 2008).

For laboratory thermometers that require measurements at 0.1°C or better, the alternatives are electronic thermometers (Lassen et al., 2008). For laboratory measurements that need high temperature measurements gallium or electronic thermometers can be used.

Room temperature thermometers, including Six's thermometers, can be replaced directly by liquid-in-glass alternatives (Lassen et al., 2008). This would also apply for the thermometers that are inside hydrometers. For meteorological applications that would require higher precision than 0.1°C, the situation is similar to laboratory thermometers.

Maximum thermometers were mentioned by one producer to be an essential use in the consultation ECHA carried out for preparing this restriction report (Lassen et al., 2010). However there is no known reason to treat them differently from other mercury thermometers that require high precision (Lassen et al., 2010), and are therefore not treated separately in the report.

According to a producer, electronic alternatives to psychrometers (hygrometers) could in '*some cases not be used because of the structure of their temperature and chemical resistant sensor housing*' (Lassen et al., 2010). According to Lassen et al. (2010), this seems not to be justified: psychrometers have been banned for many years in Denmark, and consulted calibrating laboratories were not able to identify any applications where it has been difficult to replace mercury psychrometers. Klif confirmed that placing on the market of psychrometers is prohibited in Norway. It seems that psychrometers have successfully been replaced in Denmark, Sweden and Norway without any reported problems (see section B.5).

In industrial settings a resolution of 0.1°C is generally not necessary (Lassen et al., 2010). For temperature measurements above 200°C at a resolution of 1°C, dial thermometers with coiled bimetal or a liquid or air filled metal cylinder with a dial for manual reading are available (Lassen et al., 2008).

According to the Commission's review (Appendix 5), a company would have defended the use of mercury in a limited number of highly specialised professional

uses, such as retort[77] thermometers in the canning industry (Appendix 5). However, several producers offer electronic alternatives for retort thermometers, such as "Palmer Wahl DST600" (Palmer Wahl, 2010), and "Digital Temperature Gauge for Retort Applications" (Anderson, 2010). In addition bi-metal thermometers can be used in the canning industry (Omega, 2010).

Mercury heat indicators and other non-electrical thermometric applications

Producer AGA Rangemaster Limited informed ECHA that it has alternative solutions in place for its mercury heat indicator in their *electric* ovens. The producer says there are no known alternatives for the heat indicator for ovens that operate *without electricity*, and function on gas or oil. It is also said that the area where the heat indicator is located would be 'far too hot for an electronic solution'. In addition, supply of replacement parts for existing devices are mentioned as an obstacle. The producer indicated that to date suppliers have been unable to provide a high temperature infill which lasts more than 4 months, although they would have samples on trial. Producer AGA Rangemaster Limited estimates a need of 12 months for substitution of the mercury heat indicator with alternatives in new devices. (AGA Rangemaster, pers. comm., 2010)
On the basis of this information it is understood that there will be feasible technical alternatives available before the potential entry into force of a restriction.

There are no known technical feasible alternatives to mercury triple point cells for calibration of platinum resistance thermometers. As described in section 1 it is one of the elements *defining* the 1990 International Temperature Scale (ITS-90). The Dutch mercury restriction has a derogation for "*equipment for the calibration of platinum resistance thermometers using the triple point of mercury*" for these reasons.

Based on the available information it is concluded that there are technically feasible alternatives available for the minor use of mercury in mercury heat indicators, and possible other non-electrical thermometric applications. It would not be technically feasible to restrict the use of equipment for the calibration of platinum resistance thermometers using the triple point of mercury.

[77] Retort: A retort is a machine similar to a domestic pressure cooker, where batches of cans are heat processed under pressure. The retort has temperature and pressure gauges and should also have temperature / time recording charts. (http://www.cip.ukcentre.com/keywords.htm#R)

Table A5a-2 Overview of the technical feasible alternatives to mercury thermometers

Application area & product type	Alternatives	Applicability	remarks
Mercury-in-glass thermometers *(T range -58℃ to +800℃ and accuracy up to 0.01℃ for high precision thermometers)*			
For laboratory use, including industry labs for material testing (precision and high precision thermometers). Reading scale Hg thermometer up to 0,01℃	Liquid-in glass thermometers	T range <250℃, accurac y 1℃, and up to 0,1℃	Typically replace mercury-in-glass thermometers for T-range < 200℃, where accuracy >0,1℃ is not required
	Gallium thermometers	T-range 0-1200℃, accuracy 5℃ or 2℃ (possibly more accurate as well)	Seems to be a niche market for economical and it appears also technical reasons. Seems to be used as a very wide range thermometer
	Electronic thermometers	More accurate than Hg in glass, very large T range (-200 to 1800℃), resolution 0.1℃ (or better)	Advantages are data recording and remote reading. Might replace many mercury thermometers.
	High precision electronic thermometers	Resolution up to 0.001℃, T range -200 to +400℃	Higher resolution than high precision Hg-in-glass thermometers. Might replace many mercury thermometers.
For industrial use. Reading scale Hg thermometer usually 1-5℃, sometimes 0,5℃	Liquid-in glass thermometers	T range <250℃, accurac y 1℃	Typically replace for T-range < 200℃
	Dial thermometers	T range -70℃ to +600℃, accuracy 1℃	Replacement for T-range > 200℃, also used as a mechanical back-up for electronic thermometers
	Electronic thermometers	More accurate than Hg in glass, very large T range (-200 to 1800℃), resolution 0.1℃ or better	Accuracy higher than 1℃ is normally not an issue for industry thermometers. Reasons to choose electronic thermometers might be: data logger, possibilities for remote reading, real-time monitoring & feedback mechanisms, alarm systems,…
Meteorological measurements and room temperature measurement. Reading scale of Hg meteorological thermometers usually not smaller than 0,2℃.	Liquid-in glass thermometers	Accuracy 1℃, and up to 0,2℃	All room temperature thermometers and Six's thermometers, and most if not all other meteorological applications such as psychrometry, can be directly replaced by LiG thermometers.
	Electronic thermometers	Resolution 0.1℃ (or better)	Data recording and remote reading. Widespread use in meteorology. For soil temperature much better than mercury thermometers.
Mercury dial thermometers (5-200g Hg/piece)	Dial thermometers	T range -70℃ to +600℃, accuracy 1℃	Replacement for T-range > 200℃, also used as a mechanical back-up for electronic thermometers
	Electronic thermometers	More accurate than Hg in glass, very large T range (-200 to 1800℃), resolution 0.1℃ or better	Data logger, possibilities for remote reading, real-time monitoring & feedback mechanisms, alarm systems,…
Mercury heat indicators (approximately 1.8g Hg/piece)	other liquids or other systems		Producer AGA Rangemaster Limited estimates a need of 12 months for substitution of the mercury heat indicator with alternatives in new devices
Mercury triple point cells used for calibration of platinum resistance thermometers	none		Application is prescribed in the 1990 International Temperature Scale (ITS-90)

Standards prescribing the use of a mercury thermometer

Analysis standards often list equipment and techniques to be used, and step-by-step instructions how to use the equipment. Such analysis standards might specifically refer to the use of mercury thermometers, and might therefore constitute a practical obstacle for using alternatives to the mercury thermometers in laboratories.

These references to mercury thermometers in *analysis standards (test methods)* can be made in the form of references to a certain specific *technical standard (technical specification)* of a mercury thermometer. Technical standards are defining technical specifications including accuracy and dimensions. They play an important role for production and choice of industrial as well laboratory thermometers. An example of such a technical standard is ASTM E1 - 07 Standard Specification for ASTM Liquid-in-Glass Thermometers[78].

According to Ripple and Strouse (2005), many hundreds of ASTM test methods would rely on mercury-in-glass (ASTM E1) or liquid-in-glass thermometers (ASTM E1 for low accuracy and E 2251 for high accuracy[79]).
In addition, according to information from one producer, 60 to 80 %, and in some sectors nearly a 100% of thermometers used in laboratories would be used for measurements where procedures prescribe standard thermometers (Lassen et al., 2010). The latter does not imply that these standard thermometers are mercury thermometers.

Although traditionally many standards have prescribed mercury thermometers in analysis, many standards now allow for the use of alternatives (Lassen et al., 2010)[80]. Standards for testing in the petrochemical sector in general allow for electronic devices to be used, and automatic equipment is available for most tests (Lassen et al., 2010). An example of this is flash-point determination where standards often have been cited to prescribe mercury thermometers. In fact, currently the standards fully allow for the use of electronic alternatives (at least all ISO and ASTM standards), and in fact it seems that at least in Germany the use of automatic apparatus for flash point determination is common practise (Lassen et al., 2010).[81]

[78] ASTM International is a major standardisation organisation.

[79] ASTM E1 is a technical standard for mercury thermometers, and low-precision liquids. ASTM standard E2251 - Specification for Liquid-in-Glass ASTM Thermometers with Low-Hazard Precision Liquids, has a list of thermometers with alternative liquids that can replace some of the mercury thermometers specified in ASTM standard E1, Specification for ASTM Liquid-in-Glass Thermometers.

[80] Relevant standards for materials' testing are developed by ISO, CEN, ASTM, DIN and IP/BS (Lassen et al., 2010). The focus here is on ASTM because most of the available information describes ASTM standards (Lassen et al., 2010 and ASTM International (2010)). ISO and CEN appear to develop standards together, at least in the area of flash point determination (Lassen et al., 2010).

[81] **This footnote was added due to a comment received in the public consultation on draft opinion of SEAC.** During the preparation of the original restriction report an industry consultation was carrried out by Lassen et al. (2010) (see Appendix 3). A manufacturer of thermometers proposed a derogation amongst others for "all thermometers whose range exceeds 200°C". One of the justifications given for the derogation is that "both non-mercury glass thermometers and electronic thermometers can lead to much slower response and to erroneous and incorrect evaluations of measurement results". Furthermore, during the public consultation on the draft opinion of SEAC, a comment was received claiming that electronic thermometers "… have a much slower reaction-time, which can lead to wrong

Three cases of analysis standards that still would prescribe the use of mercury thermometers were identified in the course of the information gathering and consultations by Lassen et al. (2010):

- method A1 "Melting/freezing temperature", in the Test Method Regulation (Regulation (EC) No 440/2008) would specify technical standards for thermometers that require mercury;
- Regulation (EC) No 1031/2008 requires testing according to the Abel-Pensky method which is specifically defined as DIN 51755, a national standard for flash point; and
- a drop point apparatus with a mercury thermometer is described in the European Pharmacopoeia 5.0 from 2005.[82]

Concerning Regulation (EC) No 1031/2008, it seems sufficient that the standard DIN 51755 (from March 1974) would be amended (if that has not yet happened). Note that this Regulation is amending Council Regulation (EEC) No 2658/87 on the tariff and statistical nomenclature and on the Common Customs Tariff. Amendment of the relevant annex to this Regulation (Annex I) occurs several times a year.

Regarding the CLP Regulation (Regulation (EC) No 1272/2008), it seems sufficient that the standards that are mentioned for flash point testing (Table 2.6.3 of the CLP Regulation) would be updated where required, without the need to amend the Regulation itself.

According to ASTM, there would still be many standards referring to the use of a thermometer according to ASTM standard E1 or call out the usage of a mercury thermometer (ASTM, pers. comm., 2 June 2010). However this does not necessarily mean that the standard does not allow for alternatives to be used. As examples of standards that call out for the usage of a mercury thermometer, ASTM mentioned D97, D566, D938, D972 and D2595 (ASTM, pers. comm., 14 June 2010).

ASTM standards have to be reviewed every 5 years, but can be updated at any time. Since the start of the mercury initiative of ASTM in 2006, ASTM International is working to identify industrial standards and test methods that require the use of mercury thermometers in order to determine whether the use of alternatives is feasible

evaluation of measuring results". Evidence is available that the reaction time for other liquid-in-glass thermometers is signicantly slower than for mercury-in-glass thermometers. However, no evidence has been found that this statement would apply to electronic thermometers. On the contrary, evidence such as the response times of the high temperature electronic alternatives of one second (Amarell 2011) compared to available response times of several minutes for mercury-in-glass thermometers (Miller & Weber 2011) indicates that a slow reaction time is not an issue. In addition, the response times of electronic fever thermometers have been reported to be faster than for the mercury devices (Ng et al., 2002). However, the reaction (including response time) of electronic thermometers is different from mercury-in-glass thermometers, which can make comparison of measurement results difficult (see discussion on measurement bias further in the text).

[82] **This footnote was added after the public consultation on the draft opinion of SEAC.** According to the German "Apothekenbetriebsverordnung – ApBetrO" from 1987, each pharmacy needs to have a basic set of equipment for getting a licence to operate. According to Annex 1 to ApBetrO, a set of seven mercury-in-glass thermometers is required. However, technically equivalent mercury-free alternatives are available and could be allowed instead for the use in pharmacies.

(ASTM 2010). This action is supported by the US EPA initiative to phase-out mercury thermometers used in industrial and laboratory settings (US EPA 2010).
Where removal of the reference or requirement from an ASTM standard was relatively straightforward, changes have been completed (ASTM, pers. comm., 2 June 2010). Reasons for cases where this has not yet happened can be because of a lack of industry support for the change; lack of testing for a suitable replacement; and needs for new interlaboratory studies (costs and time associated with it and lab participation) (ASTM, pers. comm., 2 June 2010).

As ASTM points out, although electronic alternatives might be preferable because of their higher accuracy, there might be issues of bias between temperature readings from electronic thermometers in comparison with mercury thermometers: *"Most electronic thermometers considered as alternatives are minimally or not at all affected by emergent stem temperature. Therefore, in this type of test method, as in many ASTM test methods, the use of an alternative temperature measurement device may provide more accurate temperature measurements but may not reproduce the previously accepted values of the test method."*(ASTM, 2009). Because of these reasons, there is a need for research comparing data obtained with an alternate device of well-defined geometry and construction and the specified mercury-in-glass thermometers with samples of the same test material. The ASTM subcommittee E20.05 will determine effects on charts, data, and precision & bias statements (ASTM, 2009).

Information that ECHA has received from Denmark, the Netherlands and Norway in early 2010 shows that current national restrictions on mercury thermometers foresee exemptions for mercury thermometers where analysis standards prescribe a mercury thermometer (see section B.5). This information is to a certain extent supportive to the evidence that standards would constitute a technical obstacle.

Sweden seems to be an exception. With regard to CEN and ISO standards, Sweden has not implemented standards that prescribe the use of mercury measuring devices since 1998 (KemI, 2004). According to information received from the Swedish Chemicals Agency (KemI), the only remaining exemption on mercury thermometers is issued for flash point determination according to Directive 67/548/EEC, which was granted in 2007 and will expire on the 30th of June 2011.

Conclusions on technical feasibility of alternatives

For all known applications, there are technically feasible alternatives that can replace all mercury thermometers and other non-electrical thermometric devices using mercury, with the exception of

- **thermometers used for testing according to analysis standards (test methods) that prescribe mercury thermometers, and**
- **mercury triple point cells that are used for the calibration of platinum resistance thermometers.**

For AGA heat indicators, technically feasible alternatives are estimated to be available well before the entry into force of the proposed restriction.

This conclusion is supported by the conclusion of the US National Institute of Standards and Technology (NIST) that there are no fundamental barriers to the replacement of mercury thermometers. NIST and US EPA are collaborating to resolve difficulties in using alternative thermometers in certain elevated temperature applications, such as autoclave operations and asphalt processing. However, some Federal and State Regulations contain requirements to use mercury thermometers either directly or through citations of standards and methods from organizations such as ASTM International and the American Petroleum Institute (API). The US EPA is taking steps to revise its regulations to allow non-mercury alternative thermometers. In addition, US EPA is working with ASTM International and the API to revise their standards to include flexibility allowing non-mercury alternatives. (US EPA, 2011)

3.4 Economic feasibility

The analysis of economic feasibility builds on the technical feasibility of alternatives, and on the compliance cost calculations for thermometers that are presented in Annex 5b.

Both mercury thermometers and their alternatives have variable properties – even within each market segment. The best endeavour is made to compare mercury containing devices with alternatives that have similar technical properties for each of the main market segments. Factors that seem to influence the price of mercury thermometers and their alternatives are accuracy, temperature range and level, compliance with standards, calibration certification, and suitability to measure temperature in adverse environmental conditions. For electronic alternatives also additional features and optional interfaces can be added to this complexity of elements influencing the price of a particular thermometer. The combinations of all factors results in a substantial price diversity of thermometers. Therefore, the analysis of economic feasibility (including compliance costs calculations in Annex 5b) is based on what is considered by producers to be a "typical mercury containing thermometer" and a "typical alternative thermometer" taking into account all available information, in particular from Lassen et al. (2008) and Lassen et al. (2010).

The price of liquid-in-glass thermometers is roughly the same as for mercury thermometers. For this reason, and because of the many common technical properties, liquid-in-glass thermometers are the most common replacement for mercury thermometers up to 200°C and with resolution not better than 0.1°C (Lassen et al., 2008 and Lassen et al., 2010). They can directly replace mercury room temperature thermometers (Lassen et al., 2008). Gallium thermometers are reported to have a low market share, which seems to be related to their (higher) price (Lassen et al., 2010). They are not further considered in the assessment.

Prices of the electronic alternatives are higher than mercury thermometers. However, the electronic devices have additional features such as automated temperature recording, alarm systems, real-time process monitoring and feedback systems[83]. Thus,

[83] Amongst additional features are higher precision and automation offered by electronic thermometers. These advantages can result in additional savings in industrial applications, e.g. lower operational costs due to the use of less energy to, for example, heat large industrial volumes to a certain temperature.

the prices cannot be compared directly. In fact, the advantage of electronic reading for example is one of the drivers for replacing mercury thermometers with electronic devices. Due to the additional features customers are willing to pay a higher price for the electronic devices (Lassen et al., 2010). No information is available to quantify the value of these additional features and to deduct it from the investment costs of the electronic alternatives. Therefore, the costs associated with the transitioning from a mercury thermometer to an electronic alternative are likely to be overestimated.

The users of analysis standards that prescribe mercury thermometers might have to pay an additional cost for a standard update originating from a restriction (a restriction would require standards to be amended in order to allow for the use of non-mercury alternatives, see also section 3.3). It seems that the cases where an update would be a direct result from a restriction would be limited. It is not considered possible to estimate the compliance costs related to the purchase of standards, but it is thought that the additional cost for the lab thermometer market segment would not be substantial[84].

A problem that has been mentioned is the need for modification of existing equipment, also called retrofitting (Lassen et al., 2010)[85]. On the basis of the available information, it was concluded that usually the effect on the investment costs would be negligible. See Annex 5b for a more detailed discussion.

The economic feasibility of the following main market segments are discussed in this section: laboratory thermometers, industrial thermometers, and thermometers for meteorological measurements.

Laboratory thermometers

Mercury-free liquid-in-glass lab thermometers are one of the most common replacements for mercury-in-glass thermometers used to measure temperature below 200°C in applications where high precision is not needed. Their price is roughly the

Automatic reading and data storage are likely to reduce the need for labour due to less time spent to collect temperature readings manually and additional savings associated with reducing human reading errors. Automated temperature feedback mechanisms might result in higher efficiency of reactions, or to a better quality of the end-product. Temperature alarm systems (and to a certain extent automated temperature feedback mechanisms) might substantially reduce the risks of damage. All these benefits may have substantial value, however, whether these additional functions are of importance depends on the application (see also Annex 5b).

[84] It is unknown how many standards would actually prescribe mercury thermometers to be used, and therefore it is not known how many standards would have to be changed as result of a restriction. Considering the difficulty in identifying standards that would *prescribe* mercury thermometers during the information gathering and consultations carried out in the course of preparing this dossier, it is thought that the amount would be limited. When a new version of a standard is published, customers need to purchase the entire standard again, but note that one analysis standard is likely to cover several thermometers in one lab (ASTM standards vary in price from $34 to $120 USD each (ASTM, 2010, pers. comm.)). However, in so far a standard is updated during the normal update process it is thought there would be no additional cost that can be attributed to a restriction. In the case of ASTM standards that are already in the process of being modified under the mercury initiative, it would be difficult to argue if, and to what extent, an update would result from a restriction in the EU.

[85] This is considered to be an economical issue rather than a technical feasibility issue since it seems that these modifications can always be carried out (at a certain cost).

same as for mercury thermometers or about 10% lower (Lassen et al., 2010). In the main scenario used for laboratory thermometers in this segment, investment costs are assumed to be the same. However, the operating costs for the liquid-in-glass thermometers would be lower due to their assumed lower waste treatment costs in comparison to their mercury-containing counterparts. Table A5a-3 shows that the lower operating costs would result in savings of €2.6 per year for each liquid-in-glass thermometer compared to a mercury-in-glass lab thermometer in this market segment. Therefore, liquid-in-glass thermometers are an **economically feasible alternative** to the mercury-containing devices when measuring temperature **below 200°C** in applications where **high precision is not needed**.

Table A5a-3 also shows the costs for mercury-in-glass thermometers used in laboratories where an **accuracy of 0.1°C or better** is needed **or** for temperature measurements **above 200°C**. The purchase price of an electronic system is higher than their mercury counterparts. However, as it is assumed that mercury thermometers can be replaced by 60% fewer electronic alternatives, the analysis concludes that laboratories would pay €3 (i.e., 4%) more per year to replace each mercury containing device. Calibration frequency of mercury thermometers is considered to be once every two years – twice more frequent that industrial thermometers due to the higher precision needed, while the electronic alternatives are assumed to be calibrated annually similar to the assumptions made in the industrial segment. The life-times are considered to be similar. In sum, electronic thermometers are an **economically feasible alternative** to the mercury-containing devices in this market segment.

Table A5a-3: Costs of mercury containing thermometers and their alternatives in laboratory applications[86]

	Lab (res >0.1°C and T<200°C)		**Lab** (res 0<.1°C or T>200°C)	
Device Costs (€)	**Mercury-in-glass**	**Liquid-in-glass**	**Mercury-in-glass**	**Electronic**
Investment cost	40.0	40.0	80.0	180.0*
Lifetime of device (years)	5	5	5	5 (10)**
Annualised investment cost	9.0	9.0	18.0	31.9
Recurrent costs	27.0	24.4	52.9	41.9
Annualised total cost	**35.9**	**33.7**	**70.9**	**73.8**
Additional annualised total cost	0.0	-2.6	0.0	2.9

Source: Tables 1-4 and 7-10 in Annex 5b

Notes: * The investment cost for electronic thermometers is much lower than the purchase price of a full measurement set because of the assumption that 60% fewer electronic alternatives can replace mercury-in-glass thermometers.

**5 years for the probe and 10 years for the data reader.

[86] The costs in the analysis represent factory gate prices excluding VAT for investment costs, but for other costs (recurrent costs) it is not known if the VAT is included or not. All values used in this analysis refer to year 2010 price levels.

Industrial thermometers

In the market segment of industrial mercury-in-glass thermometers measuring temperatures **below 200°C**[87], mercury-free liquid-in-glass industrial thermometers cost somewhat less than mercury-containing devices. Table A5a-4 shows that the transition to liquid-in-glass thermometers will result in annual savings to users (assuming that the waste treatment costs of the alternatives are lower than the mercury-containing devices). Thus, in this market segment there **are economically feasible alternatives**.

Mercury-in-glass thermometers used in industry to measure temperature **above 200°C**, can be replaced by electronic or mercury-free dial thermometers. When excluding the labour time savings, the additional annualised costs for users of the alternative are about €98 per device[88]. Since the electronic alternatives offer the advantage of automation, thereby reducing the need for an individual to visually verify the temperature, the cost calculations were refined to reflect labour time savings. The additional annualised costs per device are €13 ±€42[89] per annum per device, including labour time savings (Table A5a-4).

The calibration costs and calibration frequency of the alternative devices have a major impact on the costs. These factors are uncertain and it is thought that there are differences between the recommended calibration frequency and the real frequency in practice. The analysis in Annex 5b assumes that alternatives have a four times higher calibration frequency. In the extreme case, when calibration costs are ignored and labour time savings are taken into account, the annualised *savings* per electronic device are €61. When both calibration costs and labour time savings are ignored, the additional annualised costs would be lower, i.e. €23.3 and €40.2 per device per annum for respectively the electronic and mercury-free dial thermometers[90].

In addition, the economic impact of the transition to alternatives on users of industrial mercury thermometers measuring temperature above 200°C will be relatively small because:

- the additional annualised costs associated with the transition to the alternatives are estimated to be a small percentage of the users' total costs for purchases of goods and services;[91]

[87] Precision is not a critical characteristic for industrial thermometers, see section 3.3.
[88] There are a number of reasons why the transition to alternatives in the high resolution/T>200°C lab segment is more cost-effective than the industry segment over 200°C. The main factors include: the lower long-term investment cost of the alternative due to the assumption that mercury lab thermometers can be replaced by fewer electronic alternatives; and the shorter lifetime (5 years in lab instead of 13 years in industry) that is equal for both mercury and alternative lab thermometers (see Annex 5b).
[89] Labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are assumed.
[90] The mercury-free dial thermometers are in this case more expensive due to their short life-time
[91] As an illustrative example, the additional annualized total cost of €13 per thermometer can be compared to the total purchases of goods and services (TPGS) for high volume users of industrial thermometers measuring temperature over 200°C, e.g., manufacturing companies. In the EU-27, the average TPGS for a manufacturing company was €2.3 million (TPGS and number of enterprises, Eurostat, 2007). Assuming that a manufacturing company in the EU-27 purchases between 1 and 100

- the measurement costs overall do not represent a substantial portion of the total production costs; therefore, the additional annualised costs due to the transition to the alternative are expected to contribute only marginally to the final product cost and thus, are not expected to lead to (sizeable) price increases to consumers downstream;
- the alternatives have additional benefits over the mercury-containing devices which were not fully taken into account in the cost calculations:
    - cost savings due to lower spill cleanup costs[92];
    - cost savings due to avoidance of contamination of batch with mercury upon breakage;
    - other potential benefits in addition to reduced labour time savings, e.g., increased accuracy of process control;
- alternatives have already taken over the market for industrial thermometers (Lassen et al., 2008) and the majority of users are no longer heavy users of mercury-containing devices.

It can be concluded that the alternatives to industrial mercury-in-glass thermometers measuring temperature over 200°C can also be considered economically feasible. This is due to the fact that the possible additional annual costs associated with the transition to the alternatives are estimated to be a small outlay in comparison to other expenditures on goods and services of users of these thermometers. Consequently, these additional expenditures will not lead to significant price increases of the final goods or services produced by the users of these thermometers.

non-mercury thermometers every five years (the lifetime of the cheaper alternative), the additional total costs associated with the use of the alternatives (€13 – €1,300) are estimated to be between 0.0006% and 0.06% of the average TPGS per manufacturing company. Two other sectors were also analysed – the mining & quarrying and electricity, gas & water supply industries – which are also estimated to be high volume users of thermometers measuring temperature over 200°C. The share of the additional annualised total cost of €13 (or €98 if labour cost savings are taken into account) per thermometer represents even smaller percent of the TPGS per enterprise in these sectors.

[92] Although specific estimates for spill cleanup costs for thermometers have not been obtained, the following estimates for sphygmomanometers can assist the reader to put the costs in perspective: €400 clean up cost per spill (cost of spill kit, person-hours, spill area closure and cost of downtime, waste disposal, etc.), and €30 per sphygmomanometer for staff training on spill response. (Concorde East/West 2009)

Table A5a-4: Costs of mercury-in-glass thermometers and their alternatives in industrial applications[93]

Device Costs (€)	Industry (T<200°C)		Industry (T>200°C & Dial)		
	Mercury-in-glass	Liquid-in-glass	Mercury-in-glass	Mercury-free Dial	Electronic
Investment Costs	22.5	22.5	45.0	125.0	134.2
Lifetime of device (years)	13	13	13	3	5
Annualised Investment Costs	2.3	2.3	4.5	45.0	26.0
Recurrent Costs					
- excluding labour time savings	28.6	27.8	28.6	85.6	104.7
- including labour time savings	28.6	27.8	28.6	85.6	20.4
Annualised Total Costs					
- excluding labour time savings	**30.9**	**30.0**	**33.1**	**130.6**	**130.7**
- including labour time savings	**30.9**	**30.0**	**33.1**	**130.6**	**46.4**
Additional Annualised Total Costs					
- excluding labour time savings		-0.8		97.5	97.6
- including labour time savings		-0.8		97.5	13.2

Source: Annex 5b

Mercury dial thermometers used in industry can be replaced by electronic or mercury-free dial thermometers. In the absence of information, the costs of mercury dial thermometers and their alternatives are assumed to be the same as the mercury-in-glass industrial thermometers for measuring temperatures above 200°C (Table A5a-4). The reported figures do not include labour time savings resulting from the use of electronic alternatives, but since the figures are the same as for mercury-in-glass thermometers, the additional annualised cost including labour time savings would also drop from €98 to €13 (in the 2010 price level). Mercury dial thermometers are confirmed by producers to hold only a very limited residual market because alternatives have taken over (Lassen et al., 2008), and no consulted producers have mentioned that alternatives to dial thermometers would not be economically feasible (Lassen et al., 2010). The economic importance of mercury dial thermometers is thought to be marginal[94].

[93] The costs in the analysis represent factory gate prices excluding VAT for investment costs, but for other costs (recurrent costs) it is not known if the VAT is included or not. All values used in this analysis refer to year 2010 price levels.

[94] In addition, because the market of these thermometers was known to be marginal, minimal effort has been given to better estimate costs and life-times of these devices. Therefore the data from mercury-in-glass thermometers was used. It has to be emphasised that the cost estimate is conservative in several ways. The assessment used a conservative estimate of a lifetime of 13 years for mercury dial thermometers vs. three years for gas or liquid actuated dial alternatives, and a yearly calibration of the alternatives vs. once every 4 years for the mercury dial thermometer. It seems however that the technology of the mercury dial thermometers gas or liquid actuated dial alternatives is not very different, and in reality the lifetimes and calibration frequencies might be equal or similar (analogue to the situation of mercury-in-glass and liquid-in-glass alternatives). Assuming that the mercury dial thermometers have the same lifetime and calibration frequency as their gas-actuated alternative systems (and ignoring labour time savings), the additional annualised total cost would be €24.30 (for mercury-free dial) and €24.40 (electronic) instead of €97.5/ device and €97.6/ device respectively.

For these reasons it can be concluded that the alternatives to mercury dial thermometers can be considered economically feasible.

Thermometers for measuring ambient temperature and other meteorological measurements (including Six's thermometers and psychrometers)

The transition from mercury-containing to mercury-free ambient thermometers, psychrometers (hygrometers), and most other thermometers for meteorological applications, is expected to result in additional annualised savings, similar to mercury-in-glass lab and industrial thermometers for measuring temperature below 200°C and with a resolution not better than 0.1°C. This is likely to take place due to the following reasons:

- the price of the liquid-in-glass alternatives in ambient temperature is similar to the mercury-containing thermometers (no resolution <0.1°C needed);
- Six's thermometers with organic liquids are available at similar or lower prices than the mercury filled counterparts (Lassen et al., 2010);
- electronic or spirit-filled psychrometers are available for most applications at approximately the same price as mercury psychrometers (Lassen et al., 2010);
- it costs less to dispose of a mercury-free device at the end of its useful life;
- the calibration frequency and costs of the mercury and liquid-in-glass devices are similar; and
- the lifetime of the mercury and liquid-in-glass devices is similar.

Therefore, it can be concluded that alternatives to mercury thermometers for measuring ambient temperature and other meteorological measurements (including Six's thermometers and psychrometers) are economically feasible.

Conclusions on economic feasibility of alternatives

It is concluded that the alternatives for all laboratory thermometers, mercury dial thermometers, industrial mercury-in-glass thermometers for measuring temperature below 200°C, and thermometers for measuring ambient temperature and other meteorological measurements are economically feasible.

The analysis of the market segment of industry mercury-in-glass thermometers measuring temperature over 200°C showed that the transition to non-mercury containing alternatives will induce approximately €97.5 additional annualised total cost per device, or when the assessment is refined by including the labour time savings, approximately €13±42[95] per annum per device. Possible additional annual costs associated with the transition to the alternatives are estimated to be a small outlay in comparison to other expenditures on goods and services of users of these thermometers. Therefore, it can be concluded, although with less certainty than the other market segments, that **the alternatives for industry mercury-in-glass thermometers measuring temperature over 200°C are economically feasible.**

[95] Labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are assumed.

4. Justification why the proposed restriction is the most appropriate Community-wide measure (PART E)

4.1 Identification and description of potential risk management options

4.1.1 Risk to be addressed – the baseline

As described in section B.2, the total estimated amount of mercury placed on the market in measuring devices containing mercury is used to describe the maximum potential for mercury emissions to the environment that might ultimately occur.
In 2007, between 0.7-1.6 tonnes of mercury was placed on the market in the EU in new thermometers (Lassen et al., 2008). Based on the declining trend in the thermometer market, as described in Box 1 in section 2 of this annex, it is assumed that without additional legislative action the European market of mercury thermometers will decline by about 5% annually. Thus, in 2010 this would result in a volume brought on the market of 0.6-1.5 tonnes. For the purposes of the analysis of the baseline of thermometers, it is assumed that the mid-point, i.e. 1 tonne, will be placed on the market in 2010 and that this amount will decline by 5% annually. Table A5a-5 and Figure 5a-1 give the baseline for thermometers. In addition, the accumulated amount in the years 2015-2034 is presented in Table A5a-5 for use in section 4.2.

Although not the primary concern, it is worth mentioning that direct exposure of workers can occur during production, professional/industrial use of thermometers and during waste management operations.

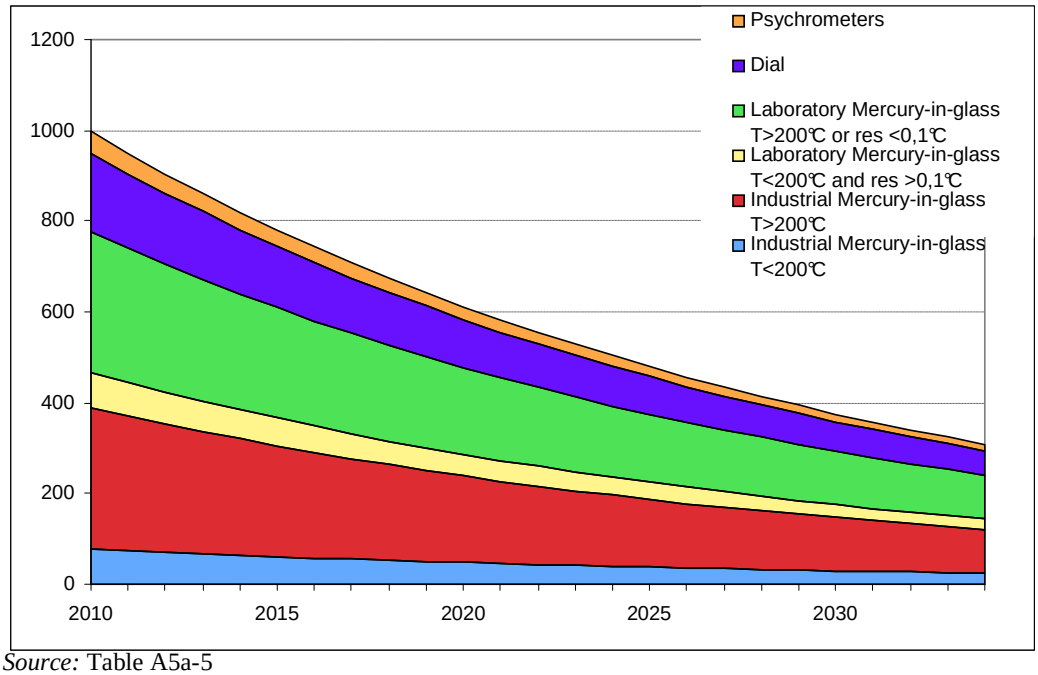
Table A5a-5: Estimates of the amount of mercury placed on the market each year in mercury containing thermometers for 2010-2034 - Baseline assumptions (kg per year)

Year	**Thermometer type**						*Total*
	Industrial			***Laboratory***		***Psychro-meters***	
	Mercury-in-glass		*Dial*	*Mercury-in-glass*			
	T<200° C	*T>200° C*		*T<200°C and res >0,1°C*	*T>200°C or res <0,1°C*		
2010	78	311	173	78	311	48	998
2011	74	296	165	74	296	45	950
2012	71	282	157	71	282	43	905
2013	67	269	149	67	269	41	862
2014	64	256	142	64	256	39	820
2015	61	244	135	61	244	37	781
2016	58	232	129	58	232	35	744
2017	55	221	123	55	221	33	708
2018	53	210	117	53	210	32	675
2019	50	200	111	50	200	30	642
2020	48	191	106	48	191	28	612
2021	45	182	101	45	182	27	583
2022	43	173	96	43	173	26	555
2023	41	165	92	41	165	24	528
2024	**39**	**157**	**87**	**39**	**157**	**23**	**503**
2025	37	150	83	37	150	22	479
2026	36	142	79	36	142	21	456
2027	34	136	75	34	136	20	434
2028	32	129	72	32	129	19	414
2029	31	123	68	31	123	18	394
2030	29	117	65	29	117	17	375
2031	28	112	62	28	112	16	357
2032	27	106	59	27	106	15	340
2033	25	101	56	25	101	15	324
2034	24	96	54	24	96	14	309
Σ 2015-2034	**800**	**3,190**	**1,770**	**800**	**3,190**	**470**	**10,210**

Source: Estimate based on figures from Lassen et al. (2008).

Note: No estimates were available for other meteorological applications than psychrometers, but the volumes are thought to be very small.

Figure 5a-1: Estimates of the amount of mercury placed on the market each year in mercury containing thermometers for 2010-2034 - Baseline (kg per year)



Source: Table A5a-5

As described in the Chapter 2 of this annex, the pool of mercury in lab and industry thermometers currently used in society is estimated to be roughly 90 tonnes in 2010.

As described in section B.4 of the BD collection efficiencies of mercury in measuring devices, including mercury thermometers, in accordance with requirements set out in the hazardous waste legislation are estimated to be low. It is difficult to estimate the future trend of collection and share of proper waste management, however, there is no indication that the collection rate would improve without new targeted action and considerable efforts by the Member States in the future. Even with improved collection compared to the current situation, it seems unlikely that high enough collection rates would be achieved[96].

4.1.2 Options for restrictions

A tentative identification of possible restriction options was carried out based on the conclusions from the technical and economic feasibility in sections 3.3 and 3.4 of this Annex. The main results are presented in Table A5a-6. Based on those conclusions, two main issues need to be assessed further. These relate to analysis standards that refer to mercury thermometers for certain laboratory applications (including laboratories in industry), and to temperature measurements above 200°C in industry. Since these issues impact a separate market segment, it is considered more practical to

[96] Collection efficiencies above 50% should in general not be expected (Lassen et al., 2008Lassen et al., 2008).

assess the restriction options of industry and laboratories separately[97]. For the sake of that approach, the meteorological applications were included in the laboratory assessment.

Table A5a-6: Information to help determine options to reduce mercury placed on the market in thermometers

Market segment	Technically feasible?	Economically feasible?	Volume Hg in thermometers in 2015-2034 (kg)	Cost-effectiveness to reduce mercury (€/kg)
Laboratory thermometers				
Lab res>0.1°C and T<200°C	Yes, **but** standards	Yes	800	-3,700
Lab res<0.1°C or T>200°C	Yes, **but** standards	Yes	3,190	4,185
Industrial thermometers				
Industry T<200°C	Yes	Yes	800	-3,100
Industry T>200°C	Yes	**Yes**	3,190	
- excluding labour time savings				362,200
- including labour time savings				49,200
Dial thermometers	Yes	Most likely	1,770	12,400
Meteorological thermometers				
Psychrometers	Yes	Yes	470	*
Others	Yes	Yes	**	*

Source: Sections 3.3 and 3.4, and Table A5a-5 of this Annex, and Annex 5b.
Notes: Negative value means saving
*Cost calculations for psychrometers and other meteorological thermometers are not available but due to the reasons described in section 3.4 and Annex 5b, their cost-effectiveness is expected to be high (even resulting in negative values), similar to mercury-in-glass lab and industrial thermometers for measuring temperature below 200°C and with a resolution not better than 0.1°C.
**No data is available about the size of this market segment.

Based on the tentative identification of possible restriction options, 5 options to reduce the risk from mercury contained in thermometers in the EU have been assessed

[97] The described options are considered to be independent from one another. In real life, a restriction in one of the market segments might have an influence on other market segments. As an example, a reduced overall market after restriction of a segment can influence prices in another segment, and there may be some issues in relation to enforceability or implementability. However, such effects are thought to be minor.

in greater detail ('options for analysis'). It was concluded to repeat two limited derogations, namely:

1) a derogation for mercury triple point cells that are used for the calibration of platinum resistance thermometers in the options for the laboratory market segment (on the basis of technical feasibility, see section 3.3); and
2) a derogation to allow the placing on the market of thermometers with historic or cultural value in all options (See Part E of main document for details).

The impact of these two derogations on risk reduction capacity and economic feasibility of the restriction options is considered negligible. See Part E of the main document for the derogation on thermometers with historic or cultural value. The mercury placed on the market in mercury triple point cells that are used for the calibration of platinum resistance thermometers is estimated to be negligible (Lassen et al., 2008).

Options for analysis

Laboratory (& meteorology)

- Option 1a: Restriction on the placing on the market of all mercury laboratory thermometers and thermometers for meteorological applications from 2015[98] onwards with the two recurring derogations.

- Option 1b: A restriction as in option 1a, and in addition a *time-limited* derogation of 5 years[99] for mercury laboratory thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers.

Industry

- Option 2a: Restriction on the placing on the market of all industrial mercury thermometers from 2015 onwards with the derogation on thermometers with historic or cultural value.

- Option 2b: A restriction as in option 2a, and in addition a derogation for mercury-in-glass thermometers used in industrial applications for temperature measurements above 200°C as demonstrated by the reading scale.

- Option 2c: A restriction as in option 2b, and in addition a derogation for dial thermometers.

[98] Assuming that a restriction would apply 18 months after the entry into force, it is estimated for the purpose of this assessment that the restriction comes into effect in the year 2015.

[99] Based on the available information (see section 3.3) it seems that not many standards would prescribe mercury thermometers to be used anymore, and at least ASTM is already in the process of phasing out mercury thermometers from its standards from 2006. Since ASTM standards would have to be reviewed every 5 years, it seems reasonable to assume that all remaining ASTM and other standards still prescribing mercury can be amended by approximately 2018.

Options not retained for further assessment

In addition to the restriction options described above and that were assessed in detail, the following additional aspects have been considered, but for reasons explained not retained for further assessment:

- A derogation for mercury-in-glass thermometers in laboratories > 200°C or with a resolution <0.1°C.

  Similarly to the derogation in restriction Option 2b for the market segment of mercury-in-glass thermometers in industry for measurements above 200°C, a derogation on the restriction for lab thermometers for all applications that need a resolution better than 0.1°C or used for measurements >200°C could be envisaged. However, unlike for the industry segment, the estimated additional annualised cost per thermometer is only marginally higher[100] and the measure is cost-effective (€2600€/kg of mercury not placed on the market, see Annex 5b). A derogation was not deemed warranted and this option was not analysed further.

- Restriction on the placing on the market of mercury thermometers with a derogation for all industry mercury-in-glass thermometers

  This restriction would be similar to Option 2b with the difference that in addition thermometers measuring temperature below 200°C would be derogated. This would imply that during 2015-34 some 4 tonnes of mercury would still be placed on the market in thermometers for measuring temperature below 200°C. Derogating all industrial mercury-in-glass thermometers might be legally somewhat clearer and easier to enforce, but since the transition to alternatives would be cost neutral or even imply savings, enforceability and legal clarity were not deemed to be sufficient reasons for such a derogation (Table A5a-6).

- A system might be installed by which users or suppliers could apply for an exemption on the general restriction (as in the Swedish and Norwegian restriction, see section B.5 in the main report).

  Administrative efforts to implement such a system were deemed to be disproportionately high, and the risk reduction capacity is unlikely to improve substantially in comparison with derogations in the options. Also the enforceability of such a system might be slightly reduced. For these reasons, this option was not considered further.

[100] There are a number of reasons why the transition to alternatives in the high resolution/T>200°C lab segment is more cost-effective than the industry segment over 200°C. The main factors include: the lower long-term investment cost of the alternative due to the assumption that four mercury lab thermometers can be replaced by one electronic alternative; the calibration neutrality of the cost calculations for lab thermometers as the calibration frequency and cost of both mercury and alternative thermometers is assumed to be the same, and the shorter lifetime (5 years in lab instead of 13 years in industry) that is equal for both mercury and alternative lab thermometers (see Annex 5b).

- A restriction on the professional use of mercury fever thermometers.

  It was considered whether a use ban of existing fever thermometers in the medical sector, might be combined with a possible use ban of sphygmomanometers. The total volume of the mercury included in fever thermometers still in society is estimated to be 12 tonnes in 2010, but is steeply declining to an estimated volume of 0 already in 2014 (the restriction of placing on the market fever thermometers entered into force in April 2009). At the time the use restriction would come into effect, due to the short estimated useful lifetime of fever thermometers, there could only be some amount of fever thermometers recuperated that are 'lingering on' in store rooms in hospitals and with general practitioners. Because of the low volumes, and because a use ban on sphygmomanometers was not considered to be proportionate (see Annex 3a), this option was not analysed further.

- A derogation for long-term studies for laboratory mercury thermometers.

  There might be a bias between temperature readings from alternatives to mercury thermometers. Lowe (2009) suggests that readings of mercury thermometers, Galinstan thermometers and electronic thermometers do not differ significantly. This study was limited to fever thermometers, however.

  Conversely, according to ASTM (2009) there is a need for research comparing data obtained with alternate devices and the mercury-in-glass thermometers. All ASTM test methods (see section 3.3) are required to have a Precision and Bias statement, and based on information received from ASTM (2010) it seems that such issues would have to be resolved before a standard can be published in its updated form (i.e. allowing the use of alternatives). Because of this, the issue is directly linked to a possible derogation for analysis standards. A separate derogation for laboratory thermometers is therefore not considered further.

4.2 Assessment of risk management options

4.2.1 Option 1a: Restriction on all laboratory thermometers

Restriction to place mercury on the market in non-electrical equipment used to measure or indicate temperature in laboratories and for meteorological applications, after 18 months of entry into force with derogations for:

- mercury triple point cells that are used for the calibration of platinum resistance thermometers; and
- placing on the market thermometers with historic or cultural value (see details in Part E of the main document).

4.2.1.1 Effectiveness

Risk reduction capacity

The risk reduction capacity that can be achieved by introducing restriction Option 1a is described as an annual reduction of mercury placed on the market in the EU (see section B.2 of the main report). Assuming an annual declining trend of 5%, restriction Option 1a would avoid placing on the market a volume of around 220 kg of mercury in 2024[101], or a cumulatively amount of about 4.5 tonnes of mercury would not be placed on the market in the period 2015-34 (Table A5a-5). Note that the amounts for other meteorological applications other than psychrometers are not estimated and thus, not included in this number. This volume is a measure for reduction of the maximum potential for mercury emissions to the environment that might ultimately occur. In addition, it can be mentioned that the volume also reduces direct exposure of workers in production, use and waste phase -with the exception of exposure related to remaining production for exports.

Emissions related to the service-life and waste phase of mercury thermometers already in use will not be affected by restriction Option 1a.

The risk associated with placing on the market of alternatives to mercury thermometers is not considered to be significant in comparison to the risk associated with mercury thermometers (see Section 3.2).

Proportionality

Technical feasibility

In section 3.3 it was concluded that – apart from the issue relating to standards and the two recurring derogations – there are no known technical obstacles to replace all mercury thermometers for all applications.

Until standard organisations have updated their analysis standards referring to mercury thermometers in order to support the use of alternatives, it will in practice not be possible to replace mercury thermometers in certain laboratory applications.

As a conclusion it is not considered technically feasible to restrict placing on the market of mercury thermometers with the limited derogations as proposed in Option 1a.

Economic feasibility (including the costs)

Section 3.4 of this Annex described the economic feasibility of alternatives. This section summarises the compliance and administrative costs associated with the proposed restriction Option 1b from the compliance cost analysis in Annex 5b. Table A5a-7 presents the main outcomes.

[101] The year 2024 is a chosen as a representative year for compliance cost calculations, see section E of the main document for the justification.

As a result of the implementation of Restriction Option 1a, the replacement of 220 kg[102] of mercury in 2024[103] (or cumulatively 4.5 tonnes for the period 2015-34). This is estimated to cost €0.6 million in 2024 (or €6.9 million cumulatively in 2015-34).[104]

Table A5a-7: Restriction Option 1a: Amount of mercury not placed on the market in thermometers, compliance costs and cost effectiveness for laboratory thermometers

	Amount of mercury not placed on the market in thermometers		Additional annualised costs for alternative	Total compliance cost		Cost effective-ness
	in 2024	cumulative 2015-34		in 2024	cumulative 2015-34	
	(kg)	(kg)	(€ /device /annum)	(€ million)	(€ million)	(€/kg)
Lab res>0.1°C and T<200°C	39	797	-2.6	-0.2	-2.0	-3,692.5
Lab res<0.1°C or T>200°C	157	3,188	2.9	0.7	8.9	4,185.2
Psychrometers	23	470	*	*	*	*
Total	**220**	**4,455**		**0.6**	**6.9**	**2,609.7**

Notes:
Negative values represent cost savings.
*Cost calculations for psychrometers are not available but due to the reasons described in section 3.4 and Annex 5b, their additional annualised and total compliance costs are expected to be low and even negative, similar to mercury-in-glass lab and industrial thermometers for measuring temperature below 200°C and with a resolution not better than 0.1°C. Similarly, the cost effectiveness of psychrometers is expected to be high (even resulting in negative values).
Source: Annex 5b

Although the socio-economic benefits of reducing mercury use have not been estimated, the cost-effectiveness of the alternatives (Table A5a-7) in comparison to other measuring devices and other implemented policies (Appendix 2) suggests that Option 1a is economically feasible.

Administrative costs resulting from the restriction of placing on the market of mercury laboratory thermometers is considered to be small, or might even result in savings (see section 4.2.1.2 Practicality).

[102] The mid-point of the estimated mercury use in the EU in 2010: 780-1,040 kg.
[103] The year 2024 is a chosen as a representative year for compliance cost calculations, see section E of the main document for the justification.
[104] No cost estimates are available for psychrometers.

4.2.1.2 Practicality

Implementability and manageability

As the cost difference of electronic alternatives is small, and as laboratories are already using such equipment for the advantages they have, no major problems are foreseen in terms of implementability or manageability of this market segment, with the exception of thermometers for measurements according to analysis standards prescribing mercury thermometers.

No problems concerning implementability have been reported by Denmark, The Netherlands, Norway and Sweden with regard to implementation of their national restrictions (see also section B.5 of the main report). However, Denmark, the Netherlands and Norway have an exemption for thermometers used for analysis standards or laboratory use in general.

Because of the simplicity of a restriction with only two limited derogations, the legal clarity of restriction Option 1a would be high for all actors, including enforcers.

The administrative burden for laboratory operators of restriction Option 1a would be negligible. In fact there may be savings since many of the thermometers would be replaced by electronic thermometers that have significant advantages concerning keeping temperature records, and inserting data in computer models etc.

As mentioned before, for mercury laboratory thermometers that are used for measurements according to analysis standards, the restriction Option 1a is not considered to be technically feasible, and thus not implementable.

Enforceability

The compliance with restriction Option 1a can be assessed by inspecting producers (at least 11 in the EU according to Lassen et al., 2008), and by verifying if importers and distributors still supply mercury thermometers. Amongst importers can be users (labs or meteorological institutes) that buy thermometers from outside the EU. This last group would be more difficult to inspect. The clarity of the legal obligations would be high.

It would often be sufficient to visually inspect the thermometers to ensure that they do not use mercury as a thermometric liquid. In some circumstances gallium fillings might initially be confused with mercury, because gallium has a similar silvery liquid metal appearance. However, the capillary would have a concave instead of convex meniscus observed with mercury in a glass capillary.

4.2.1.3 Overall assessment of restriction Option 1a

The advantage of the restriction option is the legal clarity and the highest achievable risk reduction capacity for the laboratory segment. Restriction Option 1a would avoid placing on the market a volume of around 220 kg mercury (including in

psychrometers) in 2024 (or cumulatively 4.5 tonnes between 2015 and 2034). This is estimated to cost €0.6 million in 2024 (or €6.9 million cumulatively for the period 2015-34).[105] The restriction would be cost-effective.

However, this option has as a major shortcoming originating from the fact that it does not address the issue of analysis standards. This issue is addressed in option 1b.

4.2.2 Option 1b Restriction on laboratory thermometers with a time-limited derogation for use according to analysis standards.

Restriction to place mercury on the market in non-electrical equipment used to measure or indicate temperature in laboratories and for meteorological applications, after 18 months of entry into force with derogations for:

- mercury triple point cells that are used for the calibration of platinum resistance thermometers;
- placing on the market thermometers with historic or cultural value (see details in Part E of the main document); and
- *a time-limited derogation of 5 years for mercury laboratory thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers.*

4.2.2.1 Effectiveness

Risk reduction capacity

The avoided volume of mercury placed on the market in the EU would be slightly lower than in Option 1a during the 5 year period the derogation on analysis standards would apply (it has not been possible to estimate the derogated volume).

In the years after the derogated period, the risk reduction capacity would be similar to Option 1a (from approximately the year 2018 onwards).

Proportionality

Technical feasibility

The only problem concerning technical feasibility that was identified and discussed in Option 1a, would be lifted with the derogation for laboratory thermometers exclusively intended to perform specific analytical tests according to established standards. Based on the available information (see section 3.3) it seems that not many standards would prescribe mercury thermometers to be used anymore, and at least ASTM is already in the process of phasing out mercury thermometers from its standards from 2006. Since ASTM standards would have to be reviewed every 5

[105] No cost estimates are available for psychrometers.

years, it seems reasonable to assume that all remaining ASTM and other standards still prescribing mercury can be amended by approximately 2018.

Economic feasibility (including costs)

The compliance cost of implementation of the Restriction Option 1b is estimated to be similar to Option 1a, but with the following differences:

- The total compliance cost would be somewhat lower as the total number of thermometers that have to be replaced would be lower (5 year derogation);
- The cost-effectiveness of Option 1b would be the same (as the cost effectiveness is not affected by the number of thermometers on the market).

Overall, Option 1b is in all aspects similar to Option 1a in terms of economic feasibility.

4.2.2.2 Practicality

Implementability and manageability

Option 1a had a problem relating to technical feasibility due to the fact that it did not take into account the need to perform specific analytical tests according to established standards with mercury containing thermometers in laboratories. Option 1b remedies this problem with the time-limited derogation for laboratory thermometers exclusively intended to perform specific analytical tests according to established standards.

However, legal clarity would be reduced in comparison with Option 1a as a result of the derogation.

Enforceability

A temporarily decreased enforceability would be the main difference with Option 1a. In the 5 years the derogation would be applicable, enforcement would have to take place on the level of users (laboratories) in order to confirm that laboratory thermometers placed on the market are indeed used for measurements according to analysis standards. Enforcing the derogation might require a high level of technical knowledge from enforcement authorities, and additional resources would be required for enforcers to familiarise themselves with the analysis standards that are prescribing mercury thermometers. The need for resources would significantly increase (in terms of personnel, time, travelling costs, administrative costs, etc.) and would therefore represent an obstacle for the enforceability of a derogation as proposed in this Option.

4.2.2.3 Overall assessment of restriction Option 1b

The risk reduction capacity would be slightly lower in Option 1b than in Option 1a. However, implementability and technical feasibility would be optimised in

comparison with Option 1a. However, effective enforcement of the time-limited derogation might be problematic.

4.2.3 Option 2a Restriction on all industrial mercury thermometers

Restriction to place mercury on the market in non-electrical equipment used to measure or indicate temperature in industrial applications, after 18 months of entry into force with derogations for:

- placing on the market thermometers with historic or cultural value (see details in Part E of the main document).

4.2.3.1 Effectiveness

Risk reduction capacity

The risk reduction capacity that can be achieved by introducing restriction Option 2a is described as an annual reduction of metallic mercury used in the EU (see section B.2 of the main report). Assuming an annual declining trend of 5%, restriction Option 2a would avoid placing on the market a volume of around 280 kg of mercury in 2024, or a cumulative amount of about 5.8 tonnes of mercury would not be placed on the market in the period 2015-34 (Table A5a-5). This volume is a measure for reduction of the maximum potential for mercury emissions to the environment that might ultimately occur. In addition, it can be mentioned that the volume also reduces direct exposure of workers in production, use and waste phase -with the exception of exposure related to remaining production for exports.

The risk associated with placing on the market alternatives to mercury thermometers is not considered to be significant in comparison with the risk associated with mercury thermometers (see section 3.2).

Emissions associated with the production of mercury thermometers will remain where production continues for export. Emissions related to the service-life and waste phase of mercury thermometers already in use in the industry will not be affected by restriction Option 2a.

Proportionality

Technical feasibility

The technical feasibility of Option 2a has been demonstrated in section 3.3 of this Annex. The current national restrictions on mercury thermometers in Denmark, The Netherlands, Norway, and Sweden have no exemptions on industrial thermometers. This would support the assessment that from a technical point of view there is no obstacle to replace mercury thermometers with alternatives for all industrial applications.

Economic feasibility (including the costs)

Table A5a-8 presents the main outcomes of the compliance cost analysis. As a result of the implementation of Restriction Option 2a the replacement of 280 kg of mercury in 2024 (or cumulatively 5.8 tonnes between 2015 and 2034) will take place. This is estimated to cost €8.4 (±24 million[106]) in 2024 including labour cost savings from the use of electronic alternatives (or €90 ±256 million[107] cumulatively for the period 2015-34). When labour cost savings are excluded, the figures become €56 million in 2024 and €602 million for the period 2015-2034.

In terms of cost effectiveness, this means €30,600 per kg of mercury for the restriction of the whole industrial segment (restriction option 2a), when labour time savings are taken into account. Assuming a range of 2 to 6 hours of labour time savings per annum, the cost effectiveness figures range between €117,400 (assuming 2 hours per annum) and savings of €56,100 (assuming 6 hours per annum) per kg of mercury. When labour cost savings are excluded, the figure becomes €204,000 per kg of mercury removed from the market.

In the segment of mercury industrial thermometers for measuring temperature above 200°C, the transition to alternatives will be associated with higher costs to society if no labour time savings are assumed (362,165 €/kg in Table A5a-8). As explained in Annex 5b, labour time savings are realised from the transition to electronic alternatives. Therefore, labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are here assumed. The cost effectiveness is €49,200 (±€156,700) per kg of mercury. The "break-even" point of using an electronic thermometer would be if the employer would save 4.7 hours of work per year.

Table A5a-8: Restriction Option 2a: Amount of mercury not placed on the market in thermometers, compliance costs and cost effectiveness for industrial thermometers

Thermometer Market Segment	Amount of mercury not placed on the market in thermometers		Additional annualised costs for alternative	Total compliance cost		Cost effecti-veness
	in 2024 (kg)	cumulative 2015-34 (kg)	(€ / device / annum)	in 2024 (€ million)	cumulative 2015-34 (€ million)	(€/kg)
Industry T<200°C	39	797	-0.84	-0.12	-1.28	-3,127
Industry T>200°C	157	3,188				
- excluding labour time savings			97.5	55.1	591.6	362,165
- including labour time savings			13.2	7.5	80.4	49,201
Dial thermometers	87	1,771	97.5	1.1	11.3	12,367
Total (excluding labour time savings)	**284**	**5,757**		**56**	**601.6**	**203,956**
Total (including labour time savings)				8.4	90.4	30,622

Note: Negative values represent cost savings.
Source: Annex 5b

[106] Labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are assumed.
[107] Labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are assumed.

To better understand the compliance costs in relation to other actions and policies to reduce mercury, one can compare the cost effectiveness of the restriction Option 2a (€30,600/kg Hg) with the other policy options reviewed in Appendix 2. Furthermore, the fact that there are no reported problems related to the national restrictions in Denmark, The Netherlands, Norway and Sweden which have no derogations for industry thermometers (see also section B.5), provides indication that the costs are proportionate to the risks. Based on the information described above, it is concluded that the costs of restriction Option 2a are proportionate to the risk reduction capacity.

4.2.3.2 Practicality

Implementability and manageability

For most industrial applications electronic alternatives are replacing mercury thermometers due to the advantage of automation (Lassen et al., 2008). Mercury dial thermometers are confirmed by producers to hold only a very limited residual market because alternatives have taken over (Lassen et al., 2008). In fact, when the estimated volumes of mercury included in thermometers that are placed on the EU-market is considered, it is evident that there is in general a steep decline in thermometers used in all segments of the market.

No problems concerning implementability have been reported by Denmark, The Netherlands, Norway and Sweden with regard to implementation of their national restrictions (see also section B.5). None of the national restrictions foresees any derogations for industry thermometers. From this experience it appears that a restriction for all thermometers in industry would be implementable as well as technically feasible in those countries.

Because of the simplicity of a restriction with only two derogations, the legal clarity of restriction Option 2a would be high for all actors, including enforcers.

The administrative burden for industry of restriction Option 2a would be negligible. In fact, there may be administrative cost savings since many of the thermometers would be replaced by electronic thermometers that have significant advantages concerning keeping temperature records, and inserting data in computer models.

Enforceability

The compliance with restriction Option 1a can be assessed by inspecting the fairly limited number of producers (at least 11 in the EU according to Lassen et al., 2008), and by verifying if importers and distributors still supply mercury thermometers. The clarity of the legal obligations would be high.

It would often be sufficient to visually inspect the thermometers to ensure that they do not use mercury as a thermometric liquid. In some circumstances gallium fillings might initially be confused with mercury, because gallium has a similar silvery liquid metal appearance. However, the capillary would have a concave in stead of convex meniscus observed with mercury in a glass capillary.

Mercury dial thermometers have a mercury filled metal bulb, and thus visual inspection would not be sufficient. For these devices mobile XRF analysers can be used to verify if mercury is used as the thermometric liquid (non destructive analytical method) (see also First Advice of the Forum on the enforceability of the proposed restriction on mercury measuring devices, adopted 19 November 2010).

4.2.3.3 Overall assessment of restriction Option 2a

The advantage of the restriction option is the legal clarity and the highest achievable risk reduction capacity for the industrial market segment. Restriction Option 2a would avoid placing on the market a volume of around 280 kg of mercury in 2024 (or cumulatively 5.8 tonnes in 2015-34). Although not as clear-cut as in the other thermometer segments, the alternatives for the mercury industrial thermometers for measuring temperature above 200°C are considered economically feasible, and the overall cost-effectiveness of industrial segment acceptable.

4.2.4 Option 2b Restriction on industrial mercury thermometers with a derogation for mercury-in-glass thermometers for temperature measurements above 200°C

Restriction to place mercury on the market in non-electrical equipment used to measure or indicate temperature in industrial applications, after 18 months of entry into force with derogations for:

- placing on the market thermometers with historic or cultural value (see details in Part E of the main document); and
- *industrial mercury-in-glass thermometers that have a reading scale indicating a maximum temperature that is higher than 200°C.*

4.2.4.1 Effectiveness

Risk reduction capacity

The risk reduction capacity that can be achieved by introducing restriction Option 2b is much lower than in Option 2a. The restriction would avoid placing on the market a cumulative volume of around 2.6 tonnes of mercury between 2015 to 2034 (Table A5a-9), which is close to 60% lower than Option 2a which has a risk reduction of approximately 5.8 tonnes over the same period.

Proportionality

Technical feasibility

The technical feasibility of Option 2b has been demonstrated.

Economic feasibility (including the costs)

As a result of the implementation of Restriction Option 2b, 130 kg of mercury will be replaced in 2024 (or cumulatively 2.6 tonnes for the period 2015-34). This is estimated to cost €0.9 million in 2024 (or €10 million cumulatively in 2015-34). See also Table A5a-9.

Table A5a-9: Restriction Option 2b: Amount of mercury not placed on the market in thermometers, compliance costs and cost effectiveness for industrial thermometers. Derogation for industrial thermometers for temperature measurements above 200°C.

Thermometer Market Segment	Amount of mercury not placed on the market in thermometers		Additional annualised costs for alternative	Total compliance cost		Cost-effective-ness
	in 2024 (kg)	cumulative 2015-34 (kg)	(€ / device / annum)	in 2024 (€ million)	cumulative 2015-34 (€ million)	(€/kg)
Industry T<200°C	39	797	-0.84	-0.12	-1.28	-3,127
Dial thermometers	87	1,771	97.5	1.1	11.3	12,367
Total	**127**	**2,568**		**0.9**	**10.0**	**7,558**

Note: Negative values represent cost savings.
Source: Annex 5b

The cost-effectiveness is much higher than in Option 2a due to the derogation on industrial thermometers measuring temperatures above 200°C, and in addition, for reasons described in section 3.4 of this annex, the cost estimates for dial thermometers might be too conservative.

In sum, the cost-effectiveness of the alternatives (Table A5a-9) in comparison to other measuring devices and other implemented policies (Appendix 2) suggests that Option 2b is economically feasible.

4.2.4.2 Practicality

Implementability and manageability

Legal clarity of Option 2b would be slightly reduced in comparison with Option 2a as a result of the derogation.

Enforceability

Enforcing the derogation would be similar to Option 2a, although enforcers would have to check the maximum temperature level that an industrial mercury-in-glass thermometer can indicate on its reading scale. If the maximum is below 200°C a breach can be concluded. This can easily be verified by visual inspection. However,

the difference between industrial mercury-in-glass thermometers sold as inserts for metal cases and laboratory thermometers is not considered to be straightforward (general purpose thermometers in laboratories do not require high precision). Thus, when inspecting producers, importers and distributors it might be difficult for enforcers to prove that a thermometer is not compliant or vice-versa for the actor to provide evidence of the contrary.

4.2.4.3 Overall assessment of restriction Option 2b

Restriction Option 2b would avoid placing on the market a cumulative volume of approximately 2.6 tonnes of mercury in thermometers between 2015 and 2034. The risk reduction capacity is close to 60% lower compared to Option 2a. In return, however, Option 2b increases economical feasibility due to the derogation for industrial mercury-in-glass thermometers measuring temperature above 200°C, which was the reason for the comparatively high compliance costs of Option 2a.

4.2.5 Option 2c Restriction on industrial mercury thermometers with a derogation for mercury-in-glass thermometers for temperature measurements above 200°C and a derogation for mercury dial thermometers.

Restriction to place mercury on the market in non-electrical equipment used to measure or indicate temperature in industrial applications, after 18 months of entry into force with derogations for:

- placing on the market thermometers with historic or cultural value (see details in Part E of the main document);
- *industrial mercury-in-glass thermometers that have a reading scale indicating a maximum temperature that is higher than 200°C; and*
- *mercury dial thermometers.*

4.2.5.1 Effectiveness

Risk reduction capacity

The risk reduction capacity that can be achieved by introducing restriction Option 2c is much lower than in Option 2a and Option 2b. A cumulative amount of mercury of about 0.8 tonnes would not be placed on the market between 2015 to 2034 (Table A5a-10), instead of 5.8 tonnes in Option 2a or 2.6 tonnes in Option 2b.

Proportionality

Technical feasibility

The technical feasibility of Option 2c has been demonstrated.

Economic feasibility (including the costs)

The implementation of Restriction Option 2c will result in the replacement of 39 kg of mercury in 2024 (or cumulatively 0.8 tonnes between 2015 and 2034) (Table A5a-10). The implementation of this restriction option can result in cost savings of approximately €120,000 in 2024 (or €1.3 million cumulatively for the period 2015-34), due to the assumed lower waste treatment costs of the alternative liquid-in-glass thermometers than their mercury counterparts. Clearly Option 2c is economically feasible.

Table A5a-10: Restriction Option 2c: Amount of mercury not placed on the market in thermometers, compliance costs and cost effectiveness for industrial thermometers. Derogation for dial as well as industry thermometers that have maximum temperature measurements above 200°C.

Thermometer Market Segment	Amount of mercury not placed on the market in thermometers		Additional annualised costs for alternative	Total compliance cost		Cost-effective-ness
	in 2024 (kg)	cumulative 2015-34 (kg)	(€ / device / annum)	in 2024 (€ million)	cumulative 2015-34 (€ million)	(€/kg)
Industry T<200°C	**39**	**797**	**-0.84**	**-0.12**	**-1.28**	**-3,127**

Source: Annex 5b
Note: Negative values represent cost savings.

4.2.5.2 Practicality

Implementability and manageability

The implementability and manageability of restriction Option 2c would be similar to Option 2b, however, legal clarity of Option 2c would be slightly reduced in comparison with Option 2b as a result of the introduction of an additional derogation.

Enforceability

Option 2c has the same enforcement issues in relation to the derogation of industrial mercury-in-glass thermometers measuring temperature above 200°C as Option 2b. Enforceability of Option 2c will be just slightly improved with regard to Option 2b as a result of the derogation on dial thermometers: enforcers would not need to check if dial thermometers would contain mercury or not.

4.2.5.3 Overall assessment of restriction Option 2c

The restriction would avoid placing on the market a cumulative amount of mercury of about 0.8 tonnes from 2015 to 2034 – much lower than in Option 2a and Option 2b. Option 2c would be cost neutral or even result in savings, but the risk reduction capacity is considered insufficient to address the risk. In sum, Option 2c seems not to be a proportionate response to the concern related to mercury.

4.3 Comparison of the risk management options

Table A5a-11 summarises the risk reduction capacities and costs associated with the implementation of different restriction options.

Table A5a-11: Summary of risk reduction capacities and costs associated with the implementation of different restriction options

Options	Amount of mercury not placed on the market in thermometers		Total compliance cost		Cost Effec-tiveness (weighted average)
	in 2024	cumulative 2015-34	in 2024	cumulative 2015-34	
	(kg)	(kg)	(€ mill)	(€ mill)	(€ million)
Option 1a	220	4,455	0.6	6.9	2,610
Option 1b	<220	<4,455	<0.6	<6.9	<2,610
Option 2a	284	5,757			
- excluding labour time savings			56	601.6	203,956
- including labour time savings			8.4	90.4	30,622
Option 2b	127	2,568	0.9	10	7,558
Option 2c	39	797	-0.1	-1.3	-3,127

Source: Annex 5b

* The risk reduction capacity and the costs related to Option 1b are estimated to be slightly lower than Option 1a.

Table A5a-12 gives a qualitative overview of the risk management options. The table can be seen as summary of the main elements of the assessment, and allows for a rough comparison of the options on the basis of technical feasibility, risk reduction capacity, economic feasibility, and practicality. Based on the assessment, a combination Options 1b and 2a is considered the most appropriate risk management measure.

Table A5a-12 Overview of the risk management options

Options	derogation	Technically feasible?	Risk reduction capacity	Economic feasibility	Remarks practicality
Lab					
Option 1a	none	yes, but standards	++++	+++	/
Option 1b	standards	yes	+++	++++	Enforceability issue (temporary)
Industry					
Option 2a	none	yes	++++	+	/
Option 2b	MiG* >200°C	yes	++	+++	Enforceability issue
Option 2c	MiG >200°C +dial	yes	+	++++	/

*MiG = mercury-in-glass thermometers
Note: The indication "/" means that no major additional concerns relating to practicality have been identified

4.4 The proposed restriction(s) and summary of the justifications

The restriction that is proposed for thermometers is a combination Options 1b and 2b:

Restriction to place mercury on the market in non-electrical equipment used to measure or indicate temperature after 18 months of entry into force with derogations for:

- mercury triple point cells that are used for the calibration of platinum resistance thermometers;
- placing on the market thermometers with historic or cultural value (see details in Part E of the main document); and
- a time-limited derogation of 5 years for mercury laboratory thermometers exclusively intended to perform tests according to standards that require the use of mercury thermometers.

Justification

Based on the assessment of risk management options and on the comparison of restriction options in section 4.3, a combination of Options 1b and 2a is the most appropriate risk management measure.

The main purpose of the proposed restrictions is to reduce the mercury pool in the society, thus avoiding negative impacts on human health and the environment. The

proposed restriction would avoid placing on the market of around 500 kg of mercury in 2024. Cumulatively, the proposed restriction would avoid placing on the market an amount of mercury of about 10 tonnes in the period 2015-34. The costs of this reduction effort are estimated to be €9 ±24 million per annum or €97 ±256 million for the period 2015-34.[108] If labour time savings related to the use of electronic alternatives are excluded, the estimated cost impact is €56.6 million per annum or €609 million for the period 2015-34.

To better understand the relevance of the estimated compliance costs, a literature review estimating the compliance costs of other policies to reduce mercury and the human health benefits of reduced mercury emissions, as well as the restoration costs is presented in Appendix 2. As indicated in Table A5a-6, the cost-effectiveness of restricting different thermometer market segments varies considerably.

The transition to alternatives in the segment of mercury industrial thermometers for measuring temperature above 200°C will be associated with substantial costs to society if no labour time savings are assumed (362,165 €/kg Hg). As explained in Annex 5b, this assumption would not be true to the real-life situation. Therefore, labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are here assumed, resulting in a cost effectiveness figure of 49,200 ±156,700 €/kg Hg.[109] Furthermore, some other additional benefits offered by electronic alternatives could not be taken into account in the cost effectiveness estimate. Considering the relatively small impact to users, and aspects related to enforceability of the proposed restriction, this cost-effectiveness estimate for this segment is considered acceptable.

In the case of dial thermometers, the cost effectiveness was estimated to be €12,000/kg Hg. and the proposed restriction for dial thermometers is deemed proportionate. In addition, they are known to hold only a very limited residual market,[110] and consequently the economic importance of mercury dial thermometers is thought to be marginal (see section 3.4[111]).

Certain analysis standards (test methods) currently require the use of mercury thermometers and are thus preventing the use of alternatives. A time-limited derogation of 5 years for mercury laboratory thermometers exclusively intended to perform tests according to such standards is therefore considered justified.

In conclusion, the proposed restriction is considered proportionate, implementable, manageable and enforceable.

[108] Labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are assumed.
[109] Labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are assumed.
[110] It is estimated that the mercury dial thermometers represent less than 1% of the estimated total industrial and lab thermometers in 2010.
[111] In addition the cost is likely overestimated

Annex 5b: Compliance cost calculations for thermometers

Contents

1. Introduction

This annex presents the compliance costs calculations of substituting mercury-containing thermometers with mercury-free alternatives in support of the development of restriction options for thermometers in the Annex XV restriction report (Annex 5a). From section 1 "Technical description of mercury thermometers" in Annex 5a it is apparent that the applications and types of mercury thermometers on the market are very diverse. Similarly to section 3.3 of annex 5a on the technical feasibility of alternatives, the thermometer market was split in three main groups for the purposes of calculating the costs of compliance with the proposed restriction:

- Mercury-in-glass laboratory thermometers
  - Thermometers measuring temperature typically from -58°C to up to 200°C and where an accuracy of 0.1°C or better is not needed, i.e. generic thermometers;
  - Thermometers measuring temperature above 200°C or where an accuracy of 0.1°C or better is needed. This includes certain meteorological measurements; and
  - Mercury thermometers measuring ambient temperature and for most other meteorological measurements (including Six's thermometers and psychrometers).[112]
- Mercury-in-glass industrial thermometers
  - Thermometers measuring temperature typically from -58°C to up to 200°C, i.e. generic thermometers; and
  - Thermometers measuring temperature above 200°C (e.g., with application in the processing industry, marine applications, engines, etc.).
- Mercury dial thermometers

2. Defining the temporal scope and choosing a representative year

The temporal scope of the analysis is from the time when the restriction is assumed to become effective in 2015 to 2034.[113] Taking into account the uncertainties related to available data and the assumed declining trend in the number of mercury thermometers, 20 years scope is regarded sufficient. This temporal scope was also selected for consistency purposes to present comparable results to the analysis of sphygmomanometers.

[112] No specific cost information on this market segment has been gathered, since it is considered to be a residual market. For the sake of simplicity they are combined with the laboratory market segment (see Section 5.1.3)

[113] This temporal scope is chosen for illustrative purposes. In reality the time when the restriction becomes effective (2015 in this analysis) depends on the speed of the decision-making process and the transitional periods after entry into force.

The costs are reported in two ways:

1. In the cumulative approach, the present values of costs are calculated for 2015-2034.
2. In the representative year approach, the annualised costs, using the year 2024 as a representative year, are calculated.

3. Data sources and approach

The main sources of data used in the analysis are Options for reducing mercury use in products and applications, and the fate of mercury already circulating in society published by DG Environment (Lassen et al. 2008)[114] and Appendix 3 of the restriction report (Lassen et al., 2010).

The calculations have been carried out in Excel using NPV (for net present value) and PMT (for annualised cost) worksheet functions.

4. Main assumptions

Mercury volume in thermometers for the EU-market

The mercury volume in mercury-in-glass thermometers for the EU-market is estimated at 0.6-1.2 tonnes for 2007. Based on information from producers, it is estimated that approximately half of the mercury is used in thermometers for laboratory use and the other half is used for industrial and marine applications (Lassen et al. 2008). For the purposes of this analysis, it is assumed that the number of mercury-containing thermometers sold per year in the next 20 years will decline annually by 5%. This reduction in using mercury-containing devices is partly due to increased awareness of the harmful properties of mercury and partly because of the advantages of some alternatives, particularly related to automation.

Therefore, it is estimated that in 2010 the use of mercury for placing on the EU market industrial and lab mercury-in-glass thermometers is approximately 390kg each.[115] As it is unclear what portion of that is for thermometers measuring temperature above 200°C, for the purpose of this analysis it is assumed that they represent 80% of the volume in the total lab and industry segment of the EU thermometer market. This number is supported by information from a German producer that estimated the market to be 100 kg of mercury per year for the industry thermometer segment (>200°C), and 100 kg for lab >200°C segment in Germany alone. If this is compared to the estimated EU volume of 300 – 600 kg mercury per year[116], the percentage has to be relatively high. The impact of this assumption is assessed in the sensitivity analysis.

The use of mercury for placing on the EU market mercury dial thermometers is estimated to be 0.1-0.3 tonnes for 2007 in the EU (Lassen et al., 2008). Based on the

[114] Available at http://ec.europa.eu/environment/chemicals/mercury/pdf/study_report2008.pdf
[115] Based on the 50% mid-point of the 2007 consumption level in the EU of 0.6-1.2 tonnes.
[116] Total of 0.6-1.2 tonnes per year, where the industry and lab market represent about half each.

assumption of 5% annual decline, for the purpose of this analysis it is estimated that the volume in the European Union is approximately 150kg in 2010.

Psychrometers represent a small marker segment of the mercury market. The mercury volume in psychrometers placed on the EU-market is estimated at 0.01-0.1 tonne in 2007 (Lassen et al., 2008). No data is available for thermometers used for other meteorological applications, but the residual market is thought to be limited (see Section 5.1.3).

Mercury content

The mercury content of thermometers used for laboratories and in industry range from 1 to 20 g per thermometer, with an average content of 3-4 g (Lassen et al. 2008). The analysis assumes that all mercury-in-glass thermometers contain on average 3.5g of mercury. This average was also supported by producers describing "typical" thermometers (Lassen et al., 2010). The sensitivity analysis assesses the influence of the mercury content on compliance costs taking into account that some high precision, broad temperature range thermometers can have higher mercury content.

The mercury content of dial thermometers tends to be very variable, ranging from about 5 to 200 g (Lassen et al., 2008). The "rigid" type has relatively low mercury content, whereas the "remote" type can have a much higher content, since they can have a mercury filled capillary up to 40 m or more. The mid-point of 102.5g mercury per device is assumed for this analysis.

Lifetime

Mercury-in-glass industrial thermometers

The average technical lifetime of mercury thermometers can exceed 25 years. As no data are available for the breakage rate and other influencing factors such as changing of production lines, etc., a shorter useful life estimate of 13 years is adopted, as per the response of a major producer of mercury thermometers that a realistic average lifetime of these thermometers in practice is between 10 and 15 years (Lassen et al., 2010).

Mercury dial thermometers

It is likely that the actual lifetime of the "rigid" type will be very different from the "remote" type, since it can be expected that the capillaries are especially vulnerable to breakage, wearing, and loss of accuracy. It is possible that the actual lifetime of dial thermometers is comparable to the alternative liquid- or gas-actuated systems. However, as there is no specific information for the lifetime of mercury dial thermometers, as a conservative assumption, the same average lifetime as other industrial thermometers is used for the analysis.

Mercury-free dial thermometers

The lifetime of bi-metal and liquid- or gas-actuated dial thermometers varies depending on the type of the dial thermometer and the conditions in which it is used. The average lifetime for the dial thermometer is indicated by the mercury thermometer manufacturer to be 1-2 years whereas the manufacturer of alternatives indicates 1-5 years for mechanical systems depending on the environment. A Danish manufacturer of mechanical thermometers estimates the typical lifetime of bimetallic

thermometers at 2-5 years and of gas-filled thermometers at 5-10 years (Lassen et al., 2010). A three-year lifetime for all mechanical systems is assumed for the purpose of this analysis.

Electronic thermometers

The lifetime of the electronic probes (sensors) is generally shorter than for the rest of the system (the data reader or indicator), as the probes are often placed in more harsh environments (vibration, temperature, humidity, corrosive gases, etc.) and are in general more delicate than the rest of the system. The lifetime of thermocouple probes can vary between one and five years and 1-10 years for the resistance thermometers. In very harsh environments with higher temperatures (e.g. waste incinerators) the lifetime of the probes is less than half a year. Based on the available data a typical lifetime for the electronic sensors is considered three to six years (Lassen et al., 2010). A five-year lifetime for all electronic probes is assumed for the purpose of this analysis. As there is no detailed information for the lifetime of the data reader, a 10 year lifetime is assumed for the purpose of this analysis.

Mercury-in-glass lab thermometers

The analysis assumes a lifetime of five years for this market segment, which is based on an estimate of the University of Minnesota, Floyd *et al.* (Lassen et al. 2008, Lassen et al., 2010). It is assumed that a high rate of breakage would be indeed more typical for the lab thermometers, since the thermometers are frequently handled manually, are often not fixed in a device, can have a long stem length of 30-70cm, and, compared to industry thermometers, are usually not protected by sturdy encasings. All these factors will result in a shorter lifetime than the lifetime of industrial thermometers.

Replacement ratio of mercury thermometers with alternatives

The analysis assumes that one mercury-containing device can be replaced by one mercury-free mechanical alternative. However, when it comes to electronic alternatives, in certain circumstances, one electronic system can replace a number of mercury thermometers. Therefore, different replacement ratios are assumed for mercury in glass thermometers in labs for measuring temperature above 200°C. The assumptions made are explained in greater detail in the respective sections for laboratory and industry thermometers.

Device prices

The price of mercury thermometers and their alternatives is assumed to be a function of factors such as accuracy, temperature range and level, compliance with standards, calibration certification, and suitability to measure temperature in adverse environmental conditions. Prices of the electronic alternatives are also driven by additional features such as automated temperature recording, alarm systems, real-time process monitoring and feedback systems, etc. The various combinations of these factors (based on customer requirements) results in a substantial price diversity of thermometers available on the market. Therefore, the analysis is based on prices of what is considered by producers to be a “typical thermometer” and a “typical alternative” taking into account information in the Lassen et al. (2008) and Lassen et al. (2010).

Due to the uncertainty associated with the device prices and as the alternative market is thought to have reached maturity, it is assumed that the prices of mercury-containing and alternative devices do not change between 2015 and 2034. In reality, there could be a change in prices in favour of the alternatives as the technology further matures.

The costs in the analysis represent factory gate prices excluding VAT for investment costs. Recurrent costs also likely exclude VAT. All values used in this analysis refer to year 2010 price levels, i.e. the prices are "real" as the effect of inflation has not been included in the analysis.

Alternatives considered

The analysis takes into account technically feasible alternatives identified in Section 3.3 of Annex 5a. Investment and recurrent costs of the mercury containing devices are specifically compared to alternatives identified as "typical" in Lassen et al. (2010). When several alternatives are shown to be technically feasible, the analysis assumes that customers will replace the mercury-containing thermometers with the cheaper alternatives.

Gallium thermometers are technically feasible alternatives to the mercury thermometers, in particular as a very wide range thermometer and for measuring temperature outside the range of mercury thermometers (above 750°C). These thermometers are difficult to manufacture as each thermometer has to be individually filled resulting in high prices for these thermometers (Lassen et al., 2010). Gallium thermometers are excluded from the cost calculations due to their limited application in practice because of their high costs and because their use is rather complementary to mercury thermometers (outside the temperature range of mercury thermometers).

Comparability of alternatives

As far as possible, alternative devices with technical properties similar to mercury-containing thermometers are considered in the analysis. Electronic alternatives have additional features that mercury thermometers do not possess. These include: automated temperature recording, alarm systems, real-time process monitoring and feedback systems, etc. These additional benefits may lead to energy savings, labour cost savings, minimisation of human reading errors, higher efficiency of reactions, a better quality of the end-product, reduced risks of damage, etc. These additional benefits present a challenge in the direct comparison of the alternatives to the mercury-containing thermometers (and impact the price of the alternatives). In fact, the advantage of electronic reading for example is one of the drivers for replacing mercury thermometers with electronic devices, which for many customers offsets the extra costs of the thermometers (Lassen et al., 2010). Insufficient information was available to estimate the value of these additional features and to deduct it from the investment costs of the electronic alternatives. However, since the real-life situation is that the market has moved (and is moving) to the use of electronic alternatives for the additional benefits they bring, the impact of the value of these benefits on the cost effectiveness has been estimated by taking into account assumptions for labour time

savings[117] due to automatic reading and monitoring. This approach was taken only for the compliance cost calculations of industrial mercury-in-glass thermometers because the economic feasibility and cost effectiveness of restricting the market segment is clearly shown without taking into account the value of these additional benefits. On the basis of qualitative indication, labour cost savings due to replacement of a mercury industrial thermometer measuring temperature above 200°C with an electronic alternative were estimated to be on average 4 hours a year (or 40 seconds per day). Due to the substantial uncertainty on the true average labour cost savings in the whole market segment of the industrial thermometers measuring temperature over 200°C, the estimated average impact on the cost calculations is reported with an uncertainty margin of ±2 hours per annum. The "break-even" point is presented as well.

Calibration frequency

Calibration frequency is particularly difficult to estimate due to the diverse requirements for calibration and industry practices. For the purposes of this analysis it is assumed that all devices are bought calibrated.

Mercury-containing industrial thermometers

Mercury thermometer producers reported that industrial mercury-in-glass thermometers do not need frequent recalibration because its glass capillary keeps its accuracy for 30 years and more. The actual calibration frequencies, however, are dependent on the procedures set up by the users in their quality management system. Thermometers are thought to be checked regularly when used to measure temperature in industrial processes where temperature is of high importance (e.g., in the diary industry). Lassen et al. (2010) estimates that calibration once every three to five years would be typical (based on information from producers and a Danish reference lab). For the purpose of this analysis it is assumed that all industrial mercury thermometers (including dial) will be calibrated once every four years for all industrial (including dial) segments.

Mercury-free industrial thermometers

According to the information in Lassen et al., 2010, the calibration frequency of the alternative mechanical (dial) system is 6-12 months, while the frequency for the electronic systems is 6-24 months. According to a Danish producer it is typically necessary to recalibrate the probe after installation where the probe is "aged" by changing the temperature about 10 times. After the aging, the probe is often stable for some 5 years and does not drift more than 0.1°C. Many customers calibrate the thermometers every year because it is required by their quality management system. The analysis assumes that both dial and electronic alternatives are calibrated once a year for all thermometer segments.

Liquid-in-glass industrial thermometers

As no specific information was gathered for liquid-in-glass thermometers, and because of their similarities, it is assumed that they have the same calibration frequency as mercury-in-glass thermometers.

[117] Other possible benefits are: energy savings; minimisation of human reading errors; higher efficiency of chemical reactions; a better quality of the end-product; reduced risks of damage (automated warning/alarm function); etc.

Mercury-in-glass and mercury-free lab thermometers

Similar to industrial mercury thermometers, it is difficult to determine the frequency of calibration of a typical mercury lab thermometer. For mercury and mercury-free liquid-in-glass devices that do not need a high accuracy and do not need to measure temperatures above 200°C, the calibration frequency is assumed to be the same (once every fourth year) as in the industry segment for measurements below 200°C, as high accuracy is not considered a critical factor in either of these segments.

For mercury and mercury-free devices with accuracy of 0.1°C or better or measuring temperature above 200°C, one manufacturer indicated that the mercury thermometers do not need calibration while another – a 15 year validity of calibration. According to a Danish manufacturer, certified test laboratory mercury thermometers are usually calibrated every 3-5 years (Lassen et al., 2010). However, it was noted that in many laboratories the frequency of calibration is one to two calibrations per year independent on thermometer type (Lassen et al., 2010). For the purpose of this analysis, it is assumed that mercury-free (electronic) laboratory thermometers will be calibrated annually, while mercury lab thermometers – once every two years which is twice more frequent than the industrial market segment and the low precision/low temperature lab segment due to the higher need for accuracy in this lab segment.

Calibration costs

The cost of a calibration depends among others on the number of calibration points used. Lassen et al, (2010) indicates a price of €100-€150 for the calibration of an electronic thermometer. For this study the cost of calibration, done by a certified laboratory in Denmark, is reported to be about €200-€300, where the calibration of high precision thermometers tends to be more expensive. A price of €200 has been reported by a major German producer of electronic thermometers. With a traceable certificate the cost of calibration from the producer is about €350 (Lassen et al., 2010). As all the estimates for calibration costs in Lassen et al. (2010) are for Western European users, this analysis assumes the mid-point of the lowest estimates (€125) for all thermometers, to take into account the lower labour costs in Eastern Europe. These calibration costs are assumed for all thermometers included in the compliance cost calculations.

The cost of calibration is higher than the cost of new electronic equipment, but used electronic equipment is more stable than new equipment (Lassen et al., 2010).

Other recurrent costs

In addition to calibration costs, the analysis also takes into account other recurrent costs such as costs for power or batteries for the electronic device and waste handling. It is assumed that the device is purchased with batteries.

Waste treatment expenditures are assumed to occur the year after the end of the useful life of the device. As no specific data was gathered for these recurrent costs for thermometers, the analysis is based on assumptions presented in the cost calculations for sphygmomanometers. It is not known whether this estimate for sphygmomanometers considers that not all users dispose of the mercury devices in accordance with hazardous waste legislation. The values presented for

sphygmomanometers were reduced by half to reflect the lower mercury content and the smaller size of thermometers.

In the event of breakage of a mercury containing thermometer, there are costs associated with the cleaning of the spill. As no information was gathered regarding these costs they are not considered in the analysis.

One particular problem mentioned is the need for modified/additional installations in existing facilities if spare mercury thermometers are not available ("retrofitting") (Lassen et al., 2010). Mercury-free replacement thermometers (spare parts) fitting into the existing installations are sometimes claimed not to be readily available. A Danish producer of thermometers informed that the price of the adjusted alternatives is only slightly higher than the standard thermometer (Lassen et al., 2010). This is supported by product catalogues and on-line information assessed by ECHA. The alternatives encountered all use the same industry standards (such as DIN) for dimensions, fittings, etc. that are used for mercury thermometers. Usually producers mention that besides the standard versions, also custom dimensions, connection heads, transmitters, etc. can be supplied upon request.

As a specific case of retrofitting, finding solutions to accommodate certain older autoclaves with electronic alternatives has been reported as problematic. For these reasons, mercury-containing maximum thermometers to be placed inside older autoclaves are exempted from the restriction in Norway.[118] However, a report by the Swedish Chemicals Agency (KemI) indicates that mercury thermometers are being replaced with for example thermocouples in this equipment, and that this has advantages with respect to automated data collection and recording (Lassen et al., 2010).

It is concluded that on average there is no problem with retro-fitting, since in general the alternatives use the same industry dimensions, and that for the cases where customisation is needed, in most cases this has little effect on the investment costs. Therefore, for the purpose of the cost calculations, the installation/modification costs are considered immaterial and therefore, ignored in the analysis.

Discount factor

Throughout the analysis a 4% discount rate is used and the expenditures are assumed to occur in the beginning of each year, i.e. 1 of January.

[118] The Norwegian Climate and Pollution Agency (Klif) mentioned two possibilities for retrofitting of older autoclaves (where the thermometers are placed inside the autoclave) that both seem to be problematic. One is to place an electronic thermometer with data logger inside the autoclave, but the loggers are said not to withstand high temperatures. Another alternative is to place a thermocouple inside with connections to a meter outside. Some laboratories would have tried to lay thin conducting wires through the gasket, but it would have been difficult to avoid leakage caused by the high pressure. (Klif, 2010, pers. comm.)

5. Cost calculations

5.1. Mercury-in-glass lab thermometers

5.1.1. Mercury-in-glass lab thermometers (<200°C and resolution not better than 0.1°C)

5.1.1.1. Introduction

A number of mercury-in-glass thermometers are used to measure temperature below 200-250°C in applications where high precision and broader temperature range is not needed. Mercury-free liquid-in-glass thermometers are one of the most common replacements of these thermometers. Most mercury-free liquid-in-glass thermometers are not suitable for accurate measurements at 0.1°C resolution, but are fully suitable for less accurate measurements (Lassen et al., 2010). Their price is roughly the same as for mercury thermometers or about 10% lower (Lassen et al., 2010). It is assumed that the prices of these devices is approximately half the price of the mercury-in-glass lab thermometer for measuring temperature above 200°C, as it is assumed that high-precision, broad temperature range thermometers command higher prices.

Other thermometers that can replace mercury devices in this marker segment include electronic thermometers and gallium-indium thermometers. These thermometers command higher prices (up to 10-times the price of mercury-thermometers) due to their additional features such as data logger (for electronic thermometers) or broader temperature range (gallium thermometers). Therefore, for the purposes of estimating the cost effectiveness of substituting the mercury-in-glass thermometers measuring temperature below 200°C, only liquid-in-glass thermometers are considered.

Assuming 3.5g of mercury content for thermometers in this market segment, it is estimated that there are approximately 22,200 thermometers in the EU in 2010.

Table A5b-1 presents the input data used in the analysis.

Table A5b-1: Input data – Mercury-in-glass lab thermometers (<200°C)

Parameter	Device	Central case
Discount rate		4%
Mercury devices sold per year 2010		22,200
Annual decrease in number of devices sold		5%
Mercury per device (kg)		0.0035
Average lifetime (years)	Mercury Liquid-in-glass	5 5
Investment cost (price of device)	Mercury Liquid-in-glass	€ 40 € 40
Calibration costs (per calibration)	Mercury Liquid-in-glass	€ 125 € 125
Calibration frequency (once in *x* years)	Mercury Liquid-in-glass	4 4
Batteries (per year)	Mercury Liquid-in-glass	€ 0 € 0
Waste treatment (per device)	Mercury Liquid-in-glass	€ 16 € 2

5.1.1.2. Cost calculations

Investment costs

Table A5b-2 presents the investment costs of the mercury- and liquid-in-glass thermometers for measuring temperature below 200°C.

Table A5b-2: Annualised investment costs per device (in 2010 price level) – Mercury-in-glass lab thermometers (<200°C)

Year	Total Investment costs (€) per device	
	Baseline: Mercury-in-glass Lab Thermometer	Alternative: Liquid-in-glass Thermometer
Investment costs	40	40
Present value (for lifetime)	40	40
Average lifetime (years)	5	5
Annualised	**9**	**9**
Additional annualised		**0**

As the price of the alternative is the same as the mercury-in-glass thermometer, the transition to the alternative results in no additional annualised investment costs per device.

Recurrent costs

Table A5b-3 presents the recurrent costs of the mercury- and liquid-in-glass thermometers for measuring temperature below 200°C.

Table A5b-3: Annualised recurrent costs per device (in 2010 price level) – Mercury-in-glass lab thermometers (<200°C)

Year	Recurrent costs (€) per device	
	Baseline: Mercury-in-glass Lab Thermometer	Alternative 1: Liquid-in-glass Thermometer
1	0	0
2	0	0
3	0	0
4	0	0
5	125	125
6	16	2
7	0	0
8	0	0
9	0	0
10	0	0
11	0	0
12	0	0
13	0	0
14	0	0
15	0	0
16	0	0
17	0	0
18	0	0
19	0	0
20	0	0
21	0	0
Present value (for lifetime)	**120**	**108**
Annualised	**27**	**24.4**
Additional annualised		**-2.6**

The lower waste treatment costs result in an annualised savings of recurrent costs of €2.60 per device when the mercury lab thermometer is replaced with a liquid-in-glass thermometer.

Total costs and compliance costs

Table A5b-4 presents the calculations of total costs of mercury thermometers and liquid-in-glass thermometers.

Table A5b-4: Annualised total costs per device (in 2010 price level) – Mercury-in-glass lab thermometers (<200°C)

Year	Total costs (€) per device	
	Baseline: Mercury-in-glass Lab Thermometer	Alternative: Liquid-in-glass Thermometer
Present value (for lifetime)	160	148
Average lifetime (years)	5	5
Annualised	**36**	**33**
Additional annualised		**-2.6**

Due to lower waste treatment costs of the liquid-in-glass thermometers, it is estimated that the transition to the alternative will result in additional annualised savings per device of €2.60. The results in the table above can be obtained by addition of the investment and recurring costs presented in Tables A5b-2 and A5b-3.

Table A5b-5 presents the compliance costs from replacing the mercury-in-glass lab thermometer with a liquid-in-glass thermometer.

Table A5b-5: Annualised and present value compliance costs (in 2010 price level) – Mercury-in-glass lab thermometers (<200°C)

	Compliance costs (€) Alternative 1: Liquid-in-glass Thermometer
2015	-44960
2016	-87780
2017	-128560
2018	-167399
2019	-204388
2020	-194655
2021	-185386
2022	-176558
2023	-168150
2024	-160143
2025	-152517
2026	-145255
2027	-138338
2028	-131750
2029	-125476
2030	-119501
2031	-113811
2032	-108391
2033	-103230
2034	-98314
Compliance cost (present value 2015-2034)	**-1,963,574**
Annualised compliance cost (2024)	**-160,143**

Assuming that approximately 22,200 mercury thermometers are placed on the market annually (with a 5% declining rate over the study period), the compliance costs savings of replacing the mercury-filled with liquid-in-glass thermometers over the study period is close to €2 million (NPV) or €160 thousand as of 2024 on the representative year basis.

This tendency to replace the mercury containing thermometers with liquid-in-glass alternatives is already observed in the market. The reasons for continued use of the mercury containing thermometers can be explained with perceived higher level of quality of the mercury thermometers (which is a trusted, time tested method of measuring temperature) or customers' failure to take into account the long-term (recurrent) costs associated with the mercury thermometers.

5.1.1.3. Cost effectiveness

As the alternative has lower recurring costs, reducing the marketed volume of mercury by 1kg when replacing mercury lab thermometers with liquid-in-glass thermometers results in cost savings of approximately €3,700. The calculation is based on the present value compliance costs and on the assumption that one mercury thermometers contains 3.5g of mercury.

Table A5b-6 presents a summary of the compliance cost calculations associated with the transition from mercury-in-glass thermometers to liquid-in-glass thermometers.

Table A5b-6: Annualised and present value compliance costs (in 2010 price level) – Mercury-in-glass lab thermometers (<200°C)

Main assumptions for device			
Number of devices per year (2010)		22,200	
Trend		-5%	per year
Amount of mercury per device		0.0035	kgs
Lifetime of device		5	years
Costs (€)		**Baseline: Mercury-in-glass Lab Thermometer**	**Alternative 1: Liquid-in-glass Thermometer**
Investment cost	annualised	9	9
Recurrent cost	annualised	27	24
Total cost	annualised	36	33
Additional total cost	annualised		-2.6
Cost effectiveness	**per kg of Hg**		**-3,693**
Compliance cost	2024		-160,143
Compliance cost	total		-1,963,574

5.1.1.4. Sensitivity analysis

If waste treatment costs are ignored in the cost calculations, the transition to the liquid-in-glass alternative will be cost neutral, i.e., total compliance costs and the cost effectiveness will be 0€/kg Hg.

If we assume that the price of the liquid-in-glass alternatives is approximately 10% lower than the mercury containing device (Lassen et al., 2010), the transition to the alternative will result in higher cost savings: €5,000 per 1kg of mercury (cost effectiveness) or a total compliance cost for 22,200 mercury devices of €2.7 million (NPV) or €216 thousand (as of 2024).

Depending on the size of this market segment, the total compliance costs can range from €0 (assuming that all lab thermometers are used to measure temperature above 200°C) to €3.9 million savings on NPV basis or €320 thousand as of 2024 on representative year basis when it is assumed that this market segment represents 40% of all lab mercury-in-glass thermometers (44,400 devices as of 2010). The cost-effectiveness under this scenario will remain the same.

5.1.2. Mercury-in-glass lab thermometers (resolution better than 0.1°C or >200°C)

5.1.2.1. Introduction

This section addresses thermometers used in laboratory applications where an accuracy of 0.1°C or better is needed or to measure temperature above 200-250°C. Other technical requirements may include: a broad temperature range, high maximum temperature, and certification requirements for quality management (related to standards and calibration).

Assuming mercury content of 3.5g per thermometer, it is estimated that in the European Union, in 2010 there are approximately 88,900 mercury-in-glass thermometers in this market segment (assuming the segment represents 80% of total mercury-in-glass lab thermometers). The impact of this assumption on the compliance cost calculations is tested in the sensitivity analysis.

There are a number of technically feasible alternatives that have replaced mercury-in-glass lab thermometers with accuracy <0.1°C or for the temperature range above 200°C. These mainly include electronic thermometers such as thermocouples and platinum resistance thermometers (PRTs), as described in Section C: Technical feasibility.

Thermocouples and PRTs are three to five times more expensive and require additional data readers, which cost three to four times the cost of the mercury thermometers (Lassen et al., 2010). However, their higher prices are partially attributable to additional features such as data logger, possibilities for remote reading, alarm systems, etc. Due to lack of detailed information no attempt has been made to quantify the value of these additional features. For the purposes of this analysis, it is assumed that the price of the electronic system is €450.

An electronic thermometer typically has a much broader temperature range than mercury thermometers. It can be assumed that more than one mercury thermometers can be replaced by one electronic thermometer (probe with a data reader). One electronic thermometer could replace a whole set of narrow range (high) precision mercury thermometers, or even several of those sets. Such sets typically consist of six to 11 thermometers. However, other factors come into play and the actual replacement rate will be highly dependent on the needs of a lab.

In addition, several probes may be connected to one indicator (data reader), but on the other hand measurements might have to be done simultaneously on different locations in the lab. It was not considered possible to estimate the respective influence of these parameters.

Therefore, the analysis assumes a moderate replacement ratio of 2.5:1 for both the probe and the data reader. The impact of this assumption on cost effectiveness and compliance cost calculations is tested in the sensitivity analysis.

Table A5b-7 below presents the input data used in the analysis.

Table A5b-7: Input data used in the analysis – Mercury-in-glass lab thermometers (>200°C)

Parameter	Device	Central case
Discount rate		4%
Mercury devices sold per year 2010		88,900
Annual decrease in number of devices sold		5%
Mercury per device (kg)		0.0035
Average lifetime (years)	Mercury Electronic	5 5
Investment cost (price of device)	Mercury Electronic	€ 80 € 240
Calibration costs (per calibration)	Mercury Electronic	€ 125 € 125
Calibration frequency (once in *x* years)	Mercury Electronic	2 1
Batteries (per year)	Mercury Electronic	€ 0 € 3
Waste treatment (per device)	Mercury Electronic	€ 16 € 2
Investment cost (price of data reader)	Mercury Electronic	€ 0 € 210
Average lifetime per data reader (years)	Mercury Electronic	0 10
Replacement (Hg : electronic)		2.5:1

5.1.2.2. Cost calculations

Investment costs

Table A5b-8 presents the calculation of investment costs of mercury-in-glass lab thermometers and electronic thermometers.

Table A5b-8: Annualised investment costs per device (in 2010 price level) – Mercury-in-glass lab thermometers (>200°C)

Year	Total Investment costs (€) per device	
	Baseline: Mercury-in-glass Thermometer	Alternative: Electronic (probe & data reader)
Investment costs	80	180
Present value (for lifetime)	**80**	**180**
Average lifetime (years)	**5**	**5**
Annualised	**18**	**32**
Additional annualised		**14**

Due to higher price compared to mercury-containing devices, the additional annualised investment cost is estimated to be €14 for the alternative.

Recurrent costs

Table A5b-9 presents the calculations of recurrent costs for mercury-in-glass lab thermometers and electronic thermometers. The assumed lower waste disposal costs and the replacement ratio of the electronic thermometer result in small savings per device of an estimated €11 annually.

Table A5b-9: Annualised recurrent costs per device (in 2010 price level) – Mercury-in-glass lab thermometers (>200°C)

Year	Recurrent costs (€) per device	
	Baseline: Mercury-in-glass Thermometer	Alternative: Electronic
1	0	0
2	0	51
3	125	51
4	0	51
5	125	51
6	16	1
7	0	0
8	0	0
9	0	0
10	0	0
11	0	0
12	0	0
13	0	0
14	0	0
15	0	0
16	0	0
17	0	0
18	0	0
19	0	0
20	0	0
21	0	0
Present value (for lifetime)	236	187
Annualised	**53**	**42**
Additional annualised		**-11**

Total costs and compliance costs

Table A5b-10 presents the calculations of total costs of mercury-containing thermometers and the alternative device. The results in the table above can be obtained by the addition of the investment and recurring costs presented in Tables A5b-8 and A5b-9.

Table A5b-10: Annualised total costs per device (in 2010 price level) – Mercury-in-glass lab thermometers (>200°C)

Year	Total costs (€) per device	
	Baseline: Mercury-in-glass Thermometer	Alternative: Electronic
Present value (for lifetime)	316	367
Average lifetime (years)	5	5
Annualised	**71**	**74**
Additional annualised		**3**

When taking into account the replacement ratio of the probe and the data reader, the shorter lifespan and the higher investment costs of the alternative result in annualised cost of €3 per mercury device.

Table A5b-11 presents the compliance costs from replacing the mercury-in-glass lab thermometer with an electronic thermometer. The calculations are made assuming 5% annual decrease in the number of mercury-containing thermometers sold per year in the next 20 years, i.e. approximately 44,900 devices in 2024.

Table A5b-11: Annualised and present value compliance costs (in 2010 price level) – Mercury-in-glass lab thermometers (>200°C)

	Compliance costs (€)
	Alternative: Electronic
2015	204,067
2016	398,416
2017	583,511
2018	759,791
2019	927,677
2020	883,502
2021	841,431
2022	801,363
2023	763,203
2024	726,860
2025	692,247
2026	659,283
2027	627,889
2028	597,989
2029	569,514
2030	542,394
2031	516,566
2032	491,967
2033	468,540
2034	446,229
Compliance cost (present value 2015-2034)	**8,912,294**
Annualised compliance cost (2024)	**726,860**

The present value compliance costs for 2015-2034 are estimated at close to €8.9 million and the annualised compliance costs (2024) at approximately €727 thousand.

5.1.2.3. Cost effectiveness

As the alternatives have higher investment costs, reducing the marketed volume of mercury by 1kg when replacing mercury lab thermometers with electronic thermometers results in compliance costs of approximately €4,185. The calculation is based on the present value compliance costs and on the assumption that one mercury thermometer contains 3.5g of mercury. It is important to note that due to the additional features of the electronic thermometers (such as automatic data-logging, alarm, etc.), the mercury and electronic alternatives are not completely comparable, and that the compliance cost might be slightly overestimated because this factor is not quantified.

Table A5b-12 presents a summary of the main results of the compliance cost calculations associated with the transition from mercury-in-glass lab thermometers (>200°C) to an electronic alternative.

Table A5b-12: Cost effectiveness of replacing the mercury thermometers (in 2010 price level) – Mercury-in-glass lab thermometers (>200°C)

Main assumptions for device			
Devices per year (2010)		88,900	number
Trend		-5%	per year
Amount of mercury per device		0.0035	kgs
Lifetime of device (probe)		5	years
Costs (€)		**Baseline: Mercury-in-glass Thermometer**	**Alternative: Electronic**
Investment cost	Annualised	18	32
Recurrent cost	Annualised	53	42
Total cost	Annualised	71	74
Additional total cost	Annualised		3
Cost effectiveness	**per kg of Hg**		**4,185**
Compliance cost	2024		726,860
Compliance cost	total		8,912,294

It is important to note that the analysis above does not take into account the need to use mercury devices to meet requirements set in certain standards.

5.1.2.4. Sensitivity analysis

The mercury content of high precision lab thermometers can range between 1 and 20g (Lassen et al. 2008). Assuming a higher average mercury content for lab thermometers in this market segment – 11g (Lassen et al., 2010), the costs of reducing the volume of mercury placed on the EU market will be three times lower or €1,330

per kg (see also section 2 of this annex). The total compliance costs under this scenario will remain the same as in the central case.

When relaxing the central case assumptions for the replacement ratio, i.e., assuming a one-to-one relationship between the mercury thermometer and the probe and data reader of the electronic thermometer, the costs of reducing the marketed volume of mercury can reach €162,400 per kg. The total compliance costs are €345.7 million (NPV) and €28.2 million (2024 on annualised basis). The plausibility of this scenario is difficult to assess due to lack of information of the replacement rate of mercury thermometers with electronic alternatives.

Depending on the size of this market segment (based on central case assumptions), the total compliance costs can range (on NPV basis) from €6.7 million (assuming that this market segment represents 60% of all mercury-in-glass lab thermometers or 66,600 devices as of 2010) to €11 million, assuming that this market segment represents 100% of all lab mercury-in-glass thermometers (111,100 devices as of 2010). Under this scenario, as of 2024, on representative year basis, the total compliance costs will range from €545 thousand to €908 thousand. The cost effectiveness under these scenarios will remain the same, as this measure is not impacted by the number of devices on the market.

5.1.3. Mercury thermometers used in meteorological applications

As stated in section 3.4 of Annex 5a, mercury-in-glass thermometers for ambient air temperature measurements (including for min/max measurements) are almost fully substituted by liquid-in-glass thermometers or, where additional accuracy and features (e.g., remote reader) are desired, by electronic thermometers.[119] Similarly, electronic and liquid-filled alternatives to psychrometers with mercury thermometers dominate the market. Psychrometers represent a small market segment of the mercury market: the mercury volume in psychrometers placed on the EU-market is estimated at 0.01-0.1 tonnes in 2007 (Lassen et al., 2008). A proportion of psychrometers may require higher accuracy. These are considered to be included in the assessment for mercury-in-glass lab thermometers with resolution better than 0.1°C or for temperatures >200°C.

Because the residual market is thought to be very limited, detailed information for this market segment was not gathered; and therefore, no compliance cost calculations could be prepared. However, the transition from the mercury-containing ambient thermometers for meteorological applications is expected to result in additional annualised savings because:

- the price of the liquid-in-glass alternatives for ambient temperature measurement is similar to the mercury-containing thermometers (when no resolution <0.1°C needed);
- Six's thermometers with organic liquids are available at similar or lower prices than the mercury filled counterparts (Lassen et al., 2010);
- electronic or spirit-filled psychrometers are available for most applications at approximately the same price as mercury psychrometers (Lassen et al., 2010);

[119] This is also true for hydrometers that have a mercury thermometer inside.

- it costs less to dispose of a mercury-free device at the end of its useful life;
- the calibration frequency and costs of the mercury and liquid-in-glass devices are similar; and
- the lifetime of the mercury and liquid-in-glass devices is similar.

For the purpose of exploring restriction options, the meteorological applications are included in the laboratory assessment.

5.2. Mercury-in-glass industrial thermometers

5.2.1. Mercury-in-glass industrial thermometers (<200°C)

5.2.1.1. Introduction

This section discusses thermometers measuring temperature typically from -58°C to up to 200°C, i.e., generic thermometers which do not require certification and high precision. For the purpose of this analysis it is assumed that the price of the mercury-in-glass industrial thermometers (<200°C) is about half of the industrial thermometers (>200°C) to reflect the lower temperature range (and lower level of protection needed in the form of high quality encasings, which is included in the price of the industrial thermometers for above 200°C). Assuming 3.5g of mercury content for thermometers in this market segment, it is estimated that there are approximately 22,200 thermometers in the EU in 2010 (20% of the total number of mercury-in-glass industry thermometers).

The liquid-in-glass thermometers can directly replace mercury thermometers to measure temperature in industrial processes where high temperature and accuracy are not a requirement. Their price is roughly the same as for mercury thermometers or about 10% lower (Lassen et al., 2010). Mercury-free liquid-in-glass thermometers are not suitable for accurate measurements at better than 0.1°C resolution, but in industrial processes it is generally not necessary to measure the temperature at this high resolution (Lassen et al., 2010).

Other thermometers that can replace mercury devices in this marker segment include electronic thermometers and gallium-containing thermometers. These thermometers command higher prices (up to 10-times the price of mercury thermometers) due to their additional features such as data logger (for electronic thermometers) or broader temperature range (gallium thermometers). Therefore, for the purposes of evaluating the cost effectiveness of substituting the mercury-in-glass industrial thermometers measuring temperature below 200°C, only the cheapest alternative, being the liquid-in-glass thermometers are considered. If more expensive electronic thermometers are used as replacement, it is assumed that this would be because of their advantages of automatic reading and other features not directly applicable to mercury-containing devices.

The Table A5b-13 presents the input data used in the analysis.

Table 5b-13: Input data – Mercury-in-glass industrial thermometers (<200°C)

Parameter	Device	Central case
Discount rate		4%
Mercury devices sold per year 2010		22,200
Annual decrease in number of devices sold		5%
Mercury per device (kg)		0.0035
Average lifetime (years)	Mercury	13
	Liquid-in-glass	13
Investment cost (price of device)	Mercury	€ 23
	Liquid-in-glass	€ 23
Calibration costs (per calibration)	Mercury	€ 125
	Liquid-in-glass	€ 125
Calibration frequency (once in *x* years)	Mercury	4
	Liquid-in-glass	4
Batteries (per year)	Mercury	€ 0
	Liquid-in-glass	€ 0
Waste treatment (per device)	Mercury	€ 16
	Liquid-in-glass	€ 2

5.2.1.2 Cost calculations

Investment costs

Table A5b-14 presents the investment costs of the mercury-in-glass industrial thermometer (<200°C) and the lowest cost alternative: liquid-in-glass thermometers. As the price of the alternative is the same as the mercury-in-glass thermometer, the transition to the alternative results in no additional annualised investment costs per device.

Table A5b-14: Annualised investment costs per device (in 2010 price level) – Mercury-in-glass industrial thermometers (<200°C)

Year	Total Investment costs (€) per device	
	Baseline: Mercury-in-glass Industrial Thermometer	Alternative: Liquid-in-glass Thermometer
Investment costs	23	23
Present value (for lifetime)	23	23
Average lifetime (years)	15	15
Annualised	**2**	**2**
Additional annualised		**0**

Recurrent costs

Table A5b-15 presents the recurrent costs of the mercury-in-glass industrial thermometer (<200°C) and the lowest cost alternative: liquid-in-glass thermometers.

The lower waste disposal costs of the alternative result in small savings per device of an estimated €0.80 annually.

Table A5b-15: Annualised recurrent costs per device (in 2010 price level) – Mercury-in-glass industrial thermometers (<200°C)

Year	Recurrent costs (€) per device	
	Baseline: Mercury-in-glass Industrial Thermometer	Alternative 1: Liquid-in-glass Thermometer
1	0	0
2	0	0
3	0	0
4	0	0
5	125	125
6	0	0
7	0	0
8	0	0
9	125	125
10	0	0
11	0	0
12	0	0
13	125	125
14	16	2
15	0	0
16	0	0
17	0	0
18	0	0
19	0	0
20	0	0
21	0	0
Present value (for lifetime)	286	277
Annualised	**29**	**27.8**
Additional annualised		**-0.8**

Total costs and compliance costs

Table A5b-16 presents the calculations of total costs of mercury-containing thermometers and the alternative device for this industry segment (<200°C). The results in the table can be obtained by the addition of the investment and recurring costs presented in Tables A5b-14 and A5b-15.

Table A5b-16: Annualised total costs per device (in 2010 price level) – Mercury-in-glass industrial thermometers (<200°C)

Year	Total costs (€) per device	
	Baseline: Mercury-in-glass Industrial Thermometer	Alternative 1: Liquid-in-glass Thermometer
Present value (for lifetime)	308	300
Average lifetime (years)	15	15
Annualised	**30.9**	**30.0**
Additional annualised		**-0.8**

The additional annualised savings per device is estimated to be €0.80 compared to the mercury-containing device.

Table A5b-17 presents the compliance costs from replacing the mercury-in-glass industrial thermometer with a liquid-in-glass thermometer. The results are based on the assumption that this market segment represents 20% of the industrial mercury-in-glass thermometers, i.e. 11,200 in 2024, assuming 5% annual decline of mercury thermometers on the market.

Table A5b-17: Annualised and present value compliance costs (in 2010 price level) – Mercury-in-glass industrial thermometers (<200°C)

	Compliance costs (€) Alternative: Liquid-in-glass Thermometer
2015	-14646
2016	-28595
2017	-41879
2018	-54531
2019	-66581
2020	-78057
2021	-88986
2022	-99395
2023	-109308
2024	-118749
2025	-127740
2026	-136304
2027	-144459
2028	-137580
2029	-131029
2030	-124789
2031	-118847
2032	-113188
2033	-107798
2034	-102664
Compliance cost (present value 2015-2034)	**-1,275,721**
Annualised compliance cost (2024)	**-118,749**

The compliance cost savings of replacing the mercury-filled with the mercury-free alternative over the study period is close to €1.3 million (NPV) or €119 thousand as of 2024 on the representative year basis.

A tendency to replace the mercury containing thermometers with liquid-in-glass alternatives is already observed on the market (Lassen et al., 2008). The reasons for continued use of the mercury containing thermometers can be explained with perceived higher level of quality of the mercury thermometers (trusted, time tested method of measuring temperature) or customers' failure to take into account the long-term (recurrent) costs associated with the use of mercury thermometers.

5.2.1.3. Cost effectiveness

As the alternative has lower recurring costs, reducing the volume of mercury placed on the EU market by 1kg when replacing mercury industrial thermometers with liquid-in-glass thermometers results in cost savings of approximately €3,130. The calculation is based on the present value compliance costs and on the assumption that one mercury thermometer contains 3.5g of mercury.

Table A5b-18 presents a summary of the compliance cost calculations associated with the transition from mercury-in-glass thermometers (<200°C) to liquid-in-glass thermometers.

Table A5b-18: Cost effectiveness of replacing the mercury thermometers (in 2010 price level) – Mercury-in-glass industrial thermometers (<200°C)

Main assumptions for device			
Devices per year (2010)		22,200	number
Trend		-5%	per year
Amount of mercury per device		0.0035	kgs
Lifetime of device		13	years
Costs (€)		**Baseline: Mercury-in-glass Industrial Thermometer**	**Alternative 1: Liquid-in-glass Thermometer**
Investment cost	annualised	2	2
Recurent cost	annualised	29	28
Total cost	annualised	31	30
Additional total cost	annualised		-0.8
Cost effectiveness	**per kg of Hg**		**-3,127**
Compliance cost	2024		-118,749
Compliance cost	total		-1,275,721

It is important to note that the analysis above does not take into account the need to use mercury devices to meet requirements set in certain standards.

5.2.1.4. Sensitivity analysis

If waste treatment costs are ignored in the cost calculations, the transition from a mercury-in-glass industrial thermometer to the liquid-in-glass alternative for measuring temperature up to 200°C is cost neutral, i.e., total compliance costs and the cost effectiveness will be zero.

If we assume that the price of the liquid-in-glass alternatives is approximately 10% lower than the mercury containing device (Lassen et al., 2010), the transition to the alternative will result in higher cost savings: €3,960 per 1kg of mercury (cost effectiveness) or a total compliance savings of €1.6 million (NPV) or €150.5 thousand (as of 2024).

Depending on the size of this market segment, the total compliance savings range (on NPV basis) from €0 (assuming that all industrial thermometers are used to measure temperature above 200°C) to €2.6 million or €237.5 thousand as of 2024 on a representative year basis when it is assumed that this market segment represents 40% of all industrial mercury-in-glass thermometers (44,400 devices as of 2010).

5.2.2. Mercury-in-glass industrial thermometers (>200°C)

5.2.2.1. Introduction

A number of mercury-in-glass thermometers are used to measure temperature in industrial processes. The technical requirements include high temperature measurements (up to 800°C), endurance to aggressive environments, and certification requirements for quality management (related to standards and calibration).

The mercury content of the industrial thermometers ranges from about 1 to 20 g with an average content of 3-4 g (Lassen et al. 2008). Assuming mercury content of 3.5g per thermometer, it is estimated that in the European Union, in 2010 there are approximately 88,900 mercury-in-glass thermometers in this market segment (assuming the segment represents 80% of total mercury-in-glass industrial thermometers). The impact of this assumption on the compliance cost calculations is tested in the sensitivity analysis.

The price of a typical mercury thermometer for industry in this segment is reported to be €30 - 60 (Lassen et al., 2010) inclusive of the casing for the thermometer. The mid-point is selected for the purpose of this analysis.

There are a number of technically feasible alternatives that have replaced mercury-in-glass thermometers for the temperature range above 200°C. The analysis focuses on two: mechanical (liquid- or gas-filled or bi-metal dial) thermometers and electronic thermometers (thermocouples).

Producers of mercury thermometers have indicated that the prices of the mechanical (dial) thermometers are typically 3-5 times the price of the mercury thermometer. Other data shows that the price of the dial thermometers replacing the assumed typical industrial thermometer (>200°C) ranges between €100 and €150 (Lassen et al., 2010).[120] The mid-point is selected as the price of a typical dial replacement for the purpose of this analysis.

Thermocouples are three to five times more expensive and require additional data readers, which costs three to four times the price of the mercury thermometers (Lassen et al., 2008). The analysis assumes an average price for electronic alternatives of €175. Their higher prices are partially attributable to additional features such as data logging, possibilities for remote reading, real-time monitoring and feedback mechanisms, alarm systems, etc. No data have been available by which it can be estimated how the price of the data acquisition systems can be allocated to the individual thermometers (Lassen et al., 2010). To obtain such data extensive market

[120] This is consistent with the estimate that prices of the electronic alternatives are three to five times higher than the mercury containing device.

surveys need to be conducted. Therefore, taking into account that several probes and other inputs such as pressure gauges can be connected to one data reader, a replacement ratio of 2:1 is used in the central case for the data reader. This replacement ratio is not applied to the probes as in most if not all circumstances they are installed in equipment.

In addition, it is generally known that the life of the probe is shorter than for the rest of the system, as the probes are often placed in more harsh environments (vibration, temperature, humidity, corrosive gases, etc.) (Lassen et al., 2010). As no specific information is available, for the purpose of the analysis, it is assumed that the lifetime of the data reader is twice as long as that of the probes.

As mentioned in section 4 (Main assumptions), electronic alternatives have several additional benefits that mercury thermometers do not possess and that may lead to cost savings. These additional benefits are considered in fact the main drivers for replacing mercury thermometers with electronic devices (Lassen et al., 2010). Insufficient information was available to estimate the value of these additional features to take it into account in the central case of the compliance cost calculations. However, since the real-life situation is that the market has moved (and is moving) to the use of electronic alternatives for the additional benefits they bring, the impact of the value of these benefits on the cost effectiveness has been estimated by taking into account assumptions for labour time savings[121] due to automatic reading and monitoring.[122] On the basis of qualitative indication, labour cost savings due to replacement of a mercury industrial thermometer measuring temperature above 200°C with an electronic alternative was estimated to be on average 4 hours a year (or 40 seconds per day). Due to the substantial uncertainty on the true average labour cost savings in the whole market segment of the industrial thermometers measuring temperature over 200°C, the estimated average impact on the cost calculations is reported with an uncertainty margin of ±2 hours per annum (see section 5.2.2.4).

Table A5b-19 below presents the input data used in the compliance costs calculations associated with the transition from mercury industrial thermometers to mercury-free dial thermometers and thermocouples.

[121] Other possible benefits are: energy savings; minimisation of human reading errors; higher efficiency of chemical reactions; a better quality of the end-product; reduced risks of damage (automated warning/alarm function); etc.

[122] A similar approach was not taken for laboratory thermometers because economic feasibility and cost effectiveness of restricting the market segment was already clearly shown without taking it into account the value of these additional benefits.

Table A5b.19: Input data used in the analysis – Mercury-in-glass industrial thermometers (>200°C)

Parameter	Device	Central case
Discount rate		4%
Mercury devices sold per year 2010		88,900
Annual decrease in number of devices sold		5%
Mercury per device (kg)		0.0035
Average lifetime (years)	Mercury	13
	Dial	3
	Electronic	5
Investment cost (price of device)	Mercury	€ 45
	Dial	€ 125
	Electronic	€ 93
Investment cost (price of data reader)	Mercury	€ 0
	Dial	€ 0
	Electronic	€ 82
Calibration costs (per calibration)	Mercury	€ 125
	Dial	€ 125
	Electronic	€ 125
Calibration frequency (once in *x* years)	Mercury	4
	Dial	1
	Electronic	1
Batteries (per year)	Mercury	€ 0
	Dial	€ 0
	Electronic	€ 3
Waste treatment (per device)	Mercury	€ 16
	Dial	€ 2
	Electronic	€ 2
Average lifetime per data reader (years)	Mercury	0
	Dial	0
	Electronic	10
Replacement (Hg : electronic probe)		2:1

5.2.2.2. Cost calculations

Investment costs

Table A5b-20 presents the calculation of investment costs of mercury-in-glass industrial thermometers (>200°C) and two alternative devices.

Recurrent costs

Table A5b-21 presents the calculations of recurrent costs for different devices. The values of different parameters of recurrent costs are listed in Table A5b-19. The more frequent calibrations and shorter lifespan of the alternatives result in higher recurrent costs in comparison to the mercury thermometer: additional annualised costs per device of €57 for Alternative 1 and €76 for Alternative 2.

Due to the shorter lifetime and higher price compared to the mercury-containing device, the additional annualised investment cost for the alternatives are estimated to be €41 for Alternative 1 and €21,5 for Alternative 2.

Table A5b-20 Annualised investment costs per device (in 2010 price level) – Mercury-in-glass industrial thermometers (>200°C)

Year	Total Investment costs (€) per device		
	Baseline: Mercury-in-glass Thermometer	Alternative 1: Mercury-free Dial Thermometer	Alternative 2: Electronic (probe & data reader)
Investment costs	45	125	134
Average lifetime (years)	**13**	**3**	**5**
Annualised	**5**	**45**	**26**
Additional annualised		**40.5**	**21.5**

Table A5b-21: Annualised recurrent costs per device (in 2010 price level) – Mercury-in-glass industrial thermometers (>200°C)

Year	Recurrent costs (€) per device		
	Baseline: Mercury-in-glass Thermometer	Alternative 1: Mercury-free Dial Thermometer	Alternative 2: Electronic
1	0	0	0
2	0	125	128
3	0	125	128
4	0	2	128
5	125	0	128
6	0	0	2
7	0	0	0
8	0	0	0
9	125	0	0
10	0	0	0
11	0	0	0
12	0	0	0
13	125	0	0
14	16	0	0
15	0	0	0
16	0	0	0
17	0	0	0
18	0	0	0
19	0	0	0
20	0	0	0
21	0	0	0
Present value (for lifetime)	**286**	**238**	**466**
Annualised	**29**	**86**	**105**
Additional annualised		**57**	**76**

Total costs and compliance costs

Table 5b.22 presents the calculations of total costs of mercury-containing thermometers and the two alternative devices. The results in the table above can be obtained by the addition of the investment and recurring costs presented in Tables A5b-20 and A5b-21.

The more frequent calibrations, shorter lifespan and higher investment costs of the alternatives result in additional annualised costs per device in comparison to the mercury-containing device: respectively €97.50 for Alternative 1 and €97.60 for Alternative 2.

Table A5b-22 Annualised total costs per device (in 2010 price level) – Mercury-in-glass industrial thermometers (>200°C)

Year	Total costs (€) per device		
	Baseline: Mercury-in-glass Thermometer	Alternative 1: Mercury-free Dial Thermometer	Alternative 2: Electronic
Present value (for lifetime)	**331**	**363**	**600**
Average lifetime (years)	**13**	**3**	**5**
Annualised	**33.1**	**130.6**	**130.7**
Additional annualised		**97.5**	**97.6**

Table A5b-23 presents the compliance costs from replacing the mercury dial thermometer with the mercury-free dial or electronic alternative as described above.

Table 5b-23: Annualised and present value compliance costs (in 2010 price level) – Mercury-in-glass industrial thermometers (>200°C)

	Compliance costs (€)	
	Alternative 1: Mercury-free Dial Thermometer	Alternative 2: Electronic
2015	6791832	6798510
2016	13260244	13273281
2017	19420637	19439730
2018	25287677	25312539
2019	30875334	30905690
2020	36196913	36232500
2021	41265083	41305653
2022	46091911	46137227
2023	50688891	50738726
2024	55066966	55121106
2025	59236562	59294801
2026	63207606	63269749
2027	66989552	67055414
2028	63799574	63862299
2029	60761499	60821237
2030	57868094	57924988
2031	55112471	55166655
2032	52488067	52539671
2033	49988635	50037782
2034	47608224	47655031
Compliance cost (present value 2015-2034)	**591,585,833**	**592,167,456**
Annualised compliance cost (2024)	**55,066,966**	**55,121,106**

Assuming that 88,900 new mercury containing industrial thermometers are placed on the market in 2010 (with 5% annual rate of decline), the present value of the compliance costs for the period 2015-2034 are estimated to range between €591.6 million and €592.2 million and on annualised compliance costs (2024) basis between close to €55.07 million and €55.12 million depending on whether the mercury thermometer is replaced exclusively with Alternative 1 or Alternative 2.

5.2.2.3. Cost effectiveness

The analysis in this section assumes that 100% of the mercury-containing thermometers will be replaced with the slightly cheaper alternative - the mercury-free dial thermometer, even though in reality some of the users would replace the mercury thermometer with mercury-free dial thermometer, some with electronic devices and some with alternatives not covered in this analysis. In fact, it is thought that users will in most circumstances prefer the electronic alternative because of the low price difference between the two alternatives in combination with the additional features the electronic alternative offers (such as automation).

As the alternatives have higher investment costs, reducing the volume of mercury placed on the EU market by 1kg when replacing mercury industrial thermometers (>200°C) with mercury-free dial thermometers results in compliance costs of close to €362,200. The calculation is based on the present value compliance costs and on the assumption that one mercury thermometer contains 3.5g of mercury and 100% of the mercury-containing thermometers will be replaced with the slightly cheaper alternative: the mercury-free dial thermometer.

Table A5b-24 presents a summary of the main results of the compliance cost calculations associated with the transition from mercury-in-glass industrial thermometers (>200°C) to a mercury-free dial thermometers. These figures do not take into account additional benefits from the use of more accurate (electronic) alternatives.

Table A5b-24 Cost effectiveness of replacing the mercury thermometers (in 2010 price level) – Labour time savings for electronic alternatives not included – Mercury-in-glass industrial thermometers (>200°C)

Main assumptions for device				
Devices per year (2010)			88,900	number
Trend			-5%	per year
Amount of mercury per device			0.0035	kgs
Lifetime of device			13	years
Costs (€)		**Baseline: Mercury-in-glass Thermometer**	**Alternative 1: Mercury-free Dial Thermometer**	**Alternative 2: Electronic (probe)**
Investment cost	annualised	5	45	26
Recurrent cost	annualised	29	86	105
Total cost	annualised	33	131	131
Additional total cost	annualised		97.5	97.6
Cost effectiveness (per kg of Hg)			**362,165**	**362,522**
Compliance cost	2024		55,066,966	55,121,106
Compliance cost	total		591,585,833	592,167,456

5.2.2.4. Effect of labour time savings on cost effectiveness

When labour time savings are taken into account, the electronic alternative becomes the cheaper alternative. Table 5b-25 shows the impact of the estimated value of additional benefits, i.e., labour time savings[123] due to automatic reading and monitoring, on the cost effectiveness.

Table A5b-25 Cost effectiveness of replacing the mercury thermometers (in 2010 price level) – Labour time savings for electronic alternatives included – Mercury-in-glass industrial thermometers (>200°C)

Main assumptions for device				
Devices per year (2010)			88,900	number
Trend			-5%	per year
Amount of mercury per device			0.0035	grams
Lifetime of device			13	years
Costs (€)		**Baseline: Mercury-in-glass Thermometer**	**Alternative 1: Mercury-free Dial Thermometer**	**Alternative 2: Electronic (probe)**
Investment cost	annualised	5	45	26
Recurrent cost	annualised	29	86	20
Total cost	annualised	33	131	46
Additional total cost	annualised		98	13
Cost effectiveness	annualised		27,859	3,785
Cost effectiveness (per kg of Hg)			**362,165**	**49,201**
Compliance cost	2024		55,066,966	7,480,953
Compliance cost	total		591,585,833	80,368,074

Assuming average labour time savings of 4 hours per year (or 40 seconds per day) due to automatic and remote reading/monitoring and €20 per hour wage cost, the additional annual total cost of the cheaper alternative – in this scenario the electronic alternative – is €13 – about 85% lower than under central case assumptions. The cost of reducing mercury use by 1 kg is €49,200 or seven times lower than under the central case assumptions.

To reflect the substantial uncertainty on the true average labour cost savings in the whole market segment of the industrial thermometers measuring temperature over 200°C, the estimated average impact on the cost calculations is reported with an uncertainty margin of ±2 hours per annum. Assuming in the lower bound 2 hours of labour time savings per year (20 second per day), the additional annualised cost associated with the transition are €55.40 annually over the lifetime of the electronic alternative. The cost effectiveness under this scenario is approximately €205,900 per

[123] Other possible benefits are: energy savings; minimisation of human reading errors; higher efficiency of chemical reactions; a better quality of the end-product; reduced risks of damage (automated warning/alarm function); etc.

kg of mercury reduced or about 40% less than under the central case. Assuming 6 hours of labour time savings annually (i.e., 60 seconds per day), the transition to the alternative electronic thermometer is associated with cost savings to users of approximately €28.90 annually over the lifetime of the electronic alternative. This translates into cost savings of reducing mercury use by 1 kg of approximately €107,500. The "break-even" point of using an electronic thermometer would be if the employer would save 4.7 hours of work per year.

It is important to note that the analysis above considers only labour time savings and does not fully reflect all additional benefits from the use of the more accurate (electronic) alternatives. These other benefits may lead to energy savings, minimisation of human reading errors, higher efficiency of reactions, a better quality of the end-product, reduced risks of damage, etc.

5.2.2.5. Sensitivity analysis

Relaxing the assumption of replacement ratio

Relaxing the replacement ratio assumption (of 2:1) for the data reader of the thermocouple does not change the cost effectiveness and total compliance costs for the transition from mercury-in-glass industrial thermometers (>200°C) to alternatives, as the analysis assumes that the mercury devices are replaced with the slightly cheaper alternative: mercury-free dial thermometers to which the replacement ratio does not apply. However, when labour time savings are taken into account, the electronic alternative becomes the cheaper alternative; therefore, when assuming no replacement ratio, the cost effectiveness and the compliance costs increase by 38% to €67,900 and €10.3 million in 2024 (annualised) or €111 million for the period 2015-2034.

Relaxing the assumption for market size

Depending on the size of this market segment, the total compliance costs can range from €443.2 million (assuming that this market segment represents 60% of all industrial thermometers or 66,600 devices as of 2010) to €739.3 million on NPV basis when it is assumed that this market segment represents 100% of all industrial mercury-in-glass thermometers (111,100 devices as of 2010). Under this scenario, as of 2024, on representative year basis, the total compliance costs will range from €41.3 million to €68.8 million.

Assuming labour time savings, the total compliance costs range from €60.2 million (assuming that this market segment represents 60% of all industrial thermometers or 66,600 devices as of 2010) to €100.4 million on NPV basis when it is assumed that this market segment represents 100% of all industrial mercury-in-glass thermometers (111,100 devices as of 2010). Under this scenario, as of 2024, on representative year basis, the total compliance costs will range from €5.6 million to €9.3 million or 25% lower.

The cost effectiveness under these scenarios will remain the same as it is not impacted by the number of devices on the market.

Relaxing the assumption for calibration

During the data gathering stage of preparation of the Annex XV restriction report, it was noted that some users do not follow the recommended frequency of calibrations. Assuming that there are no calibration costs for the mercury-in-glass and the cheaper under this scenario alternative - dial thermometer, the cost effectiveness is lower by 2.5 times or €149,000 per kg mercury.

When labour time savings are taken into account, the electronic alternative becomes the cheaper alternative; therefore, when it is assumed that there are no calibration costs, the cost effectiveness ratio and the compliance costs translate into savings of €226,600 and €34.5 million in 2024 (annualised) or €370 million for the period 2015-2034.

5.3. Mercury dial thermometers

5.3.1. Introduction

The mercury content of dial thermometers depends largely on whether the dial thermometer is of the "rigid" or "remote" type (whether it has a capillary or not). It can range from about 5g to 200g (Lassen et al. 2008). Between 0.1 and 0.3 tonnes/year of mercury was used in mercury dial thermometers for the European market in 2007. For the purpose of this analysis, the mid-point in these ranges are taken, i.e., 102.5g of mercury per thermometer or 150kg of mercury used in mercury dial thermometers for the EU-market in 2010 (assuming 5% annual decline in volume).

A number of bi-metal and liquid- and gas-actuated dial thermometers are available as alternatives to mercury dial thermometers (Lassen et al. 2008). Other technically feasible alternatives include electronic thermometers such as thermocouples and RTDs (resistance temperature device). From the available information, there is no indication that liquid-in-glass thermometers would be alternatives to the dial thermometers for measurement below 200°C[124]. Taking into account that several probes and other inputs such as pressure gauges can be connected to one data reader, a replacement ratio of 2:1 is used in the central case for the data reader, similar to the industrial mercury-in-glass thermometers (>200°C). This replacement ratio is not applied to the probes as in most if not all circumstances they are installed in equipment. In addition, it is assumed that the lifetime of the data readers of the electronic devices is twice as long as that of the probes.

The Table A5b-25 below presents the input data used in the compliance costs calculations associated with the transition from mercury dial thermometers to

[124]Lassen et al. 2008 report (Table 2-23) suggests that liquid-in-glass thermometers are not used as replacements for mercury dial thermometers. However, it cannot be entirely excluded that in some applications liquid-in-glass thermometers might be replacements for dial thermometers for temperature measurements <200°C. Given the small market size of this segment and the almost full replacement of the mercury dial thermometers (Lassen et al., 2008), the analysis assumes that if a substitution with liquid-in-glass was possible it was already adopted by users. Therefore, for the purpose of this analysis, we examine the transition from mercury dial thermometers to mercury-free dial thermometers and thermocouples.

mercury-free dial thermometers and thermocouples. As no specific pricing information is available for mercury dial thermometers, it is assumed that these thermometers and their alternatives will have similar costs as the mercury-in-glass industrial thermometers (>200°C).

Table 5b-25: Input data used in the analysis – Mercury dial thermometers

Parameter	Device	Central case
Discount rate		4%
Mercury devices sold per year 2010		1,700
Annual decrease in number of devices sold		5%
Mercury per device (kg)		0.1025
Average lifetime (years)	Mercury Dial Thermocouple	13 3 5
Investment cost (price of device)	Mercury Dial Thermocouple (probe)	€ 45 € 125 € 93
Investment cost (price of data reader)	Mercury Dial Thermocouple	€ 0 € 0 € 82
Calibration costs (per calibration)	Mercury Dial Thermocouple	€ 125 € 125 € 125
Calibration frequency (once in *x* years)	Mercury Dial Thermocouple	4 1 1
Batteries (per year)	Mercury Dial Thermocouple	€ 0 € 0 € 3
Waste treatment (per device)	Mercury Dial Thermocouple	€ 16 € 2 € 2
Average lifetime per data reader (years)	Mercury Dial Thermocouple	0 0 16
Replacement (Hg : electronic)		2:1

5.3.2. Cost calculations

Investment costs

Table A5b-26 presents the calculation of investment costs of mercury-containing dial thermometers and two alternative devices.

Due to their assumed shorter lifetime (respectively three and five years) and higher price compared to mercury-containing devices, the additional annualised investment cost is estimated to be €40.5 for Alternative 1 and €21.5 for Alternative 2.

Table A5b-26: Annualised investment costs per device (in 2010 price level) – Mercury dial thermometers

Year	Total Investment costs (€) per device		
	Baseline: Mercury Dial Thermometer	Alternative 1: Mercury-free Dial Thermometer	Alternative 2: Thermocouple (probe & data reader)
Investment Cost	45	125	134
Average lifetime (years)	13	3	5
Annualised	**5**	**45**	**26**
Additional annualised		**40.5**	**21.5**

Recurrent costs

Table A5b-27 presents the calculations of recurrent costs for the three devices.

Table A5b-27 Annualised recurrent costs per device (in 2010 price level) – Mercury dial thermometers

Year	Recurrent costs (€) per device		
	Baseline: Mercury Dial Thermometer	Alternative 1: Mercury-free Dial Thermometer	Alternative 2: Thermocouple
1	0	0	0
2	0	125	128
3	0	125	128
4	0	2	128
5	125	0	128
6	0	0	2
7	0	0	0
8	0	0	0
9	125	0	0
10	0	0	0
11	0	0	0
12	0	0	0
13	125	0	0
14	16	0	0
15	0	0	0
16	0	0	0
17	0	0	0
18	0	0	0
19	0	0	0
20	0	0	0
21	0	0	0
Present value (for lifetime)	286	238	466
Annualised	**29**	**86**	**105**
Additional annualised		**57**	**76**

The values of different parameters of recurrent costs are listed in Table A5b-25. The more frequent calibration and shorter lifespan of the alternatives result in higher additional recurrent costs in comparison to the mercury dial thermometer: an estimated €57 for Alternative 1 and €76 for Alternative 2.

Total costs and compliance costs

Table A5b-28 presents the calculations of total costs of the mercury dial thermometers and the two alternative devices.

Table A5b-28 Annualised total costs per device (in 2010 price level) – Mercury dial thermometers

Year	Total costs (€) per device		
	Baseline: Mercury Dial Thermometer	Alternative 1: Mercury-free Dial Thermometer	Alternative 2: Thermocouple
Present value (for lifetime)	**331**	**363**	**600**
Average lifetime (years)	**13**	**3**	**5**
Annualised	**33**	**131**	**131**
Additional annualised		**97.5**	**97.6**

The assumed more frequent calibration, shorter lifespan and higher investment costs of the alternatives result in additional annualised costs per device in comparison to the mercury-containing device: respectively €97.5 for Alternative 1 and €97.6 for Alternative 2. These results can be derived from Tables A5b-26 and A5b-27 as sums of additional investment and recurrent costs.

Table A5b-29 presents the compliance costs from replacing the mercury dial thermometer with alternatives as described above.

The present value compliance costs for 2015-2034 are estimated to be between €11.31 million and €11.32 million depending on whether all mercury dial thermometers are replaced only by Alternative 1 or Alternative 2. In reality some of the users would replace the mercury dial thermometer with a mercury-free dial thermometer, some with electronic devices and some with alternatives not covered in this analysis.

Further on this analysis assumes that 100% of mercury dial users will replace the devices with the cheaper alternative – the mercury-free dial whose recurrent cost are slightly lower than those of thermocouple.

Table A5b-29 Annualised and present value compliance costs (2010 price level) – Mercury dial thermometers

	Compliance costs (€)	
	Alternative 1: Mercury-free Dial Thermometer	Alternative 2: Thermocouple
2015	129878	130005
2016	253570	253820
2017	371373	371738
2018	483566	484042
2019	590417	590997
2020	692179	692860
2021	789096	789872
2022	881398	882264
2023	969304	970257
2024	1053024	1054059
2025	1132758	1133871
2026	1208694	1209883
2027	1281015	1282275
2028	1220014	1221214
2029	1161918	1163061
2030	1106589	1107677
2031	1053894	1054930
2032	1003709	1004696
2033	955913	956853
2034	910393	911289
Compliance cost (present value 2015-2034)	**11,312,665**	**11,323,787**
Annualised compliance cost (2024)	**1,053,024**	**1,054,059**

5.3.3. Cost effectiveness

As the alternative has higher annualised costs, reducing the use of mercury by 1kg when replacing mercury dial thermometers with thermocouples results in compliance costs of approximately €12,370. The calculation is based on the present value compliance costs and on the assumption that one mercury dial thermometer contains 102.5 g of mercury.

Table A5b-30 presents a summary of the main results of the compliance cost calculations associated with the transition from mercury dial to mercury-free dial thermometers.

Table A5b-30 Cost effectiveness of replacing the mercury thermometers (in 2010 price level) – Mercury dial thermometers

Main assumptions for device				
Devices per year (2010)			1,700	number
Trend			-5%	per year
Amount of mercury per device			0.1025	kilograms
Lifetime of device			13	years
Costs (€)		**Baseline: Mercury Dial Thermometer**	**Alternative 1: Mercury-free Dial Thermometer**	**Alternative 2: Thermocouple (probe)**
Investment cost	annualised	5	45	26
Recurrent cost	annualised	29	86	105
Total cost	annualised	33	131	131
Additional total cost	annualised		98	98
Cost effectiveness	**per kg of Hg**		**12,367**	**12,379**
Compliance cost	2024		1,053,024	1,054,059
Compliance cost	total		11,312,665	11,323,787

5.3.4. Sensitivity analysis

In the absence of information, the assessment used a conservative estimate of a lifetime of 13 years for mercury dial thermometers vs. three years for gas or liquid-actuated dial alternatives, and a yearly calibration of the alternatives vs. once every 4 years for the mercury dial thermometer. It appears, however, that the technology is not very different, and the lifetimes and calibration frequencies might be equal or similar of the mercury and gas- or liquid-actuated thermometers. Assuming that the mercury dial thermometers have the same lifetime and calibration frequency as their gas-actuated alternative systems, the cost effectiveness is lower by 94% or €710. The total compliance costs are also much lower as under this scenario mercury dial thermometers have higher annualised total costs per device (€106) and due to the early retirement of the mercury thermometers. They are €0.9 million (NPV) or €66 thousand on a representative year basis (2024).

The assumption of an annual decrease of 5% of the thermometer market might be conservative, as according to the manufacturers of mercury dial thermometers, there is a very limited remaining market (see section 3.4). Assuming a faster replacement of mercury dial thermometers of 10% annually, the total compliance costs are more than five times lower than the central case scenario: €2.2 million (NPV) or €144 thousand on a representative year basis (2024).

Relaxing the replacement ratio assumption (of 2:1), i.e., no replacement ratio, for the data reader of the thermocouple, will result in an increase of the annualised investment cost of the alternative. Under this assumption, the mercury-free dial will

remain the cheaper alternative; therefore, the total compliance costs will remain as presented in Table 5b-29.

During the data gathering stage of preparation of the Annex XV restriction report, it was noted that some users do not follow the recommended frequency of calibrations. Assuming that there are no calibration costs for the thermocouple and the cheaper alternative (mercury-free dial), the cost effectiveness of decreasing the volume of mercury placed on the EU-market by 1kg is 60% lower or €5,100. Total compliance costs under this scenario are €1.5 million (NPV) or €109 thousand on a representative year basis (2024).

6. Summary

Table A5b-31 presents a summary of the main results of the compliance cost calculations associated with the transition from mercury-containing thermometers to feasible alternatives.

Table A5b-31 Cost effectiveness and total compliance costs related to the transition from mercury-containing thermometers to feasible alternatives (in 2010 price level)[125]

Thermometer Market Segment	Mercury volume in 2010 (kg)	Estimated cost Effectiveness (€/kg)	Total Compliance Cost for 2024 (€)
Industry (T<200°C)	80	-3,127	-118,749
Industry (T>200°C)			
- excl. labour time savings	310	362,165	55,066,966
- incl. labour time savings	310	49,201	7,480,953
Dial	170	12,367	1,053,024
Industry - total			
- excl. labour time savings	390	203,956	56,001,242
- incl. labour time savings	390	30,622	8,415,229
Lab (>0.1°C res T<200°C)	80	-3,693	-160,143
Lab (<0.1°C res or T>200°C)	310	4,185	726,860
Lab - total	390	2,610	566,717
Total (excluding labour time savings)	**950**	**121,587**	**56,567,958**
Total (including labour time savings)		**19,162**	**8,981,945**

[125] Excludes psychrometers and ambient thermometers.

Table A5b-31 shows that the transition from mercury industrial thermometers, in particular of thermometers designed to measure temperature above 200°C, to feasible alternatives, will be associated with substantial costs for users if no labour time savings are assumed. If labour time savings of 4 hours with an uncertainty margin of ±2 hours per year are assumed, the cost effectiveness is 49,200 ± 156 500 €/kg.

Lab and dial thermometers will have lower compliance costs with the proposed restriction of the placing on the market of mercury-containing devices. Although there are a number of similarities in the assumptions for industry and lab segments for thermometers measuring temperature above 200°C, the compliance cost for lab thermometers is calculated to be lower. The main factors influencing this outcome include: the lower long-term investment cost of the alternative due to the assumption that 2.5 mercury lab thermometers can be replaced by one electronic alternative; and the shorter (5 years instead of 13 years in industry) and equal lifetime of both mercury and alternative lab thermometers.

The transition to the alternatives from thermometers designed to measure temperature up to 200°C (including ambient thermometers and psychrometers) will likely result in long-term savings for users.

Annex 6: Mercury electrodes used in voltammetry

Content

1. Technical description of mercury electrodes[126]

Voltammetry

Voltammetry is an analytical technique, measuring the current flowing through an electrode dipped in a solution containing the sample, under an applied potential (Amel, 2001).

The voltammetric techniques allow to distinguish between the different oxidation status of metals, the differentiation between the free and bound metal ions, (Amel, 2001, Lassen et al., 2010) the analysis of the environmentally relevant anions like cyanides, sulphides, nitrites and nitrates and the specification of the biological availability of heavy metals (UNESCO, 2002, Lassen et al., 2010).

Measuring devices based on voltammetry

The *polarograph* comprises of a potentiometer for adjusting the potential, a galvanometer for measuring the current and a polarographic cell (made of glass or teflon) containing three electrodes, a reference one with a constant potential, an auxiliary electrode (a platinum wire inserted on a teflon rod) and the working electrode, a capillary connected to a mercury reservoir. A tube for bubbling nitrogen is inserted into the polarographic cell. (Lassen et al., 2008)

Example of a Modern polarograph from Metrohm

During the polarographic measurements the voltage is increased linearly with time (a voltage ramp) and the current variations are recorded automatically. The working electrode can be for instance mercury electrode. If the electrode is formed by a drop of mercury hanging from a tip or capillary, the technique is called *polarography* (Amel, 2001).

[126] Mercury reference electrodes are not covered by this title, and are not assessed because they are dependant on electric current and contain mercury as an integral part of the device (See also appendix 4).

Besides polarography, mercury electrodes are used in the *stripping voltammetry*, and they usually consist of either a drop or a film of mercury. This technique follows two main steps: a preconcentration of the analyte onto the electrode and the successive stripping of the accumulated compound in an inverse direction, onto the electrode towards the solution (it is also named inverse voltammetry). It allows to considerably enhance the sensitivity during the preconcentration stage and to reduce the quantity of the mercury used as electrode. (Amel, 2001)

The devices based on voltammetry are relatively simple, fast, and the theoretical background is precise. All together with the high reproducibility of the curves (current-voltage or current-potential) makes the method one of the most sensitive and versatile one (Electrochemistry Encyclopedia, 2010).

Mercury electrodes

The mercury electrodes used in voltammetry (e.g. with above mentioned devices), serve as sensor electrodes. According to a producer of polarographs, mercury is considered the best metal for cathodic scanning because of its large overpotential and for the possibility to be renewed before each analysis (Amel, 2001).

The mercury electrode is a drop of mercury hanging at the orifice of a fine-bore glass capillary. The capillary is connected to a mercury reservoir so that mercury flows through it at the rate of a few milligrams per second. The outflowing mercury forms a drop at the orifice, which grows until it falls off. The lifetime for each drop is 2 to 5 seconds. Each drop represents a new electrode with the surface practically unaffected by processes taking place on the previous drop. The dropping electrode is immersed in the investigated solution from the cell. (Electrochemistry Encyclopedia, 2010)

The Metrohm 3 electrode system. (the real physical diameter of the mercury drop is typically between 0.3 mm and 0.4 mm; the size is adjustable in certain narrow limits).

The modern versions of mercury electrodes used in polarography are:

- *The dropping mercury electrode* (DME); a flow of mercury passes through an insulating capillary producing a droplet which grows from the end of the capillary in reproducible way. Each droplet grows until it reaches a diameter of about a millimeter and releases. As the electrode is used mercury collects in the bottom of the cell (Amel 2001).
- *The hanging mercury drop electrode* (HMDE) is a variation on the dropping (DME). It consists of a partial mercury drop of controlled geometry and surface area at the end of a capillary in contrast to the dropping mercury electrode (DME) which steadily releases drops of mercury during an experiment; the whole potential sweep takes place at this single drop.

- *The static mercury electrode* (SMDE) combines the properties of the dropping mercury electrode (DME) and the hanging mercury electrode (HMDE). It comprises of a capillary (0.15 to 0.2 mm ID) connected to the mercury container. A valve, operated by a PC, adjusts the dimension of the drop, while a platinum wire ensures the electrical connection with the electrical circuit. The drop surface is constant during the measurement (Amel 2001).

The modern instruments allow the use of any of these electrodes, depending on the application they are used for (Schröder &Kahlert, 2002).

The mercury electrodes used in voltammetry usually have very small surfaces in order to assume quickly and accurately the potential imposed by the electrical circuit. (Amel, 2001)

Application areas

As voltammetry is a non-destructive technique it allows the sample to be analyzed for several times and with different analytes. It also allows the determination of metals at different oxidation numbers (e.g. Cr(III), Cr(IV), Fe(II), Fe(III), As(III), As(V)) and has a high sensitivity for Pb, Cd and Se. (Amel, 2001)

Nickel (Amel 2001), Cd, Pb, Cu, Cr and Fe (Metrohm, 2009) can be analysed (and the speciation is also possible) in sea water only using voltammetry and by this the ability of the water sample to form heavy metal complexes can be characterized (the complexing agents like natural organic compounds of anthropogenic origin, humic acids can mobilize heavy metals) (Metrohm, 2009).

The voltammetric method for metal trace analyses are recommended for small and medium sized laboratories with a low number of samples and a large variety of elements or other compounds to be determined and it has to be used in large laboratories for sensitivity or matrix problems or when a validation of the method is required (Amel, 2001).

The applications for mercury electrodes used in voltammetry are for instance:

- Mechanistic studies (especially of organic compounds) which are important for basic research, structure-activity relationship investigation, study of supramolecular interactions etc.
- Trace metal determination and speciation (information on the oxidation state of the metal, free metal and metal ion in different individual complexes)
- Trace determination of organic substances in the field of pharmaceutical analysis, food analysis, forensic analysis, toxicology and environmental analysis
- Voltammetric immuno assays (UNESCO, 2002, Metrohm, 2009)

2. Description of release and exposure

As described in the approach to assess the risks related to measuring devices using mercury as described in Section B.4 of the main document, there is no single parameter to sufficiently describe the potential release and exposure from either the use or the waste phase. However, according to Lassen et al. (2008) around 0.1-0.5 tonnes of mercury is used per year in polarography.

During the service-life of the polarograph, the mercury has to be continuously added to the device (Lassen et al., 2008), indicating that the use phase may cause both occupational exposure and releases to the environment. The amount of mercury used in measurements is used to describe the potential release and exposure from both the use and the waste phase.

Box 1: General qualitative description of potential release and exposure

Production phase

The mercury is not included in the polarographs during the production of the devices, thus the production phase of polarographs is not relevant for potential release and exposure.

Use phase

Mercury has to be continuously added to the polarographs (Lassen et al., 2008). According to Lassen et al. (2008) around 0.1-0.5 tonnes of mercury is used per year in polarography. This is in the same order of magnitude as the estimation of world-wide use of 0.35 tonnes per year by a producer of devices containing mercury electrodes and used in voltammetry (Metrohm, 2009).

The amount of mercury used is significantly reduced in the modern instruments and one filling requires 6 ml of mercury (81g). This can be used to create 200,000 drops necessary for 0.5 to 1 year of use (Metrohm, 2009). According to one manufacturer, the modern instruments are fully sealed (Amel, 2001).

According to a user of a polarograph, the mercury drops are collected during the analysis in the polarography cell. After the analysis the whole liquid including the mercury amalgam is collected in a special vessel for mercury waste and covered by a water layer. When the accumulated waste reaches a reasonable quantity, the mercury can be either distilled in- house, or sent to external specialized companies. Only pure mercury can be used in polarography (Diacu, 2010).

There is no data available to quantify or assess further the emissions from the use phase. Due to relatively low tonnages (e.g. compared to mercury used in porosimeters) and the way the mercury is used in the measurements, the exposure of workers and releases to the environment from the use phase are assumed to be limited

and in any case covered by the occupational limit value (coming into force in December 2010).

Waste phase

As the mercury is used in the analysis the waste stage of the device is not relevant, but the waste handling of mercury is, according to a polarograph user (Diacu, 2010), the mercury used in polarography is either distilled in-house, or sent to specialised companies after measurements. There is no data available to assess further the waste stage and the situation may vary between users and possibly also between Member States.

3. Available information on alternatives (Part C)

3.1 Identification of potential alternative techniques

There are several methods and combinations of methods which can replace polarography or mercury electrodes used in voltammetry only in certain applications. They can be divided in the following categories.

Spectroscopic techniques (usually coupled with another separation technique):

- Atomic absorption/emission spectroscopy (AAS/AES) is an instrumental technique for detecting concentrations of atoms to parts per million by measuring the amount of light absorbed/emitted by atoms or ions vaporized in a flame or an electrical furnace.
- Inductively coupled plasma (ICP), an analytical technique used for the detection of trace metals with A(O)ES atomic (optical) emission spectroscopy (ICP-A(O)ES). A(O)ES is a type of emission spectroscopy that uses the inductively coupled plasma to produce excited atoms and ions emitting characteristic electromagnetic radiation http://www.answers.com/topic/electromagnetic-radiation of a particular element. Its intensity is used to determine the concentration of the element.
- Mass Spectrometry (MS) is an analytical technique by which substances are identified by sorting the mass of gaseous ions using electric and magnetic fields. The molecules ionized in the target sample, are accelerated in the mass spectrometer. The speed of the molecules attain during acceleration is proportional to their mass (their mass-charge ratio), which thus can be calculated (answers.com, 2010).

Other non-electrochemical techniques (than spectroscopic techniques)

- High performance liquid chromatography (or high pressure liquid chromatography (HPLC) usually coupled with mass spectrometry (MS) (HPLC-MS) is a form of column chromatography to separate, identify, and quantify compounds based on their polarities and interactions with the column's stationary phase.

- Neutron Activation Analysis (NAA) is a sensitive multi-element analytical technique used for both qualitative and quantitative analysis of major, minor, trace and rare elements, via the element characteristic emission of particles, or gamma-rays. The activation nuclear process is used for very accurately determining certain concentrations of elements in a vast amount of materials.
- X-ray emission; measure these X-rays having characteristic energy of elements . E.g. following X-ray emission methods exist:
    - X-ray fluorescence (XRF) is the emission of characteristic "secondary" (or fluorescent) X-rays from a material that has been excited by bombarding with high-energy X-rays or gamma rays.
    - Particle-Induced X-ray Emission or Proton Induced X-ray Emission (PIXE) analyses atomic interactions occurring in the X-ray part of the electromagnetic spectrum specific to elements.
    - microPIXE; Recent extensions of PIXE using tightly focused beams (down to 1 μm) gives the additional capability of microscopic analysis. This technique can be used to determine the distribution of trace elements in a wide range of samples (answers.com, 2010).

Electrochemical techniques using electrodes (others than mercury electrodes):

Other electrochemical techniques exist that work on the same voltammetry principle but use different types of electrodes.

- voltammetric solid sensors (gold, carbon silver or bismuth electrodes),
- rotating disk electrodes,
- disposable electrodes (Metrohm, 2009).

Using alternative electrodes in polarography

Galinstan, a registered trademark of the German company Geratherm Medical AG, is an eutectic alloy of gallium, indium, and tin, liquid at room temperature, and is considered to be a promising alternative to the commonly used mercury electrodes in polarography (Surmann, P. and Zeyat, H., 2005, Channaa,H. and Surmann, P.,2009). It can be employed as a liquid electrode instead of mercury in the voltammetric analysis of different metal ions, such as lead and cadmium, in supporting electrolytes.

3.2 Human health and environment risks related to alternatives

The risks associated with the alternative devices/methods vary, as the methods/techniques are very different.

Due to its low toxicity and low reactivity of its compounds, galinstan is considered to be safer than mercury (reachinformation.com, 2010). For more information on gallium and indium see Annex 4.

The other substances used in the alternative electrodes have lower toxicity compared to mercury: gold is well-known as a non-toxic substance and for its inertness, the

carbon-silver electrodes are safely used in health-care devices and bismuth is one of the least toxic heavy metals. The other alternative methods include mechanical and electronic parts, not posing notable risks to human health or the environment (see description in part C).

Since the technical feasibility of alternatives could not be established (see further in section 3.3), it has not been possible to compare the risks of mercury electrodes used in voltammetry and their non-mercury alternatives.

3.3 Technical feasibility of alternatives

As some of the alternatives apply totally different methods and principles than the mercury electrodes used in voltammetry, their technical feasibility is difficult to be assessed. Nevertheless, below are presented some problems and limitations related to alternative methods.

Spectroscopic techniques

The ion matrices analyzed by spectroscopic techniques require custom-designed analysis, usually an additional pre-separation phase (by co-precipitation, extraction, hydride generation, separation on cathion exchange resin, adsorption) and often pre-concentration are required to provide acceptable levels of detection when using AAS or HPLC. The flame emission instruments (used in AES) lack the sensitivity offered by the mercury devices (Thompson, 1991).
The spectroscopic techniques allow only the total metal content determination, and they do not distinguish between different oxidation stages of metal ions, or between free and bound metals (Lassen et al., 2010).

Other non electrochemical methods

All the non-electrochemical methods (excluding spectroscopic techniques) described above are well accepted. Nevertheless, most of them allow only the total element detection and need high investments (for purchasing, running and maintenance), have limited mobility and require special laboratory infrastructure. There are some problems with some sample matrices (sea water, pure chemicals), as they can generate more interferences and by this, they are less sensitive.

When using Neutron Activation Analysis (NAA) the irradiated sample remains radioactive for many years. As the number of suitable activation nuclear reactors is declining, the technique may become more expensive.

Other electrochemical techniques using other types of electrodes (than mercury hanging drop electrodes)

Other electrochemical techniques have high sensitivity and may replace some mercury applications but have limited analytical performance due to dynamic range and versatility (less elements can be determined). In addition they generate more

interference and by this, they are less sensitive. The lifetime of sensors is limited and they need more electrode maintenance (Metrohm, 2009).

Using alternative materials for the hanging drop electrodes

Galinstan tends to wet and adhere to many materials, including glass, which limits its use compared to mercury (HERC, 2010). The inner glass tubes must be coated with gallium oxide to prevent the alloy from wetting the glass surface. In addition, its aggressiveness could be a major obstacle for its use: it corrodes many other metals by dissolving them (Cadwallader, 2003). With the existing information it is difficult to assess the technical feasibility of galinstan in polarography.

3.4 Economic feasibility

The modern voltammetry instruments using mercury electrodes have a low price, low running costs and compact dimensions (they do not require special build laboratory space) (Lassen et al., 2010, Metrohm, 2009).

Two most relevant and widely used alternative techniques could in principle be assessed against their economic feasibility, namely, atomic absorption spectroscopy (AAS) and Inductive coupled plasma (ICP) spectrometers with OES (Optical emission detection) or with MS (Mass spectrometric detection). However, even these alternatives can replace the mercury electrodes only in certain subsets of applications not necessarily in all uses (Metrohm, 2010).

Secondly, there is not enough data available for either of the alternatives for the full economic comparison. However, below we sketch a comparison given the existing data.

The one-time investment cost of one polarograph is €20,000 compared to over €40,000 for AAS and €40,000-100,000 for ICP (Lassen et al., 2010). The comparison of the numbers is hindered as the average lifetime of the two alternatives is not available. Furthermore, the difference in the investment costs is underlined as the two aforementioned alternatives i) generally require laboratory infrastructure, ii) are less mobile and iii) have smaller number of suitable applications.

Recurrent costs for polarography is suggested to be about €2000-2500 annually translating to about €1 per analysis given generally 100-5000 analysis per year. A full comparison of the recurrent costs can neither be done as the data for recurrent costs and annual number of analysis is missing for alternatives. However, first one of the alternatives, AAS, is reported to require costly accessories (lamps, graphite furnaces), and users of the ICP alternatives are reported to need to spend € 20 000 – 30 000 per year only for argon gas needed in the process. (Lassen et al., 2010)

Given the scarcity of the data it can only be said, that the relatively higher investment costs, more narrow uses and special needs for laboratory infrastructure in case of the two alternatives would require that the lifetime and/or the productivity of the

alternatives would need to be considerably higher in order for those to be able to compensate the limitations.

4. Justification why the proposed restriction is the most appropriate Community-wide measure (PART E)

4.1 Identification and description of potential risk management options

4.1.1 Risk to be addressed – the baseline

As discussed in Part B, the current pool of mercury in measuring devices is used as an indicator of maximum emission potential for most of the devices in this report. For the mercury drop electrodes there is not such a pool as the mercury is used in the measurements, and it does not accumulate in the products. For mercury drop electrodes the maximum potential for emissions is the amount of mercury used annually by the users. As described in Chapter B.4. it is estimated to be 0.1-0.5 tonnes yearly. According to the only identified European producer, the world-wide use of mercury is estimated to be 350 kg per year (Metrohm, 2009).

According to a producer of the devices (Metrohm, 2009) the risks related to both use and waste phase are very much reduced in the most modern devices as a result of the minimization of the mercury used (around 80 grams for one filling, necessary for 0.5 to 1 year of use). As a result of the replacing existing devices by modern equipments, the trend of mercury used in voltammetry is likely to be declining. Nevertheless, there is no information available to assess the trend in the number of mercury drop electrodes used in voltammetry, placed on the market annually.

4.1.2 Options for restrictions

As a result of the low quantities of mercury used in voltammetry and strong evidence suggesting that feasible alternatives do not exist, only one restriction option is assessed:

> Restriction on the placing on the market of mercury to be used as mercury electrodes in voltammetry.

4.2 Assessment of risk management options

Restriction of the placing on the market of mercury to be used as mercury electrodes in voltammetry

The maximum risk reduction capacity of this option is estimated to be between 0.1 and 0.5 tonnes annually. As described in Part B.2 (Scope and approach), the restrictions do not apply to the manufacture, placing on the market or use of a substance for scientific research and development provided that the conditions in Article 3(23) of REACH are achieved. Article 3(23) of REACH defines scientific research and development as "*any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year*". It is possible that some of mercury electrodes used in voltammetry fulfil the above mentioned requirements, namely mercury is used under controlled conditions in a volume less that 1 tonne per year, and consequently benefit from this exemption. If this is a case, the risk reduction capacity would be reduced accordingly, i.e. it would be lower than estimated above.

As described in Section 3.3 the alternatives for polarographs have limitations related to both technical and economic feasibility. Thus no restriction on the placing on the market of mercury used as electrodes in voltammetry is proposed.

Due to obvious limitations on technical and economic feasibility of alternatives, no further efforts have been taken to assess the restriction option.

4.3 The proposed restriction(s) and summary of the justifications

Proposal:

No restriction proposed.

Summary of justification:
Technically feasible alternatives for mercury electrodes used in voltammetry are not available in all applications. In addition two main alternatives seem not to be economically feasible.

Annex 7: Porosimeters

Content

1. Technical description of porosimeters

Porosimeters are instruments that are capable of measuring pore volume and their distribution, based on the principle of either liquid intrusion or extrusion into or from pores. They are used e.g. in automotive, biotechnology, pharmaceuticals, ceramic, catalysis, energy, building materials, geology, agricultural and textile industry. According to a producer of porosimeters around 60% of porosimeters are used for research and 40% for quality control purposes (Commission, 2009b; Lassen et al., 2010). Contrary to devices containing mercury as an integral part, mercury is used when measuring with mercury porosimeters and the equipment must be refilled regularly.

The application of mercury porosimeters is based on the gradual increase in pressure to enable mercury to enter the pores in a sample, as there is a relationship between the applied pressure and the pore diameter. Mercury porosimeters can be used for wide range of pore sizes i.e. routinely from 0.003 μm to ca. 1000 μm. In addition to pore volume and distribution, mercury porosimeters can provide information about the surface area, particle size distribution, tortuosity, permeability, fractal dimension, compressibility, pore shape, network effects and the skeletal and bulk density. (IUPAC task group, 2010)

2. Description of release and exposure

As described in the approach to assess the risks related to measuring devices using mercury in Section B.4 of the main document, there is no single parameter to sufficiently describe the potential release and exposure from either the use or the waste phase.

Waste management of mercury and mercury contaminated samples and other materials is one part of the normal operation of the laboratories performing measurements with these devices. The reported practices in laboratories appear to support the view that the waste handling of mercury used in the measurements would be conducted in accordance with the requirements of the hazardous waste legislation (Lassen et al., 2010, see Appendix 3). Thus, the annual amount of mercury disposed of as a waste does not reflect the emissions that could occur from the uncontrolled waste streams. Nevertheless it describes the magnitude of mercury involved in the waste phase. Similarly, the amount of mercury used annually in the measurements gives an idea of the quantity of mercury involved in the use phase of porosimeters, and thus gives an impression of the magnitude of releases and exposure that can occur in the use phase.

Based on the calculations and information presented in Box 1:

- The amount of mercury bought annually by the users of porosimeters is estimated to be around 5-14 tonnes per year in the EU. However, the amount of mercury used in the measurements is estimated to be 12-58 tonnes per year,

as some of the mercury is used several times by the users as described in Box 1.

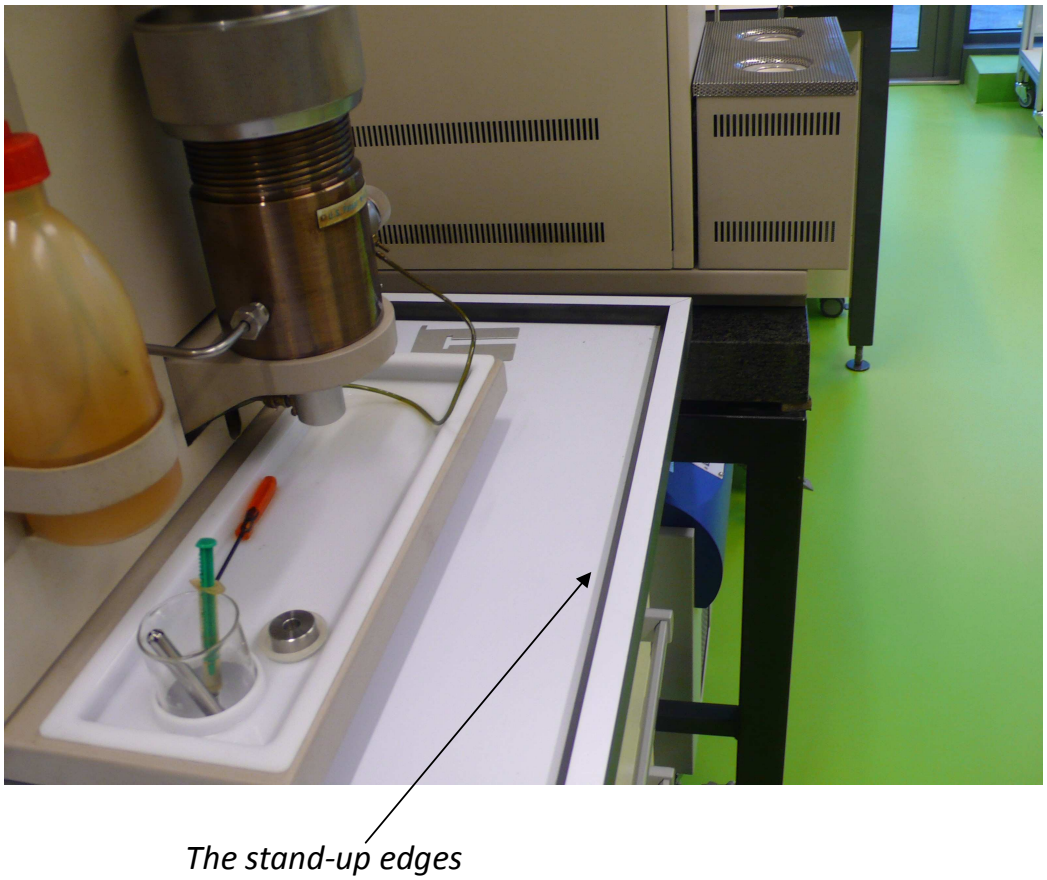
- The amount of mercury disposed of annually as hazardous waste is estimated to be around 1.2-3.4 tonnes.
- The mercury that is not disposed of as hazardous waste by the users is sent to specialised companies for purification or regeneration.

There is no data available to quantify the amounts of mercury released during the normal use of porosimeter or the amounts of mercury ending up to non-controlled waste streams. Nevertheless, based on the information gathered during the preparation of this report, these amounts are likely to be relatively small (Lassen et al. (2010) in Appendix 3).

In addition to general qualitative description of potential release and exposure presented in Box 1, Appendix 3 (Lassen et al. 2010) contains a detailed description of the actual measuring activity and a screening of potential release sources for porosimeters. Furthermore, during the public consultation additional information describing measures taken to prevent mercury releases were provided. The illustrative pictures from the University of Amsterdam (pictures 1, 2 and 3) should be considered together with above mentioned information and pictures presented in the appendix 3.

Picture 1. A thresdhold separating the area were mercury is used from the rest of the laboratory and a special table (see also picture 3) used in the University of Amsterdam.
Source: University of Amsterdam (received during the public consultation)

Picture 2. The suction located below the working area in the University of Amsterdam.
According to the user, a fume hood above the working area is not the best option as the vapours are heavy. Furthermore, using a good filter will create some pressure drop and lower the suction rate.
Source: University of Amsterdam (received during the public consultation)



Picture 3. The stand-up edges in the University of Amsterdam.
Source: University of Amsterdam (received during the public consultation)

Box 1: General qualitative description of potential release and exposure

Amounts of mercury bought and used by the users of porosimeters

According to a survey carried out by the Commission (see Appendix 5), a user of porosimeter buys on average 7.2 kg of new mercury per year. Assuming that 700-2000 porosimeters are in use in the EU (Commission, 2009; Lassen et al., 2008), a total amount of 5-14 tonnes of new mercury is bought annually by these users[127]. This estimate does not consider the fact that some users have a lot of mercury in storage, e.g. 400 kg reported by one user (see Appendix 5), and they do not need to buy new mercury annually.

As visualised in Figure A7-1 below, oil is needed in the measurements. Around 35 %

[127] 7.2 kg (Hg bought annually by user) x 700-2000 (Number of users in EU) = 5-14 t/y

of the users of porosimeters are able to separate the mercury from the oil themselves (see Appendix 5)[128] after the measurement and some laboratories send the mercury and oil to specialised companies for separation. Laboratories can use a batch of mercury 5-10 times or even more often (Lassen et al., 2010). Based on these assumptions it can be estimated that 12-58 tonnes of mercury is used annually for the measurements[129].

The cycle of mercury when using porosimeters

There are several steps in the "cycle of mercury" when using porosimeters as described in the figure A7-1. After measurement some of the mercury can be used again after separation from oil.

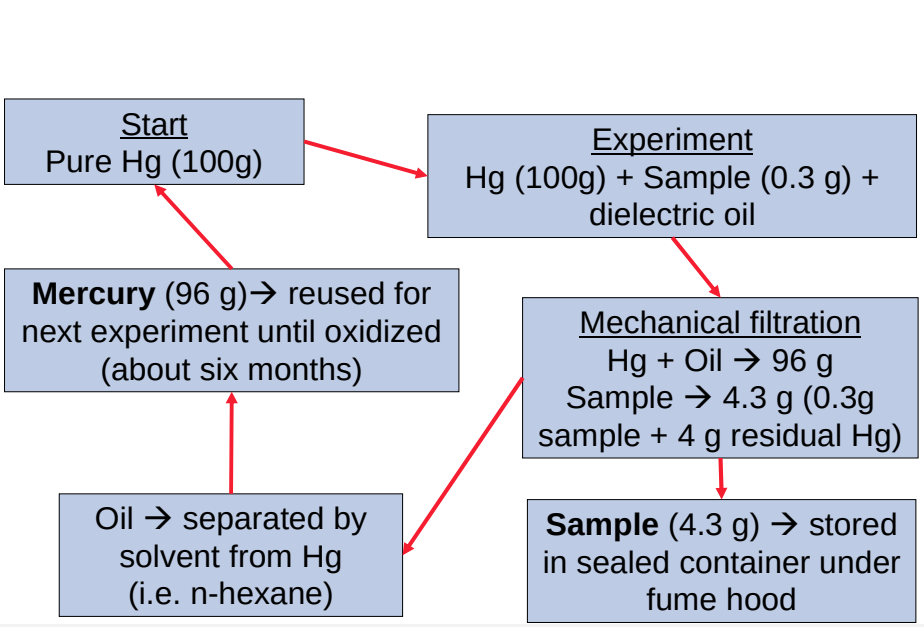


Figure A7-1: The cycle of mercury in measurement with mercury porosimeter
Source: Thermofisher, as cited in Lassen et al., 2010 (see Appendix 3)

Around 4% of mercury used in a measurement will stay in the sample and 96% of mercury is mixed with the oil and needs to be separated. The separated (in-house or externally) mercury can be used in a new measurement until it is oxidised. There is no data available on the rates of oxidation of mercury during or between the measurements, but it is dependant on the material of the measured samples. The oxidised mercury may be sent to specialised companies to be regenerated, i.e. reduced back to the metallic form. (Lassen et al. 2010, see Appendix 3)

[128] This result is not reported in the Commission's review report (COM, 2009), but is based on the individual responses for the survey which have been made available for ECHA.
[129] 5-14 t (Hg bought annually) x 0.35 (35% of laboratories conducting in-house separation of Hg from oil) x 5-10 (Hg reused 5 to 10 times) + 5-14 (Hg bought annually) x 0.65 (65% of laboratories not using Hg several times) = 12-58 t/y
[130] 1.7 kg (Hg disposed as waste by one user) x 700-2000 (number of porosimeters in EU) = 1.2-3.4 t
[131] 0.04 (4% of Hg stays in the sample) x 13-58 t (Hg used for measurements) = 0.5-2.3 t

Production phase

The mercury is not included in the porosimeters during the production of the devices, thus the production phase is not relevant for potential release and exposure of mercury.

Use phase

Some of the mercury is likely to evaporate during the use of porosimeters and causes occupational exposure or ends up in the environment. There is no data available to estimate the possible release from the use, but the relevance can not be excluded due to relatively high volumes of mercury used. The release is highly dependant on the risk management measures and safety procedures used in the laboratories, and may vary significantly between laboratories and Member States. Note that in this respect it is relevant to mention that a Community-wide occupational exposure limit value (IOELV) has been adopted for mercury (0.02 mg/m^3), see also Part B.5 (Summary of existing legal requirements and their effectiveness).

The following release routes of mercury from the use and waste phase are identified by Lassen et al. (2010):

1. Releases from the porosimeter through the exhaust of the porosimeter. From mercury spilled by filling of container, droplets on penetrometer, cleaning of valves, cleaning of high pressure tank, etc.
2. Releases from the fume hood through the exhaust of the fume hood. From mercury spilled or directly evaporated by emptying and cleaning the penetrometer and mercury spilled or directly evaporated by regenerating the mercury. Mercury releases from small droplets on gloves, cleaning pads, etc.
3. Release from the fume hood through the drain of the sink (if the fume hood has a sink). From mercury spilled by emptying and cleaning the penetrometer, mercury spilled by regenerating the mercury, from small droplets on gloves, cleaning pads, etc. the mercury may inter into a sink in the fume hood.
4. Releases from the laboratory's general ventilation system. From mercury spills outside the fume hood or porosimeter.
5. Long term releases from mercury contaminated waste. All mercury contaminated waste (>0.1 % w/w) has to be disposed of as hazardous waste, in accordance with EU waste regulation.
6. Releases from recycling of mercury by recycling companies.
7. Mercury in solvent disposed of as solvent waste. Mercury is not dissolved in the solvents and the waste solvent seems not to be considered mercury containing.

No data has been available for quantification of any of these releases, but according to Lassen et al. (2010) the main source of mercury releases from the use phase of porosimeters is assumed to be from the fume hood, where several operations with mercury are conducted.

A detailed description of the measuring process of porosimeter and description of

potential releases can be found in the Appendix 3.

Waste phase

Most of the mercury used in analysis is regenerated to be used again. This regeneration is not recycling as described in the revised waste framework directive (2008/98/EC), as the mercury is not intended to be discarded by the user. In addition, some of the mercury waste disposed of as a hazardous waste will be recycled. It is highly unlikely that the mercury mixed with the oil or the oxidised mercury would end up to non-controlled waste streams, but it can not be excluded either.

The main mercury waste fraction is the contaminated sample. In addition, some mercury ends up in the waste stream from the protecting gloves filters etc. Based on the individual responses to Commission's survey (see Appendix 5) and interviews with users of porosimeters (Lassen et al., 2010) it seems that the users dispose of the mercury in accordance with the requirements of the hazardous waste legislation. Thus the proportion of mercury ending up in non-controlled waste streams seems to be small.

Based on the reported amounts of mercury disposed as waste by users (see Appendix 5), it can be estimated that around 1.2-3.4 tonnes of mercury would be disposed of as waste per year[130]. According to Lassen et al. (2008) most of the mercury losses are expected to be caused by the mercury-saturated samples. Assuming that 4% of mercury stays in the sample after a measurement (Thermofisher as cited in Lassen et al. 2010) results in having around 0.5-2.3 tonnes of mercury in the samples annually[131]. The amount depends on the material of the sample, and a rate as high as 20% has been reported (Lassen et al., 2010)

There is no data to further assess the amounts of mercury ending up in hazardous or non-controlled waste streams from the waste fractions or to assess the recycling rate for the mercury disposed of as waste.

3. Available information on alternatives (Part C)

3.1 Identification of potential alternative techniques

There are several alternatives for mercury porosimeters with different kind of limitations on the feasibility. The following alternative techniques and methods have been identified in a report by IUPAC task group on liquid intrusion and alternative methods for the characterization of macroporous materials (2010).

Intrusion of other non-wetting liquids

Alternative liquid metals e.g. gallium, indium and their alloys can be used instead of mercury in devices relying on the same method as mercury porosimeters.

Methods based on capillary condensation equilibria obtained through drainage and/or evaporation

Liquid porosimetry (i.e. extrusion porosimetry) can utilize any wetting fluid e.g. pure water and hexane. Instead of positive pressure to intrude the liquid into sample, liquid porosimetry applies negative pressure to drain the wetting liquid from the pores. The sample is exposed, in a test chamber, to varying and precisely controlled air pressure. With the variation of pressure, different size pore groups drain the liquid and their pore volume is equal with the one of the liquid.

Gas adsorption porosimeter is based on the adding (or removing) a quantity of gas (nitrogen, argon or krypton, CO_2) to samples, at cryogenic temperatures, where weak molecular attractive forces cause the gas molecules to adsorb on material in order to obtain adsorption-desorption isotherms. The volume of the gas adsorbed by the sample can be determined from the ideal gas law and also the surface area and pore size distribution of the sample can be derived (ZAG Ljubljana, Micromeritics Analytical Services, Green Chemistry Centre of excellence). According to Mitchell et al. (2008) gas adsorption is the most commonly used method for determining pore size distributions in addition to mercury porosimetry.

Contact (or standard) porosimetry is based on the gravimetric measurements of the liquid in the sample and by simultaneously investigating from adsorption and capillary isotherms the pores at the thermodynamic equilibrium conditions. The automated version, automated standard porosimeter (ASP), includes a computer, an electronic balance, an automatic manipulator, a device with electromagnetic valves for a controlled drying of the porous samples by a flow of dry inert gas. It is used e.g. for the investigation of porous materials used in electrochemical devices (electrodes, membranes).

The bulk condensation method consists in the oversaturation of the sample in order to fill all the pores and then the analysis of the desorption branch from the adsorption isotherms.

Water desorption calorimetry consists in the saturation of the porous medium with a liquid which is then slowly desorbed in quasi-equilibrium conditions. The equilibrium relative pressure is deduced from a differential transducer between the sample cell and the reference cell that is filled with pure liquid. The desorbed liquid is determined by using the heat flow.

Permeation of a liquid (permeameters)

Porous samples can be characterized by permeation of a gas or a liquid through the sample material followed by a prediction, or at least correlation of the pressure drop to the flow rate by using various equations for the laminar flow regime. (IUPAC task group, 2010)

Freezing-melting porosimetry

When a liquid fills a porous sample its freezing and melting points are depressed. These changes are connected with the width of the pore. Together with the volume of

molten liquid in a given temperature it is possible to get information on pore-size distribution. The method is completed by *Differential Scanning Calorimetry (i.e. Thermoporometry) when* the measured temperature depression is determined and directly related to the pore width or *Nuclear Magnetic Resonance (NMR) cryoporometry*, when the depression of the melting point of a crystalline solid is determined by analyzing the proton NMR signal as function of temperature.

Imaging techniques

Imaging techniques including e.g. *Magnetic Resonance Imaging*, *X-ray Tomography*, *Electron Microscopy*, *Light microscopy/Laser methods*, *Pulsed-field Gradient* and *Hybrid Imaging* allow pore size mapping.

Statistical reconstruction of porous materials

Statistical modelling can be used to characterise a disordered porous medium with several pore shapes presented. Structural correlations aim to correlate the structural state of different points with functions such as bulk, surface autocorrelation or pore-surface correlations functions and use of statistical geometrical analysis, mathematical morphology.

3.2 Human health and environment risks related to alternatives

Some alternatives use other liquids than mercury to measure the porosity of the sample. They vary from water to liquid metals like Indium, Gallium and their alloys (IUPAC task group 2010). The environmental and health risks related alternative substances and methods are not assessed further in this report[132], but there are no indications that risks would be at the same level as related to mercury. For most of the alternatives the risks would be significantly lower.

3.3 Technical and economic feasibility of alternatives

Only one producer of mercury porosimeters (out of four contacted) responded to the questionnaire in the stakeholder consultation. The producer with wide selection of alternative devices did not respond (based in the USA). Thus, the following information is based on a (limited) literature search and one response during the stakeholder consultation. Identified alternatives have different limitations related to e.g. applicable pore sizes, applicable size and material of samples, measured parameters and duration of measurement. The mercury porosimeter has limitations in applicability as well e.g. limited pore size range (0.003-1000 μm) and requirements on the durability of the sample as high pressure is applied. Below some identified limitations and advantages of different alternative devices.

[132] Some information on gallium can be found in Annex 5b (Thermometers).

Intrusion of other non-wetting liquids

According to a brochure of a producer of porosimeters, a specific porosimeter is able to use both mercury and other liquids (only water mentioned) (Porous Materials, 2010). Based to the brochure the only limitation seems to be that the fluid needs to be non-wetting to the tested material. There is no data available on the potential fluids (in addition to water) to be used or their wetting properties in different sample materials (and thus in different application areas).

Intrusion of water is applicable only on hydrophobic samples and the preliminary surface treatment to make the sample hydrophobic (if needed) is a time consuming task. According to a producer of porosimeters, the hydrophobic materials cover less than 5% of applications and the water intrusion porosimeter is only applicable to samples with pore sizes between 0.001-20 μm. (Lassen et al., 2010)

According to a producer of water intrusion porosimeters, potential application areas include automotive, chemical, pharmaceuticals, battery separator, fuel cells, powder metallurgy, ceramic, paper and filtration industries (Porous Materials, 2010).

Methods based on the capillary condensation equilibria obtained through drainage and/or evaporation

Liquid porosimetry (i.e. extrusion porosimetry)
Liquid porosimetry can be used for deformable materials (IUPAC task group, 2010). According to Lassen et al. (2010) a producer of porosimeter has indicated that the method involves a very expensive gravimetric technique and is applicable to pore sizes between 1-1000 μm, even though an application range of 0.06-1000 μm is indicated by another producer. According to a producer of liquid extrusion porosimeters, potential application areas include automotive (particle filters for diesel fuels), filtration, nonwovens, biotechnology & healthcare, geotextiles, pharmaceuticals, ceramic, household & personal hygiene and textiles industries (Porous Materials, 2010).

Adsorption (nitrogen) porosimeter is applicable only for pore sizes below 0.05-0.1 μm. (IUPAC task group, 2010).

Contact (or standard) porosimetry is applicable for pore size between 0.01-100 μm. (IUPAC task group, 2010)

The bulk condensation method is not applicable for pore size above 0.4 μm

Water desorption calorimetry still has some problems related to kinetics and is not applicable for pore sizes above 10 μm.

The methods based on the capillary condensation equilibria are applied at least to some extent for the same pore sizes as mercury porosimetry and are thus possible alternatives to replace the mercury porosimetry in the future. (IUPAC task group, 2010)

Permeation of a liquid (permeameters)

The results can be linked to pore size in the 0.1 to 1000 μm range, or other characteristic of the material. A major problem is with samples composed of different pore sizes, as the flow rate though the larger pores will be more than proportionally larger than flow through smaller pores. In addition no standard equipment is readily available with broad applicability. (IUPAC task group, 2010)

Freezing-melting porosimetry

The freezing-melting porosimetry is applicable for wet and fragile samples which do not withstand drying or outgassing. It has also advantages of being a clean method (usually using water), relatively fast measurement (around 3 hours), requirement of small sample (10 mg) and reasonably comparable results with other methods. (IUPAC task group, 2010)

Nevertheless, the sample must withstand the liquid and avoid any unwanted transformation (IUPAC task group, 2010). In addition, nuclear magnetic resonance cryoporometry has the disadvantage over mercury intrusion of having an upper measurable size limit below1 μm (Vargas-Florencia et al., 2006).

Conclusions on technical and economic feasibility

The IUPAC task group (2010) concludes that there are no technically feasible well-established alternatives to mercury porosimeters in pore sizes between 0.05μm and 400μm. Nevertheless, it has not been possible to rule out during the preparation of this report that a combination of several devices and methods would allow measuring more or less similar parameters as by mercury porosimeters. It is possible that the technical infeasibility is more related to the comparability of the results measured by mercury porosimeters and alternatives than physical limitations like pore sizes. This problem could be solved at least partly by allowing adequate time for the users to run measurements concurrently. According to Lassen et al. (2010) a producer of porosimeters has indicated that some 3 years would be needed for validation and re-calibration of quality control procedures and 4 years for development of new certified reference materials for the results validation. There are no data available on the relevance of the comparability of results for research purposes.

Three national bans in Denmark, Netherlands and Norway have derogations for use in porosimeters. In addition in Sweden companies have a possibility to apply for national authorisation for purchase of porosimeters and between 1996 and 2010 this possibility has been used twice. This indicates that the technical feasibility of alternatives has not been easily established in those Member States which already have wide national restrictions related to mercury in other measuring devices.

It has not been considered proportionate in the framework of this restriction report to fully screen and assess all the alternative devices and methods, and their technical feasibility in each application area. This is due to highly technical nature of the work requiring very specific expertise and a high workload (there are many different application areas, as well as different parameters measured, see section 1). Moreover, it has not been possible to identify a single application or group of applications

covering a significant share of measurements, which would allow a targeted restriction. In addition, after identifying technically feasible alternatives (or combination of alternatives) for some application areas, resources would need to be allocated in the assessment of the economic feasibility. In conclusion, a further assessment was not considered proportionate in the framework of preparing this report considering the anticipated workload and results.

As the technical feasibility of alternatives could not be established, the economic feasibility is not assessed in the report either. However, some available information gathered in the stakeholder consultation is reported below. According to Lassen et al. (2010) a mercury porosimeter cost around €20,000-€40,000. At least some alternative devices are cheaper than the mercury porosimeters (Lassen et al., 2008). Nevertheless, several alternative devices may be needed to cover all the measured parameters and all the sample materials that can be measured by a mercury porosimeter. The information received from a producer of porosimeters suggests that the costs of using flow porometer would be in the same magnitude as using mercury porosimeter (Lassen et al., 2010).

4. Justification why the proposed restriction is the most appropriate Community-wide measure (Part E)

4.1 Identification and description of potential risk management options

4.1.1 Risk to be addressed – the baseline

As discussed in Part B, the annual amount of mercury used in measuring devices is used as an indicator of the potential release and exposure in this report. For mercury porosimeters, one way to describe the annual use is the amount of mercury purchased by the users which is estimated to be 5-14 tonnes per year. However, the possibility to reuse the mercury several times means that around 12-58 tonnes of mercury is fed in to porosimeters annually to conduct the measurements. This amount describes the relevance of mercury porosimeters as source of exposure and emissions during the use phase. In addition, it is estimated that around 1.2-3.4 tonnes of mercury is disposed of as waste.

The risk related to both use and waste phase might be slightly reduced over time as devices and instructions, e.g. ISO standard, will be developed further. Nevertheless, these effects would not apply to all the users and old devices. There is no data available to estimate the trend in number of measurements done with mercury porosimeters.

4.1.2 Options for restrictions

The following tentative options to reduce the risks related to use of mercury in porosimeters were identified when preparing this restriction report. Options 1a, 1b and 1c are aimed to reduce the amount of mercury used in porosimeters and thus affect both the use and waste phase. Option 2 is only considering the waste phase, whereas options 3a and 3b concentrates on the use phase. Option 4 is a way to collect information to further assess the technical feasibility of the alternatives, as it was not possible to fully assess it when preparing this report. The variety of options reflects the fact that the mercury used in porosimeters could cause risks at both the use and the waste phase.

After tentative consideration only options 1a and 4 are considered more in detail in Chapter E.2 for the reasons presented below.

Reducing the amount of mercury used in porosimeters

1a) Ban on using the mercury in porosimeters
All the risks from both the use and waste phase would be totally eliminated. However, this option would also introduce high costs as mercury porosimeters would need to be replaced before the end of their service-life. For some applications several alternative devices would be needed to cover the same range of pore size measurements and to measure all the parameters offered by a porosimeter. As no technically feasible alternatives are identified for some applications, it would no longer be possible to carry out certain types of measurements. However, the impacts of this are extremely difficult to assess. Due to lack of technically feasible of alternatives, this option as such is not considered further. The following elements could be considered to reduce the negative impacts described above:

- long transitional period (e.g. 10 years) to allow users to adapt their quality control or research processes
- banning the use of mercury only in the porosimeters placed on the market after entry into force (i.e. ban placing on the market of mercury porosimeters)
- combination of above elements

This option with additional elements is further assessed in section E.2.

1b) Ban on using mercury in porosimeters with derogations for specific applications where technically feasible alternatives do not exist

Compared to 1a this option introduces lower costs as the impacts of not being able to carry out all types of measurements would be avoided. Likewise also the risk reduction capacity would be lower. As some laboratories are using porosimeters for several applications, this option might still introduce additional costs related to the need to buy additional devices to be used concurrently with the mercury porosimeter. The enforcement could be particularly problematic as mercury porosimeters would still be allowed, but only their use for specific applications would be restricted. In addition, it would be very difficult to go through all the applications to definitively assess the technical feasibility of alternatives, running the risk that some important

applications could be banned. Thus, this option is not considered further. The additional elements described for option 1a could be included to this option as well.

1c) Ban on using mercury in porosimeters in specific applications

This option is the same as 1b, but allows banning only those uses for which technically feasible alternatives exist for sure. The risk reduction capacity depends on the amount of mercury used for applications with technically feasible alternatives. We have not been able to identify a single application or group of applications covering a significant share of measurements. As in option 1b, some laboratories are using porosimeters for several applications. Thus this option might introduce higher costs as there would be a need to buy additional devices to be used concurrently with the mercury porosimeter. In addition, the enforcement could be problematic if mercury porosimeters would be allowed but only their use for specific applications would be restricted. Thus, this option is not considered further. The additional elements described for option 1a could be included to this option as well.

Promoting appropriate waste handling of mercury

2) Setting waste handling requirements

Risks related to the waste phase of mercury originating from the use of porosimeters could be reduced by promoting appropriate waste handling. However, the current waste legislation requires treating mercury properly, and according to available information there seem not to be problems with the compliance. Without any specific reasons the problems related to waste stage should be addressed through waste legislation and this option is not considered further. Nevertheless, the following two aspects to affect the waste stage were considered:

- The users of porosimeter could be obliged to deposit a pledge (x € per kg of Hg) which would be returned only when the mercury (including mercury in the samples) is returned to the supplier, and all the suppliers of mercury would need to adopt the system. The risk reduction capacity would be highly depending on the value of the pledge. Enforcement of this kind of scheme would be difficult, as mercury will be on the market for other applications than porosimetry without the pledge. In addition, some laboratories use mercury for other purposes than porosimeters as well and they would need to have separate fractions of mercury for different purposes. Setting this kind of system is not regarded necessary as there seem to be high compliance with waste legislation.
- Suppliers of porosimeters could be obliged to arrange take-back scheme for mercury used for porosimeters and the scheme would be obligatory for users. All the mercury for porosimeters would have to be purchased from the suppliers of porosimeters or from a company authorised by the supplier. The involvement of suppliers of porosimeters could make the enforcement easier. It would be also easier to inform these companies about the requirements. This scheme would include all the mercury containing waste fractions. Enforcement of this kind of system could be challenging, as mercury will be on the market from other sources than the suppliers of porosimeters. Setting this kind of system is not regarded necessary as there seem to be high compliance with the existing waste legislation.

In addition to setting waste handling conditions in the Annex XVII of REACH, another option would be to have a voluntary agreement with the users to improve waste handling. However, the reasoning above applies also to some extent to the voluntary agreements with the users of porosimeters. If later on new data becomes available – suggesting significant problems in the waste handling - the voluntary action with the users could be worth examining.

Promoting appropriate handling of mercury during the use phase

3a) Setting use conditions

Laboratories have different safety measures in place to prevent emissions and exposure to mercury e.g. exhaust systems, mercury spill kits and fume hoods. This option would try to promote and codify current best practices to be used by all the users. Use conditions would reduce the risks related to use phase including also the in-house separation of mercury. With the available data it is difficult to estimate the risk reduction capacity and costs related to this option.

There is an ongoing work to revise the ISO-15901-1 standard (Pore size distribution and porosity of solid materials by mercury porosimetry and gas adsorption) to include recommendations on the safe use of mercury. These recommendations could be used as an example when setting the use conditions. However, a straight forward reference to prevailing the ISO standard is not a suitable option as the standards are not available free of charge for actors and they might be amended (or even closed down) without involving chemical authorities. The possible impact of the ISO standard revision on the risk reduction capacity of setting the use conditions is difficult to be assessed as there is no data available on the share of users following the standard in question, nor on how well they already fulfil the recommendations.

Occupational health legislation has already addressed the concern related to exposure at the workplace by setting an occupational exposure limit value for mercury (0.02 mg/m^3). We have not identified reasons why the limit value would not be in a sufficient level or reasons why a condition in Annex XVII entry would be needed to ensure that actors comply with this limit value. Thus this option is not assessed further. See Part B.5 (Summary of existing legal requirements and their effectiveness) for further discussion on the occupation exposure limit value for mercury.

3b) Setting monitoring requirements in the workplace

Laboratories have different safety measures in place to prevent exposure to mercury. Due to relatively high tonnages of mercury used and several steps of measuring with porosimeters where mercury is handled, relevant exposure may take place. To support the implementing of the occupational exposure limit for mercury, monitoring requirement by monitoring batches or urine tests could be required.

As mentioned above, occupational health legislation has already addressed the concern related to exposure at the workplace by setting an occupational exposure limit value for mercury. We have not identified reasons why a condition in Annex XVII entry would be needed to ensure that actors comply with this limit value and this option is not assessed further.

Supporting further assessment of technical feasibility of the alternatives

4) Information gathering

Due to challenges related to assessment of technical feasibility of the alternatives, it was not possible to conclude if technically feasible alternatives for all applications of mercury porosimeters exist or not. This option is aiming to support the collection of additional information to allow full assessment of both technical and economic feasibility by setting a requirement for the users of porosimeters to provide information to competent authorities of the Member States on the technical features needed in their field. This option is assessed further in the next Chapter.

In addition, the users of mercury porosimeters could be obliged to register themselves to competent authorities of Member States. This information could be later on used to collect further information.

4.2 Assessment of risk management options

4.2.1 Option 1: Restriction on the use of mercury in porosimeters that are placed on the market after 5 years of the entry into force

Adopting this restriction option would in practise mean that mercury porosimeters shall not be placed on the market after five years of the entry into force. The reason to introduce this as a use ban, rather than restricting the placing on the market of mercury porosimeters, is that at least one type of device can utilize both mercury and other liquids. Thus it would be possible to argue that the supplier would not be placing on the market mercury porosimeters but porosimeters in general. Nevertheless, to promote effective enforcement, it should be considered to ban also the placing on the market of mercury porosimeters (or porosimeter designed to be used with mercury), as it would be more practical to enforce the placing on the market of the devices than using them. The use of porosimeters placed on the market before the ban would become effective, would still be allowed.

4.2.1.1 Effectiveness

Risk reduction capacity

Following the approach described in Part B, the risk reduction capacity of this restriction option is described as the annual amount of mercury used in porosimeters. As the mercury is regenerated to be used again, the amount used does not reflect the risk reduction capacity for the waste phase. For that, the relevant figure is the amount of mercury disposed annually as waste. For both indicators, the capacity is 1/10 of the annual amount in the first year the restriction is effective, assuming 10 years service-life for porosimeters. In 10 years the restriction would have its full effect and the risk reduction capacity would be the same as the annual amount. Using averages of ranges calculated above, the risk reduction capacity can be estimated to be rising from 0.2 to 2.3 tonnes per year for the waste phase and from 3.6 to 36 tonnes per year for the use phase. Nevertheless, the real emissions from the use of porosimeters are much lower

due to relatively high rate of mercury being collected according to hazardous waste legislation and risk reduction measures already in place in laboratories.

As described in Part B.2 (Scope and approach), the restrictions do not apply to the manufacture, placing on the market or use of a substance for scientific research and development provided that the conditions listed in Article 3(23) of REACH are achieved. Article 3(23) of REACH defines scientific research and development as "*any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year*". It is possible that some use of mercury porosimeters fulfil the above mentioned requirements, namely mercury is used under controlled conditions in a volume less that 1 tonne per year, and consequently benefit from this exemption. If this is a case, the risk reduction capacity would be reduced accordingly, i.e. it would be lower than estimated above..

Proportionality

Technical feasibility

Even though it has not been possible to fully assess the technical feasibility of the alternatives or combination of alternatives, different devices and methods are available to measure the porosity of the materials. In the product control, it seems that measurements with alternatives can offer adequate data to assure the quality even though the results would not be exactly the same as with mercury porosimeters. The five years transitional period for placing on the market and the possibility to continue using porosimeters already in use would allow users to adapt their quality control procedures.

Economic feasibility (including the costs)

As the technical feasibility of alternatives has not been fully established and the economic feasibility has not been assessed, it is not possible to assess the economic feasibility of this restriction option.

4.2.1.2 Practicality

Implementability and manageability

Because of the limited information on the technical and economic feasibility of alternatives, the implementability of this option is difficult to asses. Nevertheless, problems related to implementability and manageability should be significantly reduced by the five years transitional period and by the possibility to continue using existing devices.

Enforceability

The enforcement would in practise be done by enforcing the placing on the market of porosimeters, even though the restriction entry of this option is formulated to restrict the use of mercury. As there are only few suppliers of porosimeters in the EU, the enforcement should not be a problem.

4.2.1.4 Overall assessment of restriction option 1

Based on the limited information on the technical and economic feasibility of the alternatives it is not possible to draw conclusions on the proportionality of the restriction option. Even though it has not been possible to verify the technical feasibility of alternatives, it is not possible to rule out that technically feasible alternatives may exist. Also the risk reduction capacity of this option is difficult to assess. The comparison of the risk reduction capacity with other mercury measuring devices should not be done directly with annual tonnages, as the waste handling situation seem to be better for porosimeters and the risks related to the use phase seem to be higher.

4.2.2 Option 2: Information gathering with further assessment of the technical and economic feasibility

The assessment of the technical feasibility of the alternatives to mercury porosimeters is not finalised in the framework of this report due to the highly technical nature of the issue. The application areas where mercury porosimeters are used are very diverse and different features from the alternative devices might be required to get the desired results. This is naturally affecting the possibilities to transfer to the alternatives.

In depth assessment of the technical feasibility of the alternative devices would require involvement of both the suppliers of the different alternatives and the users from different application areas. As at least some alternative devices are new for the users of mercury porosimeters, it can be doubted if they would be able to directly argue whether an alternative is feasible without a detailed knowledge on the properties of devices. Thus a research program with possibly a workshop could be beneficial.

To support the further assessment of alternatives the users of mercury porosimeters could be required to provide information on their use as a requirement in the restriction entry. That information could include for instance the results (parameters) needed in each application area, the costs of measuring and also the argumentation on the technical feasibility of alternatives based on the descriptions provided in the questionnaire/reporting format. At the same time it would be possible to get a more detailed picture on the risks related to both use and waste phase of mercury.

4.2.2.1 Effectiveness

Risk reduction capacity

This restriction option does not have a significant risk reduction capacity without further regulatory action. Nevertheless, awareness of alternatives may lead to voluntary replacement of mercury porosimeters. The possible future risk reduction is naturally related to the outcome of the further assessment of the technical and economic feasibility of the alternatives and to the consequent actions taken on the

basis of this assessment. If the assessment later on concludes that feasible alternatives exist and a ban is introduced, the future risk reduction would be more or less similar to what is described for restriction option 1 above. It is difficult to estimate the quality of responses that would be received from the user especially related to technical feasibility of the alternatives. Thus it could be argued that the assessment of alternatives could be conducted without the legislative requirement and a voluntary involvement for instance in workshops might be more effective.

Proportionality (technical and economic feasibility)

As described above, the success of this option is related to the quality of data collected. It can be technically challenging to formulate the questions and additional information in a way that allows the users to provide useful information. To achieve a high response rate (compliance), it could be useful to require the users of mercury porosimeters to register themselves to competent authorities as a first step. At least some contact details can also be provided by the suppliers of porosimeters.

This option could support possible other efforts taken to assess the alternatives. The costs of information gathering are related to the time required for preparation of questionnaires and additional information, distributing the questionnaires, answering (time consumed by users) and analysing the data. These costs are not quantified in this report.

4.2.2.2 Practicality

The users of mercury porosimeters should be able to provide the requested information if the questionnaire and additional information is properly drafted. No specific problems related to implementability and manageability have been identified.

The enforcement of this option could be done in the margins of the general enforcements of the laboratories. Enforcement authorities could check if the users have provided the required information to Member State competent authorities when a mercury porosimeter is found in the laboratory. If the register of users would be established it could also be used for targeted enforcement of the users of the mercury porosimeters.

4.3 Comparison of the risk management options

The two restriction options described above are not comparable with each other in terms of risk reduction capacity, proportionality and practicality. The restriction option 1 is not regarded proportional due to uncertainties related to technical feasibility of alternatives. The restriction option 2 is not proposed either as having a legal requirement to provide information which does not automatically lead to receiving helpful data for the further assessment. Nevertheless, the information gathering combined to other suitable efforts to assess the alternatives could be useful.

4.4 The proposed restriction(s) and summary of the justifications

Proposal:

No restriction is proposed for mercury porosimeters.

Summary of justifications:

No restriction is proposed for mercury porosimeters due to high uncertainties in the technical feasibility of the alternatives. Consequently the economic feasibility was not assessed.

The waste handling of mercury used in porosimeters seems to be done in accordance with requirements of hazardous waste legislation. Nevertheless, due to relatively high tonnages of mercury needed for measurements with porosimeters, further assessment of the feasibility of alternatives could be beneficial.

Annex 8: Pycnometers

Content

1. Technical description of pycnometers

Pycnometers are used for accurately measuring the true and bulk densities of materials, by a volume displacement technique based on the fact that mercury at atmospheric pressure will not enter pores smaller than 15 microns in diameter. They are used for instance in battery separators, ceramic and fuel cells industry.

2. Description of release and exposure

As described in the approach to assess the risks related to measuring devices using mercury as described in Section B.4 of the main document, there is no single parameter to sufficiently describe the potential release and exposure from either the use or the waste phase. Waste management of mercury and mercury contaminated samples and other materials is one part of the normal operation of the laboratories performing measurements with these devices. There is no data available on the number of pycnometers in use in the EU, but according to Lassen et al. (2008) the annual use of mercury in pycnometers is estimated to be very small compared to porosimeters. In the stakeholder consultation, no response was received from the only identified producer of mercury pycnometers (based in the USA). According to a producer of mercury porosimeters (not pycnometers), the alternatives have already substituted mercury pycnometers in all the applications (Lassen et al., 2010). This indicates that at least the number of mercury pycnometers placed on the market in the EU annually is very low if not zero.

The mercury is not included in the pycnometers during the production of the devices. Thus the production phase is not relevant for potential release and exposure. The mercury used in measurements is cleaned and dried and returned to the reservoir of the device. The mercury does not end up in the sample, indicating that potential emissions from waste phase are small compared to the situation with porosimeters. (Lassen et al., 2008).

3. Available information on alternatives (Part C)

Alternatives using a gas replacement technique to measure the volume are available (Lassen et al., 2008). Inert gases such as helium or nitrogen are used as the replacement media. According to a producer of mercury porosimeters and non-mercury pycnometers, the alternatives have already substituted mercury in all the applications: "*As far as I know mercury is no more used in pycnometry as envelope or helium pycnometers have substituted mercury pycnometry in all the application.*" (Lassen et al., 2010).

The only identified producer of mercury pycnometers produces also the alternative, i.e. the gas pycnometer. According to a brochure of the producer, the application areas covered by the mercury pycnometer are also covered by gas pycnometers, and the brochure does not mention any specific advantages of mercury pycnometetry over the

alternatives. These application areas include battery separators, ceramic and fuel cells industries. In addition gas pycnometers can be applied in automotive, chemical, pharmaceuticals, powder metallurgy, nonwovens and construction industries. (Porous Materials, 2010)
This producer of mercury pycnometers (based in the USA) did not provide a response in the stakeholder consultation.

There are no derogations for pycnometers in the national restriction for mercury in Sweden. Sweden has not indicated any problems due to the restriction of these devices, which can be seen as an indication that the alternatives are technically feasible.

4. Justification why the proposed restriction is the most appropriate Community-wide measure (Part E)

4.1 Identification and description of potential risk management options

4.1.1 Risk to be addressed – the baseline

As discussed in Part B, the annual amount of mercury used in measuring devices is used as an indicator of potential release and exposure in this report. For mercury pycnometers, a way to describe the risk reduction capacity is the amount of mercury bought annually by the users, but there is no data available on that. Nevertheless this amount is assumed to be very small compared to porosimeters. Based on information received from a producer of porosimeters, the market of mercury pycnometers in the EU is very small if existing at all (Lassen et al., 2010). Thus, restricting the placing on the market of the mercury pycnometers can be seen as codifying the current situation.

4.1.2 Options for restrictions

Considering the evidence supporting the technical feasibility of alternatives and the low number of (if any) mercury pycnometers sold annually, only one restriction option is considered, i.e. a ban on placing on the market of mercury pycnometers after 18 months of the entry into force. This can be seen more or less as codifying the current situation.

4.2 Assessment of risk management options

The available data suggests that technically feasible alternatives for mercury pycnometers are available. Furthermore, the number of mercury pycnometers placed on the market annually is low (if any) and thus the risk reduction capacity is very small (if any). Accordingly the compliance costs related to the proposed restriction are small (if any) as only few users would need to move away from pycnometers after the end of their service life. The fact that replacement has already more or less

happened, indicates that the alternatives should not be significantly more expensive than the mercury device.

4.3. The proposed restriction and summary of the justifications

Proposal:

The placing on the market of mercury pycnometers after 18 months of entry into force of the amendment of Annex XVII.

Summary of justification:

Technically feasible alternatives to mercury pycnometers are available. The available data suggest that the replacement has already taken place which supports the conclusion that alternatives are also economically feasible.

Annex 9: Mercury metering device for the softening point determination[133]

Content

[133] This mercury measuring device was identified in the very last stage of the preparation of Annex XV restriction report, and no questionnaire was sent to the producer in the stakeholder consultation. However the producer was contacted by phone to collect some information.

1. Technical description of mercury metering devices

The **softening point** is the temperature at which a material softens beyond some arbitrary softness (Wikipedia, 2010f). For a substance which does not have a definite melting point, it is the temperature at which viscous flow changes to plastic flow (answers.com, 2010).

For a bitumen it represents an index of its fluidity, the temperature at which a bitumen (used in roofing or road construction) softens or melts.

The softening point can be determined by several methods, depending on the type of the tested substance (carbonaceous substances, bitumen, resin, glass, foodstuff like cheese).

Mercury metering devices are used for measuring the softening point by the Kraemer-Sarnow method. The Kraemer-Sarnow softening point of a material is the lowest temperature at which a mercury load deforms a sample under standardized conditions.

By this method, the softening points of resins and fusible carbonaceous materials are determined according to DIN 53180 from 1996, Binders for paints and varnishes - Determination of the softening temperature of resins and DIN 52025 from 2004, Testing of carbonaceous materials -Determination of the Kraemer-Sarnow softening point.

The Kraemer-Sarnow is the oldest method and uses a small glass tube that is open at both ends and the load is a small mercury drop (5g). The mercury drop is placed on a small disk made of the test material contained in a metal ring fixed at the lower end of a tube. The ensemble is warmed on a bath at a constant rate. The softening point is obtained as the Kraemer-Sarnow temperature (TKS) at which the mercury drop breaks through the softening material and falls.

2. Description of release and exposure

As described in the approach to assess the risks related to measuring devices using mercury as described in Section B.4 of the main document, there is no single parameter to sufficiently describe the potential release and exposure from either the use or the waste phase. There is no data available on the number of mercury metering devices currently used in the Kraemer-Sarnow method in the EU. Only one producer of mercury metering devices for the Kraemer-Sarnow method was identified in Europe. According to the producer, no devices have been sold in the past three or four years[134]. This indicates that the number of mercury metering devices placed on the market in the EU annually is very small (if any).

According to this producer, the mercury is not included in the mercury metering devices during their production. The mercury used in measurements can be cleaned

[134] This information was indicated in preliminary screening of the device, but could not be verified before the submission date of this report, but should be further investigated during the processing of this Background document.

and dried and returned to the reservoir of the device. Thus, the production phase is not relevant for potential release and exposure. The mercury ends up mixed with the sample, indicating that potential emissions from waste phase exist.

3. Available information on alternatives (Part C)

Alternatives using other techniques to measure the softening point are available. According to Benedek and Feldstein (2009) and a producer of mercury metering devices (Petrotest, 2010), the alternatives have already substituted mercury in all the applications.

The softening point can be determined at least by the following methods:

The Ring and Ball method (R&B), carried out according to ASTM D 3461-76 and DIN ISO 4625; it is the most frequently used method to determine the softening point of resins (pavementinteractive.org). The sample of resin is melted into a metal ring and left to cool. The ring is placed in a special metallic device, which is placed into a water or glycerol bath. A steel ball of given diameter and mass is placed on the ring and the bath is heated at a given rate. The temperature at which the ball forces the softening resin downward is noted as the softening point.

Mettler Softening Point method, carried out according to ASTM D 3461-76; it is the most recent method used for resins and it has the advantage to be automatic. The method measures the temperature at which the resin flows out of a sample cup under its own weight; the temperature is recorded when the first drop crosses the light path of a photocell; the Mettler method is quite accurate and reproducible.

Plate-plate Stress Rheometer Test is another method used for resins; the resin is placed between the two steel plates of a stress-controlled rheometer, maintaining in between them a gap. The upper plate is oscillated at a given frequency, whereas the lower plate is heated. The variation of the storage and loss moduli as a function of the temperature is monitored. The softening temperature is estimated from the temperature at the cross-over between the two moduli.

Vicat method or **Vicat hardness** is used for polycarbonates. The apparatus used consists of a heated bath with a flat ended needle penetrator so mounted as to register its penetration on a gauge. The sample is placed with the needle resting on it. The Vicat softening point is the temperature at which the sample is penetrated to a depth of 1 mm by the needle when the bath is heated. The determination of the softening point with the Vicat methode can be carried out according to standards ASTM D 1525 and the equivalent ISO 306.

Although not widely used, other methods to determine the softening point exist, such as capillary method, the flow point, the drop point, and the Kofler method. In general, the R&B method provides the highest softening point, whereas the Mettler method provides the lowest softening point for a given resin. Therefore, always both methods should be given.

There are no known considerable risks related to the alternatives to the Kraemer-Sarnow devices, as they all have a composition similar to any other mechanical or electronic article used by consumers in the everyday life.

The alternative methods are widely used at least in petrochemical, chemical, building materials industry. There are no known problems related to economical feasibility of the alternatives to the Kraemer-Sarnow devices.

The only identified producer of mercury metering devices for the determination of the softening point also produces two other alternative devices. There are no known problems related to economical feasibility of the alternatives to the Kraemer-Sarnow devices.

4. Justification why the proposed restriction is the most appropriate Community-wide measure (Part E)

4.1 Identification and description of potential risk management options

4.1.1 Risk to be addressed – the baseline

As discussed in Part B, the annual amount of mercury used in measuring devices is used as an indicator of potential release and exposure in this report. For mercury metering devices, a way to describe the risk reduction capacity is the amount of mercury bought annually by the users, but there is no data available on that. Nevertheless this amount is assumed to be very small compared to porosimeters. Based on the available information, the market of mercury metering devices for this specific use in the EU is very small if existing at all. Thus, restricting the placing on the market of the mercury metering devices can be seen as codifying the current situation.

4.1.2 Options for restrictions

Considering the evidence supporting the technical feasibility of alternatives and the low number of (if any) mercury metering devices sold annually, only one restriction option is considered, i.e. a ban on placing on the market of the mercury metering devices for the determination of the softening point after 18 months of the entry into force. This can be seen more or less as codifying the current situation.

4.2 Assessment of risk management options

The available data suggests that technically feasible alternatives for mercury metering devices are available. Furthermore, the number of mercury metering devices for the determination of the softening point, placed on the market annually is low (if any) and thus the risk reduction capacity is very small (if any). Accordingly the compliance costs related to the proposed restriction are small (if any) as only few users would need to move away from mercury metering devices after the end of their service life.

The fact that the alternatives, available from the same producer are preferred due to their accuracy, indicates that the alternatives should not be significantly more expensive than the mercury device.

4.3. The proposed restriction and summary of the justifications

Proposal:

The placing on the market of mercury metering devices for the determination of the softening point after 18 months of entry into force of the amendment of Annex XVII.

Summary of justification:

Technically feasible alternatives to mercury metering devices for the determination of the softening point are available. The available data suggest that the replacement has already taken place which supports the conclusion that alternatives are also economically feasible.

Annex 10: Mercury probes used for capacitance-voltage determinations[135]

Content

[135] This Annex 10 of the BD was not included in the original Annex XV restriction report and consequently subject to the public consultation of the restriction report. The mercury probes used for capacitance-voltage determinations were recognized as a mercury measuring device based on the information received in the last day of the public consultation on the Annex XV restriction report.

1. Technical description of mercury probes

The mercury probe, also called mercury probe contact, is an electrical junction device (Schroder, D.K.). Mercury creates the front side contact in a mercury capacitance–voltage (MCV) and in a current–voltage (IV) measurement. The mercury in the probe is used since its density allows to form non-destructive contacts of well-defined areas. Mercury probes may be connected to different devices such as capacitance–voltage (CV) plotters, computerized semiconductor measurement systems, curve tracers, and doping profilers (MDC, 2011).

There are two types of probes, depending on the configuration of the mercury contacts (MDC, 2011):

- Standard: mercury forms a concentric dot and a ring to allow contact in both front-back and front-front modes, for measurements on semi-insulating substances. The ring contact can be configured as a guard ring for special applications.
- Mapping versions, with 3 contacts: allow for repeatable contacts over a wafer using two manual positioning controls. They use a 300 mm diameter platform.

The probes are used to measure several parameters related to the sample such as permittivity, doping, oxide charge and dielectric strength. The method requires that the analysed material does not react with mercury (Wikipedia, 2011b, Mercuryprobe, 2011, Semilab, 2011b, MDC, 2011). The measurements with MCV tools are applicable for materials such as metals, semiconductors, oxides and chemical coatings (Wikipedia, 2011b). The samples need to be thinly sliced as wafers or disposed as thin films (mercuryprobe.com).

The mercury probes are used for e.g. in following applications:

- Doping profiles of bulk and epitaxial layers of SiC, GaAs, 2DEG, GaN, InP, CdS and InSb
- Mercury-oxide-semiconductor (MOS) structure characterisation
- Permittivity and thickness of dielectrics
- Detection of residual films on conducting substrates
- Current-voltage testing of photovoltaic devices
- Ferroelectric sample investigations
- Poly silicon characterization

The functioning of the MCV tool and mercury probes is described in the Box 1.

Box 1: The functioning of the MCV tool
In a MCV tool, the mercury probe has either a stainless steel cylinder or a capillary which holds mercury, a small vacuum pump and a support platform. When the probe head is lowered on the wafer to form a contact, mercury is pressurized and lowers through the capillary to form the contact. A hole bored into the underside of the platform, to which the pump is attached, allows the wafer to be held in place through the negative pressure of the vacuum. A measuring voltage is applied via a metal wire to the mercury, which is the contact itself. After the measurement is done, the mercury is sucked up into the glass capillary and the probe lifts up. The created mercury contact contains a few microns (<37 µl) of mercury. The mercury has to be changed once a week leading to 2 cm^3 of mercury used per year per device.
Source: Semilab 2011, mercuryprobe.com 2011.

2. Description of release and exposure

There is no data available on the number of mercury probes currently used in the EU. Only two producers of mercury probes located in the US have been identified. According to the information received in the public consultation, the device seems to be used mainly for R&D and quality monitoring in the semiconductors industry. Only around 1 to 5 kg of mercury is used annually in the EU in mercury probes for capacitance-voltage determination and the mercury is kept in a closed space with a very limited possibility of mercury vapour releases. (Semilab, 2011a)

The mercury is not included in the mercury probe during their production, and consequently, the production phase is not relevant for potential release and exposure. The mercury used in measurements is purified and returned to the reservoir of the device. Some of the mercury ends up mixed with the sample wafer, indicating some potential for emissions during the waste phase. (Semilab, 2011a)

3. Available information on alternatives (Part C)

A good quality contact has to be created between a probe and the front surface of the semiconductor wafer to perform the capacitance- or current-voltage measurement.
The alternatives used to perform the same measurements, are normally time consuming processes (usually a few hours for a measurement), such as metallization or photolithographic processing. As described below, these alternatives usually lack one or two key features needed by the users or they do not deliver the expected precision and repeatability, or the handling of the sample or the measurement cannot be performed automatically.

Potential alternatives include:

<u>Metallization or photolithographic processing</u>
The contact can be made by evaporating a metal, but the process is lengthy and the heat during the process may change wafer properties and the wafer may not be used anymore.

Airgap CV method
This technique uses a non-contact electrode placed at a 500nm distance from the sample. The non-contact nature makes IV measurements and generally measurements made on dielectric layers impossible. The tool is only available in fully automated versions for high-end semiconductor lines at a price of about 1 million USD. (Semilab, 2011a)

Surface charge analyzer
The technique is used mostly for dielectric measurements, has a generally weaker performance and it is not suitable for epitaxial layers. (Semilab, 2011a)

Non-contact corona charge –voltage (VQ) tools
This is a non-contact technique, suitable for dielectric layer characterization. Corona chargers are used to charge dielectric layers, and a Kelvin probe to measure the resulting change in potential. The technique has limitations or no applicability to leakage current and epitaxial layers measurements. (Semilab, 2011a)

Surface charge profiling
The method is based on the surface photo-voltage technique. It enables epitaxial layer resistivity measurements, but it does not allow dopant concentration profile. (Semilab, 2011a)

Spreading resistance profiling
The technique is applicable to epitaxial layers measurements, but not to dielectric layers. It is a destructive method and requires a lengthy sample preparation procedure which cannot be automated. (Semilab, 2011a)

Elastic metal CV
In this technique, a contact is formed by a very small sized elastic metal probe placed on the sample. This system may perform the whole range of MCV measurements, however the probe is technically difficult to produce, and different types of measurements require different probes. The technique is fully automatic and fast, and constitutes a reliable alternative, but it is much more expensive. (Semilab, 2011a and b)

The systems described above are available from the same supplier as the MCV tools but none of them is completely capable of replacing the mercury CV systems in all the applications (or in case of the elastic metal CV requires a set of different kind of probes). In most of the cases, the replacement of a mercury probe would require several other devices for purely technical reasons, and consequently the alternatives seem not to be economically feasible. This is supported by the information received in the public consultation stating that “a replacement could effectively double or triple the costs of the user because multiple tools are needed to replace all functionalities”(Semilab, 2011b).

4. Justification why the proposed restriction is the most appropriate Community-wide measure (Part E)

Identification and description of potential risk management options

Risk to be addressed – the baseline

As discussed in Part B, the annual amount of mercury used in measuring devices is used as an indicator of potential release and exposure in this report. Around 1 to 5 kg of mercury is used annually in mercury probes for capacitance-voltage determination (Semilab, 2011a).

According to the information received in the public consultation (Semilab, 2011a) the risks related to both use and waste phase seem to be very low in the modern devices as a result of the minimization of the mercury used (around 30 μl for one measurement, around 2 cm^3 mercury used/year). There is no information available to assess the trend in the amount of mercury used, or in the number of mercury probes placed on the market annually.

Assessment of risk management options

As a result of the low quantities of mercury used in capacitance–voltage and current–voltage measurements, only one restriction option is assessed: *Restriction on the placing on the market of mercury to be used as mercury probes in capacitance–voltage and current–voltage measurements.*

The maximum risk reduction capacity of this option is estimated to be less than 5 kg annually. As described in Part B.2 (Scope and approach), the restrictions do not apply to the manufacture, placing on the market or use of a substance for scientific research and development provided that the conditions in Article 3(23) of REACH are achieved. Article 3(23) of REACH defines scientific research and development as "*any scientific experimentation, analysis or chemical research carried out under controlled conditions in a volume less than 1 tonne per year*". It is possible that some of mercury probes used in capacitance- or current-voltage measurements fulfil the above mentioned requirements, namely mercury is used under controlled conditions in a volume less than 1 tonne per year, and consequently benefit from this exemption. If this is the case, the risk reduction capacity would be reduced accordingly, i.e. it would be lower than estimated above.

As described in Section 3, the alternatives for mercury probes have limitations related to both technical and economic feasibility. None of the alternatives are both economically and technically feasible. Thus, no restriction on the placing on the market of mercury used in mercury probes used in capacitance- or current-voltage determination is proposed.

The proposed restriction and summary of the justifications

Proposal:
No restriction proposed.

Summary of justification:
None of the alternatives for mercury probes used in capacitance-voltage or current-voltage measurements are both technically and economically feasible. This is mainly because in most of the cases the replacement of a mercury probe used for capacitance-voltage determinations would require several other measuring devices.

Appendices

All the following appendices are attached as separate documents:

Appendix 1: Classification and labelling

Appendix 2: Review of literature estimating the compliance costs, human health benefits and restoration costs of reduced mercury emissions to support assessment of the cost-effectiveness

Appendix 3: Services to support preparing an Annex XV restriction report on mercury containing measuring devices: Working notes based on stakeholder consultation[136]

Appendix 4: Restriction of mercury in measuring devices under Regulation (EC) No 1907/2006 (REACH) in relation to restriction of the use of certain hazardous substances in electrical and electronic equipment (RoHS)

Appendix 5: Review on the availability of technically and economically feasible alternatives for mercury containing sphygmomanometers and other measuring devices for professional and industrial uses[137]

[136] This appendix is prepared by Cowi consulting company, together with ENTEC and IOM as a part of the stakeholder consultation during the preparation of the original restriction report. The consultation took place between January and May 2010. The objective was mainly to collect input data to assess the proportionality of the restriction options and for socioeconomic analysis – in particular on costs of alternatives as well as technical and economic feasibility of replacement. This BD has been updated to take into account the comments received in the public consultation (September 2010-March 2011), and consequently there might be some inconcistancies between the information in the BD and and in the appendix.

[137] This appendix reports the results of consultation by DG-Enterprise & Industry that was launched in summer 2008 before the preparation of the original Annex XV restriction report. Questionnaires were prepared and circulated to the Members of the Commission Experts Working Group on Limitation of Chemicals (LWG) and to the Experts Working Group on Medical Devices (MDEG). This BD takes into account the additional information collected during the stakeholder consultation (see appendix 3) and also the comments received during the public consultation (September 2010-March 2011), and consequently there might be some inconsistencies between the information in the BD and in the appendix.

Appendix 1: Classification and labelling

Mercury is included under the index number 080-001-00-0 in the Annex VI, Table 3.1 of CLP Regulation**,** *List of harmonised classification and labelling of hazardous substances* and Table 3.2 *List of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC.* The substance is classified according to Annexes I and IV of the 1st adaptation to technical and scientific progress of the CLP Regulation (Commission Regulation (EC) No 790/2009).

Index No: 080-001-00-0 **International Chemical Identification:** mercury **EC No**: 231-106-7 **CAS No:** 7439-97-6			
	Classification according to Annex IV of the Regulation (EC) No 790/2009, amending the Table 3.2 *List of harmonised classification and labelling of hazardous substances from Annex I to* ***Directive 67//548/EEC*****, 31st ATP**	**Classification and labelling according to CLP Regulation, 1st ATP** from Annex I of the Regulation (EC) 790/2009	
		Hazard Class and Category Code(s)	Hazard statement Code(s)
Classification	Repr. Cat. 2; R61 T+; R26 T; R48/23 N; R50-53 **Note E**: The R phrases indicating specific effects on human health shall be preceded by the word 'Also'.	Repr. 1B: Reproductive toxicity, hazard category 1B Acute Tox. 2*: Acute toxicity, hazard category 1 (* meaning Minimum classification, see Annex VI, chapter 1.2.1 of the CLP Regulation) STOT RE 1: Specific target organ toxicity – repeated exposure, hazard category 1 Aquatic Acute 1: Hazardous to the aquatic environment, acute hazard category 1 Aquatic Chronic 1: Hazardous to the aquatic environment, chronic hazard category 1	H360D***: May damage fertility or the unborn child (***meaning the general hazard statement can be replaced by the hazard statement indicating only the property of concern, where either fertility or developmental effects are proven to be not relevant, see Annex VI, chapter 1.2.3 of the CLP Regulation) H330: Fatal if inhaled H372**: Causes damage to organs (state all organs affected, if known) through prolonged or repeated exposure (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard) (** meaning Route of exposure cannot be excluded, see Annex VI, chapter 1.2.2 of the CLP Regulation) H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects

<table>
<tr><td rowspan="2">Labelling</td><td>Symbols
 
Risk phrases:
R61: May cause harm to the unborn child,
R26: Very toxic by inhalation,
R48/2: Toxic: danger of serious damage to health by prolonged exposure through inhalation,
R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment,
S phrases:
S53: Avoid exposure - obtain special instructions before use,
S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible),
S60: This material and its container must be disposed of as hazardous waste,
S61: Avoid release to the environment. Refer to special instructions/Safety data sheets.</td><td>Pictogram, Signal Word Code(s)</td><td>Hazard Statement code(s)</td></tr>
<tr><td></td><td>GHS06: Acute toxicity (inhalation) 
GHS08: Reproductive toxicity, STOT 
GHS09: Hazardous to the aquatic environment 
- Acute hazard category 1
- Chronic hazard category 2
Dgr: Danger</td><td>H360D***: May damage fertility or the unborn child (***meaning the general hazard statement can be replaced by the hazard statement indicating only the property of concern, where either fertility or developmental effects are proven to be not relevant, see Annex VI, chapter 1.2.3 of the CLP Regulation)

H330: Fatal if inhaled

H372**: Causes damage to organs (state all organs affected, if known) through prolonged or repeated exposure (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard) (** meaning Route of exposure cannot be excluded, see Annex VI, chapter 1.2.2 of the CLP Regulation)

H410: Very toxic to aquatic life with long lasting effects</td></tr>
</table>

Appendix 2: Review of literature estimating the compliance costs, human health benefits and restoration costs of reduced mercury emissions to support assessment of the cost-effectiveness

In this appendix the literature estimating the compliance costs and the human health benefits of reduced mercury emissions, as well as the restoration costs are summarised. On the basis of these studies and assessment of them (chapters 1 to 3) chapter 4 discusses the relevance of these results when assessing the proportionality of the proposed restrictions on the placing on the market of mercury measuring devices.

1. COMPLIANCE COSTS OF REDUCING MERCURY

Hylander and Goodsite (2006) reviewed costs of removing a kilogramme of mercury from different policies (Table 1). The estimates can be roughly divided into two categories: i) The cost estimates in the upper part of the table are related to collection, returning or replacing mercury compounds or items, replacing Hg-cells in chlor-alkali plants and to amalgam separators. ii) The cost estimates in the bottom part of the table are related to removing mercury emissions from crematoria, waste incineration and from coal fired power plants. Below some of these estimates are discussed.

According to the reviewed studies the return of mercury in thermometers in Sweden in 1992-96 costs between €829 and €1047[1] per kg of mercury. These costs included the provision of information and collection, transport and deposition of mercury containing thermometers. The costs of additional working time of shop assistants and municipal officials were excluded. More importantly, the costs of purchasing alternative equipment were excluded, too. As at that time the price difference between mercury containing and mercury free thermometers was large, the costs represent only a fraction of the overall compliance costs of replacing mercury in thermometers in Sweden. In other words, the assessed policy is related to collection of devices instead of restricting the placing on the market.

The replacement of mercury containing items with mercury free items in Minnesota (US) was estimated to cost between €17 and €1745[2] per kg of mercury depending on the policy. The cost of collection of mercury and mercury compounds in school laboratories was estimated to be between €61 and €349[3] per kg of mercury. (Jackson et al., 2000).

The compliance costs of amalgam[4] separators per kg of mercury removed in Minnesota (US) have been estimated to be between €28,795 and €1,134,358[5] per kg of mercury removed (Jackson et al., 2000). The reasons for the large differences for the cost per kg of mercury estimates in this study were not reported. The dossier submitter (ECHA) did not get the information to examine in detail what is covered in these costs and

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31 From $950 to $1200 measured in 2004 US dollars

2 From $20 to $2000 measured in 2004 US dollars

3 From $70 to $400 measured in 2004 US dollars

4 About 50 % (weight) of dental amalgam is mercury (http://en.wikipedia.org/wiki/Amalgam_(dentistry)#cite_note-1)

5 From $33 000 to $1 300 000 measured in 2004 US dollars

consequently to what extent they are comparable with the costs of restricting the use of mercury in measuring devices. Furthermore, another study from the Netherlands estimates the cost of reducing mercury emissions from amalgam to be only around €1150 per kg of mercury in 2010 price level (CUWVO, 1990)[6].

Many Member States (e.g. Belgium, Denmark, Finland, Germany, Sweden and the UK) as well as Norway have national policies (either voluntary or legislative action) to encourage or require the use of amalgam separators at dentists. It should be noted that due to technical progress and the fact that amalgam separators have become standard equipment in dental care, the real costs of amalgam separators are likely to be now lower than at the time the estimates in the Netherlands and Minnesota were made. At the same time in the EU there is an overall declining trend in the amount of amalgam used to fill cavities[7].

Several studies estimate the costs of removing mercury emissions from crematoria, waste incineration and from coal fired power plants (see Table 1). The estimates vary between $465 and $2,000,000 per kg of mercury for different policies.

In Table 1, the cost-effectiveness estimates of different policies to reduce mercury are summarised.

Conclusion

Some of the cost estimates are more relevant than others for the purposes of comparison with possible restrictions for mercury in measuring devices. It would seem that the costs of replacing mercury containing items are more relevant as they relate to a similar approach to replacing the existing mercury measuring devices.

It should be noted that some of the values presented in Table 1 (e.g. estimates related to collection of mercury measuring devices) seem to underestimate the full compliance costs (because they do not consider the higher prices of alternatives). At the same time some values (estimates related to crematoria, waste incineration and coal fired power plants) are overestimates compared to the cost-effectiveness estimates for restricting sphygmomanometers and thermometers in this report, as the estimates refer to the amounts of mercury emitted instead of amount placed on the market. In addition, these values may be overestimates since the effect of the measures on the other pollutants is probably not always taken into account.

[6] 1600 NLG (Dutch guilders) x 1.6 (GDP deflator) x 0.45 (exchange rate guilders to euros) = €1150

[7] For instance, mercury free materials are used to fill cavities, and there is an overall reduction in caries in the EU) (eg. see Table 38.2 of World Bank, 2006).

Table 1: Costs for strategies avoiding Hg pollution and their potential to reduce Hg pollution, expressed in the classes: small, medium, and large

Activity	Place and year	Cost (US$/kg Hg)	*a*	Reduction potential	Reference
Return of Hg thermometers	Sweden, 1992–1996	950–1,200	*b*	Large	Rein and Hylander, 2000
Replace mercury-containing items	Minnesota, estimated 1999	20–2,000	*c*	Large	Jackson et al., 2000
Collect Hg and Hg compounds in school labs	Sweden, 1995–1999	70–400	*b*	Small	Rein and Hylander, 2000
Collect metallic Hg in school laboratories	Minnesota, estimated 1999	20	*c*	Large	Jackson et al., 2000
Collect Hg compounds in school laboratories	Minnesota, estimated 1999	1,400	*c*	Small	Jackson et al., 2000
Replacing Hg cells at chlor–alkali plants	USEPA, estimated 1996	10,100	*d*	Large	USEPA, 1997
Increase recycling of chairside traps in dentistry	Minnesota, estimated 1999	240		Medium	Jackson et al., 2000
Install amalgam separators	Minnesota, estimated 1999	33,000–1,300,000		Medium/ Large	Jackson et al., 2000
Replace dental amalgam fillings at dentists	Sweden, estimated 2004	129,000		Large	Hylander and Goodsite, 2006
Remove dental amalgam fillings at death	Sweden, estimated 2004	400		Large	Hylander and Goodsite, 2006
Flue gas cleaning with carbon at crematoria	Sweden, estimated 2004	170,000–340,000		Medium/ Large	Hylander and Goodsite, 2006
Flue gas cleaning with carbon at crematoria	UK, estimated 2004	29,000		Medium/ Large	Hylander and Goodsite, 2006; BBC News, 2005
Medical waste incinerators with scrubber	USEPA, estimated 1996	4,400–8,800		Medium/ Large	USEPA, 1997
Carbon injection into flue gases at waste incinerators	USEPA, estimated 1996	465–1,900		Medium/ Large	USEPA, 1997
Combined technologies at waste incineration	Uppsala, Sweden, 2004	40,000		Large	Hylander and Goodsite, 2006
Coal cleaning, conventional, chemical or both	Minnesota, estimated 1999	100,000–128,000		Large	Jackson et al., 2000
Carbon injection into flue gases at power plants	USEPA, estimated 1996	31,000–49,000	*e*	Large	USEPA, 1997
Carbon injection into flue gases at power plants	US Dep. Energy, estimated 1996	149,000–154,000	*e*	Large	Brown et al., 2000
Carbon injection into flue gases at power plants	Minnesota, estimated 1999	20,000–725,000		Large	Jackson et al., 2000
Combined technologies at power plants	USEPA, estimated 1996	11,000–61,000	*e*	Large	USEPA, 1997
Combined technologies at power plants	US Dep. Energy, estimated 1996	56,000–85,000	*e*	Large	Brown et al., 2000
Wind as replacement for energy from coal	Minnesota, estimated 1999	1,200,000–2,000,000		Large	Jackson et al., 2000

Source: Hylander and Goodsite (2006)

Notes

a Values in a range reflect differences across facilities of different sizes or at different recovery rates e.g. 90% or >95% of Hg recovered from flue gases, or other site-specific conditions.

b Cost calculated per kilogram Hg collected and includes costs for information, reimbursement for thermometers, and additional costs for collecting, transport and deposition, while costs for additional working time of shop assistants, municipal officials, etc. are excluded.
c Total cost per unit of Hg not emitted.
d Capital and electrical costs. Indirectly reduced Hg emissions caused by lower consumption of electricity from Hg emitting power plants have not been included. The costs increase if pollution occurred earlier needs extensive remediation.
e 90% reduction in mercury emissions. The EPA figures are based on a lower flue gas temperature when carbon is injected, thereby using the sorption capacity better, resulting in that only 2–34% active carbon is used compared to the DOE estimates.

2. MEASURING HUMAN HEALTH BENEFITS OF REDUCED MERCURY EXPOSURE

Rice and Hammitt (2005) analysed very comprehensively the health benefits of reducing mercury emissions to air from coal-fired power plants in the United States. Reductions in mercury emissions were anticipated to decrease methyl mercury concentrations in fish, whose consumption is the primary pathway of human exposure to methyl mercury.

The analysis accounted for potential changes in two health effects: cognitive abilities (i.e. changes in IQ[8]) and cardiovascular events. Overall, the health benefits of reducing mercury emissions range between about €5000 and €250,000 per kg of mercury. The lowest benefits are related to the development of the children (measured in IQ) while the higher benefits include also cardiovascular effects. Table 2 gives the main results of Rice and Hammitt (2005). The degree of certainty is discussed below.

Table 2: Health benefits from reducing mercury emissions measured in € per kg of removed mercury, 2010 price level

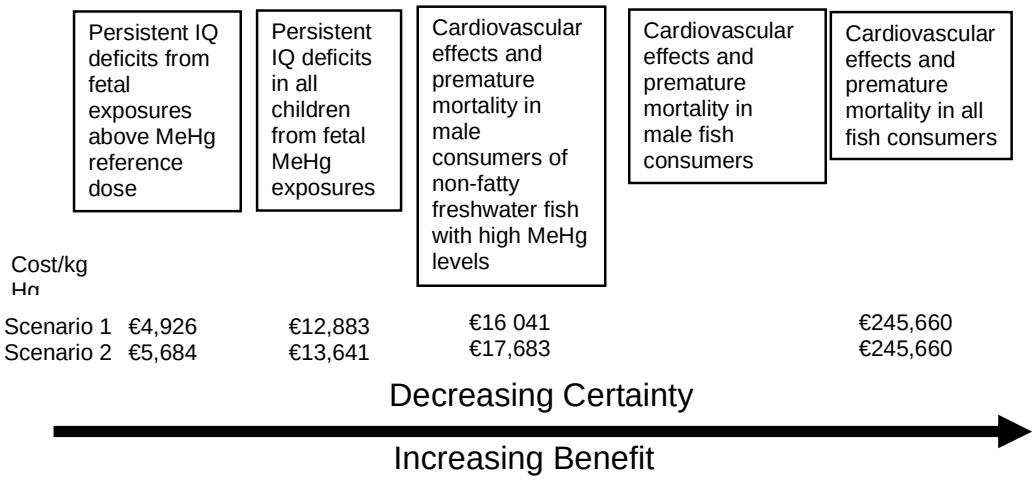
Option		Scenario 1 (19.1 tonnes of Hg removed)	Scenario 2 (26.7 tonnes of Hg removed)	Degree of certainty
1	Cost of Illness estimates for persistent IQ deficits in children exposed above the reference dose in utero	€4,926 *($3,900)*	€5,684 *($4,500)*	Highest
2	As 1 but effects occur also below the reference dose	€12,883 *($10,200)*	€13,641 *($10,800)*	Fairly high
3	As 2 but also "males that consume non-fatty freshwater fish", are assumed to have cardiovascular effects	€16 041 *($12,700)*	€17,683 *($14,000)*	Lower
4	As 3 but also <u>all</u> individuals are assumed to have cardiovascular effects	€229,873 *($182,000)*	€245,660 *($194,500)*	Lowest

Source: Page 193 in Rice and Hammitt (2005)
Note: The estimates in the study were given in US dollars 2000 price level and are given in (*italics*). They have been converted to euros in 2010 price level by first converting the dollars to euros (i.e. ECUs) in 2000 and then using the EU's GDP deflator to bring them to 2010 price level. End note 1 gives the deflators and exchange rates used.

[8] Using a cost-of-illness approach Rice and Hammitt (2005) estimated the value of a lost IQ point to be approximately $16,500 (in 2000 dollars).

According to Rice and Hammitt (2005) the neurological effects associated with *in utero* methylmercury exposures are well estabilished and thus they considered these effects relatively certain *"On the other hand, while the studies that have evaluated the association of adult methylmercury exposures with cardiovascular events and premature mortality appear to be scientifically sound and the individual study results appear to be credible, they have not been subjected to a rigorous scientific analysis as a group."* (Rice and Hammitt, 2005, p. 191) Although these relationships have been observed in several studies, there are also studies in which a relationship was not observed (Rice and Hammitt 2005, p. 37). In other words, the degree of certainty is reduced the more health effects are included in the analysis. This has been illustrated in Table 2 as well as in Figure 1.

Figure 1: Spectrum of Certainty of Causal Association of Health Effect with Mercury Exposure with Estimated Benefit Overlay



Source: Adapted from Figure 12 of Rice and Hammitt (2005)

Spadaro and Rabl (2008) analysed the global average damages from mercury emissions. The cost of an IQ loss measured in the US was applied to other countries in portion to GDP per capita and adjusted for the purchasing power parity (PPP). The resulting mean estimate of the global average of the marginal damage cost of mercury emissions was between €1,280 and €2,900[9] per kg mercury emitted. Given that the world's PPP adjusted GDP is lower than the GDP in the US, the results at global level by Sparado and Rabl (2008) were close to those by Rice and Hammitt (2005). For the EU, given that its GDP is relatively close to that of the US, the Rice and Hammitt results are considered more relevant than those of Sparado and Rabl.

Swain et al. (2007) reviewed 11 studies that have provided quantification of the benefits of reducing mercury pollution. However, they did not relate the benefits to tonnes of mercury removed and thus, the results cannot be applied in the context of the regulation of mercury in measuring devices in the EU. As regards health endpoints most of the studies focused only on IQ. Consequently, these quantitative estimates of benefits related to reduced mercury use and emissions underestimate the full benefits of Hg reduction by excluding other health endpoints (see Table 1 above) as well as environmental endpoints. The authors argued that the economic valuation models used in the reviewed studies were quite similar, however, assumptions regarding the impact of decreased mercury

[9] From $1500 to $3400 per kg mercury emitted, measured in 2005 US dollars

emissions on the changes in methyl mercury levels in different types of fish, and the health effects considered, differed markedly. There are numerous uncertainties involved in evaluating policies for mercury reduction: including (i) changes in mercury deposition rates, (ii) changes in fish methyl mercury levels, (iii) changes in human intake of methyl mercury, (iv) changes in IQ due to exposure, and (v) changes in all-cause mortality and fatal and nonfatal heart attacks in adults. Much of the variability of economic benefit estimates in these studies is explained by differing assumptions made to response to uncertainties in the physical and health sciences of mercury and methyl mercury (Swain et al. 2007).

Conclusion

It can be concluded that many studies have estimated values of reducing mercury emissions. These range from about €5,000 to €20,000 per kg of emitted mercury but could be much higher (e.g. €250.000), if the less certain cardiovascular effects are included. These values relate to emissions (to air) and are not directly comparable with the cost-effectiveness of reducing the amount of mercury placed on the market that is estimated in this report. The values relate to human health impacts, thus omitting the values of impacts that effect the environment as such.

3. OTHER METHODS

3.1. Removing costs of mercury in Sweden

Hylander and Goodsite (2006) also reported several cases of the costs of removing mercury from deep sediments in Sweden. Some costs were actual, some planned or estimated. It is assumed that actual (rather than planned or estimated) costs reflect better the willingness of the society to reduce risks related mercury. Taking these actual costs as the basis the restoration costs in Örserum Bay and Lake Thuringen have been between €8,726 and €21,815[10] per kg of mercury.

The restoration costs cannot be compared with the compliance costs of restricting the placing on the market of mercury measuring devices, as the emissions take place mainly during the waste phase and in a dispersive manner. Nevertheless, the costs give an order of magnitude in some specific cases of the value of removing mercury.

3.2. Special case – damage from mercury poisoning in Minamata, Japan

According to Hylander and Goodsite (2006) the (partial) compensation of victims of mercury poisoning in Minamata, Japan ranged between €5497 and €6544[11] per kg of mercury. In this case there were also additional restoration costs of between €3927 and €4712[12] per kg mercury. If added together, the costs of compensating mercury emissions in the Minamata case ranged between €9,424 and €11,256 per kg of mercury. It should also be noted that the compensation costs relate to damage through poisoning in an extreme case and thus are likely to be an underestimate of society's willingness-to-pay to reduce mercury.

10 From $10 000 to $25 000 measured in 2004 US dollars
11 From $6 300 to $7 500 measured in 2004 US dollars
12 From $4 500 to $5 400 measured in 2004 US dollars

It should be noted that the Minamata case is unique and not directly comparable with the compliance costs of restricting the placing on the market of mercury measuring devices.

3.3. Clean-up costs of mercury spills from measuring devices

According to calculations submitted during the public consultation of the Annex XV restriction report, the benefit of avoided mercury emissions inside the hospitals in the USA can be estimated to be at least €22,684 (for sphygmomanometers) and €636,714 (for fever thermometers) per kg of mercury. The calculations are based on the estimates from US EPA on clean-up costs of mercury spills in the hospitals (Environmental Protection Agency USA, 2002), which can be used to derive the lower bound limit for the values that society is willingness to pay to avoid the negative impacts from the breakages. The difference between the estimates for thermometers and sphygmomanometers results mainly from the different amounts of mercury in the devices.

The benefits from avoiding emissions inside the hospitals are not directly comparable with the compliance costs of restricting the placing on the market of mercury measuring devices. Most of the releases prevented by the proposed restriction on the placing on the market of mercury measuring devices are related to the waste stage of the devices, i.e. the emissions would not occur indoors. Furthermore, the spill clean-up costs are considered in the sensitivity analysis (not in the main assessment) of compliance costs calculations for sphygmomanometers and thermometers in this BD (see Annexes 3b and 5b) and should not be double-counted. The estimate for thermometers (€636,714 per kg of Hg) is based on the average content of mercury in a fever thermometer, which is lower than the average content in industrial and professional thermometers, and consequently, the estimated figure per kilogram would be lower for industrial and professional thermometers.

4. CONCLUSION

The cost-effectiveness estimates in this report (cost per kg of mercury not placed on the market) on their own do not reflect whether the costs introduced by a restriction are proportionate to the risks reduced. Thus, the data above is presented to facilitate the assessment of proportionality of the proposed restrictions.

The benefit estimates for reducing mercury emissions are not directly comparable with cost-effectiveness estimates for the proposed restrictions as the mercury placed on the market in the measuring devices (or to be used in conjunction with measuring devices) is not necessarily released (at least not immediately). However, as the rate of an appropriate collection of used mercury measuring devices is low, it is possible that significant amounts of the mercury are emitted to the environment in the long term. Therefore the estimated values of the benefits of reduced mercury emissions are considered helpful, when assessing proportionality.

None of the compliance cost estimates for other policies are directly comparable with the cost-effectiveness estimates for the proposed restrictions in this report either at least for the following reasons:

a) the costs given are related to several different type of policy measures (increase of collection rates, abatement technologies, etc.) and cannot be expressed as the costs for not placing on the market of one kg of mercury
b) the development in available technologies is not considered, and some of the studies are already quite old
c) the effects on other pollutants are not always fully taken into account.

However, these other policies have been established to reduce the overall exposure of humans and the environment to mercury which is also the aim of the suggested restrictions. Therefore, it seems reasonable to infer that when the cost per kg of mercury not placed on the market is relatively low compared to other policies, the proportionality of such a restriction would be demonstrated.

End note 1: GDP deflators and exchange rates used

	EU27 GDP deflator (Di), 2000 = 100	Exchange rates: US$ in Euros	Coefficients for converting US$ to € valued at 2010 (US$/€) / (Di/D2010)
2000	100,0	1,0827	1,2630
2001	102,1	1,1166	1,2757
2002	104,6	1,0575	1,1791
2003	105,0	0,8840	0,9821
2004	107,5	0,8039	0,8726
2005	109,9	0,8038	0,8532
2006	112,5	0,7964	0,8260
2007	115,7	0,7297	0,7357
2008	116,2	0,6799	0,6829
2009	114,4	0,7169	0,7313
2010	116,7	0,6843	0,6843

Example: 100 US dollars measured in 2000 price level would be 1.2630 x 100 dollars, i.e. 1263 euros in 2010 price level

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Services to support preparing an Annex XV restriction report on mercury containing measuring devices

Results from the information gathering and stakeholder consultation

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Preface

The following appendix includes working notes prepared December 2009 to May 2010 to support ECHA in preparing an Annex XV restriction report on mercury containing measuring devices. The notes are not considered stand alone documents presenting a comprehensive view of the use of the equipment, but reflect the information that has been requested by ECHA for the preparation of the Annex XV report. It is therefore recommended to read the notes together with the relevant parts of the Annex XV report.

In addition to the working notes the consultant has provided an inception report including a review of the Concorde East/west (2009) report "Turning up the pressure: Phasing out mercury sphygmomanometers for professional use"; feedback on drafts prepared by ECHA and regular and *ad hoc* consultation on different technical matters regarding mercury containing measuring equipment.

1 Stakeholder consultation

A stakeholder consultation has been undertaken as part of the work under this contract. The objective of the consultation was mainly to identify the need and reasons for possible derogations to the proposed restriction and to collect input for the socioeconomic analysis such as information on the costs of alternatives and economic feasibility of replacement.

As part of the consultation, questionnaires were sent to identified manufacturers of mercury containing thermometers (including hydrometers and hygrometers), manometers, tensiometers, porosimeters and pycnometers, hanging drop electrodes (polarography), strain gauges and gyrocompasses. The questionnaires were tailored to each type of equipment. The questionnaires were sent by e-mail to contact persons (that had been identified and contacted previously by telephone), and followed up with a reminder by e-mail after some weeks. In a few cases it was not possible to identify a contact person by a telephone call and the questionnaire was sent to the company's general e-mail address.

For selected applications, where more information was requested by ECHA, the questionnaire was supplemented by telephone and e-mail contact to selected manufacturers and suppliers of mercury containing equipment, alternatives and test laboratories.

The list of manufacturers was based on the EU Mercury Study (Lassen et al., 2008) and it is deemed that the contacted manufacturers represent the majority of the manufacturing of the concerned equipment in the EU. For porosimeters the contacted manufacturers represent also nearly all of the equipment marketed in the EU, whereas for the other equipment a significant import from countries outside the EU may take place.

Manufacturers of reference electrodes have not been contacted by the consultant as is was decided that ECHA would contact the only identified manufacturer in the EU.

Producers of barometers were not contacted as the evidence that feasible alternatives exist was regarded to be so strong based on the earlier work. Nevertheless, it has been investigated in by contact to reference laboratories to what extent mercury barometers are still needed as reference instruments for calibration of other instruments.

Table 1 below lists the contacted companies and organisations.

Table 1 Contacted companies and organisations

Company	Question-naire	Re-sponse obtained	Contacted by telephone or e-mail (apart from question-naire contact)	Re-sponse obtained
Manufacturers of Hg ther-mometers				
Sika Dr Siebert und Kühn & Co. K, Germany	x	x		
Ludwig Schneider GmbH & Co. KG, Germany	x	x	x	x
AMARELL GmbH & Co. KG	x	x	x	x
ALLA FRANCE,	x	x		
Gusmini & Balconi S.R.L., Italy	x			
S. Brannan & Sons Ltd	x	x		
Russell Scientific Instruments Limited	x	x	x	x
SC Termodensirom,	x			
Exatherm, Ltd., Czech Republic	x			
G H Zeal Ltd			x	x
Manufacturers and suppliers of alternative thermometers				
Carl A. Plesner A-S; Denmark			x	x
Kjærulf Pedersen a/s ; Denmark			x	x
Tempress A/S; Denmark			x	x
Bie & Berntsen A/S, Denmark			x	x
WIKA Alexander Wiegand SE & Co. KG; germany			x	x
Poulten Selfe & Lee Ltd, United Kingdom			x	x
Charnwood Instrumentation Ser-vices Ltd.			x	
Producers of porosimeters and pycnometers				
Micromeritics Instrument Corpora-tion, U.S.A. (European branch contacted)	x	x	x	x

Company	Question-naire	Re-sponse obtained	Contacted by telephone or e-mail (apart from question-naire contact)	Re-sponse obtained
Porous Materials, Inc., USA	x			
QUANTACHROME INSTRUMENTS; USA (European branch contacted)	x		x	x
Thermo Fisher Scientific Inc.; USA (European branch contacted)	x		x	x
Users of porosimeters				
MOL Plc, Hungary			x	x
L'Istituto di Tecnologie Avanzate per l'Energia, Italy			x	x
Risoe, Denmark			x	x
Core Laboratories, UK			x	x
Producers of Hg manometers				
Giussani S.r.l., Italy	x			
Dwyer Instruments Limited, USA	x			
Sphygmomanometers (Hg and alternatives)				
Rudolf Riester GmbH; Germany	x	x	x	x
A.C. COSSOR & SON (SURGICAL) LTD, UK	x	x	x	x
Spengler , France	x			
Manufacturers and suppliers of gyrocompasses				
Kelvin Hughes Limited; UK	x		x	x
Raytheon Anschuetz GmbH; Germany			x	x
Points North Ltd. Scotland, UK			x	x
Strain gauges				
D. E. Hokanson, Inc., USA	x			
Kemikalieinspektionen, Sweden			x	x
Producers of Hg Tensiometers				
SDEC, France	x			

Company	Question-naire	Re-sponse obtained	Contacted by telephone or e-mail (apart from question-naire contact)	Re-sponse obtained
Producers of hanging drop electrodes				
Metrohm A/G, Switzerland	x	x	x	x
AMEL srl, Italy	x			
Reference and calibration labo-ratories, standard organisa-tions				
Danish Technological Institute			x	x
Trescal A/S, Denmark			x	
Danish NMI (the National Metrol-ogy Institute)			x	x
Exova METECH A/S; Denmark			x	x
Danish Meteorological Institute, Denmark			x	x
National Physical Laboratory, UK			x	x
Pullman Instruments, UK			x	
Physikalisch-Technische Bunde-sanstalt (PTB), Germany			x	x
DIN-FAB, Germany			x	x
British Standards			x	x
BSI Committee Service Centre (CSC)			x	x
Material testing equipment				
Petrotest® Instruments GmbH & Co. KG, Germany			x	x
Stanhope-Seta, UK			x	x
AGA Appliances (stove with thermoindicator)				
AGA, UK				

2 Porosimeters

Porosimetry is an analytical technique used to determine various quantifiable aspects of a material's porous nature, such as pore diameter, total pore volume, surface area, and bulk and absolute densities.

Mercury intrusion porosimetry involves the intrusion of mercury at high pressure into a material through the use of a porosimeter. The pore size can be determined based on the external pressure needed to force the liquid into a pore against the opposing force of the liquid's surface tension. See Lassen et al. (2008) report for more details about the technique.

2.1 Analysis procedures

The following short description of the analysis procedure is based on the Operators Manual to AutoPore IV 9500 from Micromeritics and a demonstration of the analysis using this porosimeter provided by a laboratory using the equipment for analyses. Somewhat different procedures may be used by the use of other equipment (more details are referred to in operator's manuals from individual equipment providers). This description focuses on what happens to the mercury in the procedure.

A step-by-step description of the operating procedure this set out below as well as a photo illustration of the device below..In this laboratory the porosimeter was connected to a exhaust and not placed in a fume hut – it may be different in other laboratories.

The sample cells used in most mercury porosimeters are designated penetrometers (Thermo Scientific uses the e term dilatometers). The penetrometer consists of metal stem and a glass sample bulb where the sample is placed during the measurements.

All photos by COWI

1 Before the analyses: The reservoir in the porosimeter is filled with mercury. The porosimeter requires approximately 2.3 kg of mercury (minimum) to begin analyses and the reservoir can contain a maximum of 5.4 kg. Each analysis may extract from 3 mL (= approx. 40 g mercury) to 15 mL (app. 120 g) of mercury from the reservoir depending on the penetrometer and sample size used.

2 The penetrometer is weighed. The sample (specimen) is placed in the glass sample bulb of the penetrometer and the total weight of penetrometer + sample is determined.

3 The penetrometer is loaded in the low pressure port of the porosimeter for analysis of large pores (3.6 to 360 μm).

4 The penetrometer is evacuated and backfilled automatically with mercury through the stem of the penetrometer. The mercury extends the entire length of the penetrometer and fills the bulb and stem.

5 As pressure increases, mercury moves into the sample's pores, vacating the stem. The mercury moves from the stem into the sample bulb and further into the pores. Pore volume data are calculated by determining the volume of mercury remaining in the penetrometer stem. The volume of mercury in the penetrometer's stem is measured by determining the penetrometer's electrical capacitance. The result of the analysis is basically a dataset of different pressures versus volumes of mercury pressed into the specimen.

6 The penetrometer (still filled with mercury) is removed from the low pressure port and placed in a balance for determination of the weight of penetrometer + sample + mercury. (The weighing may be done after step 7 instead.)

7 The penetrometer is loaded in the high pressure port for analysis of small pores (0.005 to 6 μm) and step 4 and 5 are repeated.

8 The penetrometer is removed from the high pressure port and transferred to a fume hood (this may vary by laboratory).

9 A plug on the top of penetrometer is unscrewed and the mercury is drained through the stem into a container for slightly contaminated mercury.

10 The sample is poured into a container for mercury contaminated waste.

11 The penetrometer is cleaned with solvents in order to remove mercury droplets, oil and grease.

12 In some laboratories the contaminated mercury is regenerated by a cleaning for reuse. The number of analyses that can be run using the same mercury depends on the mercury oxidation status. Some laboratories indicate they reuse the mercury 5-10 times, others that they reuse the mercury more

than 5-10 times and that the mercury is renewed by the amount added in replacement of mercury being lost in the samples. The oxidation rate depends on the porous materials analysis, typically metal-based materials, may accelerate the oxidation process.

Steps 9-12 may be different in the way that the mercury is regenerated immediately after the analysis. The following description is based on the Instruction Manual, "Use of Cleaning Kit for Mercury" from Thermo Scientific PN 317 130 44, Revision June 2007. The mercury cleaner is a pyrex glass siphon device allowing removal by decanting both solid and powdered sample residues from the mercury.

1 Open the penetrometer (termed a 'dilatometer' in the manual) containing the mercury and pour the mercury and sample into a metal filter in the siphon container.

2 The sample remained inside the filter is transferred into a container for mercury contaminated waste

3 The mercury, passed though the filter, is further cleaned by slow decantation in the siphon and will be collected on the bottom of the siphon vessel passing through a solvent layer.

4 The penetrometer is cleaned with a brush and solvents in order to remove mercury droplets, oil and grease. All parts of the dilatometer is immersed into the solvent for 10 - 20 minutes.

Photo illustration from a laboratory visited

The following photos illustrate some of the procedures in a visited laboratory. The laboratory purchases annually about 30 kg of mercury from a mercury recycling company which also receive the contaminated mercury from the laboratory.

Note that some types of porosimeters are smaller and may by operated on a laboratory bench e.g. Thermo Scientific Pascal 140.

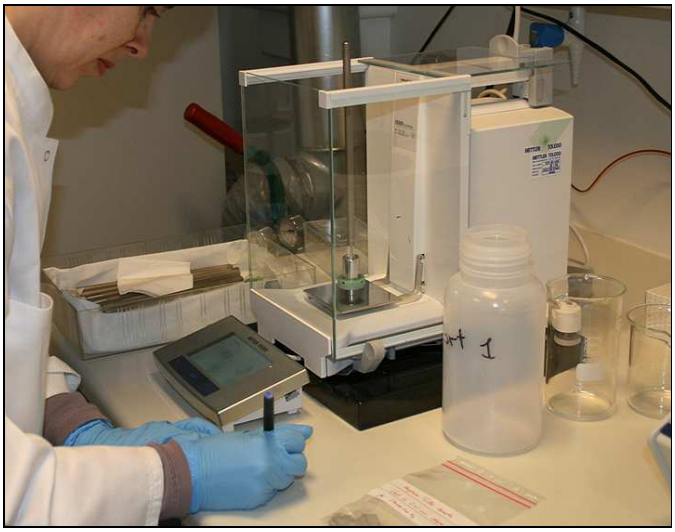
The penetrometer is removed from the high pressure chamber of the porosimeter (AutoPore IV 9500 from Micromeritics).

Note the exhaust at the right of the photo. The porosimeter is designed so it can be connected to a ventilation system that pulls ambient air over the counter, through the instrument and out a duct at the rear.

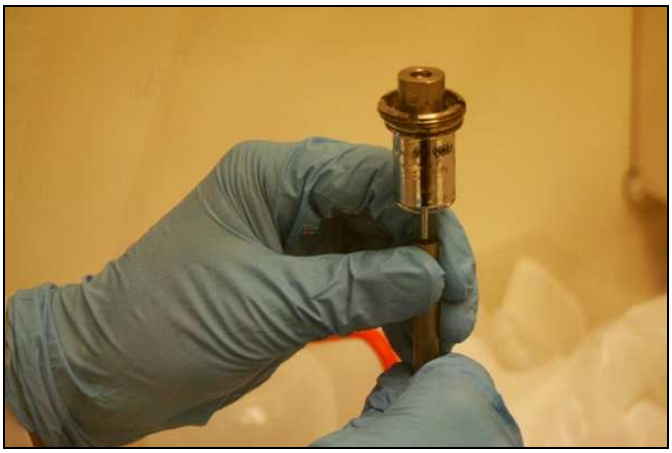
The black box on the top of the porosimeter is a mercury spill kit. The laboratory did not have any incidents with spills at least the last two years and the spill kit had been in use (the personnel had only been working with the equipment for two years).

A small mercury droplet on the penetrometer stem is wiped into the dish for collecting mercury. The dish contain approximately 3 mm of oil to prevent the escape of mercury vapours.

The mercury reservoir is located in the upper right corner of the photo. When filling the reservoir the black cap is removed and the mercury is filled in from a small container. The reservoir is filled when the instrument indicates that the level is low. Mercury is purchased in small containers holding exactly the quantity needed for filling the reservoir.



The mercury-filled penetrometer is being weighed. The penetrometer is placed in the plastic container in the front of the photo when moved between the porosimeter, the balance and the fume hood where it is emptied and cleaned.



The penetrometer before the top screw is removed and the mercury is drained into a container for slightly contaminated mercury. The penetrometer holds about 3 ml (40 g) of mercury.

In this laboratory the contaminated mercury is disposed of for recycling and no internal regeneration of the mercury takes place.

The operation takes place in a fume hood.

The mercury has been drained from the penetrometer and the specimen (with some mercury pressed into it) is poured into a containing for mixed mercury waste.

The operation takes place in a fume hood.

This waste fraction is disposed of as mercury waste to a hazardous waste company via the laboratory's general hazard-

ous waste system.

The penetrometer is cleaned for remaining mercury, oil and grease using a solvent and Mercury Collector Replacement Pads (Sigma Aldrich). The pads are used to remove small droplets of mercury from the surface of the penetrometer. The waste from the cleaning operation is disposed of as mercury waste to a hazardous waste company via the laboratory's general hazardous waste system.

Other procedures using other equipment

For porosimeters from other manufacturers somewhat different methods may be used.

For the Pascal porosimeters from Thermo Scientific, the sample cells, designated dilatometers, consist of two glass sections connectable by means of a rectified conical joint. Except for the Pascal 140 model, the degassing and mercury filling are performed before the analysis in a mercury filling unit (Duplex Dilatometer filling device). The Pascal porosimeters seems not to be equipped for direct connection to an exhaust system (e.g. not indicated in the PASCAL 240 Series. "Instruction Manual. Mercury Porosimeter"). The Pascal 140 is a low-pressure porosimeter and has only one port for analysis of the full range of poresizes that can be determined with the instrument.

Some equipment is not connected directly to an exhaust. As an example the new Autopore IV 9520 from Micromeritics is equipped with a fan and a mercury filter and do not need to be exhausted externally. Obviously the releases to the surroundings via the exhaust would be smaller with this setup, but no data are available on actual releases through the exhaust.

2.2 Possible mercury releases from the use of porosimeters and precautions

The following release routes of mercury may be considered:

1 Releases from the porosimeter through the exhaust of the porosimeter. From mercury spilled by filling of container, droplets on penetrometer, cleaning of valves, cleaning of high pressure tank, etc.

2 Releases from the fume hood through the exhaust of the fume hood. From mercury spilled or directly evaporated by emptying and cleaning the penetrometer and mercury spilled or directly evaporated by regenerating the mercury. Mercury releases from small droplets on gloves, cleaning pads, etc.

3 Release from the fume hood through the drain of the sink (if the fume hood has a sink). From mercury spilled by emptying and cleaning the penetrometer, mercury spilled by regenerating the mercury, from small droplets on gloves, cleaning pads, etc. the mercury may inter into a sink in the fume hood.

4 Releases from the laboratory's general ventilation system. From mercury spills outside the fume hood or porosimeter.

5 Long term releases from mercury contaminated waste. All mercury contaminated waste (>0.1 % w/w) has to be disposed of as hazardous waste, in accordance with EU waste regulation.

6 Releases from recycling of mercury by recycling companies.

7 Mercury in solvent disposed of as solvent waste. Mercury is not dissolved in the solvents and the waste solvent seems not to be considered mercury containing.

No data has been available for quantification of any of the releases.

2.2.1 Releases from the porosimeter through the exhaust

It is assumed that all types of porosimeters are equipped for connection to an exhaust systems or the air around the porosimeter otherwise is removed by a ventilation systems. It is assumed that the laboratories in general do not have specific mercury filters on the ventilation system and that most of the ventilated mercury is released to the surroundings.

Under normal operation, without any accidental spills, the releases to the ventilation system are considered to be negligible. The main releases would be associated with the possible spills.

The manuals of the porosimeters include a number of instructions in order to prevent spills and mercury going into parts of the porosimeter. The following is, if not mentioned otherwise, based in the instruction manual for the AutoPore IV 9500 from Micromeritics. Notes of the author of this document in square-brackets.

Incident	Instructions
Spill by filling the container or droplets spilled from the penetrometer	Any mercury spilled on the counter tray should be wiped into the drain hole in the tray, from which it will fall into a collector (mercury spill dish) and be covered by a layer of oil.
Mercury releases from the mercury spill dish	Pour approximately 1.0 to 2.0 cubic centimetres of oil into the container to prevent the mercury from vaporizing. If mercury accumulates in the dish, remove it by removing the cover and extracting the mercury with the syringe accessory.
Broken penetrometer – mercury in high pressure chamber	Should a penetrometer be broken and mercury spilled in a high pressure chamber, the glass and mercury should be removed immediately
Explosion of the penetrometer	No situation is known where pressure has caused an explosion or other dangerous reaction in a material while being evaluated by mercury porosimetry. Nevertheless, it is well to be aware of such a possibility should azides or perchlorates, for example, be considered for testing
Mercury going into the vacuum pump	Should operator error or malfunction draw mercury toward the vacuum system, the mercury will be collected in a protecting reservoir (mercury trap) with a capacity sufficient to retain all the mercury in the system at one time. A warning buzzer will signal that mercury transfer has occurred. This reservoir should be drained immediately. If, instead, more mercury is added and the error persists, subsequent quantities of mercury cannot be retained. The vacuum pump and other components will then be subject to damage Drain excess mercury from the trap into the reservoir. Remove the plug extending down from the mercury trap. Refer to Draining Spilled Mercury Dish later in this chapter. Position a container beneath the trap before removing the plug. [Porosimeters from Quantachrome are equipped with a cold trap]
Spill from low pressure port	Never remove a penetrometer or blank plug from the low pressure port when the Hg Drained indicator is not illuminated. Doing so could allow mercury to spill from the low pressure port. [further instructions on troubleshooting in manual] Mercury overfill in low pressure port [detailed instructions on troubleshooting in case of mercury overfill in the manual]
Mercury spill from the penetrometer	If the assembly is not to be placed immediately in the high pressure chamber, store it with the stem upward so that none of the mercury will be spilled.
Mercury released from the high	The high pressure fluid should be changed if mercury is

Incident	Instructions
pressure chamber	spilled into a high pressure chamber; small drops of mercury in the bottom of the chamber can cause erroneous results
Mercury releases from valves	[maintenance instructions] Make sure all mercury is below drain valves. Evacuate the reservoir and open the drain and fill valves with the low pressure manifold at atmospheric pressure. Failure to do so could result in a mercury spill. Hold a container below the valves to capture any retained mercury.

2.2.2 Releases from the fume hood

Based on the information gathered during one laboratory visit and three telephone interviews, it is assumed that handling of the penetrometers after analysis is done in a fume hood to prevent exposure of the personnel.

Incident	Instructions
Spill when pouring mercury and sample from the penetrometer	Place the mercury waste container in a shallow pan of water in case of spills. If there is any mercury in the bottom of the detergent solution, dispose of the solution properly. Do not tilt the penetrometer while removing the nut. Hold the penetrometer upright to avoid spilling mercury.

The major source of releases would be from the handling of the penetrometer and the mercury waste after the analysis. Whereas spills only happen occasionally during analysis mercury may evaporate from the handling of the penetrometer after each analysis. The minimisation of releases is mainly a question of good general laboratory procedures – for example, not leaving small droplets in the bottom of the fume hood, containers, tools and gloves.

It should be noted that the releases of mercury from the processes is a function of the total quantity of mercury used for the analysis and not the amount of new purchased mercury.

2.2.3 Releases from the laboratory's general ventilation system

Mercury spills on the floor of the laboratory or from stored mercury may be lost to the environment through the laboratory's general ventilation system. The following instructions are given in the manual for the AutoPore IV 9500 together with some mere general information on proper handling of mercury and mercury health effects.

Incident	Instructions
Spill of mercury e.g. by droplets from the penetrometer or by dropping the penetrometer or mercury containers on the floor	[No instructions on precautions by moving the penetrometer between the workplaces: porosimeter, balance, fume hood] Mercury spills should be cleaned immediately and thoroughly by mechanical, chemical or other appropriate means. Micromeritics uses and recommends that you use plastic or rubber gloves and a small vacuum pump equipped with a mercury vapour absorbing filter on the exhaust and a vacuum probe with a mercury trap on the inlet for efficient pick-up of small mercury particles in cleaning mercury spills. Afterwards, the spill area should be swabbed with a mercury decontaminant and allowed to dry.
Mercury releases from storage of mercury	Open containers for storage of mercury in the work area should be covered with an aqueous or an oil layer and kept at ambient temperatures to prevent vaporization. Because of permeability of polyethylene or plastic bottles to mercury vapor, thick glass bottles, stainless steel or cast iron containers are recommended for storing mercury. To avoid dangerous chemical reactions, mercury should not be stored with acetylene, fulminic acid, ammonia and oxalic acid.
Mercury releases from mercury contaminated clothing	Clothing contaminated with mercury should be stored in vapour-proof containers pending removal for laundering.

The manual do not mention that mercury storage in open containers should be kept at a minimum, and only placed in ventilated areas.

2.2.4 Clean up of spill

Different methods are used for cleaning up of mercury spill. One example is the QuikVac portable mercury spill vacuum.

The Mercury QuikVac portable mercury spill vacuum from Micromeritics. "*The Mercury QuickVac is the ideal tool for collecting both liquid mercury and mercury-contaminated particulate matter. Its compact size and light weight make it perfect for laboratory applications. The activated carbon filter traps the mercury vapors and exhausts clean, safe air back into the laboratory. Use it in and around vent hoods, and other areas where mercury spills may occur*."

Source: www.micromeritics.com

2.2.5 Experience of interviewed laboratories

Four laboratories have been interviewed with a focus on procedures that may lead to exposure of personnel and releases to the environment. The following information has been obtained:

Laboratory 1:

- In about 1/50 measurements a small droplet escaped the penetrometer typically because of improper filling when new materials were tested. The droplet was wiped into the mercury spill dish. In order to prevent any drip the penetrometer was kept in a container when moved from one place to another.
- By changing of the vacuum pump a visible amount of mercury was found in the valves of the pump.
- It happens that mercury is found in the high pressure port, but not often.
- No experience with broken or dropped mercury filled penetrometers. It happens that penetrometers break by the cleaning after the mercury has been removed.
- No experience with any accidents (major spills e.g. by dropping of penetrometers or explosion of penetrometers).
- Porosimeter connected to exhaust, penetrometer emptied and cleaned under fume hood.

Laboratory 2:

- No experience with broken or dropped mercury filled penetrometers. No experience with any accidents.
- The porosimeter was in this laboratory not connected directly to the exhaust (ventilation system) and not placed under a fume hood.
- Penetrometer emptied and cleaned and mercury filtered under fume hood.
- Could not describe any mercury revealed by maintenance as the maintenance was provided by the equipment supplier.

Laboratory 3:

- One incidence of broken mercury filled penetrometers.
- Old porosimeter connected to exhaust; new porosimeter equipped with fan and mercury filter and not vented externally.

- It happens that mercury is spilled. Cleaned with the use of a mercury spill kit.

- It happens that mercury is found in high pressure port, but not often

- Penetrometer is emptied and cleaned and the mercury was filtered without the use of fume hood. Urine check of personnel every half to one year – no indication of exposure.

Laboratory 4

- Penetrometer filled, emptied and cleaned and mercury filtered under fume hood.

- It happens that mercury end up in the high pressure autoclave (high pressure port), at the bottom of the autoclave.

- It happens that mercury-filled penetrometers breaks by the handling, but it is very rarely

All laboratories

All the laboratories had specific procedures for clean up of mercury spills. The procedures are slightly different. One example: "*...we use polyethylene scoop and relevant brush for collecting the majority of the spilled mercury and we have a special mercury collector which allows to collect the small drops of mercury and then we chemically treat the surface contaminated by tiny mercury drops by spreading them with sulphur. The operator (technician) wears appropriate coat, shoes, gloves and protective screen".*

2.2.6 Safety recommendations of the IUPAC Working Group

The IUPAC Working Group on "Liquid intrusion and alternative methods for the characterization of macroporous materials" has addressed the safety of using mercury porosimeters (Provisional document dated of 15th February 2010). Besides recommending checking country specific regulations and recommendations regarding occupational safety and health the groups provides the following guidelines:

" *(i) The operator should use appropriate personal protective clothing and equipment effective in preventing skin contact with mercury*

(ii) Always work with mercury over a spill tray. Keep all containers with mercury sealed when not in use. Waste mercury in any work area must be in spill trays covered with oil.

(iii) Ensure that containers of mercury are securely capped when not actually being poured from, or into. Handle containers of mercury, including sam-

ple cells, in a well-ventilated area. It is strongly recommended to clean mercury porosimeter measurement cells in a fume hood.

(iv) Use the mercury vapor traps supplied on the equipment and never override or disable any safety device.

(v) If at all possible any operation with mercury should be performed in a separate room with proper ventilation and less 'lab-traffic'. A so-called " Tacky Mat" outside the Mercury Test area…on which mercury porosimeter users must step with both feet, when exiting the Mercury test area is also recommended.

....it is advisable to periodically check the actual concentration for instance by monitor badges which are worn by the operator of the mercury porosimeter. This test should be performed at least annually, but always after a spill has occurred. All mercury spills should be cleaned immediately and thoroughly by mechanical, chemical, or other appropriate means.

Individuals dealing with the clean-up need to wear a respirator, and of course protective clothing effective in preventing skin contact with mercury.

It is not only from environmental standpoint important to stress, that used mercury should be recycled, i.e., it can be send to appropriate institutions/companies which specialize in the recycling of mercury, i.e. re-distilled (i.e. triple distilled) mercury can be used again in mercury porosimetry applications."

2.2.7 Safety measures in place in one visited laboratory in DK

The measures in place in the laboratory visited for this study can be summarised as follows:

- The porosimeter is connected to an exhaust system.
- The operator use appropriate personal protective clothing for preventing skin contact with mercury, and has been trained in the use of the equipment.
- The porosimeter is maintained in accordance with the manual and in case of malfunction the instructions of the manual (described above) are followed.
- The porosimeter is equipped with a dish for collecting mercury. The mercury in the dish is covered by oil to prevent evaporation and the collection dish is emptied regularly.
- The porosimeter is equipped with a mercury trap for preventing mercury going into the vacuum pump.

- In case of spill of mercury in high pressure port the mercury is removed from the port.

- When moving the mercury filled penetrometer between different work-places it is kept in an open container to prevent spill.

- In case of improper filling of the penetrometer, the penetrometer is checked for droplets before transferred to the balance for weighing. Drop-lets are collected in the collection dish of the porosimeter

- Mercury for filling the porosimeters is supplied in containers with exactly the amount needed for one filling, in order to reduce the risk of spill by the filling.

- A mercury spill kit for immediate response in case of spill is placed at the workplace. The personnel have been informed to follow the instructions on the use of the spill kit.

- Mercury and mercury waste is kept in capped containers and only opened when mercury is poured from, or into the container.

- Handling of penetrometer after analysis takes place in a fume hood. All handling takes place over a spill tray to prevent spill in the bottom of the fume hood. The spill tray is cleaned after handling each penetrometer.

- Contaminated material from cleaning of the penetrometers is collected in plastic bags for mercury waste and the bags are placed in a container.

- Contaminated/oxidized mercury and mercury containing samples are placed in closed containers kept in a fume hood.

- Contaminated mercury is disposed of for external recycling.

- Mercury contaminated samples and other waste is disposed of as hazard-ous waste via the laboratory's general hazardous waste system.

In addition to the measures above, the authors of this note suggests that the fol-lowing measures could be considered:

- Any operation with mercury should be performed in a separate room with a minimum throughput of other laboratory personnel

- All operations should be kept close proximity in a "Mercury Test area" with proper ventilation. When leaving the area, porosimeter users must step with both feet on a so-called "tacky mat".

- Contaminated samples should be disposed of for recycling of the mercury.

- A respirator for use in case of spill should be kept near to the working area

- The actual mercury concentration should be periodically checked.

- The ventilation from the fume hood and porosimeter should be equipped with a mercury filter [has to be further investigated whether relevant].

No data on actual concentrations in outlet air have been available. As mentioned consideration may be made of the requirement for mercury specific filters on the exhaust However, it would be relevant to first measure actual concentrations in the outlet air.

No data on actual mercury concentrations in the air of the laboratories has been obtained. None of the visited or interviewed laboratories had any data.

Waste containing > 0.1% mercury is considered hazardous in the EU and should be disposed of accordingly. The contaminated samples in general contain > 0.1% mercury whereas it is not clear whether waste from the cleaning of the penetrometers also contain > 0.1%.

2.2.8 Quantification of releases

No data have been available on the possible mercury releases through the laboratories' ventilation systems. Data on mercury concentration in the ventilation air from laboratories using porosimeters may be available, but have not been identified.

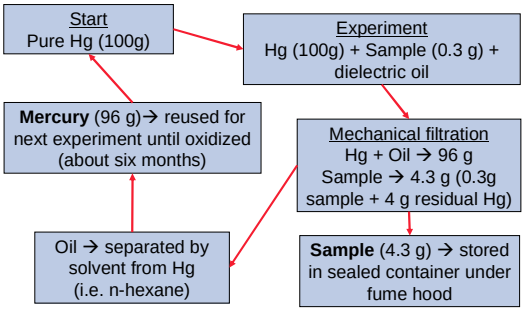
The data do not allow calculation of the releases on the basis of the known mercury input and outputs.

The main source of mercury releases from the laboratories using porosimeters is assumed to be from the fume hood where penetrometers are emptied and the mercury regenerated.

2.3 Mercury flow

The mercury flow through the process is highly dependent on whether internal recovery and recycling takes place in the laboratory and the types of samples (for example, if the samples are powders a larger amount of mercury will be disposed of with the samples).

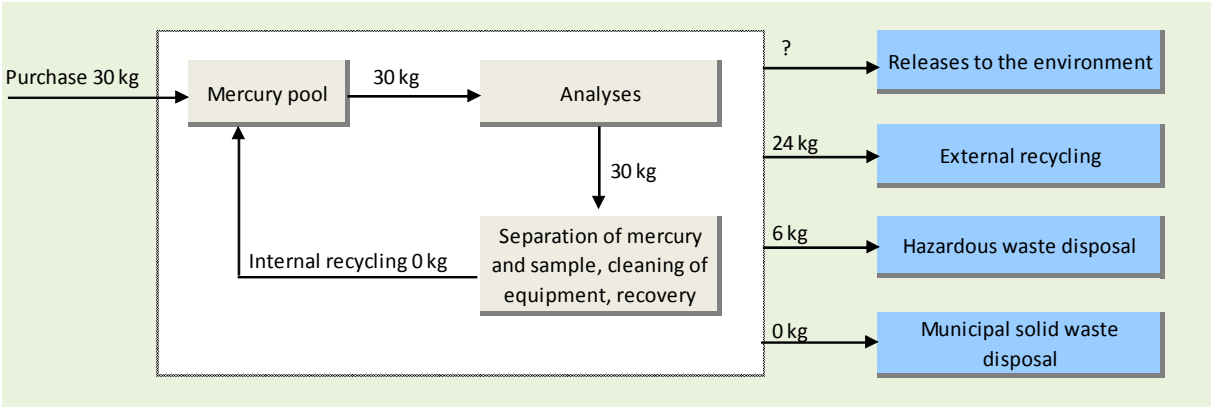
The following flowchart from Thermofisher Scientific indicated the overall flow of mercury (Thermofisher, 2009).



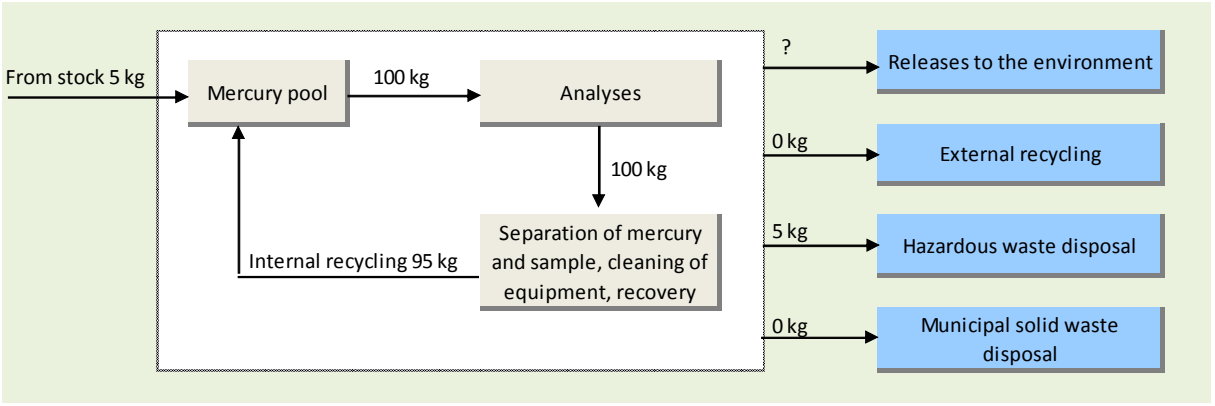
According to this scheme, for each 100 g of mercury used in the analysis, 4.3 g ends up in the waste with the sample and has to be replaced by new mercury. It is indicated that the mercury is reused for about six months. It is in this description not clear what happens to the mercury when it is oxidized.

More generalised flowcharts showing the annual flow are presented below. Examples of three interviewed laboratories and the total EU wide flow is shown (the latter based on data presented in ECHA Annex XV draft report). Note that in the case internal recovery takes place, a larger proportion of the mercury outflow will be as hazardous waste. For one laboratory, an accurate mass balance could not be established on the basis of the available information. The flowcharts do not address the issue of occupational exposure, which potentially may take place at all stages. All quantities are in kg/year.

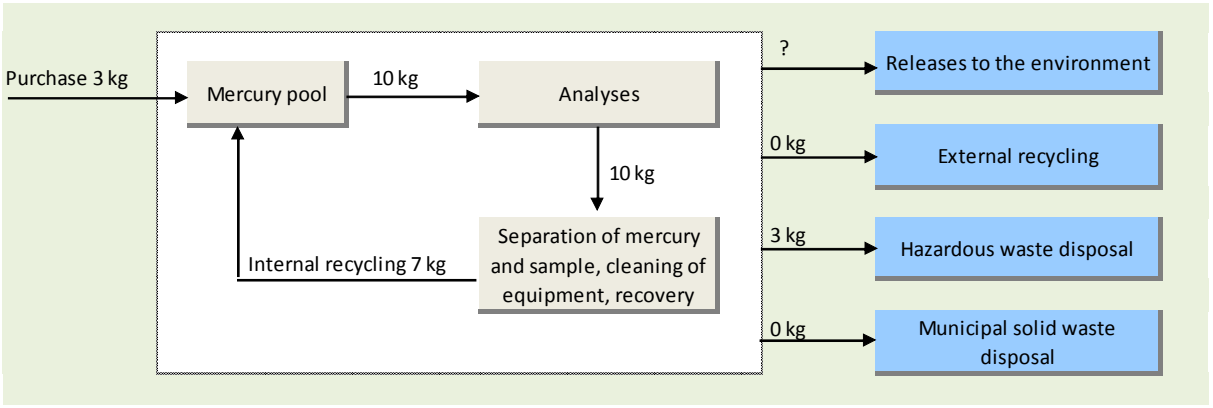
Laboratory 1: No internal recovery. About 20% of the mercury follows the sample and other waste whereas 80% of the mercury is disposed of for external recycling.



Laboratory 2: Mercury is on average recovered and recycled about 20 times. No oxidized mercury for external recycling. For each analysis about 5% of mercury is disposed of with the samples. Mercury is not purchased as the laboratory holds a large stock of pure mercury.



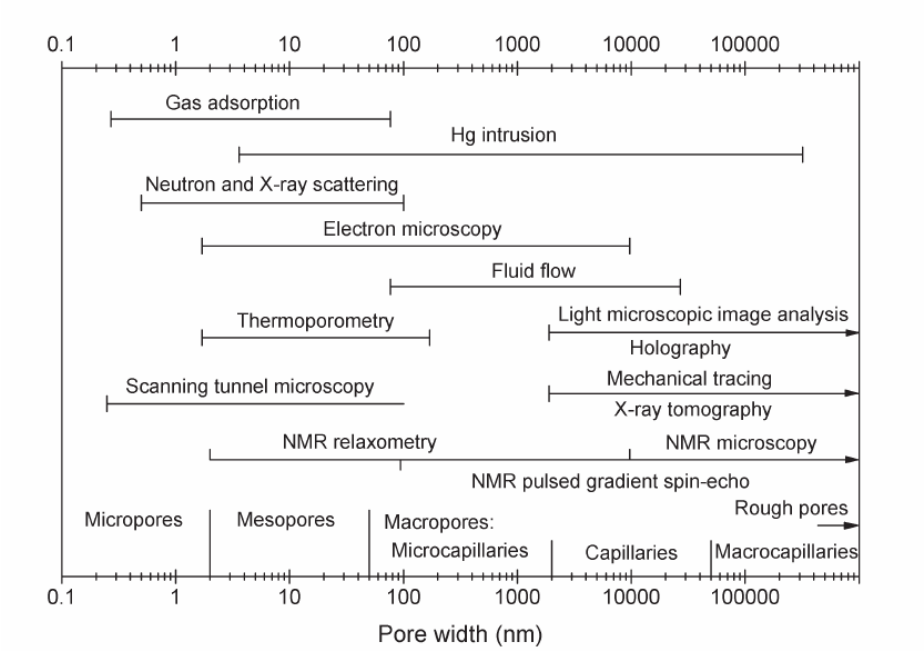
Laboratory 3: The mercury is on average recovered and recycled about 3 times. On average 25% of mercury is disposed of with samples, but it varies greatly with the porosity of the samples. All mercury is disposed of as hazardous waste.



2.4 Availability of alternatives

A number of techniques for characterizing porous materials are applied. The different techniques provide different parameters and can be applied for different pore sizes. An overview of measuring ranges for different techniques, based on a 1997 report is shown below (NIST, 2006):

Figure 1 Measuring ranges of methods for pore size determination (NIST, 2006. after Meyer 1997) [1]



Most of the techniques are rather supplementary to the mercury intrusion porosimetry than actual alternatives, as they measure other parameters.

As indicated in the 2008 EU mercury report at least one company, Porous Materials inc. (U.S.A.), manufactures equipment which is specifically marketed as alternatives to mercury porosimeters:

- Mercury-free intrusion porosimetry (water intrusion).
- Mercury-free extrusion porosimetry;

The following table shows some characteristics of the different techniques according to Porous Materials.

[1] Porosity and Specific Surface Area Measurements for Solid Materials. National Institute of Standards and Technology Special Publication 960-17. September, 2006. http://www.nist.gov/public_affairs/practiceguides/SP960-17_RPG_Porosity1.pdf

Table 2 Characteristics of mercury porosimeters, liquid extrusion porosimeters and water intrusion porosimeters (Based on Porous Materials)

	Characteristics	Mercury intrusion porosimeter	Liquid extrusion porosimeter	Water intrusion porosimeter
Pore structure characterization	Mean pore size	x	x	x
	Pore size distribution	x	x	x
	Total pore volume	x	x	x
	Liquid permeability		x	
	Porosimetry surface area	x	x	x
	Bulk density	x		x
	Absolute density	x		
	Particle size distribution	x		
Sample characteristics	Pore size range	0.0035 - 500 µm	0.05 - 2000 µm	0.001-20 µm
	Surface area range	1-100	not indicated	1-100
	Dead end and through-pores	x		x
	Special sample characteristics	indicated as N/A	not indicated	Hydrophobic
Applications	Automotive industry	x	x	x
	Battery/fuel cell industry	x		x
	Ceramic industry	x	x	x
	Chemical industry	x		x
	Filtration industry	x	x	
	Geotextiles/textiles industry		x	
	Nonwovens industry		x	
	Paper industry	x		x
	Pharmaceutical/medical industry	x	x	x
	Powder metallurgy industry	x	x	x

Mercury-free intrusion porosimetry

The Water Intrusion Porosimeter offers an alternative to mercury porosimetry for hydrophobic samples only (samples not wetted by water). According to Porous Materials the Water Intrusion Porosimeter performs a wide array of tests including total pore volume, pore volume distribution, mean pore size, and bulk density. According to the manufacturer, the water intrusion porosimeter is ideal

for quality control of hydrophobic materials, as tests are non-destructive and less than 10 minutes in length.

The availability of alternatives has been addressed by the IUPAC Working Group on "Liquid intrusion and alternative methods for the characterization of macroporous materials" (Provisional document (dated 15th February 2010)

According to the IUPAC review a major problem when using water intrusion in hydrophobic materials is that the wetting behaviour of water depends on details of the surface chemistry of the test material and consequently the contact angle of water is very often not known. The review does not provide any conclusion regarding the applicability of the method.

According to the specifications for the Aquapore water porosimeter, the porosimeter can be applied for pore sizes of 0.0005 - 20 µm.

According to the presentation from Thermofisher Scientific the hydrophobic materials cover less then 5% of applications and the determination of analytical parameters is difficult and a long surface treatment is needed.

No information has been received upon request from Porous Materials on the actual applications of the water intrusion porosimeter and the specific applications where the mercury porosimeter could be replaced. No data have been available indicating whether the same users typically analyse both hydrophobic and hydrophilic samples and in this case would need both a water intrusion and a mercury intrusion porosimeter. Porous Material market bout porosimeters which can be used for both mercury and water porosimetry (Mercury/Nonmercury Intrusion Porosimeter) and a porosimeter exclusively for water porosimetry (Water Intrusion Porosimeter (Aquapore)).

Mercury-free extrusion porosimetry

The mercury-free liquid extrusion porosimetry applies a different principle than the intrusion porosimetry. Whereas the intrusion methodology measures the pressure needed for the intrusion of the liquid into the sample, the extrusion porosimetry measure the porosity of the material by the pressure needed for pressing a wetting liquid that spontaneously has filled the pores out of the material.

The IUPAC review uses the term "liquid porosimetry" for this analytical method (IUPAC, 2010). The method is employed by the TRI/Autoporosimeter™ from TRI/Princeton (USA) and the liquid extrusion porosimeter produced by Porous Material. (USA)

TRI/Princeton mention about the instrument that it *"provides accurate measurements of pore size distributions in the range of pore radii 1 to 1000 microns and, unlike mercury porosimetry, is applicable to fragile, soft and deformable materials."*

According to the IUPAC review the method measures not only the surface area, pore volume, and pore size distribution, but also the actual uptake and retention capillary pressure at different liquid content, , and the liquid uptake/drainage hysteresis.

The review does not discuss in detail the applicability and limitations of the method as compared to mercury intrusion porosimetry. It reaches the conclusion that "*As long as the main objective is the assessment of a pore volume and a pore-size distribution (with the acceptation of simplifying assumptions about the uniform shape of the pores), methods like liquid or contact porosimetry and water desorption calorimetry certainly deserve being developed*". And "*Now, these methods are still far behind mercury intrusion porosimetry in terms of experience and know-how gathered about the experiment with a variety of materials.*"

The presentation from Thermofisher Scientific (2009) indicated that the technique involves a very expensive gravimetric technique and that the technique has a limited pore size range. As described above the TRI/Princeton instrument is limited to the 1-1000 µm range whereas Porous Materials indicate a range of 0.06-1000 µm for their instrument.

Development of methods for product control

Mercury is currently used for both research and product quality control (QC/QA) in production of different materials e.g. particle filters for diesel motors.

For product control (ensuring a uniform material quality), it may be possible to develop methods where only a few parameters are analysed as an indicator of the desired quality and these parameters could be determined using alternative methods. In the presentation by Thermofisher Scientific it is indicated that three years would be needed for validation and re-calibration of QC/QA procedures and four years would be needed for development of new certified reference materials (such as BAM and NISTreference materias) for the results validation. The presentation does not indicate which methods may be used for the product control.

2.4.1 Questionnaire results

Mercury porosimeters are used for analysis if pore sizes in the range of 0.003 to 400 micrometers in materials used in many sectors. The table below shows applications for which technically feasible alternatives are not considered by to exist, as answered by one manufacturer of mercury porosimeters. Two of the manufacturers did not answer the questionnaire as they considered the questions being answered by the IUPAC review (IUPAC 2010).

Table 3 Applications of mercury in porosimetry for which technically feasible alternatives are not regarded to exist (answer from one manufacturer)

Application of mercury porosimeter	Sectors	Potential alternatives	Reasons for these alternatives of not being technically feasible (1)
Particle filters (PM10) for diesel motors	Automotive	none	Very large pores must be measured, fast and inexpensive experiments for QC/QA in production
Heterogeneous catalyst supports	Catalysis	none	Pores in the upper meso and lower macro range typically from 4 to 500 nm, need a lot of info not given by other techniques
Battery separators, anode and cathodes	Energy	none	Anodes and cathodes should be treated as a non wetted surfaces. Difficult and long preparation, not practical for QC/QA purposes
Fuel cell matrix	Energy	none	Very large pores
Drugs support for controlled release	pharma	none	Soluble in water
Bones replacement ceramics	Medicine	none	Very large pores
Particle size analysis of solvable materials	General	none	Difficult sample preparation and difficult deaggregation of particles
Cements, Concrete	Building materials	None	Impossible to use wetting liquid, cements reacts with water
Frost resistance determination of exterior materials	Building materials	none	Pores in the lower macropore range (below 1 micron)
Raw materials for ceramics	Ceramics		
Moulding for ceramics preparation	ceramics	none	Small pores must be carefully determined
Refractory materials heat transfer properties	Industrial ovens	none	
Soil and rocks drainage properties	Geology, agricultural		
Resins and polymers raw materials	Plastic		
Geological samples	General	None known	Pore structures need to be characterized
Gas & Oil recovery	Energy	none	Pore structure of reservoir rocks to determine how to best extract the most natural gas and oil
Ceramic Insulators	General	None	Determine pore structure related to strength of materials and dielectric qualities
Dental Ceramics	Medical	None	Detemine pore structure and strength of dental materials
Paper products	General	None for the range used	Determine paper coating properties and paper porosity

Note: QC/QA = Product Quality Control/Quality Assurance

2.5 Standards

The table below shows some of the main standards for mercury porosimetry and their application in different sectors (based on the response from one manufacturer). The manufacturer consulted mentioned that a number of U.S., European and Japanese patents specify the use of mercury porosimetry for testing products. Many manufacturing companies have internal procedures for production of materials which specify the use of mercury porosimetry because no other equivalent method exists for determining the same information.

Table 4 Analysis for which national or international standards prescribe the use of mercury porosimeters

Analysis	Industrial sectors	Standard	Alternatives that potentially may be used for the analysis if the standard is changed*1
Standard Test Method for Interior Porosity of (PolyVinyl Chloride) (PVC) Resins	Plastic	ASTM D2873-94(1999)e1	
Standard Test Method for Determination of Pore Volume and Pore Volume Distribution of Soil and Rock	Geology, agricultural	ASTM D4404-84(1998)e1	
Standard Test Method for Determining Pore Volume Distribution of Catalysts	Catalysis	ASTM D4284-03	
Standard Test Method for Bulk Density and Porosity of Granular Refractory Materials	Ovens	ASTM C493-98	
Porosity and pore size distribution of materials	General	BS 7591-1:1992	
Evaluation of Pore Size Distribution and Porosity of Materials by Mercury Porosimetry and Gas Adsorption - Part 1: Mercury Porosimetry	General	ISO 15901-1	
European Pharmacopoeia	Pharma	07/2008:20932	
Pore volume distribution and specific surface area	General	DIN 66133	
Bulk and tap density (Roh und Schüttdichte)	General	DIN 51065	
Density of granules	Powders	DIN EN 993-17	

*1 The column is empty as the answerer considers that no alternatives are available.

2.6 Key cost elements

For a comparison of cost elements between mercury porosimetry and alternatives, information has been requested from manufacturers. The table below is based on the answer from the same manufacturer as previous the tables.

Two alternatives are indicated - each considered for a specific application:

- Flow porometer (only for membranes): pore size (passing through).
- Water porosimeter (only for hydrophobic materials): pore size and volume.

Table 5 Key costs elements for a comparison of mercury porosimetry with alternative methods

	Mercury porosimeter	Alternative
Measured properties	Pore size and pore volume distribution, specific pore volume, % porosity, intra-inter particle porosity, envelope, bulk and apparent density, particle size distribution, specific surface area and area distribution, compressibility, tortuosity, permeability, frost resistance factor, surface fractal dimension	Flow porometer (only for membranes): pore size (passing through) Water porosimeter (only for hydrophobic materials): pore size and volume
Typical price of meter (factory gate price without VAT in €)	20.000 euro to 40.000 euro depending on configuration	Porometer → from 25.000 euro to 50.000 euro depending on brand and model
Typical number of analysis per year – industrial setting	1000 to 3000	Don't know
Typical number of analysis per year – research	150 to 1000	Don't know
Average lifetime of porosimeter (in years)	20 years (depends on availability of spares)	Don't know
Recurrent costs per analysis (excl. salary) (€/analysis) (specify)	About 30 euro per analysis	Don't know
Average time needed for one analysis including sample preparation (minutes)	From 30 to 90 minutes depending on material and pressure range required	Don't know
Costs of waste disposal (€/analysis)	Estimated about 1 euro per analysis	Don't know
Other factors influencing the costs estimates (specify):	Lab safety (fume hood, tools for handling mercury, etc), personnel training, regular service (needed max 2 service inspection per year), periodic BioAssay of personnel to make sure no mercury exposure has occurred.	Don't know

3 Pycnometers

From consultation for this study one manufacturer of mercury porosimeter and pycnometers has answered that "*As far as I know mercury is no more used in pycnometry as envelope or helium pycnometers have substituted mercury pycnometry in all the applicatio*n." The other thee contacted manufacturers has not responded to this part.

Mercury pycnometers are still marketed by Porous Materials,USA.
http://www.pmiapp.com/products/mercury_pycnometer.html

Porous Materials has not answered the questionnaire and subsequent requests by email and telephone.

4 Thermometers

4.1 Introduction

The following chapter is drafted on the basis of information obtained by a questionnaire sent to nine manufacturers of mercury thermometers in early 2010 and an extract from the report "*Options for reducing mercury use in products and applications, and the fate of mercury already circulating in society*" (Lassen et al. 2008) (referred to as the 2008 EU Mercury Report in the following). Furthermore, seven manufacturers and suppliers of non-mercury thermometers have been contacted by telephone and e-mail.

Six manufacturers, from Germany, the UK and France, have answered the questionnaire (which is included in Section 11). Several of the manufacturers only filled in a few of the tables in the questionnaire. The questionnaire responses have been followed up with additional questions by extensive e-mail correspondence with the manufacturers which has been most informative.

Mercury thermometers may, in principle, be used for manual reading of all temperatures in the interval from the freezing point of mercury, -39°C, up to about 800°C, with an accuracy of 0.01°C. For measurements at lower temperatures, down to -58°C, a mercury-thallium thermometer may be used, while for even lower temperatures hydrocarbons such as toluene or pentane are used. For temperatures higher than 800°C, thermometers with a gallium filling are used.

Three types of mercury-containing thermometers have traditionally been used in the EU:

- Mercury-in-glass thermometers:
  - Medical thermometers;
  - Ambient temperature thermometers (wall thermometers);

  - Minimum-maximum thermometers (Six's thermometers) and maximum thermometers;
  - Laboratory thermometers;
  - Thermometers for combustion and industrial processes.

- Mechanical mercury thermometers with a dial; and

- Contact thermometers (electric thermoregulators – these are covered by the RoHS directive and were not addressed by the questionnaire and are not further addressed in this note).

Furthermore, mercury-in-glass thermometers may be used as a part of other measuring equipment, among these:

- Hygrometers (to measure humidity). A mercury hygrometer consists of two mercury thermometers mounted together, one of which has a cloth wick over its bulb and is called a wet-bulb thermometer.

- Hydrometers (to measure density or specific gravity of a liquid). Some hydrometers have a mercury thermometer inside the hydrometer for simultaneous reading of the temperature.

The most common mercury thermometers consist of mercury encased in a thin glass tube that rises and falls (expands and contracts) with temperature. This thermometer has traditionally been widely used as a fever thermometer, in laboratories, as an ambient temperature thermometer and for temperature monitoring of machines, combustion processes and industrial processes.

The mercury content of thermometers used by laboratories and in industry ranges from 1 to 20 g Hg per thermometer, with an average content of 3-4 g.

Mercury dial thermometers consist of a mercury filled metal tube with a bourdon coil and a pen or needle for reading the temperature. They are applied mostly in the process industry and for marine applications. Similar thermometers for high temperature measurements, e.g. in foundry applications for measurements of the temperature of diesel exhaust, are also referred to as pyrometers. For remote control of large engines or combustion processes, thermometers consisting of a sensor on the machine and a mercury-filled capillary up to 40 m long connecting the sensor to a gauge in the control room have been and may still be in use. The mercury content ranged from about 5 to 200 g (Maag *et al.* 1996). These thermometers have mainly been used for marine engines and within the power sector.

In their questionnaire responses, manufacturers have pointed to the need for derogations for three application areas of mercury thermometers, each of which which will be addressed in this note:

- Thermometers used for combustion and industrial processes measuring at temperatures >200°C.

- Thermometers used in laboratories and other applications where a resolution of 0.1 °C and better is needed (one manufacturer mentions 0.5 °C resolution while the remaining answered 0.1 °C).

- Hygrometers.

The discussion about availability and feasibility of alternatives is different for the three application areas and they are consequently addressed separately in the following.

None of the manufacturers have pointed at minimum-maximum thermometers (Six's thermometers) or thermometers for measuring temperatures <200°C at a resolution of >0.5 °C as essential uses.

Minimum-maximum thermometers

Minimum-maximum thermometers with mercury are still marketed, but thermometers with mercury-free filling are available at similar prices or lower (see e.g. http://www.brannanshop.co.uk/acatalog/maximum_minimum_thermometers.html#18). Electronic minimum-maximum thermometers are readily available at somewhat higher prices.

Other thermometers

Non-mercury thermometers for measuring temperatures <200°C at a resolution of >0.5 °C are readily available at prices similar to or lower than the price of the mercury thermometers. A check by a Danish supplier of thermometers for laboratories revealed that the prices of the non-mercury thermometers were about 10% lower than the price of mercury thermometers for the same range and resolution.

Maximum thermometers

Maximum thermometers are used to measure the maximum daily temperatures or the maximum temperature of a process. The thermometer has a small area where the glass tube is narrowed and works by the same principle as the fewer thermometer. When the temperature begins to drop, the constriction prevents the mercury from flowing back down the tube. The mercury will not move back down the tube until the thermometer is shaken.

Maximum thermometers have been specifically mentioned by one manufacturer as an essential application. Maximum thermometers are available for different ranges and resolutions. For ranges including low temperatures, a mercury-thallium alloy is used. Mercury maximum thermometers are provided by several manufacturers, with a resolution down to 0.1°C e.g. "maximum precision thermometers for shaking, enclosed scale" in a catalogue from Ludwig Schneider (http://www.ludwig-schneider.de/). The maximum thermometers with high resolution are included in the general applications of thermometers mentioned below.

4.2 Thermometers used for combustion and in industrial processes

Technical feasibility of alternatives

For temperatures below 200-250°C, mercury-free liquid-in-glass thermometers and electronic thermometers are the most common replacement for the mercury thermometers used in industrial processes. Mercury-free liquid-in-glass thermometers are, in general, not suitable for accurate measurements at 0.1°C resolution, but in the industrial processes it is generally not necessary to measure the temperature at this level of precision.

The following discussion thus concerns thermometers for the range of 200-800°C.

The main alternatives are:

- **Dial thermometers**. These thermometers may consist of a liquid- or air-filled metal cylinder with a dial for manual reading. Another type is a bi-metallic dial thermometer that senses and indicates temperature using a bimetallic coil, which consists of two dissimilar metals bonded together. These materials have different coefficients of thermal expansion and, when subjected to temperature change, rotate the coil.

- **Thermocouples:** These thermometers consist of two lengths of dissimilar metals, joined at one end to form a measuring junction. Each length, referred to as a thermoelement, develops a voltage (or more accurately, a thermoelectric electromotive force) along its length wherever the thermoelement passes through a temperature gradient. Different thermocouple types can be used for applications in temperature ranges from -40°C to +1800°C. Thin-film resistance thermometers provide accuracy over a wide temperature range (from -200°C to 850°C). Electronic thermometers are used throughout industry for automatic temperature measurements. For some applications, e.g. diesel engines for marine applications, the automatic measurements may be supplemented with mechanical thermometers for manual reading.

- **Platinum resistance thermometers** (PRTs) rely on the known variation of electrical resistance with temperature of a specially constructed resistor to convert temperature into a measurable electrical property. Different type e.g Pt 100, Pt 200, Pt 500, and Pt 1000.

- **Gallium thermometers.** These are applied today for high range thermometers where the upper temperature is 750°C or higher. Thermometers with a gallium filling are e.g. available for the range 0-1,050 °C with 5 °C resolution or 0 – 800 °C with 2°C resolution. (See for example http://www.amarell.de/thermometers/quartzglassthermometers.htm)

Table 6 shows the merged response from three manufacturers of the mercury thermometers comparing the mercury thermometers with three alternatives: thermocouples, dial thermometers and gallium thermometers. According to the

responses, the thermocouple and dial thermometers alternatives suffer from aging which results in decreasing accuracy and more frequent re-calibration. Furthermore, they need additional power supply and there will be some requirement for modified/additional installations in existing facilities. A UK thermometer manufacturer stated previously for the EU Stakeholder Consultation that adequate alternatives and technologies already exist for this application area (referred to in the 2008 EU mercury report).

According to the information in the table, dial thermometers have the disadvantage in large diesel engines of being sensitive to vibration. Contrary to this, Danish suppliers of thermometers indicated – for a previous study in 2006 – that for measurements in engines, the mercury-in-glass thermometers have the disadvantage that droplets may be introduced by the vibrations from the engine, if the thermometer is not held vertically (Lassen and Maag 2006). Furthermore long mercury-in-glass thermometers have the disadvantage that they can easily break when handled. Mercury thermometers used for combustion and industrial processes have been banned for many years in Denmark and the study concluded, on the basis of information from market actors, that it was unlikely that mercury thermometers would be reintroduced even if they were no longer banned (Lassen and Maag 2006).

Gallium thermometers

For the gallium thermometer no reasons for these alternatives not being technically feasible were mentioned, but in Table 7 it is indicated that it is difficult to manufacture gallium thermometers, resulting in high prices for these thermometers. One manufacturer indicates that they have used liquid gallium in thermometers for the high temperature range above 750 ° C for more than 80 years. They have subsequently been contacted for obtaining more information which is included in the follwing.

The contacted company use today pure gallium, as experiments with gallium-indium gave no useful results. According to the manufacturer, working with gallium is very difficult because it melts only at 30 °C and the thermometer cannot be filled - unlike mercury - in large numbers and under high-vacuum conditions. Each thermometer has to be individually filled, which is a costly operation.

The filing has to be done at high temperatures. The gallium thermometers produced today with a wide temperature range are made of heat resistant quartz glass with a coarse capillary, and in this case there are no specific problems with the temperature.

According to the manufacturer, however, this type of glass is not suitable for precision thermometers which have to comply with certain specific requirements. For the precision thermometers a special type of glass is used, and this glass is only suitable for working at temperatures up to 480 °C which is close to the working temperature used by filling of the gallium. For many types of gallium thermometers this leads to a large amount of waste from the manufactur-

ing process. An example of a precision thermometer is shown in table 8 with a price of about 20 times that of the similar mercury thermometer.

In solid-stem thermometers the gallium thermometer has, except for minor differences in the size of the bulb, the same dimensions as the mercury thermometer. They seem in principle to be suitable for retrofit (although at higher prices), but the manufacturer indicates that they would not comply with the thermometer manufacturing standards.

Fever thermometers filled with an alloy of gallium, indium and tin (galinstan), are widely marketed. In order to avoid the galinstan wetting the glass, the inner tube of the thermometer must be coated by gallium oxide. No examples of the use of this alloy for thermometers used in industry or laboratories have been identified.

Retrofit

One particular problem, mentioned in Table 6, is the need for modified/additional installations in existing facilities if spare mercury thermometers are no longer available. Mercury-free replacement thermometers (spare parts) that will fit into the existing installations are often not available. In the marine sector in Denmark this problem has to some extent been solved by buying spare mercury thermometers abroad.

In Sweden mercury thermometers have been banned since 1991 with a few exemptions. In an investigation of a general mercury ban, the Swedish authorities address the question of retrofitting: *"A large number of mercury thermometers are fitted in autoclaves, and warming cabinets used in laboratories and in health care. When the thermometers have been broken or no longer register correctly, the equipment has been modified to allow the installation of, for example, a thermocouple, or the thermometer has been replaced with a more modern digital temperature-measuring device. These two techniques offer certain advantages as regards automation and the collection/recording of data. There are probably still several thousand mercury thermometers in autoclaves, and warming cabinets, which will be replaced as they are become unserviceable. "* (Kemi 2004)

No information has been made available on the typical cost for retrofitting existing installations in order to be able to use mercury-free alternatives. The actual costs will be highly dependent on the timing of a restriction.

A Danish manufacturer of thermometers indicates that the company often provides thermometers (both PT100 and dial) which are adjusted to a specific machinery (specific length and diameter) and that the price of these is only slightly higher than the standard thermometer. The screw thread is typically ½'' on all thermometers. The company indicates that they know of examples where mercury thermometers may be used as spare parts in the marine industry, but have never heard about it in other sectors. In Danish industry there has been a focus on automatic reading which has been the driver for changing to electronic equipment - this may be different in other Member States.

Table 6 Applications of mercury thermometers for combustion and industrial processes for which no technically feasible alternatives are regarded to exist (based on answers from three manufacturers of mercury thermometers for industrial processes)

Application of thermometer	Sector	Potential alternatives	Reasons for these alternatives not being technically feasible
Temperature >200℃	Industry	- Thermocouple - RTD (Resistance Temperature Device)	- Aging -> decreasing accuracy -> frequent re-calibration - Requires electric indicator (digital or analogue) - Requires additional power supply - Requires modified/additional installations in existing facilities
Temperature >200℃	Industry	Dial thermometer	- Agin g -> decreasing accuracy -> frequent re-calibration - Requires modified/additional installations in existing facilities
Temperature >200℃	Industry	Gallium thermometers	-
Temperature >200℃	Engineering Large Diesel engines	Thermocouple	- Aging -> decreasing accuracy -> frequent re-calibration - Requires electric indicator (digital or analogue) - Requires additional power supply - Requires modified/additional installations in existing facilities
Temperature >200℃	Engineering Large Diesel engines	Dial thermometer	- Aging -> decreasing accuracy -> frequent re-calibration - Vibration resistance may be a problem - Requires modified/additional installations in existing facilities

Economic feasibility

According the responses from three manufacturers of mercury thermometers the price of alternative thermometers is 3-5 times the price of the mercury thermometers (Table 7). For electronic thermometers this is the price of the probe and the cost of the data acquisition system is in addition to this.

Table 7 Applications of mercury thermometers for combustion and industrial processes for which technically feasible alternatives exist, but these are not regarded as economically feasible (based on answers from three manufacturers of mercury thermometers for industrial processes)

Application of thermometer	Sector	Available technically feasible alternatives	Price of alternatives as compared to mercury thermometer	Other reasons for these alternatives of not being economically feasible
Temperature >200℃	Industry Engineering Large Diesel engines	Dial thermometer Thermocouple RTD (Resistance Temperature Device) Gallium	3 - 5 times more 3 - 5 times more + cost for additional indicator (3 - 4 x cost of the thermometer) 5 times	- High investments for replacement of all mercury filled industrial glass thermometers in existing facilities - (Re-)Installation costs - Costs for re-calibration - Energy costs for extra power (Thermocouple/RTD) - For local power supply disposal of batteries after service life - Cost of additional indicator (Thermocouple) Difficult to produce

The manufacturers point to the fact that electrical sensors and indicators for temperature measurement make the measurement dependent on an external power supply. For safety reasons there will, in certain applications, be a need for measurements which are not dependent on an external power supply.

As an example in the marine sector, insurance contracts in Denmark prescribe that the engines be equipped with thermometers which can work without external power (Lassen and Maag 2006). Manual dial thermometers can be used for this purpose and they often serve as a back-up for electrical thermometers with automatic reading.

The dial thermometer is the meter which can most immediately be compared with the mercury industrial thermometer as it is used for manual reading and does not need an additional data acquisition system.

Table 8 shows some cost elements for three different types of thermometers according to a manufacturer of thermometers for industrial processes. The company also supplies non-mercury thermometers.

According to the manufacturer the major difference influencing the cost estimate is the indicated average lifetime of the equipment. It is indicated by the manufacturer that the mercury thermometer has an average lifetime of >25 years, whereas the lifetime is only 1-2 years for the dial thermometer.

The manufacturer indicates in the response that 7,629 pieces were sold in the EU in 2009, but these figures seem to concern the specific manufacturer only. In the 2008 EU mercury report it is roughly estimated that the EU market for mercury thermometers used in industry is around 50,000 - 100,000 pieces per year.

Table 8 Comparison of mercury industrial high-temperature thermometer, up to 600 °C with alternatives (answer from one manufacturer of mercury thermometers for industrial processes)

Type of thermometer	Industrial thermometer	Thermocouple with display	Dial thermometer
Typical price of thermometer (factory gate price without VAT in €)	30 - 60 EUR	150 - 200 EUR	100 - 150 EUR
Typical mercury content	3.5g/piece	-	-
Number of thermometers sold annually in the EU (best estimate)	12,550 pieces in 2008 7,629 pieces in 2009 *1		
Average lifetime	> 25 years	5 years	1- 2 years
Costs of calibration	-	100 - 150 EUR	-
Frequency of calibration	> 25 years	12 - 24 month	
Other recurrent costs (specify):	-		
Other factors influencing the costs estimates (specify):	-		

*1 Consultants note: It is not clear whether the figures only include thermometers produced by the specific manufacturer

Table 9 shows data on possible alternatives according to a major global manufacturer of alternative thermometers. The manufacturer does not supply mercury thermometers and cannot compare the prices of mercury thermometers for the same application.

For the electrical systems, prices and lifetime are for the sensors (or probes) only. A thermometer system consists of the sensor, a transmitter (which can be analogue or digital) and a data reader. Furthermore, a digital temperature indicator for manual reading may be connected to the thermometer. The prices and lifetimes indicated in table 9 are for the sensor only. The transmitter may proc-

ess data from more than one sensor, and the data reader may also read data from other types of sensors e.g. pressure gauges.

The lifetime of the probe is generally shorter than for the rest of the system, as the probes are often placed in more harsh environments (vibration, temperature, humidity, corrosive gases, etc.). The manufacturer was not able to provide average lifetimes for all thermometers and the indicated lifetimes relate to the range of lifetimes, which are dependent on the environment where the thermometer is placed.

Table 9 Possible alternatives to mercury thermometers in industrial processes (answer from one major German manufacturer of non-mercury thermometers for industrial processes)

Temperature measurement systems	Measurement Range ℃	Accuracy °C	Average Lifetime Years	Calibration Frequency Months	Basic List Price €
Mechanical systems					
Bi-metal thermometers	-70 … +500	acc. to DIN EN 13190	1-5	6-12	> 105
Gas actuated thermometers	-200 … +600	acc. to DIN EN 13190	1-5	6-12	> 170
Electrical systems					
Resistance thermometers *2	-200 … +600	acc. to DIN EN 60751	1-10	6-24	> 110
Thermocouples *2	-200 … +1200 (standard)	acc. to DIN EN 60584	1-5	6-24	> 85
	-0 … +1700 (special)	acc. to DIN EN 60584	1-2	6-24	no data

*1 List price for basic configuration – higher prices for special configurations. The list price indicates the price the customer has to pay excl. VAT.
*2 Prices are for the probe (sensor) only. The system consists of a transmitter and an indicator which can transmit and read more thermometers and other measuring equipment. The average lifetime is for the probe alone.

Prices

The price of a typical mercury thermometer for industry is reported to be 30 - 60 EUR (Table 8) and this may be used as the baseline price. The price includes the casing for the thermometer.

Prices of **mechanical systems** allow for a straightforward comparison with mercury thermometers as the mechanical thermometers represent a 1:1 substitution. The manufacturers of mercury thermometers have indicated that the prices of mechanical thermometers are typically 3-5 times the price of mercury thermometers. The prices indicated in table 9 for mechanical systems are quite well

in accordance with the price of the dial thermometer in table 8 although the prices in table 7 are "factory gate prices" and the prices in table 9 are minimum list prices for the end-customer. For a previous Danish study it was indicated that the price of the dial thermometer was some 2-4 times the price of the mercury thermometers (Lassen and Maag 2006). We considerer that the 3-5 times indicated by the manufacturers of mercury thermometers is the best available estimate.

For **electronic systems** the price of the sensor is reported to be 3-5 times the price of mercury thermometers. Table 8 indicates that the cost of the systems would be 3-4 times the cost of the thermometer (it was not indicated whether it is 3-4 times the price of the sensor or the mercury thermometer). No data have been made available to estimate how the price of the data acquisition systems can be allocated to the individual thermometers. For the previous Danish study it was reported that the price of PT100 resistance machine thermometers was in the order of 10 times that of a simple mercury-in-glass machine thermometer (Lassen and Maag 2006). It is estimated to be very difficult to obtain a better estimate as the electronic systems consist of several elements with different lifetimes (the data reader typically has a longer lifetime than the sensors). Based on the available data a price of the electronic thermometers of 5-15 times the mercury thermometers seems reasonable, but it should be noted that the thermometers are not comparable. The driver for replacing the mercury thermometers with electronic systems is the advantage of electronic reading which apparently for many customers offsets the extra costs of the thermometers. It should be noted that the electronic thermometers typically have to be recalibrated shortly after they are put into use.

Lifetimes

The average lifetime for the dial thermometer is indicated by the mercury thermometer manufacturer to be 1-2 years (Table 8) whereas the manufacturer of alternatives indicates 1-5 years for mechanical systems depending on the environment (Table 9). A Danish manufacturer of mechanical thermometers estimates the typical lifetime of bimetallic thermometers at 2-5 years and of gas-filled thermometers at 5-10 years. It seems reasonable to use a range of 2-5 years as a best estimate for the mechanical systems.

For electronic systems the estimated lifetimes concern the sensors only. Data in table 8 suggest a lifetime of 5 years for a thermocouple while data in table 9 suggests 1-5 years for the thermocouples and 1-10 years for the resistance thermometers. A major Danish manufacturer of PT100 temperature sensors for industry, diesel engines and laboratories estimates that the typical lifetime of PT100 resistance sensors used in industry at temperatures up to 800°C is 5-10 years. The maximum guaranteed lifetime for some applications is 5 years, but usually the guarantee time is shorter. In very harsh environments with higher temperatures (e.g. waste incinerators) the lifetime of the probes is <0.5 year. Based on the available data a typical lifetime for the electronic sensors of 3-6 years seems reasonable.

The average lifetime of mercury thermometers is indicated to be >25 years. No data are available on the breakage rate of the thermometers but the >25 years seems rather to be the technical lifetime than the actual lifetime. According to a major manufacturer of mercury thermometers, it is realistic to assume an average lifetime of 10-15 years.

Calibration frequency and costs

According to the answers from manufacturers of mercury thermometers, the electronic equipment needs frequent calibration to guarantee accurate measurement values, i.e. to ensure congruence of actual and indicated values. According to these manufacturers, industrial glass thermometers do not need frequent recalibration because its glass capillary keeps its accuracy for 30 years or more. The frequency of recalibration required for mercury thermometers is indicated in Table 8 to be >25 years.

The actual calibration frequencies will probably be dependent on the procedures set up by the users in their quality management system.

In the UK British Standard BS 1041 Section 2.1 (Guide to selection and use of liquid-in-glass thermometers) recommends that verification of the ice point should take place at least annually and that complete re-calibration should take place at intervals of not more than five years [2]. The Danish National Reference Laboratory for temperature reports that the frequency for calibration of mercury thermometers in Denmark has typically been once per 3-5 years. The calibration frequency is not only dependent on the equipment, but also the seriousness of inaccurate temperature measurements and in many industries the equipment is calibrated more often to be on the safe side. According to a major manufacturer of mercury thermometers the calibration certificates of thermometers from this company are valid for a maximum of 5 years. The manufacturer estimates that calibration once every 3-5 years would be typical.

One manufacturer points to the requirements for calibration according to the ISO 9001 quality management standard. The ISO 9001 standard does, however, not set up specific frequencies for calibration of equipment, but require that the company define procedures. The actual frequencies will be different for different companies.

According to the information in Table 8, the calibration frequency of the alternative mechanical system is 6-12 months while the frequency for the electronic systems is 6-24 months. A Danish supplier of PT100 and dial thermometers recommends calibration once a year but reports that 95% of the customers do not calibrate the mechanical dial thermometers because they are mainly used as a backup for the electronic thermometers for automatic reading.

According to a Danish manufacturer it is typically necessary to recalibrate the probe after installation where the probe is “aged” by changing the temperature

[2] http://www.brannan.co.uk/products/cal_index.html.

about 10 times. After the aging process, the probe is often stable for some 5 years and does not drift by more than 0.1°C. Many customers calibrate the thermometers every year because it is required by their quality management system.

It seems appropriate to assume that both mechanical and electronic equipment is calibrated once a year.

For the cost estimates it is of high importance how the calibration is done. Table 8 indicates a price of 100 - 150 EUR for the calibration of an electronic thermometer. For this study the cost of calibration, done by a certified laboratory in Denmark, is reported to be about 200-300 EUR with the highest prices for calibration of high precision thermometers. The cost of a calibration depends on the number of calibration points used. A price of 200 EUR has been reported by a major German manufacturer of electronic thermometers. With a traceable certificate the cost of calibration from the manufacturer is about 350 EUR.

The cost of calibration is higher than the cost of new sensors, but used equipment is more stable than new equipment. All interviewees indicate that the cost of calibration is a significant cost element and is of importance when comparing mercury thermometers with alternatives.

Different procedures may be applied for the calibration of the thermometers:

- The thermometers are sent to a certified laboratory for calibration;
- A reference thermometer is sent for calibration by a certified laboratory; while the other thermometers are calibrated in-house. Different temperature calibration instruments are marketed for in-house use.
- The thermometers are calibrated by mobile units providing on-site calibration of the company's pressure and temperature instruments.

According to a Danish reference laboratory it varies whether the companies prefer to do the calibration in-house or have all equipment calibrated at the laboratory. For in-house calibration it is necessary to have the appropriate equipment and facilities and to have trained personnel, and therefore some companies find it more cost efficient to outsource the calibration. This indicates that the actual costs of in-house calibration may not be much less than calibration at a laboratory.

A cost element of importance is also to what extent it is necessary to stop production when the equipment is calibrated. As an example is it common in the Danish dairy industry to stop the production for one week, while all equipment is being calibrated and maintained.

No information has been made available on costs of the option with the mobile unit. The price is based on used man-hours and transport costs and varies considerably.

To obtain a better estimate on actual calibration costs it would be necessary to obtain information on total annual costs of calibration and total number of thermometers for a number of companies.

4.3 Thermometers used in laboratories and other applications

This section addresses thermometers used in laboratories and other applications where a resolution of 0.1 °C and better is needed. For convenience the term "laboratory thermometers" is used for all types. For thermometers of a resolution of 0.2 °C or less, non-mercury liquid-in-glass thermometers are available.

The following alternatives to mercury thermometer with high resolution are marketed today:

- **Platinum resistance thermometers** (PRTs) and **thermistors** both rely on the known variation of electrical resistance with temperature of a specially constructed resistor to convert temperature into a measurable electrical property. Thermistors have stabilities approaching a few thousandths of a degree Celsius per year when properly constructed, and are highly sensitive (approximately 4% change in resistance per degree Celsius). However, the usable temperature range is limited to not more than 100°C for a single thermistor, and the approximate maximum temperature of use is 110°C (Ripple and Strouse 2005). The best stability is obtained with thermistors coated or encapsulated in glass. Platinum resistors have a substantially wider operating range compared to thermistors, but they have a sensitivity 10 times smaller (approximately 0.4% change in resistance per degree Celsius).

- **Thermocouples** (TCs) consist of two lengths of dissimilar metals, joined at one end to form a measuring junction. Each length, referred to as a thermoelement, develops a voltage (or more accurately, a thermoelectric electromotive force) along its length wherever the thermoelement passes through a temperature gradient (Ripple and Strouse 2005). Different thermocouple types can be used for applications in temperature ranges from -40°C to +1800°C. Thin-film resistance thermometers provide accuracy over a wide temperature range (from -200°C to 850°C).

- **Gallium thermometers** may be used for some applications, but the thermometers seem to be produced for this purpose today in only very limited numbers.

- **Liquid-in-glass thermometers with an organic filling** (PerformaTherm™).

One of the manufacturers points to the fact that people mix resolution and accuracy. A digital thermometer showing the temperature with a resolution of 0.1°C, does not necessarily measure the temperature with an accuracy of 0.1°C. However, if properly calibrated the best electronic thermometers in general have a high accuracy, and the discussion about their use more concerns the need for frequent calibration.

The responses provided (Table 10 and Table 11) confirm the existing information: that the questions regarding the suitability of alternatives concern measurements at a resolution of 0.1°C or better and the drawbacks of alternatives are the price and stability of the probes. One of the has responded with an extensive list of thermometers with different application areas, but these areas are covered by the general description in the tables below.

The responses indicate that that these thermometers are used within a wide range of sectors: scientific research, breeding, the environmental sector, and the chemical, petroleum, pharmaceutical, medical, and food sectors.

Thermometers with a resolution of 0.5°C.

In principle thermometers with non-mercury fillings can be used down to a resolution of 0.2°C. However, one manufacturer points to the need for mercury thermometers for specific measurements even at 0.5°C. An example is an instrument for flash-point determination, where the different expansion coefficient and response time of the non-mercury filling would result in incorrect determination of the temperature. In this case another setup would be needed if non-mercury thermometers had to be used.

PerformaTherm

One liquid-in-glass thermometer with an organic filling, with a resolution of 0.1°C, has been introduced. According to the manufacturer , the PerformaTherm™ thermometers from Miller & Weber Inc, USA, meet the ASTM standards for accuracy, tolerance and uncertainty. Each thermometer is supplied with a two-page report of calibration. According to the manufacturer the proprietary blue liquid is biodegradable, nontoxic, noncaustic, and nonhazardous. About 15 different ASTM thermometers are available. The thermometers have the same dimensions as similar mercury thermometers.

The maximum temperature of the thermometers is 105 ºC. The limited temperature range has been mentioned as an obstacle for its use.

The liquid of the thermometer has, according to the manual, a tendency to separate, especially during storage or transit and needs to be rejoined using cooling methods. According to a supplier the column has a tendency to separate during shipping and when stored in a horizontal position, whereas this does not happen when the thermometer is stored in a vertical position (e.g. placed within equipment). The column can be reunited in the laboratory by a specific procedure.

According to information obtained from some users in the petrochemical industry the slower response time and the separation of the liquid are serious re-

straints for the use of the thermometers for applications such as fuel specifications (including freezing point of jet fuels and flash point of diesel). It has not been possible to identify any scientific papers evaluating the performance and limitations of the PerformaTherm thermometers.

According to the web-site of Miller & Weber Inc, PerformaTherm is also supplied for the food industry with a so-called HACCP [hazard analysis and critical control points] Compliance Kit.

A supplier of PerformaTherm^{TM} on the EU market has been asked for further information on the use of the thermometers in the EU. Sales to date have reportedly been very limited due to supply limitations and it has not been possible to obtain an evaluation of the use of these thermometers in different sectors.

No information on calibration frequency has been provided. According to the supplier mentioned above the frequency is normally determined by the quality management procedures of the users.

The price of PerformaTherm ASTM thermometers is 2-3 times the price of ASTM mercury-filled thermometers with the same specification, produced by Miller & Weber Inc.

Table 10 Applications of mercury laboratory thermometers for which technically feasible alternatives are not regarded to exist (based on answers from two manufacturers of mercury thermometers for industrial processes)

Application of thermometer	Sector	Potential alternatives	Reasons for these alternatives of not being technically feasible
Temperature total range but with accuracy and resolution of 0.1℃ or better	R&D, Quality Control, Breeding, Calibration, equipment control for ISO QMS, FDA, Standard methods Environmental, Water, Food, methods	Thermocouple RTD (Resistance Temperature Device)	3-5 times higher prices + cost for additional indicator (3…4 x cost of the thermometer)
		Gallium filling	10-15 times the price of the Hg thermometers. Limited measurement range, many failures during manufacturing, therefore, difficult to calculate price
Impossible to list all applications	Chemical Petroleum Food (Lab. Not consumers) research	Digital but with limits about accuracy due to stability of the probe	When speaking about high precision (0.1℃ and more), the stability of the probe moves and the thermometer becomes not sufficiently accurate. The user cannot see that the accuracy has changed. The only way is to control regularly the thermometer, which is costly.
Different thermometers with a resolution of 0,5℃ or better or for measurements above 250℃ Thermometers made in	Science and research, quality control, chemical, pharmaceutical and medical engineering	Thermometer with mercury-free fluids	Thermometers with mercury-free fluids not applicable at higher resolution than 0.5 ℃ and above 200℃. Significantly slower temperature response of glass thermometers with mercury-free fluids may lead to erroneous evaluation of measurement results

Application of thermometer	Sector	Potential alternatives	Reasons for these alternatives of not being technically feasible
accordance with specific standards [reference is made to the full response indicating a wide range of different thermometer types for different applications]		Electronic thermometer	Electronic thermometers can in some cases not be used because of the structure of their temperature and chemical resistant sensor housing No calibration with a validity of 15 years possible.

Economic feasibility

Manufacturers of mercury thermometers point to a number of cost elements that are of importance for assessing the economic feasibility of alternatives (Table 11).

Table 11 Applications of mercury laboratory thermometers for which technically feasible alternatives exist, but these are not regarded as economically feasible (based on answers from two manufacturers of mercury thermometers for industrial processes)

Application of thermometer	Sector	Available technically feasible alternatives	Price of alternatives as compared to mercury thermometer	Other reasons for these alternatives of not being economically feasible
Temperature total range but with accuracy and resolution of 0,1 ℃ and better	R&D, Quality Control, Breeding, Calibration, equipment control for ISO QMS, FDA, Standard methods Environmental, Water, Food, methods	Thermocouple RTD (Resistance Temperature Device)	3 … 5 times more + cost for additional indicator (3…4 x cost of the thermometer)	- High investments for replacement of all mercury filled industrial glass thermometers in existing facilities - (Re-)Installation costs - Costs for re-calibration - Energy costs for extra power (Thermocouple/RTD) - For local power supply disposal of batteries after service life - Cost of additional indicator (Thermocouple)

The manufacturers have provided different examples for the comparison of a thermometer for general measurements in laboratories at resolution of 0.1 ºC and alternatives (Table 12, Table 13 and Table 14). Several manufacturers have mentioned that such a thing as “a typical thermometer” for this application does not exist as a wide range of different thermometers are manufactured.

The number of thermometers sold again seems to indicate the numbers sold by the specific manufacturer and not the total EU market, and furthermore only seems to cover the specific thermometer type.

According to the 2008 EU mercury study the total market for mercury-in-glass thermometers was estimated at 200,000 - 400,000 thermometers. It is not indicated how many of these are thermometers with a resolution of 0.1 °C. For more specific market data it would be necessary to make a detailed market analysis with collection of data from all manufacturers.

Table 12 Comparison of thermometer for general measurements in laboratories at resolution of 0.1 ºC and alternatives (based on one manufacturer response)

Type of thermometer	Precision mercury thermometer	Thermocouple + Instrument	RTD (Resistance Temperature Device) + Instrument
Typical price of thermometer (factory gate price without VAT in €)	80	600	300
Typical mercury content per thermometer (g/item)	4	0	0
Number of thermometers sold annually for general applications in laboratories in the EU (best estimate)	-	-	
Average lifetime (in years)	30	3	3
Costs of calibration (€ per calibration)	70	70	70
Frequency of calibration (per year)		1	1
Other recurrent costs (specify) (€/year/item):			
Other factors influencing the costs estimates (specify):		Power/Batteries	Power/Batteries

*1 Consultants note: It is not clear whether the figures only include thermometers produced by the specific manufacturer

Table 13 Comparison of thermometer for general measurements in laboratories at resolution of 0.1 ºC and alternatives (based on one manufacturer response)

Type of thermometer	Mercury laboratory thermometer, government tested with verification certificate *2 0 - 50 ℃ Resolution 0,1℃	Electronic thermometer with Pt 1000 4-conductor probe -20+150 0,1℃ Resolution 0,001 ℃
Typical price of thermometer (factory gate price without VAT in €)	37	826
Typical mercury content per thermometer (g/item)	3	0
Number of thermometers sold annually for general applications in laboratories in the EU (best estimate) *1	650	25
Average lifetime (in years)	Unlimited	3 - 5 years
Costs of calibration (€ per calibration)	154	266
Frequency of calibration (per year)	Validity of calibration 15 years	At least every year
Other recurrent costs (specify) (€/year/item):	None	Batteries
Other factors influencing the costs estimates (specify):	None	Additional calibration points Accessories, power supply, software, etc.

*1 Consultants note: It is not clear whether the figures only include thermometers produced by the specific manufacturer

*2 Means that the precision of the thermometer is tested by an independent test laboratory.

Table 14 Comparison of thermometer for general measurements in laboratories at resolution of 0.05 ºC and alternatives (based on one manufacturer response)

Type of thermometer	ASTM 44C mercury thermometer with official certificate +18.6 – 21.4 ℃ Resolution 0.05℃	ASTM 44C gallium thermometer with official certificate 18.6 – 21.4 ℃ Resolution 0.05℃	Electronic thermometer with Pt 1000 4-conductor probe -20+150 Resolution 0.001℃
Typical price of thermometer (factory gate price without VAT in €)	54	810	826
Typical mercury content	11 g /piece	0	0
Number of thermometers sold annually for general applications in laboratories in the EU (best estimate) *1	100	1	25
Average lifetime	Unlimited	Unlimited	3 - 5 years
Costs of calibration (€)	143,-	143,-	202,-
Frequency of calibration	Validity of calibration 15 years	Validity of calibration 15 years	At least every year
Other recurrent costs (specify):	0	0	Batteries

*1 Consultants note: It is not clear whether the figures only include thermometers produced by the specific manufacturer

Lifetime

The costs estimates are very sensitive to the indicated differences in average lifetime. It is not clear from the answers whether the lifetime of the electronic equipment only concerns the lifetime of the probe or the lifetime of both probe and data logger.

The manufacturers have indicated that the lifetime of the mercury thermometers is unlimited (two manufacturers) or 30 years (one manufacturer) whereas the lifetime of the electronic thermometers is 3-5 years. Manufacturers of electronic thermometers used in industry have indicated lifetimes of 5-10 years for the probe and this would probably also be true for the electronic thermometers used in laboratories.

The actual lifetime will depend on the actual use of the equipment as it is a question of how often the equipment is dropped. The actual lifetime of mercury thermometers is certainly not unlimited (as then there would be no market for replacement thermometers), but it has not been possible to identify any information on the actual lifetime. A possible way to reach an estimate would be to

ask large users about their stock of thermometers and annual purchase of new equipment, but it would be rather time consuming to reach a robust estimate.

Calibration

According to the tables above one manufacturer indicates that the mercury thermometers do not need calibration while the other indicates a 15 year validity of calibration. Both indicate that the electronic alternatives need to be calibrated once a year and this has also been confirmed by suppliers of electronic thermometers.

In laboratories the frequency of calibration is, however, often determined by the quality management system. In many laboratories the frequency is 1-2 calibrations per year independent of thermometer type.

The mercury thermometer is very stable unless it is subject to physical damage and it is necessary to check the thermometer by physical inspection.

According to a Danish certified test laboratory mercury thermometers are usually calibrated every 3-5 years.

The calibration/check of a mercury thermometer consists of two steps as described by an instrumentation service provider (http://www.instrumentationservices.net/mercury-thermometers.php):

- ***"Physical inspection****. The thermometer is physically inspected on arrival as we look for a broken mercury column or cracked glass. If it appears to be OK we will measure the dimensions to ensure that it meets with the required specifications: BS, ASTM, or IP.*

- ***Calibration****. The thermometer is then placed in a calibration bath at the depth required by the type of thermometer that we are calibrating. We compare the readings of the thermometer against a high accuracy AC bridge thermometer using two reference probes. Any corrections that need to be made are noted on the certificate."*

As discussed for the industry thermometers, the thermometers used in laboratories may either be sent to a certified laboratory for calibration or calibrated in-house using a calibrated reference thermometer which is calibrated at a test laboratory. The costs are expected to be more or less the same as described for industry thermometers.

Shipping

The tables above do not include information on shipping costs. One supplier of thermometers mention that the costs of shipping of the thermometers if shipped by air freight is significant. If the shipped package includes one mercury thermometers the shipping costs typically increase by some 200 €. When shipping large numbers of thermometers from the manufacturers to suppliers the extra shipping costs per thermometer may be low, but the extra costs may be significant when the suppliers ship one or a few thermometers to a customer. One

supplier indicates that this is one of the reasons that the supplier has been looking for mercury-free alternatives for the oil refinery sector.

Field testing of flammable liquids

A recent article from ASTM (ASTM 2009), which discussed the possible replacement of mercury thermometers, points at a specific application where the use of a non-electric device may be of advantage.

The custody transfer of oil and natural gas, for example, commodities that are bought and sold by volume at a stated temperature, require regular field temperature measurements to verify quantities. In such situations mercury thermometers remain the 'gold standard' according to the American Petroleum Institute in Washington, D.C. The representative of the institute notes that when temperature measurement devices are used for calibrations and measurements in the field, the environment may involve potentially flammable atmospheres and liquids that can accumulate static charges, and safety becomes an issue. Because mercury in glass thermometers have no electrical safety issues and are inherently safer than alternative devices, they will be used for such purposes until an alternative is felt to be trustworthy and safe

4.4 Hygrometers

One manufacturer has indicated that economically feasible alternatives are not available for whirling hygrometers (also known as sling psychrometers) as the price of alternatives (electronic instrument using PT100) is about 10 times the price of the mercury hygrometer. Another manufacturer has indicated that technically feasible alternatives are not available for some applications of hygrometers. The two answers are merged in Table 15. The manufacturers did not provide further information for the socioeconomic assessment of replacing this equipment.

For most applications, alternatives to mercury are spirit-filled hygrometers and electronic hygrometers which are marketed at approximately the same as the price of mercury hygrometers.

The manufacturers do not indicate specific applications of the hygrometers for which alternatives are not available or for which very expensive electronic device is needed. Hygrometers have been banned in Denmark for many years and through requests to laboratories calibrating this kind of equipment it has not been possible to identify any applications for which it has been difficult to replace the mercury hygrometers.

Prices of hygrometers from one of the responding manufacturer's web retail shop are as follows:

- Non-mercury liquid filled hygrometer: 19 € (excl. VAT)
- Dial hygrometer: 9 € (excl. VAT)

- Mercury whirling hygrometers: 59-78 € (excl. VAT)
- Digital temperature and humidity meters: 67-72 € (excl. VAT)

The digital meters are, in the retail shop, indicated as ideal for use in science, industry and engineering. The data does not indicate that electronic devices should be more expensive than mercury hygrometers, and the economics of replacing mercury hygrometers has not been further investigated.

Table 15 Applications of mercury laboratory thermometers for which technically feasible alternatives exist, but these are not regarded as economically feasible (based on answers from two manufacturers of mercury thermometers for industrial processes)

Application of thermometer	Sector	Available technically feasible alternatives	Price of alternatives as compared to mercury thermometer	Reasons for these alternatives of not being economically feasible
Whirling Hygrometer (measurement of humidity using wet and dry bulb method) Also known as "Psychrometer"	Environmental Monitoring Meteorology	Electronic instrument using PT100	Estimated figure 10:1 (ten times more expensive)	
Psychrometer	Meteorological control stations and Institutes	Thermometer with mercury-free fluids Electronic thermometer		Thermometer with mercury-free fluids not applicable at higher resolution than 0.5 ℃ and above 200℃. Significantly slower temperature response of glass thermometers with mercury-free fluids may lead to erroneous evaluation of measurement results Electronic thermometers can in some cases not be used because of the structure of their temperature and chemical resistant sensor housing.

4.5 Derogations proposed by manufacturers

As part of the questionnaire, manufacturers of thermometers have been asked to propose phrasing of derogations. Some manufacturers replied with the same phrasings. The replies are collected in Table 16.

Table 16 Derogations proposed by manufacturers of mercury thermometers

Proposed derogations			
Application area	Phrasing of derogation	Time frame of derogation	Justification for the derogation
Industrial thermometers	Thermometers containing mercury that are used for temperatures > 200℃	unlimited	Technically and economically feasible alternatives not available. Typical mercury content: approx. 3.5g/piece -> total consumption of approx. 100 kg/year *2
Precision thermometers	Thermometers containing mercury that are used for temperatures > 200℃ with accuracy and resolution of 0.1 ℃ and better *1	unlimited	Technically and economically feasible alternatives not available. Typical mercury content: approx. 3.5g/pce -> total consumption of approx. 100 kg/year *2
Precision thermometers	All thermometers with a higher resolution than 1 ℃ All thermometers whose range exceeds 200℃ All thermometers tailored to specific equipment	unlimited	All non-mercury thermometer fillings have shortcomings: wetting liquids from distillation, ionic liquids separate and remain in particles sticking to the inside of the capillary. Gallium tends to lubricate the process and is extremely difficult to work with. All non-mercury liquids are used only in very limited temperature ranges. Electronic thermometers behave differently to glass thermometers, and cannot be used everywhere where temperature measurements are essential because of its design. There are currently no calibratable instruments on the market to reach anywhere near the reliable accuracy of a precision thermometer. Both non-mercury glass thermometers and electronic thermometers can lead to much slower response and to erroneous and incorrect evaluations of measurement results.

*1 Consultants comment: Probably a mistake - considering the rest of the questionnaire the phrasing should rather be “Thermometers containing mercury that are used for temperatures > 200℃ and thermometers with an accuracy and resolution of 0.1 ℃ and better”

*2 The quantities represent Germany only and the data are in reasonable agreement with the quantities estimated in the EU Mercury Report.

4.6 Standards

An issue that may hamper the replacement of mercury thermometers is that many test methods standards make reference to the use of mercury thermometers.

In the discussion of standards it is essential to distinguish between two types of standards:

- Standards with the technical specifications of thermometers such as *ASTM E1 - 07 Standard Specification for ASTM Liquid-in-Glass Thermometers.*

- Test method standards that prescribe the use of specific thermometers. As an example the *ASTM D93 - 10 Standard Test Methods for Flash Point by Pensky-Martens Closed Cup Tester* prescribes that the temperature is measured with a thermometer in accordance with *ASTM E1 Specification for ASTM Liquid-in-Glass Thermometers* or an electronic temperature device with similar temperature response as the mercury thermometers.

Standards with the technical specifications of mercury thermometers are further described in section 4.7.2.

This section concerns standards used for laboratory use. To the knowledge of the authors standards used in meteorology prescribing the use of mercury thermometers have not been raised as an issue by statkeholders. In Denmark and Sweden the use of mercury thermometers in meteorology has been restricted for many years, without any reported discussion of the issue with standards.

4.6.1 Standards prescribing the use of mercury thermometers

Traditionally many standards have prescribed that the temperature should be determined by the use of mercury thermometers. A number of standards for analysis and materials testing still make reference to the use of mercury thermometers, but many new versions of the standards allow for the use of electronic devices with similar accuracy and temperature response.

Relevant standards used for materials testing are issued by ISO (International), CEN (European) and different national standardisation organisations including ASTM International (widely used in Europe), DIN (Germany) and IP/BS (UK) (IP = Institute of Petroleum, now the Energy Institute). For analysis within the pharmaceutical sector the European Pharmacopoeia prescribes the use of specific thermometers for some tests (see later).

The main areas identified in which standards refer to the use of mercury thermometers are listed below. Please note that for many standards alternative (i.e. non-mercury) thermometers may be used, as discussed later in this section.

For flash point determination in the petrochemical sector, all identified standards from the standards organisations ISO/EN (ISO and CEN develop standards together within this area), ASTM and IP are listed. Further, some national standards may exist.

For the other applications of thermometers, except pharmaceutical industry, only the ASTM standards are listed in the table. It is assumed that for most of the thermometer use areas similar standards are issued from the other standardization organisations. However, only the ASTM International web-site indicates specifically in the summary of the standards that the standards make reference to the liquid-in-glass thermometers. For other standards it is necessary to buy the standards to obtain this information.

A search on the ASTM International website revealed more than one hundred ASTM standards making reference to ASTM E1 *Specification for ASTM Liquid-in-Glass Thermometers.* ASTM E1 defines thermometers with the following liquids depending on the type and temperature range of the thermometer:

- Mercury,
- mercury thallium eutectic alloy, and
- toluene or other suitable liquid coloured with a permanent red dye.

The standards from ASTM International are widely used in the petrochemical and chemical industries in Europe and more than one hundred different types of ASTM E1 mercury thermometers are marketed by major manufacturers of mercury thermometers.

For non-mercury alternatives to E1 thermometers, E1 and some analysis standards make reference to ASTM E2251 *Standard Specification for Liquid-in-Glass ASTM Thermometers with Low-Hazard Precision Liquids*. Some standards make direct references to ASTM E2251 e.g. ASTM D1795 - 96(2007)e1 *Standard Test Method for Intrinsic Viscosity of Cellulose*. The reason is that less accuracy is permissible for these methods and the temperature to be measured is within the range of the alternative liquid-in-glass thermometers.

The list of standards in Table 17 is not exhaustive, but illustrates the sectors where the standards are applied and gives examples of test parameters.

The main part of the identified standards is for materials testing in the petrochemical industry, paint and varnishes industry, polymer industry and other chemicals industry. No standards used in the pulp and paper industry making reference to ASTM E1 were identified as all standards for this sector make reference to the non-mercury thermometers. The ASTM standards for product control are to some extent applied in Europe together with the ISO, CEN and national standards.

Further, examples of standards for analysis of environmental samples are listed in Table 17. These standards may not be applied in the EU, but are included for illustration. It has not been possible within the scope of this work to identify similar laboratory standards applied in the EU.

In some instances the thermometers are used as parts of hydrometers (determination of density and gravity) and hygrometers (determination of humidity).

Table 17 Examples of standards making reference to the use of mercury thermometers

Sector	Test parameter	Examples of standards
Petrochemical industry	Flash-point with closed cup - Pensky-Martens method	ASTM D93 - 10 Standard Test Methods for Flash Point by Pensky-Martens Closed Cup Tester EN ISO 2719:2002 Determination of flash point - Pensky-Martens closed cup method IP 34: Determination of flash point - Pensky-Martens closed cup method IP 35: Determination of open flash and fire point - Pensky-Martens method
	Flash-Point with Closed Cup - other methods	EN ISO 1516:2002 Determination of flash/no flash - Closed cup equilibrium method EN ISO 1523 :2002 Determination of flash point - Closed cup equilibrium method EN ISO 3679:2004 Determination of flash point - Rapid equilibrium closed cup method EN ISO 3680:2004 Determination of flash/no flash - Rapid equilibrium closed cup method EN ISO 13736 :2008 Determination of flash point - Abel closed-cup method ASTM D56 - 05 Standard Test Method for Flash Point by Tag Closed Cup Tester ASTM D3278 - 96(2004)e1 Standard Test Methods for Flash Point of Liquids by Small Scale Closed-Cup Apparatus. ASTM D3828 - 09 Standard Test Methods for Flash Point by Small Scale Closed Cup Tester ASTM D3934 - 90(2007) Standard Test Method for Flash/No Flash Test-Equilibrium Method by a Closed-Cup Apparatus ASTM D3941 - 90(2007) Standard Test Method for Flash Point by the Equilibrium Method With a Closed-Cup Apparatus IP 170: Determination of flash point — Abel closed-cup method IP 491: Determination of flash/no flash - Closed cup equilibrium method IP 491: Determination of flash/no flash - Closed cup equilibrium method DIN 51755-1 Testing of Mineral Oils and Other Combustible Liquids; Determination of Flash Point by the Closed Tester according

Sector	Test parameter	Examples of standards
		to Abel-Pensky IP 492: Determination of flash point - Closed cup equilibrium method IP 534: Determination of flash point – Small scale closed cup ramp method
	Flash- and fire-point with open cup	EN ISO 2592:2001 Determination of flash and fire points - Cleveland open cup method ASTM D92 - 05a Standard Test Method for Flash and Fire Points by Cleveland Open Cup Tester ASTM D1310 - 01(2007) Standard Test Method for Flash Point and Fire Point of Liquids by Tag Open-Cup Apparatus IP 36: Determination of flash and fire points - Cleveland open cup method
	Viscosity	ASTM D445 - 09 Standard Test Method for Kinematic Viscosity of Transparent and Opaque Liquids (and Calculation of Dynamic Viscosity
	Distillation	ASTM D86 - 09e1 Standard Test Method for Distillation of Petroleum Products at Atmospheric Pressure
	Saybolt viscosity	ASTM D88 - 07 Standard Test Method for Saybolt Viscosity
	Pour point	ASTM D97 - 09 Standard Test Method for Pour Point of Petroleum Products
	Boiling point	ASTM D1120 - 08 Standard Test Method for Boiling Point of Engine Coolants
	Freezing point	ASTM D2386 - 06 Standard Test Method for Freezing Point of Aviation Fuels
	Cloud point	ASTM D2500 - 09 Standard Test Method for Cloud Point of Petroleum Products
	Dropping point	ASTM D566 - 02(2009) Standard Test Method for Dropping Point of Lubricating Grease
	Softening point	ASTM D2319 / D2319M - 98(2008)e1 Standard Test Method for Softening Point of Pitch (Cube-in-Air Method)
	Filterability	ASTM D4539 - 09 Standard Test Method for Filterability of Diesel Fuels by Low-Temperature Flow Test (LTFT)
	Density	ASTM D1298 - 99(2005) Standard Test Method for Density, Relative Density (Specific Gravity), or API Gravity of Crude Petroleum and Liquid Petroleum Products by Hydrometer Method
	Gravity	ASTM D287 - 92(2006) Standard Test Method for API Gravity of Crude Petroleum and Petroleum Products (Hydrometer Method)
	Vapour pressure	ASTM D323 - 08 Standard Test Method for Vapor Pressure of Petroleum Products (Reid Method
	Heat of combustion	ASTM D4809 - 09a Standard Test Method for Heat of Combustion of Liquid Hydrocarbon Fuels by Bomb Calorimeter (Precision

Sector	Test parameter	Examples of standards
		Method
	Oxidation stability	ASTM D4742 - 08e1 Standard Test Method for Oxidation Stability of Gasoline Automotive Engine Oils by Thin-Film Oxygen Uptake (TFOUT) ASTM D7098 - 08e1 Standard Test Method for Oxidation Stability of Lubricants by Thin-Film Oxygen Uptake (TFOUT) Catalyst B
	Foaming Characteris-tics	ASTM D892 - 06e1 Standard Test Method for Foaming Character-istics of Lubricating Oils
	Residues	ASTM D2158 - 05 Standard Test Method for Residues in Liquefied Petroleum (LP) Gases ASTM D524 - 09 Standard Test Method for Ramsbottom Carbon Residue of Petroleum Products
	Corrosiveness	ASTM D130 - 04e1 Standard Test Method for Corrosiveness to Copper from Petroleum Products by Copper Strip Test ASTM D4310 - 09 Standard Test Method for Determination of Sludging and Corrosion Tendencies of Inhibited Mineral Oils
	Refractive index	ASTM D1747 - 09 Standard Test Method for Refractive Index of Viscous Materials
Paint, inks and varnished	Flash point	EN ISO 1523 :2002 Determination of flash point - Closed cup equilibrium method ASTM D1310 - 01(2007) Standard Test Method for Flash Point and Fire Point of Liquids by Tag Open-Cup Apparatus
	Viscosity	ASTM D4212 - 99(2005) Standard Test Method for Viscosity by Dip-Type Viscosity Cups ASTM D1200 - 94(2005) Standard Test Method for Viscosity by Ford Viscosity Cup
	Distillation range	ASTM D1078 - 05 Standard Test Method for Distillation Range of Volatile Organic Liquids ASTM D850 - 03(2008)e1 Standard Test Method for Distillation of Industrial Aromatic Hydrocarbons and Related Materials
	Nonvolatile content	ASTM D4713 - 92(2007) Standard Test Methods for Nonvolatile Content of Heatset and Liquid Printing Ink Systems
	Physical/chemical properties of materials	ASTM D740 - 05 Standard Specification for Methyl Ethyl Ketone ASTM D5958 - 99(2005)e1 Standard Practices for Preparation of Oil-Based Ink Resin Solutions
Polymers	Softening stability	ASTM D1525 - 09 Standard Test Method for Vicat Softening Tem-perature of Plastics
	Viscosity	ASTM D1601 - 99(2004) Standard Test Method for Dilute Solution Viscosity of Ethylene Polymers ASTM D1823 - 95(2009) Standard Test Method for Apparent Vis-cosity of Plastisols and Organosols at High Shear Rates by Extru-sion Viscometer ASTM D4878 - 08 Standard Test Methods for Polyurethane Raw

Sector	Test parameter	Examples of standards
		Materials: Determination of Viscosity of Polyols
	Gravity	ASTM D4659 - 09 Standard Test Methods for Polyurethane Raw Materials: Determination of Specific Gravity of Isocyanates
	Density	ASTM D1817 - 05 Standard Test Method for Rubber Chemicals—Density
	Shrinkage	ASTM D2732 - 08 Standard Test Method for Unrestrained Linear Thermal Shrinkage of Plastic Film and Sheeting
	Deflection temperature	ASTM D648 - 07 Standard Test Method for Deflection Temperature of Plastics Under Flexural Load in the Edgewise Position
	Rheological properties	ASTM D2196 - 05 Standard Test Methods for Rheological Properties of Non-Newtonian Materials by Rotational (Brookfield type) Viscometer
	Physical/chemical properties of materials	ASTM D1755 - 09 Standard Specification for Poly(Vinyl Chloride) Resins ASTM D2195 - 05 Standard Test Methods for Pentaerythritol ASTM D1045 - 08 Standard Test Methods for Sampling and Testing Plasticizers Used in Plastics ASTM D4830 - 98(2006) Standard Test Methods for Characterizing Thermoplastic Fabrics Used in Roofing and Waterproofing ASTM D1619 - 03(2008) Standard Test Methods for Carbon Black—Sulfur Content ASTM D301 - 95(2004) Standard Test Methods for Soluble Cellulose Nitrate ASTM D4028 - 07 Standard Specification for Solar Screening Woven from Vinyl-Coated Fiber Glass Yarn
Other chemical industry	Physical/chemical properties of materials	ASTM E224 - 08 Standard Test Methods for Analysis of Hydrochloric Acid ASTM E223 - 08 Standard Test Methods for Analysis of Sulfuric Acid ASTM D914 - 00(2006) Standard Test Methods for Ethylcellulose ASTM D3716 - 99(2008) Standard Test Methods for Use of Emulsion Polymers in Floor Polishes ASTM D889 - 99(2009) Standard Test Method for Volatile Oil in Rosin ASTM D5249 - 95(2006) Standard Specification for Backer Material for Use with Cold- and Hot-Applied Joint Sealants in Portland-Cement Concrete and Asphalt Joints
	Viscosity	ASTM D1986 - 91(2007) Standard Test Method for Determining the Apparent Viscosity of Polyethylene Wax
	Gravity	ASTM D891 - 09 Standard Test Methods for Specific Gravity, Apparent, of Liquid Industrial Chemicals
	Cloud point	ASTM D2024 - 09 Standard Test Method for Cloud Point of Non-

Sector	Test parameter	Examples of standards
		ionic Surfactants
Mineral resources industry	Swell Index	ASTM D5890 - 06 Standard Test Method for Swell Index of Clay Mineral Component of Geosynthetic Clay Liners
	Physical/chemical properties of materials	ASTM D5249 - 95(2006) Standard Specification for Backer Material for Use with Cold- and Hot-Applied Joint Sealants in Portland-Cement Concrete and Asphalt Joints
Other sectors	Different	ISO 15267:1998 Animal and vegetable fats and oils -- Flashpoint limit test using Pensky-Martens closed cup flash tester ASTM F482 - 09 Standard Practice for Corrosion of Aircraft Metals by Total Immersion in Maintenance Chemicals ASTM F558 - 06 Standard Test Method for Measuring Air Performance Characteristics of Vacuum Cleaners
Test of environmental samples	Dispersive characteristics	ASTM D6572 - 06 Standard Test Methods for Determining Dispersive Characteristics of Clayey Soils by the Crumb Test
	pH	ASTM D5015 - 02(2008) Standard Test Method for pH of Atmospheric Wet Deposition Samples by Electrometric Determination
	Humidity	ASTM E337 - 02(2007) Standard Test Method for Measuring Humidity with a Psychrometer (the Measurement of Wet- and Dry-Bulb Temperatures)
	Electrical conductivity and resistivity	ASTM D1125 - 95(2009) Standard Test Methods for Electrical Conductivity and Resistivity of Water
	Nitrogen oxides in the atmosphere	ASTM D3608 - 95(2005) Standard Test Method for Nitrogen Oxides (Combined) Content in the Atmosphere by the Griess-Saltzman Reaction ASTM D1607 - 91(2005) Standard Test Method for Nitrogen Dioxide Content of the Atmosphere (Griess-Saltzman Reaction)
	Mercaptan in the atmosphere	ASTM D2913 - 96(2007) Standard Test Method for Mercaptan Content of the Atmosphere
Pharmaceutical industry	Drop point	European Pharmacopoeia section section 2.2.17

According to the information obtained from suppliers of apparatus for materials testing, at least the ISO/EN and ASTM standards used for materials control in the petrochemical sector in general, allow the use of electronic thermometers. According to suppliers of equipment for determination of flash point and viscosity and equipment for distillation across sectors, at least for flash point and viscosity, the standards also allow for the use of electronic thermometers.

The flash point determination, which has been mentioned as one of the areas where it was particularly difficult to replace the mercury thermometers are discussed in more detail below.

Flash point determination

Flash point is used in shipping and safety regulations to define flammable and combustible materials. Is it used also in the determination of flammability and explosivity for classification and labelling?

A number of standards for determination of the flash point of fuels, greasing oils, paint and varnishes and other chemicals exist. ISO 1523 is used in United Nations Recommendations for Transportation of Dangerous Goods and in the International Civil Aviation Organization (ICAO) regulations and for similar regulations in the International Maritime Dangerous Goods (IMDG) code.

Currently many (if not all) standards allow for the use of electronic devices with similar temperature response as the mercury thermometers.

As an example the ASTM D93-10 *Standard Test Methods for Flash Point by Pensky-Martens Closed Cup Tester* specifies regarding the temperature measuring device: "*Thermometer having a range as shown as follows and conforming to the requirements prescribed in Specification E1 or in Annex A3, or an electronic temperature measuring device, such as resistance thermometers or thermocouples. The device shall exhibit the same temperature response as the mercury thermometers.*"

Temperature Range	*Thermometer Number*	
	ASTM	*IP*
−5 to +110°C (20 to 230°F)	*9C (9F)*	*15C*
+10 to 200°C (50 to 392°F)	*88C (88F)*	*101C*
+90 to 370°C (200 to 700°F)	*10C (10F)*	*16C"*

Mercury thermometers made in accordance with ASTM D1, 9C are marketed for flash point determination in accordance with ASTM D93, but this does not imply that only these thermometers can be used.

The ASTM D93-10 makes specific reference to the ASTM E1 Liquid-in-Glass Thermometers, but not to standards for the electronic devices. For the electronic devices it is only mentioned that the temperature response shall be similar to the response of the liquid-in-glass thermometers.

Similarly, the ISO 2719 standard *Determination of flash point — Pensky- Martens closed cup method* does not require that the temperature is measured with a mercury thermometer.

Section 6.2 on thermometers specifies that thermometers should conform to the specifications in Annex C of the standard, but adds: "*NOTE Other types of temperature-measuring devices may be used, provided that they meet the re-*

quirements for accuracy and have the same response as the thermometers specified in annex C."

Annex C specifies three types of thermometers (low, medium and high range) which are indicated to correspond to the IP thermometers IP 15C, 16C and 101C and the ASTM thermometers ASTM 9C, 10C and 88C. The accuracy of the thermometers is indicated in the annex.

Whereas the ASTM standard only opens for the use of electronic devices, any thermometer which can meet the requirements for accuracy and response can be used according to the ISO 2719 standard.

On request from the consultant a member of the ISO/CEN working group on flash point determination has provided the following information on the requirements of the different ISO standards for flash point determination. In practice all these standards allow for the use of other types of thermometers.

Standard	Requirements as to the use of thermometers
EN ISO 2719 Determination of flash point - Pensky-Martens closed cup method:	Allows for other types of thermometers
EN ISO: 13736 Determination of flash point - Abel closed-cup method (currently under revision):	Edition 1997 allows for automated equipment
EN ISO 3679 Determination of flash point - Rapid equilibrium closed cup method (currently under revision):	Edition 2004 allows for temperature measuring devices other than mercury thermometers
EN ISO 3680 Determination of flash/no flash - Rapid equilibrium closed cup method (currently under revision):	Edition 2004 allows for temperature measuring devices other than mercury thermometers
EN ISO 1523: Determination of flash point - Closed cup equilibrium method	Edition 2002 - no extra equipment is described; only a different procedure is given; equipment according to EN ISO 13736, EN ISO 2719, DIN 51755 part 1, ASTM D56 is allowed
EN ISO 1516: Determination of flash/no flash - Closed cup equilibrium method	Edition 2002 - no extra equipment is described; only a different procedure is given; equipment according to EN ISO 13736, EN ISO 2719, DIN 51755 part 1, ASTM D56 is allowed

Apparatus for materials testing

Equipment for flash point determination is today marketed as both manual apparatus with mercury thermometers or and as automatic apparatus with electronic thermometers. The electronic thermometers are electronically corrected for replicating the response time of the specified mercury thermometer.

A UK manufacturer of test apparatus e.g. supply a thermometer with a PT 100 probe for distillation control which "*...uses a unique simulation program that replicates the characteristics of mercury-in-glass ASTM 7C/F or 8C/F thermometers, including the time lag and thermal history*" [3]. This specific thermometer can be used in accordance with ISO 3405, ASTM D86, ASTM D850 and a number of other standards.

According to a major German manufacturer of test apparatus nearly all customers in Germany today use the automatic apparatus for flash point determination, while the manual apparatus is mainly requested by customers with relatively few measurements per week. The price of the electronic apparatus (about 12,000 €) is about 5 times the price of the manual apparatus with mercury thermometers.

Automatic equipment with electronic thermometers is today available for most material tests within the petrochemical industry. For some test equipment, however, the development of automatic devices may still be pending. For some test equipment some of the manufactures only market the manual equipment while others have both manual and automatic in their product range.

Table 18 lists examples of test equipment with PT-100 electronic thermometer from the product catalogues of two major manufactures of test equipment.

Table 18 Examples of apparatus for materials testing in accordance with standards provided with electronic PT-100 temperature device (based on the web page of two major manufacturers of the apparatus)

Equipment for determination of:	Standards	Name of ISO standard
Flash-point – closed cup	ISO 15267 ASTM D93	Flash Point by Pensky-Martens Method
	EN ISO 13736	Determination of flash point -- Abel closed-cup method
	ISO 1523	Determination of flash point -- Closed cup equilibrium method
Flash-point – open cup	EN ISO 2592 ASTM D92	Determination of flash and fire points -- Cleveland open cup method
Viscosity	ISO 3104 ASTM D445-IP71	Kinematic Viscosity of Transparent and Opaque Liquids and the Calculation of Dynamic Viscosity
Gum content	ISO 6246 ASTM D381-IP 131	Petroleum products -- Gum content of light and middle distillate fuels -- Jet evaporation method

[3] http://www.stanhope-seta.co.uk/product.asp?ID=2405&bShowDetail=true

Equipment for determination of:	Standards	Name of ISO standard
Distillation temperature	ISO 3405 ASTM D86 ASTM D 850 - ASTM D 1078	Petroleum products -- Determination of distillation characteristics at atmospheric pressure
Softening point	ISO 4625-1 EN 1427 ASTM D 36 EN 1238 ASTM E 28	Binders for paints and varnishes -- Determination of softening point -- Part 1: Ring-and-ball method

Changing of standards

Although the standards allow for the use of electronic devices with similar characteristics it may be relevant to change the standards, as in many cases the electronic devices would be able to measure the temperature more accurately and currently have to be modified in order to replicate the mercury thermometers.

The general principles for replacing mercury thermometers are discussed by Ripple and Strouse (2005) in an ASTM paper. According to that paper many hundreds of ASTM test methods relied on ASTM liquid-in-glass (LiG) thermometers or ASTM Liquid-in-Glass Thermometers with Low-Hazard Precision Liquid (E 2251).

At the moment a process of replacing mercury-in-glass thermometers in ASTM test methods is ongoing (ASTM 2009). In total 853 consensus documents from 94 different technical committees are being reviewed (ASTM 2008).

A recent paper from ASTM discusses some of the issues of changing the standards (ASTM 2009), which also explains why it may sometimes be difficult to replicate the response of the mercury thermometers. According to the paper, the goal of the thermometer designs was often to provide consistent results among the parties. To that end, the designs were often manipulated for optimal repeatability or ease of use within the method, not necessarily for accuracy. Examples of this manipulation include establishing arbitrary emergent stem temperature assignments for partial immersion thermometers (for example, ASTM 5C/5F cloud and pour thermometers), or use of expanded bulb thermometers in tests (thermometers conditioned at their highest temperature before use, for example, ASTM 56C and ASTM 117C calorimetric thermometers).

In many ASTM test methods, the use of an alternative temperature measurement device may provide more accurate temperature measurements but may not reproduce the previously accepted values of the test method. Switching to an electronic alternative might introduce a new bias in the method. In general, be-

cause of the unique design manipulations of the ASTM E1 thermometers, results produced by alternative temperature measurement devices in apparatus built for ASTM mercury-in-glass thermometers will not be directly comparable to results obtained using the ASTM E1 thermometer(s) specified in the test method. For some test methods, electronic thermometers are marketed with simulations for replicating the response of the mercury thermometers. Currently, such equipment seems not to have been developed for all test methods, in particular for which there have been no incentives for the development of the automatic test apparatus.

In many cases the best solution seems to be to change the standards to take advantage of the better characteristics of the electronic devises. ECHA has made direct contact to ASTM regarding the process of changing the standards and the ASTM process will not be discussed further here.

According to the European experts contacted no similar process is ongoing in ISO or CEN.

National standards

According to German experts in the field at least for the testing within the petrochemical sector the DIN standards are today replaced by the corresponding EN ISO standards except for one standard, DIN 51755. DIN 51755, requiring the use of mercury thermomters, is mentioned in several community legislation such as Commission Regulation (EC) No 1031/2008 of 19 September 2008.

IP standards, issued by the British Energy Institute are widely used in the petrochemical sector. Under the Phoenix agreement from 2006 the Energy Institute (EI), and the American Petroleum Institute (API) work together with the aim of producing joint API/EI standards in all areas of petroleum measurement.

Information on standards issued by other Member States has been beyond the current contract.

Indication of standards on thermometers

The Dutch mercury regulation [4] includes a derogation for "*a mercury thermometer exclusively intended to perform specific analytical tests according to established standards*;"

According to the explanatory notes of the regulation "*Section j discusses mercury thermometers which are explicitly prescribed in international standards, such as ASTM, DIN, BS. These thermometers can easily be distinguished from other thermometers, because they are specially designed for the application of a particular standard and the number of that standard is written on the thermometers*".

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4 English translation of "Besluit kwikhoudende producten Wms 1998". Bulletin of Acts and Decrees of the Kingdom of the Netherlands No. 553

The latter seems to be incorrect. According to information from a leading German mercury thermometer manufacturer contacted for this study, in some cases, as also described in section 4.6.2, the standard for the manufacturing of the thermometer is written on the thermometer (e.g. ASTM E1, 12F). This may give an indication of the analysis for which the thermometer is going to be used (e.g. the 12F is indicated in the standard as "density wide range") and consequently the number indicated the standard prescribing the thermometer. But the number of the standard the thermometer is designed for is not indicated. The indication of thermometer type on the thermometer applies to the ASTM thermometers, but is in general not the case for thermometers made in conformity with a specific DIN standard. The standard for the manufacturing of the thermometer e.g. DIN 12775 is usually indicated in the technical specifications of the thermometer, but not written on the thermometer.

According to information from one manufacturer 60-80 % of the thermometers used in the laboratories in the EU are used for measurements where the procedure prescribes either: 1) that the thermometers used conform to a specific standard or 2) more widely prescribes that the thermometers should be a standard thermometer (without specifying the standard). In some sectors e.g. the petrochemical industry or pharmaceutical industry it applies to nearly 100% of the thermometers. No data are available indicating the percentage of thermometers used in accordance with standards prescribing a specific thermometer.

Test methods for implementation of REACH

The new Swedish mercury regulation has an exemption for mercury thermometers for flash point determination until 31/12/2013 with reference to Directive 67/548/EEC (http://www.kemi.se/templates/Page____5487.aspx).

Directive 67/548/EEC specified in Annex XV methods for determination of flash point. As concern the flash point test method the description in the annex has been transferred without changes to Council Regulation (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 (REACH) [5]. The Regulation No 440/2008 does not specifically prescribe mercury thermometers for flash point determination but prescribes that "Only the methods which can give the temperature of the flash -point may be used for a notification." The regulation lists a number of standards for reference. The exact wording is as follows:

"1.6.3. Performance of the test

1.6.3.1. Equilibrium method

See ISO 1516, ISO 3680, ISO 1523, ISO 3679.

1.6.3.2. Non-equilibrium method

[5] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:142:0001:0739:EN:PDF

Abel apparatus:

See BS 2000 part 170, NF M07-011, NF T66-009.

Abel-Pensky apparatus:

See EN 57, DIN 51755 part 1 (for temperatures from 5 to 65 °C), DIN 51755 part 2 (for temperatures below 5 °C), NF M07-036.

Tag apparatus:

See ASTM D 56.

Pensky-Martens apparatus:

See ISO 2719, EN 11, DIN 51758, ASTM D 93, BS 2000-34, NF M07-019".

Most of these standards likely allow for the use of electronic thermometers with similar response as the mercury thermometers, but it has not been possible within the scope of this contract to consult all these standards.

On one instance the Regulation specifically prescribes the use of mercury thermometers. The Regulation specifies under A1 "Melting/freezing temperature" that "*Only those thermometers should be used which fulfil the requirements of the following or equivalent standards: ASTM E 1-71, DIN 12770, JIS K 8001*." The two first standards are standards on liquid-in-glass thermometers while the latter is a Japanese standard on "General rule for test methods of reagents". [*ASTM E 1-71 does not exist but may be the 1971 version of ASTM E 1]* Under the procedure it is further mentioned that "*The filled capillary tube is placed in the bath so that the middle part of the mercury bulb of the thermometer....".*

Test methods for implementation of Commission Regulation (EC) No 1031/2008

Commission Regulation (EC) No 1031/2008 of 19 September 2008 amending Annex I to Council Regulation (EEC) No 2658/87 on the tariff and statistical nomenclature and on the Common Customs Tariff makes reference to a German test method for flash point determination. According to the method DIN 51755 the temperature shall be determined by the use of mercury thermometers.

Page 191 of Regulation 1031/2998 states:

" (b) 'white spirit' (subheading 2710 11 21) means special spirits as defined in paragraph (a) above with a flash-point higher than 21 °C by the Abel-Pensky method (1);" and the footnote specifies...

"(1) The term 'Abel-Pensky method' means method DIN (Deutsche Industrienorm) 51755 — März 1974 published by the DNA (Deutsche Normenausschuss), Berlin 15."

European and national Pharmacopoeias

The European Pharmacopoeia is a single reference work for the quality control of medicines in Europe. The Pharmacopoeia consists of a large number of monographs addressing different issues. Several legal texts make the European Pharmacopoeia mandatory, first of all a Convention elaborated by the Council of Europe on the Elaboration of a European Pharmacopoeia and European Union directives 2001/82/EC, 2001/83/EC and 2003/63/EC (amended). The work on monographs is allocated by the European Pharmacopoeia Commission to specially constituted groups of experts and working parties. According to information at the website of the European Directorate for the Quality of Medicines and Health Care an update of a monograph takes at least 2 years.

An example of test equipment marketed with reference to the European Pharmacopoeia is a drop point apparatus with a mercury thermometer[6]. This is the only for which it has been possible to identify a direct reference to the European Pharmacopoeia and the drop point determination. Furthermore, the drop point test is the only test method mentioned by the market actors contacted for this study.

The drop point test is described in the monograph no. 33 of the European Pharmacopoeia.

The European Pharmacopoeia 5.0 from 2005 mention e.g. for 2.2.17 drop point:" *The apparatus (see Figure 2.2.17.-1) consists of 2 metal sheaths (A) and (B) screwed together. Sheath (A) is fixed to a mercury thermometer"*. The latest update of the Pharmacopoeia has not been available to the consultant within the time frame of this activity and has not been consulted.

The International Pharmacopoeia published by WHO (2008) makes reference to the use of mercury thermometers in one section. The Pharmacopoeia comprises a collection of recommended procedures for analysis and specifications for the determination of pharmaceutical substances that is intended to serve as source material for reference or adaptation by any WHO Member State wishing to establish pharmaceutical requirements. In the chapter on Methods of Analysis it is in the section of melting temperature and melting range stated that: "*Standardized thermometers should cover the range -10 to +360 °C, the length of one degree on the scale being not less than 0.8 mm. These thermometers should preferably be of the mercury-in-glass, solid-stem type with a cylindrical bulb and made of approved thermometric glass suitable for the range covered; each thermometer should have a safety chamber*". A search of the International Pharmacopoeia revealed that the mercury thermometers are mentioned in the section on melting point and melting range only.

[6] http://www.stanhope-seta.co.uk/catalogue/11610-0_pharmacopoeia_drop_point.pdf

4.6.2 Standards with technical specification of thermometers

The questionnaire sent to manufacturers included a question regarding which national or international standards prescribe the use of mercury thermometers.

The question seems to have been unclear as none of the manufacturers replied to the question, but instead replied with information on the standards the thermometers have to comply with (Table 19) and the sectors where these thermometers are used.

The objective of the question – to clarify the sectors in which analysis standards are used that prescribe that temperature is measured by the use of mercury thermometers - was consequently not met. Answers from the manufacturers are collected in Table 19.

In any case, the Table 19 shows a wide range of standards for the manufacturing of thermometers. For most applications the manufacturers indicated that alternatives are not available, but the meaning is here that none of the alternatives would comply with the standards for the mercury thermometers. It should not be interpreted that alternatives are not available for measuring the temperature in the specified range.

Table 19 also includes international standards (ISO), German (DIN), American (ASTM), British (BS, IP and STPTC) and French (AFNOR) standards. National standards are probably used in many other Member States.

One manufacturer indicated that in France the petroleum industry uses ASTM (American) or IP (British) standards.

One manufacturer mentioned that the list of thermometers connected with all standards is very long (hundreds), as every thermometer has its own specification and the manufacturer does not consider it possible to make reference to every standard and industrial sector.

Subsequently, one manufacturer was contacted for more information but, according to their response, manufacturers of the thermometers would usually not have the information on the analysis standards prescribing the use of the thermometers.

Table 19 Standards for thermometers and alternatives as reported by manufacturers of thermometers

Analysis	Industrial sector	Standard	Thermometer standard referred to by the standard	Alternatives that potentially may be used for the analysis if the standard is changed
Calorimeter Thermometer	Industry, University, R&D, Control Institutions,	DIN 12771 ISO 651 BS 791	Temperature > 200℃ and acc. 0.1℃	no alternatives available

Analysis	Industrial sector	Standard	Thermometer standard referred to by the standard	Alternatives that potentially may be used for the analysis if the standard is changed
Precision Thermometer	Industry, University, R&D, Control Institutions,	DIN 12775 DIN 12778 DIN 12781	Temperature > 200℃ and acc. 0.1℃	no alternatives available
Precision thermometers acc. To Allihn	Industry, University, R&D, Control Institutions.	DIN 12776	Temperature > 200℃ and acc. 0.1℃	no alternatives available
Precision thermometer sets, Anschütz, DIN 12777	Laboratory, Industry, University, Control Institutions Pharmacies,	DIN 12777	Measuring range Accuracy Dimensions	No alternatives available
Distillation thermometer	Industry, University, R&D, Control Institutions.	DIN 12779 DIN 12784	Temperature > 200℃ and acc. 0.1℃	no alternatives available
Precision thermometer for viscosimeter Flash-point thermometers	Industry, University, R&D, Control Institutions.	DIN 12785	Temperature > 200℃ and acc. 0.1℃	no alternatives available
Softening point thermometers	Laboratory, Petroeleum- Industry	DIN 12785, ASTM 15C ASTM 16C	Measuring range Accuracy Dimensions	No alternatives available
Breaking point thermometers	Laboratory, Industry	DIN 12785 IP 42C	Measuring range Accuracy Dimensions	No alternatives available
Determination of the distillation	Laboratory, Industry	DIN 12785 ASTM 7C ASTM 8C	Measuring range Accuracy Dimensions	No alternatives available
Thermometer sets according to Dr. Otte	Laboratory, Industry, University, Control Institutions	DIN 12786	Measuring range Accuracy Dimensions	No alternatives available

Analysis	Industrial sector	Standard	Thermometer standard referred to by the standard	Alternatives that potentially may be used for the analysis if the standard is changed
Precision adjusting thermometers acc. To Beckmann	Industry, University, R&D, Control Institutions,	DIN 12789 ASTM 115	Temperature > 200℃ and acc. 0.1℃	no alternatives available
Contact Thermometer	Industry, University, R&D, Control Institutions.	DIN 12878	Temperature > 200℃ and acc. 0.1℃	no alternatives available
Straight stem large thermometers	Industry, Chemical,pharmaceutical industry	DIN 16174	Measuring range Accuracy Dimensions	No alternatives available
Angle stem, large thermometers	Industry, Chemical,pharmaceutical industry,	DIN 16175	Measuring range Accuracy Dimensions	No alternatives available
Engine thermometers	Marine Industry, Power plants, Diesel Engine manufacturer, Chemical, pharmaceutical Industry	DIN 16181 DIN 16182 DIN 16185 DIN 16186 DIN 16189 DIN 16190 DIN 16191 - 16195	Temperature > 200℃ and acc. 0.1℃	no alternatives available
Meteorological extreme thermometers, DIN	Meteorology	DIN 58654	Measuring range Accuracy Dimensions	No alternatives available
Psychrometer August, DIN	Meteorology	DIN 58660	Measuring range Accuracy Dimensions	No alternatives available
Aspiration psychrometers, Assmann	Meteorology	DIN 58661	Measuring range Accuracy Dimensions	No alternatives available

Analysis	Industrial sector	Standard	Thermometer standard referred to by the standard	Alternatives that potentially may be used for the analysis if the standard is changed
Depth thermometers	Meteorology	DIN 58664	Measuring range Accuracy Dimensions	No alternatives available
Soil thermometers, DIN 58 655	Meteorology	DIN 58665	Measuring range Accuracy Dimensions	No alternatives available
Precision thermometer	Industry, University, R&D, Control Institutions.	BS 593 BS1365 BS1704 /ANSI BS1900 ISO R653 ISO R654 ISO R655 ISO R656 ISO R1770 ISO R1771	Temperature > 200℃ and acc. 0.1℃	no alternatives available
BS 593 laboratory thermometer	Laboratory, Industry	BS 593 A10C – F400C	Measuring range Accuracy Dimensions	No alternatives available
Meteorological Thermometers	Meteorology	BS 692	Measuring range Accuracy Dimensions	No alternatives available
BS 1704 general purpose thermometers	Laboratory, Industry	BS 1704 A/total – H/75	Measuring range Accuracy Dimensions	No alternatives available
Secondary Reference BS 1900	Laboratory, Industry,	BS 1900, SR5/20C – SR6 – 102C	Measuring range Accuracy Dimensions	No alternatives available
-	Oil industry, scientific analysis	BS 2000	Mercury in glass Laboratory thermometer	PT100
-	Oil industry, scientific analysis	IP	Mercury in glass Laboratory thermometer	PT100
-	Oil industry, scientific analysis; various	ASTM E1-07	Mercury in glass Laboratory thermometer	PT100

Analysis	Industrial sector	Standard	Thermometer standard referred to by the standard	Alternatives that potentially may be used for the analysis if the standard is changed
Precision thermometer	Industry, University, R&D, Control Institutions.	ASTM 1C/F- 133C/F	Temperature > 200℃ and acc. 0.1℃	no alternatives available
Adjustable range thermometers, Beckmann	Laboratory, University, Control Institutions	ASTM 115C	Measuring range Accuracy Dimensions	No alternatives available
ASTM thermometers	Laboratories for mineral analysis, Petroleum industry	ASTM 1C/F – 137C/F	Measuring range Accuracy Dimensions	No alternatives available
Special thermometers According to ISO ,	Laboratory, Industry, University, Control Institutions	ISO 655, ISO 656	Measuring range Accuracy Dimensions	No alternatives available
IP thermometers	Laboratories for mineral analysis, Petroleum industry	IP 1C – 102C	Measuring range Accuracy Dimensions	No alternatives available
S.T.P.T.C. thermometers	Laboratories for mineral analysis, Industry	STPTC T 1d – T 26d	Measuring range Accuracy Dimensions	No alternatives available
Short range short stem BS 1365	Laboratory, Industry,	SA 55C – SB 220 C	Measuring range Accuracy Dimensions	No alternatives available
Thermometers AFNOR	Laboratories for mineral analysis, Industry	AFNOR STL/0,1 – STL 2/	Measuring range Accuracy Dimensions	No alternatives available

4.7 Other information

One manufacturer mention in their questionnaire response that European manufacturers of glass thermometers employ approximately 800-1,000 employees for the production of mercury filled glass thermometers. In the 2008 EU Mercury Report it is estimated that some 1,000-1,500 people may be employed in this industry.

One manufacturer mentions that they sell a decontamination kit which is an amalgam (probably a metal powder which can form an amalgam). According to the manufacturer, when a thermometer is broken, this amalgam decontaminates up to 99% of the mercury. They sell the KIT with an empty hermetic box, so that the user can put the amalgam containing the mercury inside the box.

Some thermometers are produced with an outer plastic sheet to prevent loss of mercury in case the thermometer is broken.

5 Sphygmomanometers

The following chapter is not a structured note, but a collection of information obtained from manufacturers of sphygmomanometers. The information feeds into Annex XV report prepared by ECHA.

Table 20 Basic information for the socioeconomic analysis.

	Mercury sphygmomanometer			Shock-resistant aneroid sphygmomanometer			Manual (auscultatory) electronic sphygmomanometer		
Manufacturer	A	B	C	A	B	C	A	B	C
Name of equipment used as example	Diplomat Nova	Accoson Dekamet table model		R1-shock-proof	Accoson Duplex hand model			Accoson **green**light 300	
Price of meter in 2010 (factory gate price without VAT in €)	39.70	39		36.20	30			110	
Average lifetime of sphygmomanometer (in years)	10	10		10	5			15	
Manufacturer's recommendations regarding calibration frequency (years between calibrations)	5 years	2 years		5 years	1 years			4 years	
Typical price of calibration and maintenance (in € per calibration)	15	20		15	20			20	
Expected trends in prices for the period 2010-2020 (2020 prices in percentage of 2010 prices)	+ 12%	+60%		+ 12%	+50%			+25%	
Expected trend in quantity of mercury containing sphygmomanometers sold in EU without further legislative action (quantity sold in 2020)	35,000	-50% (COWI: corresponds to 22.500)		Not applicable	Not applicable		Not applicable	Not applicable	

Table 21 shows the different views of the manufacturers as to the equipment expected to replace the mercury devices.

Table 21 Manufacturers' views of the percentage of market share of different alternatives if existing mercury containing sphygmomanometers would be replaced.

	Shock-resistant aneroid sphygmomanometers			Manual (auscultatory) electronic sphygmomanometers			Oscillometric sphygmomanometers		
Manufacturer	A	B	C	A	B	C	A	B	C
Percentage	75 *1	50		3	40		22	10	

*1(including non shock-resistant aneroid devices)

5.1 Comments and additional information from manufacturers

A: In many large size emerging markets as China, India, Indonesia physicians still prefer mercury devices be-cause aneroid devices made in the Far East do no't deliver reliable readings. Despite inferior quality of aneroid devices made in the Far East there are already significant quantities in the EU market because of low market entry barriers (CE registration) compared to other registration requirements in China, USA, Japan, Brazil, etc.

If the current mercury devices will be replaced by low quality aneroid devices there is a risk of unreliable blood-pressure readings.

B: No comment

C: No answer

5.2 Additional information

Besides the questionnaire the manufacturers have been asked about the need for topping up mercury when the sphygmomanometers are calibrated.

B: "In my experience we do not find devices need topping up with mercury. In all cases for us, we do not top up mercury, as we do not see a need for it. What we do is replace all the mercury with new, and send the old mercury to our specialist recycler"

From the Concorde report[7] reviewed as part of the work under this contract: In one Czech hospital, of a total of about 180 mercury sphygmomanometers in use, one interviewee reported that about 40 of the sphygmomanometers need

[7] Concorde 2009. Turning up the pressure: Phasing out mercury sphygmomanometers for professional use. Concorde East/West for European Environment Bureau.

topping up every year, suggesting pervasive and continual slow mercury emissions to the air. Among the several Hungarian hospitals interviewed, some 10-20 percent of the mercury sphygmomanometers appeared to need mercury added each year, and in Greek hospitals around 2-3 percent.

6 Hanging drop electrodes

Two companies have been addressed with a questionnaire concerning the use of mercury hanging electrodes in polarography. Only one company answered.

The use of mercury in polarography is briefly described in the 2008 EU mercury report. The total mercury use in the EU for this application is estimated at 0.1-0.5 t/year. For a DG Enterprise mercury workshop on 28 April 2009, Metrohm (with 50% of the global market share) estimated the total global consumption at 0.25-0.35 t/year. Each unit uses on average 100 -150 g per year.

In the 2008 EU mercury report it is indicated that this equipment was banned in Sweden based on a 2004 report from the Swedish Chemicals Inspectorate mentioning that polarographs for professional measuring could be placed on the market until 31 December 2007. However the Inspectorate has answered our questions regarding alternatives to polarographs " *It is a matter of interpretation whether the use of mercury in these instrument were allowed or not under the previous Swedish legislation. Our view would probably be that they were not, but it was never tried. Under the current Swedish legislation it is allowed with reference to and subject to the conditions of the Reach restriction derogation for scientific research and development. A study in 2004 indicated no alternatives, but only a few users in Sweden (5 to 10?). To reduce mercury consumption the size of the drops have been diminished (range of a few microlitres in 2003)".*

6.1 Technical feasibility

According to the manufacturer, the use of mercury electrodes has been quite stable for a number of years. The table below lists major and important examples of applications. The list is not exhaustive, as the manufacturer see customers use the instrumentation for an extremely widespread range of applications.

For a number of applications the manufacturer indicates that no alternatives are available. For a detailed investigation of possible alternatives it would be necessary to contact a number of manufacturers of other types of analysis instruments, in order to clarify whether these methods could in fact generate useful analysis results.

Table 22 Applications of mercury in polarography for which no technically feasible alternatives are not regarded to exist

Application of polarography with hanging drop mercury electrodes	Sector	Potential alternatives	Reasons for these alternatives of not being technically feasible (1)
Metal speciation in natural water samples	Environmental research (and monitoring)	Combined techniques: • LC + ICP-MS • SPE + e.g. AAS • …	• Limited mobility • Laboratory infrastructure required • Not all applications can be replaced
Complexation capacity of natural waters, competitive ligand exchange methods	Environmental research	Unknown	
Toxic metals in sea water	Environmental research (and monitoring)	• AAS • ICP	• Problems with salt matrix in spectroscopic instruments • Limited mobility
Iodide in brine	Chloralkali electrolysis (mercury-free membrane technology)	ICP	• Problems with salt matrix • Lower sensitivity
Trace metal impurities in process solutions	Metal production (e.g. zinc smelters)	• AAS • ICP	• Laboratory infrastructure required • Not suitable for use in production environment
Organic components in plating solutions	Metal production (e.g. copper smelters, metal foil production for electronics industry)	Unknown	
Lead in electroless nickel baths	Electronics industry	• AAS • ICP	• Spectroscopic methods do not give reliable results (Total lead with AAS, “active” lead ions with VA)
Fe(II) content in iron sucrose injection solutions	Pharmaceutical	Unknown	
Elemental sulfur in gasoline	Petrochemical	Unknown	

Additional information:

Abbreviations
LC – Liquid chromatography
ICP – Inductive coupled plasma
ICP-MS – Inductive coupled plasma – mass spectrometry
AAS – Atomic absorption spectroscopy
SPE – Solid phase extraction

6.2 Economic feasibility

The listed reasons for the alternatives not being economically feasible is a copy of the reasons not being technically feasible and mainly concerns the need for laboratory infrastructure (probably meaning that different advanced laboratory equipment is needed).

Table 23 Applications of mercury polarography for which technically feasible alternatives exist, but these are not regarded as economically feasible

Application of polarography with hanging drop mercury electrodes	Sector	Available technically feasible alternatives	Reasons for these alternatives of not being economically feasible
Metal speciation in natural water samples	Environmental research (and monitoring)	Combined techniques: • LC + ICP-MS • SPE + e.g. AAS • …	• Limited mobility • Laboratory infrastructure required • Not all applications can be replaced
Toxic metals in sea water	Environmental research (and monitoring)	• AAS • ICP	• Problems with salt matrix in spectroscopic instruments • Limited mobility
Iodide in brine	Chloralkali electrolysis (mercury-free membrane technology)	ICP	• Problems with salt matrix • Lower sensitivity
Trace metal impurities in process solutions	Metal production (e.g. zinc smelters)	• AAS • ICP	• Laboratory infrastructure required • Not suitable for use in production environment

6.3 Derogations

The manufacturer does not propose any phrasing of derogations but clearly indicated the need for derogations.

6.4 Standards

The manufacturer has provided an extensive list of standards for the use of polarographic methods. Many of the standards describe the methodology, in cases where polarography is used for e.g. the determination of lead and cadmium contents of zinc (ISO 713). The presence of the standard does not imply that lead and cadmium contents of zinc cannot be determined with other methods.

It is not clear to what extent the polarographic methods are prescribed e.g. by regulation or to what extent the methods are obligatory e.g. for product control in some sectors. A closer investigation will be necessary if this is to be clarified but is out of the scope of the current contract.

Comparison of polarography with alternative techniques

The manufacturer provides the following estimates for the comparison of mercury polarographs with other instrument. It would be necessary to contact manufacturers of equipment for the alternative methods if the estimates need to be verified. This is beyond the scope of the current contract.

Table 24 Comparison of polarography with alternative techniques

	Mercury polarographs	Alternative 1 Atomic absorption spectroscopy (AAS)	Alternative 2 Inductive coupled plasma (ICP) spectrometers with • Optical emission detection (OES) or • Mass spectrometric detection (MS)
Application area	Electroactive substances: • Transition metal ions (ionic content) • Anions • Organic substances	Metals (elemental content)	Metals and non-metallic elements (elemental content)
Typical price of the total instrument (factory gate price without VAT in €)	>= EUR 20,000	Estimated: > EUR 40,000 (Graphite furnace instrument, cheaper flame emission instruments lack sensitivity)	Estimated: > EUR 40,000 to EUR 100,000

	Mercury polarographs	Alternative 1 Atomic absorption spectroscopy (AAS)	Alternative 2 Inductive coupled plasma (ICP) spectrometers with • Optical emission detection (OES) or • Mass spectrometric detection (MS)
Laboratory infrastructure required	Nitrogen gas supply (Gas cylinder, size typical 10 – 50 L)	Gas supply (types depending on application), fume exhaust installations	Argon supply (very high consumption, fume exhaust installations
Average lifetime of instrument (in years)	Min. 10 years according to our experience	Unknown	Unknown
Typical number of analyses per year with full time operation	Extremely varying on users requirements, from 100 to 5,000	Several 1,000 samples p.a. possible	Several 1,000 samples p.a. possible
Recurrent costs per instrument in normal use (€ per year)	EUR 2,000 – 2,500	Unknown Costly accessories are lamps, graphite furcaces	Unknown We have been reported that users spend often EUR 20,000 – 30,000 p.a. only for argon gas. Additional costs come on top.
Recurrent cost per analysis (€ per analysis)	In average typically around EUR 1 per analysis	Unknown	Unknown
Other factors influencing the costs estimates (specify):	Special applications • Special chemicals • Ultrapure chemicals		
Total mercury use for the application in the EU in 2009	Estimate: 100 – 180 kg		
Expected total mercury use in the EU for the application in 2020 without further legislative action	Expected: 80 – 150 kg due to partial replacement with mercury-free alternatives		

7 Use of mercury equipment for calibration

In order to make a preliminary assessment of the need of mercury devices for calibration of other measuring devices different national reference laboratories in Denmark and the National Physical Laboratory in the UK were contacted.

It would be possible to go further on with this issue by a request to The European Association of National Metrology Institutes (EURAMET), but this has been beyond the scope of the current contract. EURAMET is a Regional Metrology Organisation (RMO) of Europe. It coordinates the cooperation of National Metrology Institutes (NMI) of Europe in fields like research in metrology, traceability of measurements to the SI units, international recognition of national measurement standards and of the Calibration and Measurement Capabilities (CMC) of its members. (http://www.euramet.org/)

EURAMET has committees on “Thermometry” and “Mass and Related Quantities” (includes pressure).

7.1 Barometers

In Denmark accurate electronic barometers based on the "vibrating cylinder transducer" principle are usually used for calibration purposes. The Danish Meteorological Institute has today only one mercury barometer, "the institute reference", which is rarely used for certain calibration purposes. It is our impression that similar national references are used in other Member States.

Mercury calibration barometers are produced by Dr. Alfred Müller Meteorologische Instrumente KG, Germany. The barometers are often referred to as Fuess-Müller instruments. http://www.rfuess-mueller.de/html/mercury_barometers.html

It has been beyond the scope of the assistance to try to identify other manufacturers.

An article indicating that Japanese Meteorological Agency has adopted a Vaisala electronic barometer for replacement of the old mercury reference can be found at:
http://www.vaisala.com/files/Japan_Meteorological_Agency_adopts_Vaisala_barometers.pdf

7.2 Manometers

In Denmark electronic manometers are usually used for calibration purposes.

However, one institution holds a mercury reference manometer for calibration of other precision meters. The manometer has a 6 m mercury column with 5-10 kg mercury. The manometer is read with a laser and data are processed electronically. The mercury is changed occasionally as it needs to be 100% pure. The mercury is not directly exposed to the air and the operator could not explain how the mercury is contaminated (probably some diffusion of oxygen or other gases). The meter was originally used by the air force for calibration of height meters, but is today used for many calibration purposes.

According to the institution the manometer is the only mercury reference in Scandinavia. It is produced and maintained by Bavaria Avionic Technology GmbH, Germany (the company could not be readily found at the Internet).

Similar equipment is produced by Schwien in the USA, and marketed in the EU: http://www.chell-instruments.co.uk/schwien/schwien.htm.

The Model 1025LX Super Schwien Manometer is a laboratory-grade precision primary pressure standard designed to provide highly accurate, stable, absolute or differential pressures: http://www.schwien.com/.

It has been beyond the scope of the assistance to try to identify other manufacturers.

According to an answer from the National Physical Laboratory (NPL) in the UK there would be no need for mercury manometers and barometers. Large area piston-cylinder arrangements (pressure balances) are able to give a similar level of performance, albeit requiring a lot of effort.

7.3 Gas flow meters

At least three institutions in Denmark hold mercury-containing gas flow meters for calibration of flow meters and controllers for gases. Mercury is in the equipment used in a frictionless sealing (mercury sealed piston). The piston prover is a volumetric calibration device consisting of a precision bore borosilicate glass tube and a mercury sealed piston. The meter can be used for measuring flows to a maximum of 10 l/minute. When a gas flow enters into the vertically-mounted glass tube the piston will move upwards. A number of sensors have been mounted along the wall of the tube to detect the presence of the piston. The volume between these sensors has been calibrated and is therefore a fixed known volume. Together with the travel time, pressure and temperature in the glass tube, the flow at reference conditions can be calculated

The meters with mercury are today produced in the Netherlands by Bronkhorst High-Tech B.V.

http://www.bronkhorst.com/en/products/calibration_equipment/fluical_bench-top_calibration_system/

It has been beyond the scope of the assistance to try to identify other manufacturers.

7.4 Thermometers

In Denmark the laboratories accredited for calibration of thermometers typically use platinum resistance thermometers for calibration of other thermometers. No national mercury reference has been identified in Denmark.

For the calibration of some thermometers mercury triple-point cells are used. The triple point of mercury is one of the defining fixed-points of the International Temperature Scale of 1990. The triple point of mercury occurs at a temperature of −38.8344 °C and a pressure of 0.2 mPa. It may be questioned to what extent the triple-point cell in itself can be considered a measuring device.

Triple-point cells are among others manufacturer by the National Physical Laboratory, UK. http://www.npl.co.uk/engineering-measurements/thermal/temperature/products-and-services/supply-of-temperature-fixed-points-for-the-calibration-of-standard-platinum-resistance-thermometers-and-thermocouples

7.5 Sphygmomanometers

The assessment of SCENIHR 2009 clearly states that mercury sphygmomanometers are not essential for calibration purposes: *"No, they are not essential as reference devices for the metrological verification (calibration) needed to ensure the accuracy of the measurement of the blood pressure devices. In general, more accurate manometers are available for metrological verification." p. 31*

8 Gyrocompasses

A UK based supplier (contacted in the UK and Denmark) indicates that they are not themselves manufacturer of the gyros and they are not aware whether any of the gyros in use today contain mercury.

The CMZ 700 gyro, to which reference was made in the 2008 EU study report, was in fact not produced by Kelvin Hughes as was indicated in the report, but the actual manufacturer was the Japanese company Yokogawa. According to the UK supplier, the new types from Yokogawa do not contain mercury.

A supplier in Scotland supplies gyrocompasses of the following brands: SG BROWN (TSS), ROBERTSON, Sperry, ANSCHUTZ (Raytheon), YOKOGAWA and TOKIMEC. According to the supplier, new equipment from these suppliers should not contain mercury.

A German manufacturer has been asked about a MSDS of the liquid used instead of Hg in their gyrocompasses. They answer that "*Our compass system has a totally different technology. So our so called "Supporting Liquid" can not be used instead of mercury. This liquid is water based and contains some componants which increase the electrical conductivity. The liquid is harmless.*".

Regarding refilling or topping up of mercury, neither of the two UK suppliers have any information on alternatives which could be used instead of mercury in existing equipment.

From a German company we have been informed that YOKOGAWA probably has a replacement kit for replacement of mercury in existing gyrocompasses, but this has not been further investigated.

9 Manometers, tensiometers and strain gauges

No replies to the questionnaires were obtained from manufacturers of manometers, tensiometers and strain gauges.

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11 Example of questionnaire

Questionnaire prepared by COWI A/S for the European Chemicals Agency, ECHA.
Please address any questions regarding the questionnaire to Carsten Lassen, COWI at crl@cowi.dk.

Please return your completed questionnaire by e-mail to crl@cowi.dk before 15th February 2010. Kindly e-mail any questions to the same e-mail address.

Any reports or other additional information available in hard copy only, can be mailed to COWI A/S, Jens Chr. Skous Vej 9, DK-8000 Aarhus C, Denmark. Attn. Carsten Lassen

Contact information	
Company name	
Contact address of company	
Web site	
Contact person	
Telephone number of contact person	
E-mail address of contact person	
Date	
Additional company names and contact persons (in case the questionnaire is completed by several companies jointly)	

This questionnaire requests information about the use of mercury thermometers. The information is intended to be used by the European Chemicals Agency (ECHA) when preparing an Annex XV restriction dossier related to mercury containing measuring devices. Please also include any relevant information regarding thermometers used in hygrometers or hydrometers.

Filling in the tables
In order to be able to compile and compare the data across companies we have prepared a number of tables for a consistent reporting of the information. In case you have only partial information, please fill in what is available and leave other cells open.

Some relevant information may not fit into the tables, and in this case we would appreciate if you add this information under "additional information" or enclose the original documents. You do not need to care about the lay-out of information pasted into the questionnaire, as long as it is clearly readable and understandable.

Please add extra rows to the tables as necessary.

Supplementary material
Product brochures, or other material addressing the subjects raised in the questions below, may be of great value for the preparation of the dossier. Please submit such material to us, or supply specific links to where this material can be found on public Internet sites.

1. Essential uses of mercury thermometers

According to the available information remaining uses of mercury thermometers are in particular used for measurements at high resolution (0.1 ºC), measurements in specific environments or measurements undertaken in accordance with specific standards. For the assessment of the possible need for derogations and the timeframe of such potential derogations it is essential to obtain a better overview of the applications for which alternatives are not technically or economically feasible. For applications prescribed by analysis standards it is essential to indicate whether alternatives are not technically feasible for the analysis even if the standard is changed.

We are aware that a large number of different thermometers are marketed for many specific applications, but the tables are intended to provide an overview of the different types of applications and the sectors in which the thermometers are applied. E.g. may "determination of flash point of fuels" be mentioned only once although the thermometers may be applied for many different fuels. It may later be relevant to make a deeper assessment of some of the specific applications.

Under the heading "sector", please indicate in which sector the results of the measurement are used independent on whether the analyses are made in-house or by a laboratory providing the analytical service. Sectors may also be "scientific research" or "environmental monitoring".

Note that the information you provide in the tables should preferable be exhaustive and the tables should not cover examples only.

Technical feasibility

Applications of mercury thermometers for which no technically feasible alternatives are not regarded to exist			
Application of thermometer	Sector	Potential alternatives	Reasons for these alternatives of not being technically feasible (1)

Additional information:

Economic feasibility

For some applications, alternatives that are technically feasible exist, but due to higher price of the equipment or other factors, the use of the alternatives is not considered economically feasible. Please indicate such applications.

Applications of mercury thermometers for which technically feasible alternatives exist, but these are not regarded as economically feasible				
Application of thermometer	Sector	Available technically feasible alternatives	Price of alternatives as compared to mercury thermometer	Other reasons for these alternatives of not being economically feasible

Additional information:

Possible derogations

For the assessment we are interested in your views if there is a need for derogations and how the derogation could be phrased. Your suggestions are considered initial thoughts only and we would like to note that you may change your view later.

Proposed derogations			
Application area	Phrasing of derogation	Time frame of derogation	Justification for the derogation

Additional information:

2. Analysis standards prescribing the use of mercury thermometers

A large number of mercury thermometers are marketed with reference to different analysis standards e.g. different standards from ASTM, DIN or BS. The objective of the table below is to obtain an overview of which sectors and application areas are covered by standards specifically prescribing the use of mercury thermometers. Further the objective is to obtain an indication of to what extent national standards are used for the analysis concerned in the different Member States. We suggest that you at least fill in the table for the national standards used in your country.

Analysis for which national or international standards prescribe the use of mercury thermometers				
Analysis	Industrial sector	Standard	Thermometer standard referred to by the standard	Alternatives that potentially may be used for the analysis if the standard is changed

Additional information:

3. Basic information used for socioeconomic assessment

For the socioeconomic assessment we are seeking information that could be used as cases in the comparison between mercury thermometers and alternatives.

We are aware that hundreds of different mercury thermometers are marketed and the cases should preferably be a "representative" thermometer case and a case where replacement is expected to be relatively difficult and expensive. As a "representative thermometer" a thermometer for general measurements in laboratories at resolution of 0.1 ºC in laboratories has been selected. If you have information about more than two alternatives, please fill in a separate sheet.

Application: Thermometer for general measurements in laboratories at resolution of 0.1 ºC in laboratories			
	Mercury thermometer	Alternative 1 (please specify):	Alternative 2 (please specify):
Type of thermometer			
Typical price of thermometer (factory gate price without VAT in €)			
Typical mercury content per thermometer (g/item)			
Number of thermometers sold annually for general applications in laboratories in the EU (best estimate)			
Average lifetime (in years)			
Costs of calibration (€ per calibration)			
Frequency of calibration (per year)			

Application: Thermometer for general measurements in laboratories at resolution of 0.1 ºC in laboratories			
Other recurrent costs (specify) (€/year/item):			
Other factors influencing the costs estimates (specify):			

Additional information:

Please provide an example of applications where you consider the replacement to be relatively expensive. If you have several examples, please fill in a separate sheet.

Application (please specify):			
	Mercury thermometer	Alternative 1 (please specify):	Alternative 2 (please specify):
Type of thermometer			
Typical price of thermometer (factory gate price without VAT in €)			
Typical mercury content			
Number of thermometers sold annually for general applications in laboratories in the EU (best estimate)			
Average lifetime			
Costs of calibration			
Frequency of calibration			
Other recurrent costs (specify):			
Other factors influencing the costs estimates (specify):			

Additional information:

4: Any other information and comments

Please add any further information you may find essential for the assessment

Appendix 4: Restriction of mercury in measuring devices under Regulation (EC) No 1907/2006 (REACH) in relation to restriction of the use of certain hazardous substances in electrical and electronic equipment (RoHS)

This appendix clarifies which measuring devices containing mercury fall within the scope of Directive 2002/95/EC (RoHS Directive) as it stands now and as foreseen in the recast[1]. It explains which devices are not covered in the current proposal for a restriction of mercury in measuring devices under the REACH Regulation because they are within the scope of the proposed recast of the RoHS Directive.

Electrical and electronic equipment is not covered

Several mercury containing measuring devices are dependent on electric currents in order to work properly, and thus fall under the definition of 'electrical and electronic equipment' in the RoHS Directive[2]. This Directive does not contain a specific provision concerning the relationship to the REACH Regulation, nor vice-versa. However, Article 2(2) of the RoHS Directive provides that it shall apply without prejudice to Community legislation on safety and health requirements and specific Community waste management legislation. Similarly Article 2(4)(a) of the REACH Regulation provides that it shall apply without prejudice to workplace and environmental legislation. Thus, in principle both regulations are applicable in parallel. That being said, and acknowledging the differences of the respective legal instruments (Directive vs. Regulation), it appears, however, that the scope of the RoHS Directive affects the REACH Regulation.

To ensure regulatory coherence and consistency, mercury containing measuring devices falling under the definition of 'electrical and electronic equipment' should not be subjected to restriction under the REACH Regulation. Instead, the RoHS Directive should be regarded as sufficiently covering those devices constituting to some extent *lex specialis* in relation to the REACH Regulation.

This approach would be in line with recital 1 of the Directive 2007/51/EC that introduced the restriction on mercury in measuring devices, now subject to revision and reads: "*The Commission communication of 28 January 2005 on the Community strategy concerning*

[1] Proposal for a Directive of the European Parliament and of the Council on the restriction of the use of certain hazardous substances in electrical and electronic equipment (recast), COM(2008) 809 final. See also the voted text of the European Parliament first reading on 24 November 2010: http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P7-TA-2010-0431+0+DOC+XML+V0//EN&language=EN.
For the status in the EP see:
http://www.europarl.europa.eu/oeil/FindByProcnum.do?lang=en&procnum=COD/2008/0240
For the Presidency compromise of 12 November 2010 see:
http://register.consilium.europa.eu/pdf/en/10/st17/st17187.en10.pdf

[2] *'electrical and electronic equipment' or 'EEE' means equipment which is dependent on electric currents or electromagnetic fields in order to work properly and equipment for the generation, transfer and measurement of such currents and fields falling under the categories set out in Annex IA to Directive 2002/96/EC (WEEE) and designed for use with a voltage rating not exceeding 1 000 volts for alternating current and 1 500 volts for direct current* (Directive 2002/95/EC).

mercury, which considered all uses of mercury, concluded that it would be appropriate to introduce Community-level marketing restrictions on certain ***non-electrical or non-electronic*** *measuring and control equipment containing mercury, which is the main mercury product group not covered by Community action so far*." (emphasis added).

Mercury containing measuring devices & RoHS

The RoHS Directive requires that new equipment put on the market does not include mercury. However, it currently does not cover 'monitoring and control instruments'[3] and 'medical devices'[4] which are not listed in the reference to Annex IA to Directive 2002/96/EC (WEEE) in Article 2(1) RoHS Directive. To ensure legal consistency and clarity of the obligations it could be regarded as more appropriate to revise this omission in RoHS rather than to introduce a new restriction under another piece of legislation such as the REACH Regulation. In fact, Article 2 of the proposed RoHS recast[1] includes the above mentioned currently omitted categories in its scope, and consequently the devices listed below would be covered by the RoHS Directive in the future if adopted in the proposed version.

The RoHS Directive presents with regard to mercury in these listed measuring devices an equally effective measure as a restriction under REACH. Having all obligations related to mercury in electrical and electronic equipment in one piece of legislation would be clearer for actors that need to comply with the obligations. This could be seen beneficial also for the enforceability and monitoring of the fulfilment of these obligations.

It should be noted that the proposed RoHS recast foresees a specific exemption for reference electrodes[5], and that potentially other such exemptions might be added during the legislative procedure. It could lead to inconsistencies if 'electrical and electronic equipment' would be assessed in the restriction report for mercury in measuring devices under the legal framework of REACH.

List of mercury measuring devices using electric currents

The following mercury containing measuring devices were considered to be dependent on currents or electromagnetic fields in order to work properly, and are therefore not covered by the current proposal for a restriction of mercury in measuring devices:

1) Gyrocompasses/heading indicator
A gyrocompass is a compass that finds true north by using an (electrically powered) fast-spinning wheel whose axle is free to take any orientation. This orientation changes much less in response to a given external torque than it would without the large angular momentum associated with the gyroscope's high rate of spin. Without this electrical

[3] Directive 2002/96/EC mentions under 'monitoring and control instruments': smoke detectors; heating regulators; thermostats; measuring, weighing or adjusting appliances for household or as laboratory equipment; and other monitoring and control instruments used in industrial installations (e.g. in control panels).

[4] Directive 2002/96/EC mentions under 'medical devices': radiotherapy equipment; cardiology; dialysis; pulmonary ventilators; nuclear medicine; laboratory equipment for in-vitro diagnosis; analysers; freezers; fertilization tests; and other appliances for detecting, preventing, monitoring, treating, alleviating illness, injury or disability.

[5] Annex VI lists applications exempted from the ban in Article 4(1) as regards Categories 8 and 9 contains an item 1d: "Mercury in reference electrodes: low chloride mercury chloride, mercury sulphate and mercury oxide"

driven spin the device would not function properly. Gyrocompasses are widely used on ships and aircraft (called 'heading indicator' in that case), and can contain mercury.

2) Reference electrodes
Mercury-containing reference electrodes are used for a variety of measurements. A reference electrode provides a stable potential whatever the measurement conditions. They are considered to be 'electrical and electronical equipment' (as confirmed by the exemption in the proposal for recast of RoHS).

3) Calibration devices for gas flow meters
Calibrators of gass flow meters based on a mercury sealed piston prover have sensors in the tube that detect the presence of the piston. The volume between these sensors has been calibrated and is therefore a fixed known volume. Together with the travel time, pressure and temperature in the glass tube, the flow at reference conditions can be calculated. Thus electric current is essential for the proper functioning of the device.

4) Mercury tilt switches
Mercury tilt switches are small tubes with electrical contacts at one end of the tube. As the tube tilts, the mercury collects at the lower end, providing a conductive path to complete the circuit. When the switch is tilted back, the circuit is broken. Mercury tilt switches are used in some medical devices and laboratory equipment, motion/vibration sensors, float switches and level switches, in certain clocks, lifeboats, and thermostats[6].

5) Thermoregulators
A thermoregulator (also designated contact thermometer or accustat) is a kind of thermostat, but applies another principle than the thermostats described under tilt switches. A glass stem which contains twin capillary bores connects to a sensitive mercury filled bulb. Attached to a rider is a contact wire that extends into the capillary bore

[6] A temperature-response sensor, which is coupled to a mechanical means of activating a mercury tilt switch. The temperature-response sensor is typically either a thermocouple, resistance temperature detector (RTD), or gas activated bourdon tube.

REVIEW ON THE AVAILABILITY OF TECHNICALLY AND ECONOMICALLY FEASIBLE ALTERNATIVES FOR MERCURY CONTAINING SPHYGMOMANOMETERS AND OTHER MEASURING DEVICES FOR PROFESSIONAL AND INDUSTRIAL USES

1. INTRODUCTION-SCOPE OF THE REVIEW

In its Communication of 28 January 2005 on the Community strategy concerning mercury[1], the Commission concluded that it would be appropriate to introduce Community-level marketing restrictions on certain non-electrical or non-electronic measuring and control equipment containing mercury. The European Commission made a study concerning the risks from the use of mercury-based measuring devices[2] and taking into account technical and economic feasibility of alternatives. The outcome of this investigation indicated that marketing and use restrictions should cover those measuring devices that are intended for sale to the general public and also all fever thermometers. The Commission adopted a proposal for restrictions on 21 January 2006[3]. During the adoption of the restrictions by the European Parliament and the Council, it was decided that the restrictions should not include:

(a) the import of measuring devices containing mercury that are more than 50 years old; this concerns either antiques or cultural goods as defined in Council Regulation (EEC) No 3911/92 considering that such trade is limited in extent and seems to pose no risk to human health or the environment;

(b) mercury-containing devices for healthcare (in particular, sphygmomanometers for measuring blood pressure and strain gauges) on the basis of their essential use in the treatment of specific medical cases.

The final restrictions were adopted in Directive 2007/51/EC of the European Parliament and the Council[4]. The Directive contains a review clause indicating that: *By 3 October 2009 the Commission shall carry out a review of the availability of reliable safer alternatives that are technically and economically feasible for mercury-containing sphygmomanometers and other measuring devices in healthcare and in other professional and industrial uses. On the basis of this review or as soon as new information on reliable safer alternatives for sphygmomanometers and other measuring devices containing mercury becomes available, the Commission shall, if appropriate, present a legislative proposal to extend the current restrictions to sphygmomanometers and other measuring devices in healthcare and in other professional and industrial uses…"*

Directive 2007/51/EC has been incorporated into Annex XVII of the REACH Regulation[5] since 1 June 2009. This document contains the information and results of consultations of

[1] Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2005:0020:FIN:EN:PDF
[2] Available at: http://ec.europa.eu/enterprise/chemicals/docs/studies/rpa-mercury.pdf
[3] Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2006:0069:FIN:en:PDF
[4] OJ L57, 3.10.2007, p.13.
[5] OJ L 396, 30.12.2006, p. 1.

stakeholders conducted by the Commission until today. Consequently, the review will have to be accomplished by the European Chemical Agency (ECHA) according to REACH procedures.

2. BACKGROUND INFORMATION ON THE CURRENT USES OF MERCURY CONTAINING DEVICES IN HEALTHCARE AND IN OTHER PROFESSIONAL-INDUSTRIAL APPLICATIONS.

Following the investigation of the Commission and consultation with all interested parties, the use of mercury containing measuring devices in healthcare and in other professional and industrial applications has been identified. It should be noted that significant input (e.g socio-economic data, availability of alternatives) for the purposes of this review had been provided by a study **"***Options for reducing mercury use in products and applications, and the fate of mercury already circulating in society"*, commissioned by DG Environment in the framework of the Community Strategy on Mercury. The final report was submitted in September 2008[6] and contained a separate section concerning the mercury measuring devices for professional uses and feasibility of their substitution. Table 1 provides a summary of the mercury consumption in some professional/industrial uses of mercury measuring devices as recorded in the report.

Table 1: Mercury consumption in certain measuring devices for professional/industrial uses for 2007 (source: COWI report-2008)

[6] ": Options for reducing mercury use in products and applications, and the fate of mercury already circulating in society" (COWI A/S, Concorde East West, 2008)
Available at: http://ec.europa.eu/environment/chemicals/mercury/index.htm

Application	Consumption	
	Tonnes Hg/year	In %
Other mercury-in-glass thermometers	0.6 - 1.2	10.2% - 8.9%
Thermometers with dial	0.1 - 0.3	1.7% - 2.2%
Manometers	0.03 - 0.3	0.5% - 2.2%
Barometers	2 - 5	34.1% - 36.9%
Sphygmomanometers	3 - 6	51.1% - 44.3%
Hygrometers	0.01 - 0.1	0.2% - 0.7%
Tensiometers	0.01 - 0.1	0.2% - 0.7%
Gyrocompasses	0.005 - 0.025	0.1% - 0.2%
Reference electrodes	0.005 - 0.015	0.1% - 0.1%
Hanging drop electrodes	0.1 - 0.5	1.7% - 3.7%
Other uses	0.01 - 0.1	0.2% - 0.1%
Porosimetry		
Total	5.87 – 13.55	100%

2.1 Mercury measuring devices in Healthcare

2.1.1 Mercury containing Sphygmomanometers

Mercury sphygmomanometers have been used for more than 100 years and are still considered by many to be the “gold standard” of blood pressure measurements, although their market has been steadily decreasing in recent years in certain Member States due to legal (Sweden, Lithuania) or voluntary (e.g. Denmark, Netherlands) phase-out. Mercury sphygmomanometers manufactured in the EU typically contain 85 to 100 g mercury per instrument. The total EU-wide annual mercury consumption in sphygmomanometers for 2006 was estimated at 3-6 tonnes in 30,000 - 60,000 units, most of which were sold mainly to general practitioners.

Three manufacturers of mercury containing sphygmomanometers in the EU have been identified (Rudolf Riester GmbH & Co. KG-Germany, A.C.Cossor & Son Limited-UK and PiC Indolor- Italy) whereas several brands are also imported from non-EU countries including Japan, USA and China. There is a significant export of mercury containing sphygmomanometers manufactured within the EU to countries outside the EU. European-made sphygmomanometers are in demand because they are considered to be of higher quality by customers, and are more resistant to breakage and release of mercury. It is estimated that

annual exports comprise at least 60,000-90,000 units corresponding to a content of 5-8 tonnes of mercury.

Market shares of mercury containing sphygmomanometer and the level of substitution vary among Member States. Italy, the UK and certain new Member States constitute the largest market for mercury containing sphygmomanometers within the EU, whereas in other Member States these account for 10% or less of the total market for manual blood pressure measurement devices. Information for the main alternative devices (e.g electronic and aneroid sphygmomanometers) is given in section 4 of this report.

2.1.2 Mercury containing Strain gauges

Mercury strain gauges are used for blood flow and blood pressure measurements in body parts, mainly for diagnosing certain kinds of arteriosclerosis, and are based on a technique called strain gauge plethysmography. Considering that one major global producer of strain gauges consumed 946 grams of mercury in 2004 for production of strain gauges, it can be concluded that total EU consumption for this application may be insignificant in comparison to the amount of mercury used in sphygmomanometers. It should be noted that even in Member States that have phased out mercury containing sphygmomanometers, a certain number of strain gauges is still in use for diagnosis and monitoring of arteriosclerosis in patients (~200 devices in Sweden and ~100 in Denmark).

2.2 Other mercury containing measuring devices for professional or industrial uses

2.2.1 Mercury containing Thermometers

The following types of mercury-containing thermometers have traditionally been used in the EU:

(a) Mercury-in-glass thermometers:

- Medical thermometers;
- Ambient temperature thermometers (wall thermometers);
- Laboratory thermometers;
- Thermometers for combustion and industrial processes.
- Minimum-Maximum thermometers.

(b) Mechanical mercury thermometers with a dial

As the use of mercury in medical thermometers is now banned in the EU, further focus is given to other professional uses of mercury thermometers such as in laboratories and for specific purposes in the industry, for which the mercury consumption is estimated in the order of 0.6-1.2 tonnes per year (half of which is used in thermometers for research, and the rest for industrial and marine applications). Mercury has been widely replaced by alternatives, but mercury-in-glass thermometers seem to hold a significant market share for some specific applications. The mercury content of marketed mercury-in-steel dial thermometers used in industry and marine applications is estimated at 0.1-0.3 tonnes mercury per year.

2.2.2. Mercury containing Porosimeters

Porosimeters are used for measuring porosity, i.e. the void spaces in a material. Mercury porosimeters are typically applied for materials with pore diameters in the range of 0.0036 μm to 1 mm. EU manufacturers of porosimeters argue strongly that mercury intrusion porosimetry (MIP) has been the unique reliable and established technique for the macropore analysis for at least 30 years, as being a fast, easy to use technique with relatively inexpensive instrumentation, a wide range of pore size / pore volume measurements and well established safety procedures and recycling processes. According to the COWI-Concorde (2008) report, the total number of porosimeters in the EU is estimated at ~2000, with a total amount of mercury used estimated with high uncertainty at 10-100 tonnes per year.

2.2.3. Mercury containing Electrodes

Hanging drop electrodes in polarography are mainly used to analyse trace elements in water and environmental samples. The typical mercury use for such an instrument is ~140 gr / year. On that basis it is roughly estimated that the EU-wide mercury consumption for this application in 2007 was 0.1-0.5 tonne per year. Mercury electrodes for polarography are banned in Sweden but are exempted from a ban imposed by Norway in measuring devices until 31 December 2010.

Reference electrodes are used for a variety of measurements mainly for research purposes. It is estimated that the total mercury use in electrodes for medical equipment is ~ 2-10 kg/year and in monitoring and control instruments at about 3 kg/year, indicating a total EU mercury use at 0.005-0.015 tonnes.

2.2.4 Mercury containing Manometers

Manometers measure the difference in gas pressure between the measured environment and a reference. Mercury-containing manometers are mostly U-shaped glass or plastic tubes for laboratory use and intended for special industrial applications mainly for pressure measurements in the heating and ventilation sector. Although it is not easy to obtain a precise estimate of the current use of mercury for new manometers, the total EU consumption of mercury for filling new manometers is roughly estimated in the order of 0.03-0.30 tonnes per year.

2.2.5 Mercury containing Barometers

Barometers measure atmospheric pressure and are used for a number of professional applications, such as in weather stations (e.g. Meteorological Institutes), airports and airfields, and on ships. Compared to sphygmomanometers and thermometers, mercury containing barometers account for a minor part of mercury in measuring devices for professional uses which is estimated at 0.1-0.5 tonnes per year in the EU area. Mercury containing barometers for professional applications today hold a very small market share, as alternatives are available for all applications.

2.2.6 Other mercury containing measuring devices of minor use

(a) Tensiometers mainly used for research applications to determine the level of soil moisture tension (soil water potential). According to the COWI-Concorde (2008) report, the only one EU manufacturer informed that sales of mercury tensiometers have been in the range of 10-15 instruments per year and production would be discontinued in 2009.

(b) Hydrometers measure the density or specific gravity of a liquid. Mercury is deemed not to be used in the bulk of hydrometers in the EU today.

(c) Gyrocompasses find true north by using a fast-spinning wheel and friction forces in order to exploit the rotation of the Earth. EU annual mercury consumption for filling new gyrocompasses are in the order of 0.005-0025 tonnes.

(d) Coulter counters are used for automated counting and measuring the size of microscopic particles. The total mercury content of new Coulter counters on the EU market is assumed to be below a few kg, if any.

In total it is estimated that the mercury consumption in the above-mentioned "minor applications" is in the range of 0.01- 0.1 tonne per year.

3. CONSULTATIONS WITH STAKEHOLDERS

In summer 2008, DG-Enterprise & Industry has launched a consultation with Member States and other interested stakeholders. More specifically, questionnaires were prepared and circulated to the Members of the Commission Experts Working Group on Limitation of Chemicals (LWG) and to the Experts Working Group on Medical Devices (MDEG) asking them to provide input concerning:

- the availability of alternatives to mercury-containing sphygmomanometers in the Member States and whether these are adequately validated and calibrated;
- essential uses of mercury-containing sphygmomanometers that are required in Member States (e.g. treatment of special medical conditions);
- other mercury-containing measuring devices used for research and in industrial uses and the availability of alternatives for such devices.

In addition, the Commission sent the questionnaires to interested NGOs, industry trade associations, and scientific organisations requesting them to submit any information (reports of relevant studies/clinical trials etc.) which would be helpful for the purposes of the review. It should be noted that all responses of Member States, as well as the received material from other stakeholders (statement, reports, scientific papers) are available on CIRCA[7]. Moreover, a list of the most important submissions is given in Appendix 2. A summary of the outcome of this consultation is presented below.

[7] http://circa.europa.eu/Members/irc/enterprise/lmudsp/library?l=/thematic_folder/mercury_follow_up&vm=detailed&sb=Title

3.1 Feedback from Member States and other interested parties

(a) Positions of Member States:

There was no clear consensus within the MEDG. A number of Member States (MT, FI, DE, HU, UK and IT) claimed that mercury-containing sphygmomanometers are still essential, either for calibration purposes or the treatment of special health conditions, whereas others (IE, NL, PL and SE) were of the opinion that there are technically and economically viable alternatives for all uses.

Within the LWG, most responding Member States (LV, SE, NL, NO and FR) claimed that mercury-containing sphygmomanometers are no longer necessary and have already been replaced. However, DE and IT argued that mercury-containing sphygmomanometers should be kept for calibration purposes, while UK and FI strongly opposed an EU ban of mercury-containing sphygmomanometers stressing that these are indispensable for the treatment of certain medical conditions.

(b) Scientific organisations

The Commission also invited medical organisations to provide their expert advice concerning the substitution of mercury-containing sphygmomanometers in healthcare. The European Society of Hypertension (ESH) replied that properly validated electronic instruments (but not the aneroid devices) could serve as reliable substitutes to mercury containing-sphygmomanometers. However, ESH claimed that automated devices are not accurate for blood measurements in patients with arrhythmia, and that mercury-containing sphygmomanometers are also still essential for the calibration of electronic devices. The European Board and College of the Obstetrics and Gynecology (EBCOG) has also committed to consult the International Society for the Study of Hypertension in Pregnancy (ISSHP), in order to advise the Commission on the need for Hg-containing sphygmomanometers for the treatment of hypertension in obstetrics(No inout has been received from EBCOG until the time of completion of this report)

(c) NGOs

The Commission has received input from various NGOs (European Environmental Bureau - EEB, Health and Environmental Alliance – Health Care Without Harm-HCWH) including recent reports concerning the existence of safer alternatives to mercury-containing measuring devises in healthcare as well as recent publications from clinical journals and other worldwide initiatives. All NGOs strongly recommend that mercury-containing sphygmomanometers should be banned in the EU, considering that these devices can pose a risk to human health and the environment during use and as waste and that adequate alternatives are already available in the European market.

(d) Industry associations

The European Committee of Radiological, Electromedical and Healthcare Industry (COCIR) and the US-based Association for Advancement of Medical Instrumentation (AAMI) both claim that mercury-containing sphygmomanometers must not be banned from either practical use or from calibration purposes because they provide the most accurate reading possible today. Concerning the environmental impacts, COCIR stresses that the amount of mercury released by these devices, assuming there are spills, is negligible when compared to other sources of mercury releases, in particular industrial sources.

Input was also received from individual companies such as (a) COSSOR, a UK manufacturer of both mercury containing and mercury free sphygmomanometers, provided information on accuracy and limitations of each type of sphygmomanometers, and (b) Russell Scientific Instruments Limited who defended the use of mercury in a limited number of highly specialised professional uses such as thermometers (e.g "retort thermometers" for canning industry) and barometers (used by amateur meteorologists or breeders of reptiles and birds).

3.2 Commission Workshop on mercury in measuring devices for professional/industrial uses (April 2009)

Though the Commission consultation with stakeholders yielded a good amount of information concerning the mercury based sphygmomanometers, there was only limited input concerning the mercury containing measuring devices for other professional/industrial uses in the EU. Therefore, in order to establish a broader knowledge base for the other uses but also further develop the information on healthcare sphygmomanometers, DG Enterprise and Industry organised a workshop in Brussels in April 2009. Apart from NGOs and Member States (experts from both LWG and Medical Authorities) who recalled their above-mentioned positions, representatives of European industry were also invited to attend the workshop and present more information on the remaining applications of mercury containing measuring devices (e.g. porosimetry, polarography) and the feasibility of alternatives.

Some information of the presentations and the subsequent discussion between the participants are given in section 4 where the main arguments on feasibility of alternatives to mercury containing devices are developed. In addition more details about the actual discussions and positions are described in the Minutes of the workshop available at: http://circa.europa.eu/Members/irc/enterprise/lmudsp/library?l=/thematic_folder/mercury_follow_up&vm=detailed&sb=Title.

Concerning mercury containing measuring devices for professional and industrial uses, discussions revealed that these mainly concern quite specialised and rather small-scale applications, which probably do not significantly contribute to exposure of consumers or release to the environment. It seems that while the mercury consumption can be quite high, e.g in porosimeters, the number of such devices for use in the EU is limited and they are typically used in laboratories with well established control procedures on safety at the work place and management of dangerous waste, so that most of the mercury can be recycled and reused. On the issue of mercury recycling in porosimetry, the Commission has carried out a consultation with the industry, the outcome of which is presented and discussed in section 4.2.2.

Concerning sphygmomanometers, the workshop discussions provided much useful information to confirm that there is an ongoing tendency for substitution of mercury-containing sphygmomanometers, and that where such substitution has occurred the experience has been uniformly positive. Nevertheless, in some Member States where substitution has not yet occurred, concerns remain on calibration, validation, and on the treatment of certain medical conditions, which could at least in part be due to user-related preferences and habits, as well as lack of knowledge or training for using mercury-free sphygmomanometers.

3.3 EEB Conference on mercury in measuring devices for professional/industrial uses (June 2009)

A Conference was organized in Brussels (18 June 2009) by the NGOs (EEB-HCWH) entitled "EU Mercury phase out in measuring and control equipment". The meeting was attended by medical doctors in the EU and US, hospital representatives, experts in validation and calibration issues, manufacturers of mercury containing and mercury-free measuring devices, trade unions, NGOs and representatives of UN organisations. The Commission services participated as well. The presentations of the Conference are available at: http://www.zeromercury.org/EU_developments/090618_Meas_Dev_conference.html.
EEB and HCWH have also prepared a report from the Conference[8] summarizing the outcome and main conclusions of the discussions.

In this Conference, the EEB presented its study *'Turning up the pressure-Phasing out mercury sphygmomanometers for professional uses'*. The report[9] highlights real–life experiences of European hospitals that purchase and/or use mercury-containing and mercury–free sphygmomanometers. By means of a survey of the experiences of a number of European hospitals, this study has observed that most of the hospitals in a few EU Member States have completely phased out mercury-containing sphygmomanometers – some of them more than ten years ago. A smaller number of hospitals insists that mercury sphygmomanometers are still necessary, or at least see no immediate need to phase them out. The EEB report indicated that it is technically and economically feasible to make the transition to mercury-free sphygmomanometers that are available on the market and are approved by professional bodies, including for special cases like pre-eclampsia and hypertension.

At the EEB Conference there were also presentations about the UNEP/WHO initiatives at global level concerning restrictions of the use of mercury-containing measuring devices. According to a 2008 UNEP study[10] (*"Report on the major mercury-containing products and processes, their substitutes and experience in switching to mercury-free products and processes"*) several countries - not only European (Sweden, Netherlands, Norway etc.) but

[8] available at: http://www.zeromercury.org/EU_developments/091104EEB-HCWH-Meas-Dev-Conf-Rep.pdf
[9] Publication-Report ' Turning up the pressure : Phasing out Mercury Sphygmomanometers for professional use Concorde East/West (Commissioned and Published by European Environmental Bureau, 2009) http://www.zeromercury.org/SphygReport_EEB_Final-A5_11Jun2009.pdf

[10] available at: http://www.chem.unep.ch/mercury/OEWG2/documents/g72)/

also worldwide (e.g. Brazil, USA) - have successfully demonstrated the availability and utilisation of mercury free alternatives (such as digital or electronic and aneroid sphygmomanometers). The only remaining challenges are the direct costs or high price of some alternatives especially in developing countries and the need for the alternatives to have a regular calibration.

4 DISCUSSION ON AVAILABILITY OF ALTERNATIVES TO MERCURY-CONTAINING DEVICES FOR PROFESSIONAL/INDUSTRIAL USES

4.1 Alternatives to mercury-containing measuring devices in healthcare

4.1.1 Availability of mercury-free sphygmomanometers

For more than a century, blood pressure has been measured worldwide both in clinical practice and medical research by the auscultation technique using mercury containing sphygmomanometers together with a stethoscope to listen to the various sounds of blood flow as pressure is released from an inflatable cuff placed around the arm. The advantages and disadvantages of mercury-containing sphygmomanometers have been extensively discussed in the medical literature. Compared to other measuring devices, the main advantages of the mercury-containing sphygmomanometers are the following:

- they are relatively easy to use by people who are trained and practiced in using this instrument,
- they are relatively stable (i.e. they typically do not need to be calibrated more than once every two years),
- they may be used with virtually any medical condition,
- they are relatively easy to repair so that they may have a long lifetime,
- it is fairly easy to see when they are not functioning properly, and
- even the cheapest models may be expected to be reasonably reliable.

As a result, and certainly also because most medical personnel are familiar with these instruments, they are still considered by many to be the “gold standard” for blood pressure measurement. In fact, the vast majority of information on population blood pressure - secular trends, progression to hypertension, and prognostic implications - has so far been obtained with the use of mercury sphygmomanometers. However, the various hazards and costs associated with the life-cycle of mercury in a sphygmomanometer may be significant. Moreover, reports from hospitals and family practices have suggested that many mercury-containing sphygmomanometers are defective and with very poor maintenance.

Alternatives to mercury-containing sphygmomanometers on the market can roughly be divided into the following groups:

(I) Blood measuring devices based on the auscultatory technique, such as:

(a) *Aneroid sphygmomanometers for manual reading*

The manual aneroid sphygmomanometer works in a similar way to the mercury-containing sphygmomanometer, but with an aneroid gauge that replaces the mercury-containing manometer. While the accuracy and reliability of the aneroid manometer vary with the design and quality of the device, several aneroid mechanical sphygmomanometers have been validated for clinical use, meeting the criteria of the protocols of the British Hypertension Society (BHS). However, these devices are very sensitive to mechanical shock, easily susceptible to damage and calibration drift, particularly if they are portable, leading sometimes to inaccurate measurements. It is therefore recommended that these devices undergo a metrological check at least annually, although the implementation of this recommendation appears unlikely, especially in primary care. A recent UK study[11] in a primary care setting has shown that more than 50% of aneroid devices had a calibration error > 3 mm Hg compared to only 8% of mercury and automated devices combined.

(b) Manual digital sphygmomanometers

These devices measure the pressure in the cuff with an electrical transducer. They have the disadvantage that electrical power is required.

A relatively new type of "manual digital" sphygmomanometer marketed as an alternative to mercury-containing sphygmomanometers and as a reference manometer, combines an electronic manometer with a dial for manual reading. One such device, manufactured by A.C. Cossor & Son (Surgical) Ltd in the UK, performs an auto-calibration to zero each time it is switched on, and meets the criteria of the International Protocol for blood pressure measuring devices in adults (BHS). Although such devices are suitable for patients where clinical conditions may preclude the use of automated oscillometric devices (such as arrhythmia and pre-eclampsia), their reading cannot be assumed to be equivalent to the reading of a mercury column so that validation is required prior to their introduction on the market.

As stated in the COWI-Concorde (2008) report, aneroid and digital sphygmomanometers are widely sold in the Member States for application by general medical practitioners and in hospitals, which comprise the main market for sphygmomanometers today. An evaluation by the UK Medical Agency (MHRA) noted that the decreasing cost of automated devices, together with the improved reliability of aneroid devices and the introduction of manual digital sphygmomanometers are leading to a further reduction in the use of mercury-containing sphygmomanometers.

(II) Blood measuring devices based on the oscillometric technique

[11] Coleman AJ, Steel SD, Ashworth M, Vowler SL, Shennan A. Accuracy of the pressure scale of sphygmomanometers in clinical use within primary care. *Blood Press Monit* 2005; 10:181-188

Oscillometry measures only mean pulsation in arterial pressure and then uses software algorithms to calculate the systolic and diastolic values. The types of instruments using this principle are:

(a) Semi-automated devices

Semi-automated electronic blood pressure devices have undergone extensive development during recent years, and a large number of different devices are marketed today. They typically use the oscillometric technique and include an electronic monitor with a pressure sensor, a digital display, an upper arm cuff and a hand-operated inflation bulb. The semi-automated electronic devices are today standard for home/self assessment in many Member States and are also widely used by general medical practitioners. The European Society of Hypertension has noted that for self-assessment, electronic devices using oscillometry are becoming more popular and are replacing the auscultatory technique. The electronic devices require less training and are easier to use by patients with infirmities such as arthritis and deafness.

(b) Automated devices

Oscillometry is usually used by automated devices to determine blood pressure by analysing the pressures transmitted through arterial oscillations/vibrations that occur during cuff inflation and/or deflation. For "fully" automated measurements in hospitals, more advanced equipment, which often combines the measurement of blood pressure with monitoring of temperature, heart rate and blood oxygen level, is often used.

An accurate automated oscillometric sphygmomanometer is capable of providing printouts of systolic, diastolic and mean blood pressure, together with heart rate and the time and date of measurement, eliminating errors of interpretation and abolishing observer bias and terminal digit preference. Another advantage of automated measurement is the ability of such devices to store data for later analysis.

However, a drawback of the sphygmomanometers based on the oscillometric technique is that their accuracy is limited in special patient groups such as the elderly and those with vascular diseases that influence the oscillometric signal including diabetes, arrhythmias, and pre-eclampsia. It should also be noted that doctors are commonly uneasy about trusting algorithmic methods, which are guarded as a proprietary secret by manufacturers. In addition, the accuracy of automated oscilometric devices is user dependent as these are commonly used at home by untrained individuals.

Other considerations on substitution of mercury-containing sphygmomanometers

Concerning the cost of alternative devices, a recent EEB survey which is reflected in the Concorde (2009) report, revealed that standard EU prices are in the order of € 40-60 for a validated mercury-free sphygmomanometer, while the cost of a mercury containing sphygmomanometer, where available, was generally cited at € 50-80. High variation was indicated in the COWI-Concorde (2008) report, with a price difference between European produced alternatives and mercury containing sphygmomanometer ranging from € 0 (€ 60 for both types) for shock-proof conventional aneroid sphygmomanometers, to approximately € 100 for high performance sphygmomanometers with electronic gauges. The total extra costs

to the users in the EU of purchasing alternatives can thus be estimated at € 0-6,000,000 per year depending on which alternative is chosen.

As previously mentioned, the recent EEB survey in a number of European hospitals (an overview is given in Table 2 below) concerning the use of mercury-containing sphygmomanometers and their level of substitution noted that '*overall, nearly 90 percent of the sphygmomanometers used in these hospitals were found to be mercury-free, and 75 percent of the hospitals investigated no longer use mercury-containing sphygmomanometers – some already for more than 10 years.* Only a small number of hospitals insist that mercury-containing sphygmomanometers are still necessary, or at least see no immediate need to phase them out. Moreover, many hospitals in other Member States are merely waiting for the old mercury containing instruments to wear out.

Table 2: Results of the EEB survey on the use of mercury-containing and mercury-free sphygmomanometers in European hospitals (source: 2009 Concorde report)

Country	Number of hospitals investigated	Number of beds*	Total sphygs*	Mercury sphygs*	Mercury-free sphygs*	Hospitals with only mercury-free sphygs
Czech Repub	4	3,279	1,235	838	397	0
France	4	4,035	1,120	12	1,100	3
Germany	29	16,000	4,000	0	4,000	29
Greece	2	1,050	190	120	70	0
Hungary	5	4,375	315	115	200	1
Italy	3	1810	480	240	240	1
Spain	5	2,785	860	0	860	5
United Kingdom	3	4,700	1,700	90	1,610	2
Total	**55**	**38,034**	**9,900**	**1,413**	**8,487**	**41**
Hg vs. Hg-free				14%	86%	75%
Total without Germany	26	22,034	5,900	1,413	4,487	12
Hg vs. Hg-free				24%	76%	46%

4.1.2 Opinion of SCENIHR on the feasibility of substitution of mercury-containing sphygmomanometers in healthcare (2009)

Following the workshop in April 2009, in order to address the remaining concerns and considering that the health and safety of patients is critical, DG Enterprise and Industry has requested in March 2009 an opinion of the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) concerning the feasibility of the substitution of mercury-containing sphygmomanometers in the healthcare sector.

SCHENIHR was requested to examine whether the replacement of mercury-containing blood-pressure measuring devices (sphygmomanometers) would endanger proper healthcare including for specific groups of patients. SCENIHR was asked to comment on the essential use of mercury-containing sphygmomanometers as reference devices for (a) calibration (or technical verification) which is the regular metrological testing needed to ensure the accuracy of the blood pressure devices and (b) clinical validation which is the independent device accuracy assessment within a clinical setting commonly required before routine clinical use.

Based on the existing literature review and the information provided by the Commission and stakeholders and following a public call for information (which yielded additional relevant clinical/scientific evidence submitted by interested parties) SCENIHR adopted its opinion in September 2009[12].

In brief, SCENIHR concluded the following concerning the feasibility of alternatives:

(a) The mercury-containing sphygmomanometer is disappearing from use and there are many alternative devices available to replace it. Blood pressure measurement by a trained observer, using a mercury-containing sphygmomanometer or a validated auscultatory alternative, remains the most accurate and reliable form of indirect blood pressure measurement. The alternative devices using auscultation (e.g aneroid or digital) have similar limitations as the mercury-containing sphygmomanometers regarding the observer bias associated with auscultation itself.

(b) Even though oscillometric instruments are not considered as true "alternatives" to mercury-containing sphygmomanometers because they operate under a completely different principle, in practice these instruments do replace mercury-containing sphygmomanometers, in spite of their accuracy limitation which makes them insufficient for clinical use.

Overall, SCENIHR summarized their opinion by providing the following replies to the specific questions of the Commission's mandate:

1. *Is there sufficient evidence to demonstrate that mercury-free blood pressure measuring devices (aneroid or electronic instruments) are reliable substitutes for mercury-containing sphygmomanometers?*

Yes. There is sufficient scientific evidence that mercury-free blood pressure measuring devices (when clinically validated) are generally reliable substitutes for mercury-

[12] The opinion is available at: http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_025.pdf

containing sphygmomanometers in routine clinical practice. These alternative devices include both auscultatory devices requiring an observer and automated oscillometric devices for which some instructions are required.

2. *Have mercury-free sphygmomanometers been adequately validated over a wide range of blood pressures, ages and clinical conditions to allow routine use in hospitals and outpatient settings?*

Yes. Clinically validated, auscultatory non-mercury devices are equivalent to mercury-containing sphygmomanometers. For the oscillometric devices the situation is different as these devices have mainly been clinically validated in adult populations including a wide range of blood pressure but not in a wide range of ages and clinical conditions.

3. *Have mercury-free sphygmomanometers been adequately validated for the diagnosis of hypertension in specific clinical conditions (arrhythmia, pre-eclampsia in obstetrics etc.)?*

Yes. Clinically validated, auscultatory non-mercury devices are equivalent to mercury-containing sphygmomanometers, and are thus suitable for the specific groups of patients. In addition, some oscillometric devices have achieved accuracy in certain conditions although in others, like arrhythmias, the auscultation technique is necessary. Moreover, there is a need for more clinical validation of oscillometric devices to make them usable in specific groups of patients, including elderly patients, children and pre-eclamptic women.

4. *Are mercury-containing sphygmomanometers essential as reference devices for validation of long-term clinical epidemiological studies enrolling patients with hypertension?*

Yes. Mercury-containing sphygmomanometers are considered essential as reference devices for the clinical validation of the alternatives. For on-going, long-term epidemiological studies currently using mercury sphygmomanometers it is advisable not to change the method of measurement. Therefore, it will be necessary to keep mercury sphygmomanometers available in order to compare them with the alternatives in these studies.

5. *Are mercury-containing sphygmomanometers essential for calibration of mercury-free sphygmomanometers, when the latter are used for routine diagnostic purposes?*

No, they are not essential as reference devices for the metrological verification (calibration) needed to ensure the accuracy of the measurement of the blood pressure devices. In general, more accurate mercury free manometers are available for metrological verification.

6. *Is SCENIHR aware of any adverse effects for patients' health due to the replacement of mercury-containing sphygmomanometers by mercury-free alternatives?*

No evidence was found for adverse effects for patients' health in clinical settings due to the replacement of mercury-containing sphygmomanometers by validated mercury-free alternatives. There are adequate alternatives in most clinical condition/setting. In special conditions, such as pre-eclampsia, non-mercury auscultatory devices should be preferred until further validation of oscillometric devices.

4.1.3 Availability of alternatives to mercury-containing strain gauges

Available alternatives to mercury-containing strain gauges are:

• Strain gauges with indium-gallium;

• Photo cell or laser-Doppler techniques.

According to a 2005 survey of the Swedish Chemical Agency (KEMI), although mercury equipment is now being successfully replaced by these alternative techniques, the reason why equipment containing mercury is still in use in Sweden is mainly not medical but economic. The mercury-containing tube is developed to function together with complex electronic measuring equipment that costs more than € 20.000 and has a life span of 10-15 years. Therefore, although the mercury free products are fully competitive with mercury equipment on a price basis and on functionality, hospitals hesitate to invest in a new system unless the existing system breaks.

Moreover, as indicated by COWI-Concorde (2008), mercury-containing strain gauge plethysmographs are mostly used for research purposes. There is at present no alternative to mercury-containing plethysmographs in research where absolute blood flow in arms and legs is examined.

4.2 Alternatives for other mercury-containing measuring devices for professional/ industrial uses

4.2.1 Availability of alternatives for mercury-containing thermometers

A number of different types of mercury-free thermometers are marketed in the EU, among which:

(I) Mercury-free liquid-in-glass thermometers

The liquid-in-glass thermometer is the most common replacement of the mercury-in-glass thermometer at temperatures up to 250°C at a very similar price. Most mercury-free liquid-in-glass thermometers can directly replace mercury-containing room temperature thermometers but are not suitable for accurate measurements at 0.1°C resolution.

(II) Dial thermometers

These thermometers are available for measuring temperatures in the range between about 70°C to 600°C and have typically replaced mercury-in-glass thermometers for the

temperature range above 250°C, e.g. for measuring the temperature of exhaust gases of diesel engines. The price of a typical dial thermometer for a diesel engine is 2-4 times the price of a similar mercury-containing thermometer.

(III) Electronic thermometers

Electronic thermometers with a digital display and/or automatic data logging make up an increasing part of the thermometer market. The most common types are based on thermocouples, thermistors or resistance probes. The available electronic thermometers for laboratory use are generally more accurate than mercury-containing thermometers, if properly calibrated, which has to be done more often than with mercury-containing thermometers. However, the price of platinum resistance machine thermometers is of the order of 10 times the price of a simple mercury-in-glass machine thermometer (although price comparisons are complicated by the fact that the electronic thermometers typically consist of two separate parts: a probe (sensor) and a data logger).

For most industrial applications, electronic thermometers are replacing mercury thermometers due to the advantages of automatic reading. However, in laboratories and for some very specific applications in industry mercury-containing thermometers are still widely used. There are, in fact, 2 major constraints acting as a barrier to phasing out mercury-containing thermometers for laboratory use: (a) the higher cost of available alternatives (b) the fact that some international standards (e.g DIN-Germany, PI-UK and ASTM-USA) widely used in in the EU and elsewhere, prescribe the use of mercury-containing thermometers for laboratory use.

4.2.2 Availability of alternatives for mercury containing porosimeters (and information on mercury recycling in porosimetry

(a) Alternative mercury-free techniques

The two main alternatives to mercury intrusion porosimetry (MIP) techniques are:

- Mercury-free extrusion porosimetry:

  This technique can only measure pore sizes within the range 0.06 μm - 1000 μm, but it does not work with dead-end pores and requires that one side of the sample is cut to a plane surface (which in some cases is not desirable).

- Mercury-free water intrusion porosimetry:

  This technique can only be applied on hydrophobic (water-rejecting) materials, covers less then 5% of all applications and is a difficult and time-consuming surface treatment.

Other limitations of the alternatives techniques are: high prices of some of the components (i.e. gravimetric methods) or the long experiment time, lack of comparability with MIP, lack of international standards such as ISO or DIN etc.

(b) Mercury recycling in MIP

Following the discussions at the Commission workshop of April 2009, NGO's voiced doubts concerning the lack of data on the degree of recycling actually practiced by users of mercury

porosimeters. DG Enterprise and Industry then approached the leading EU porosimeter manufacturers (Thermofisher, Micromeritics and Quantachrome) covering together > 80% of the EU market) to ask for their assistance in surveying their customers (e.g companies, research institutes, etc.) on their use of mercury in MIP and on the extent of mercury recycling currently practiced.

In July 2009, questionnaires prepared by the Commission were sent to the users of mercury porosimeters in the EU, requesting information concerning the amount of mercury they have in stock to be used in porosimetry, the amount they recycle or dispose as waste or keep stock as oxidized, as well as the amounts of new mercury they buy per year. Information was also asked on the cost of new mercury and if they recycle the mercury in-house.

The consultation was completed in early September 2009 and yielded replies from 70 users of mercury porosimeters in the EU, of which ~65% were from university/research centers and ~35% from industrial laboratories. These account for ~10 % of mercury porosimetry users in the EU according to estimations of the manufacturers. In terms of geographical distribution, most replies were received from Germany (16) followed by France (15), Spain (14), UK (11), Italy (5), Netherlands and Belgium (3), and Hungary, Finland and Austria (1).

Appendix-1 contains the information received from the respondents (in anonymous form). The detailed replies received could be made available to ECHA on request.

According to the replies, the total amount of mercury bought by the respondents is ~ 0.52 tonnes/year, a number which if extrapolated for the total of EU users is ~ 5.2 tonnes/year. This is the amount of new mercury supplied to users each year. It should be noted that this value is lower than the range of values given in the 2008 COWI report (10-100 tonnes of mercury consumed in porosimetry/year in the EU)

The consultants having worked on the earlier studies on mercury uses (Concorde/COWI) have indicated that a level of mercury recycling around 80 % would be close to their expectations and in any case quite higher than the recycling rate of mercury in other sectors.

The price of new mercury (column 7 of Appendix 1) was found to vary enormously (from 21 to 480 € with an average value of ~93 €) depending on where and from whom the customer buys it, what quality of mercury, and in what quantities. It could be that the quite high prices correspond to very expensive extra pure distilled mercury. The costs of recycling and disposal (columns 8 and 9 of Appendix 1) also vary widely depending on quantities, country, method, etc.

4.2.3 Availability of alternatives to mercury containing electrodes

There are a few alternative techniques to mercury polarography for determination of trace metals such as: IC-ICP-MS (Ion chromatography coupled to inductively coupled plasma mass spectrometry) and SPE-AAS (Solid Phase Extraction coupled to Atomic Absorption Spectroscopy). However, according to industry stakeholders, these have certain limitations

such as: high purchase and running costs, limited mobility, specific laboratory infrastructure required, problems with some sample matrices (e.g. sea water, pure chemicals) etc.

Concerning the reference mercury-containing electrodes (e.g for pH measurements), these have mostly been replaced by electrodes based on silver/silver chloride. However these can be detrimentally affected by sulphides and can be unsuitable as reference electrodes for chemical analysis of chloride or silver concentrations.

4.2.4 Availability of alternatives to mercury-containing manometers

Electronic (or digital) manometers serve as main alternatives to mercury containing manometers and are widely used by industry for automatic and remote control.

According to a report from the Danish EPA in 2006[13], although the price of electronic manometers is estimated to be about 3-4 times the price of a mercury-containing manometer for similar pressure range, the electronic manometers have the advantage of automatic measurements and for this reason they cannot be directly compared to mercury-containing manometers. Moreover, a digital manometer can also be more precise than a mercury-containing manometer if properly calibrated. Laboratories calibrating manometers may still use mercury-containing manometers as reference instruments. As indicated in the COWI-Concorde (2008) report, according to a European manufacturer of mercury-containing manometers, there is no application for which mercury-containing manometers cannot be replaced by other devices.

4.2.5 Availability of alternatives to mercury-containing barometers

A number of alternatives to mercury-containing barometers are marketed today in the EU. For professional applications, alternatives are mainly electronic devices which are as precise as mercury-containing barometers such as:

- Electronic barometers (e.g. aneroid displacement transducers, digital piezo-resistive barometers or cylindrical resonator barometers),
- Electronic resistance or capacitance barometers.

According to the Guidelines from the World Meteorological Organisation (WMO 2006) there is an increasing move away from the use of mercury-containing barometers (due to the fact that mercury vapour is highly toxic and corrosive, mercury-containing barometers are delicate, difficult to transport clean and maintain etc.) to the use of electronic alternatives, which present many advantages. It should be noted that the price of mercury-containing barometers is generally higher or similar to the price of electronic barometers.

4.2.6 Alternatives for other mercury-containing measuring devices of minor use

[13] Alternatives to mercury-containing measuring devices (EPA, Denmark, 2006)
http://www2.mst.dk/udgiv/publications/2006/87-7052-133-6/pdf/87-7052-134-4.pdf

(a) Tensiometers: Mercury-containing tensiometers can, for all applications, be replaced by other types such as electronic tensiometers and tensiometers with mechanical bourdon.

(b) Gyrocompass: Mercury-free gyrocompasses have been available for many years and are used on all types of vessels and for the same applications as mercury-containing gyrocompasses. These gyrocompasses use a mercury-free liquid consisting of surfactants and other harmless organic compounds.

(c) Coulter counters**:** Alternatives with mercury-free gauges are available on the market.

5. PRELIMINARY CONCLUSIONS OF THE CURRENT INVESTIGATION

5.1 Sphygmomanometers in healthcare

(I) Following consultation with stakeholders and the investigations by SCENIHR, it can be concluded that mercury-containing sphygmomanometers are being steadily phased out in the EU (in particular for clinical use in hospitals) and are replaced by existing cost-effective alternatives. The fact that auscultatory rather than oscillometry technique may be preferable for high accuracy of blood pressure measurements for certain patient groups (pregnant women, persons with diabetics etc.) does not necessarily mean that mercury-containing devices are required. Indeed, several Member States (e.g Netherlands, Sweden, Denmark) have reported their positive experience over a long period with the use of mercury-free sphygmomanometers under all conditions. The majority of the existing market for mercury-containing sphygmomanometers now seems to be made up of (older) general practitioners, who consider them as the most accurate in recording blood pressure being also very experienced in their use.

(II) No matter what type of blood pressure measurement device is used, both aneroid and mercury-containing sphygmomanometers must be calibrated regularly in order to avoid errors in blood pressure measurement and consequently the diagnosis and treatment of hypertension. On the issue of calibration, manufacturers underline that a digital manometer should be used as the calibration standard rather than a mercury-containing manometer. Furthermore, SCENIHR concluded that mercury-containing manometers are not appropriate to be used as reference manometers, given their poor resolution.

(III) According to SCENIHR, given the important contribution over the years by mercury–containing manometers to the present knowledge on hypertension as a risk factor and to its control by treatment, and because of their continuing use as standard reference devices for the clinical evaluation of aneroid and automated blood pressure measuring devices, *it might be important to keep mercury manometers as a reference tools, available only in a few accredited centres around the world to perform clinical validation studies of new devices.*

5.2 Other mercury-containing measuring devices for professional/industrial uses

(I) Existing evidence and consultations reveal that mercury porosimeters and mercury electrodes in polarography are still essential for certain professional/industrial uses due to

technical limitations of their existing alternatives. In particular for porosimetry, it appears that given the use of mercury porosimeters for essential professional uses and the rather high level of mercury recycling performed by their users, such mercury use may not pose an unacceptable risk to human health or the environment and therefore should remain possible in the EU.

(II) Though substitution of certain mercury containing devices (strain gauges for blood measurements, thermometers for laboratory/industrial uses) seems technically feasible, it may still be difficult to achieve full replacement in the short term due to considerably higher cost of the existing alternatives.

(III) For the rest of mercury-containing measuring devices (manometers, barometers, tensiometers etc.) there are already available technically and economically feasible alternatives in the EU and therefore their current professional/industrial applications could be phased out without particular problems.

6. LIST OF ABBREVIATIONS

AAMI: Association for Advancement of Medical Instrumentation

BHS: British Hypertension Society

COCIR: Committee of Radiological, Electromedical and Healthcare Industry

EBCOG: European Board and College of the Obstetrics and Gynecology

ECHA: European Chemical Agency

EEB: European Environmental Bureau

EPA: Environmental Protection Agency

ESH: European Society of Hypertension

HCWH: Health Care Without Harm

IC-ICP-MS: Ion chromatography coupled to inductively coupled plasma mass spectrometry

ISO: International Standardization Organization

ISSHP: International Society for the Study of Hypertension in Pregnancy

KEMI: Swedish Chemical Agency

LWG: Limitation Working Group

MDEG: Medical Devices Expert Group

MIP: Mercury Intrusion Porosimetry

NGOs: Non-Governmental Organisations

REACH: Registration Evaluation Authorisation of Chemicals

SCENIHR: Scientific Committee on Emerging and Newly Identified Health Risks

SPE-AAS: Solid Phase Extraction coupled to Atomic Absorption Spectroscopy

UNEP: United Nations Environment Programme

WMO: World Meteorological Organisation

7. APPENDICES

(I) Summary table of the Commission's consultation concerning the Hg recycling level in porosimetry.

Summary of results of COM consultation concerning recycling on mercury porosimetery								
Code	*Stock of Hg for use in porosimetry (kg)*	*New Hg bought (kg/y)*	*Recycled Hg (kg/y)*	*Hg disposed as waste (kg/y)*	*Stock of oxidised Hg in-house (kg)*	*Price of New Hg (€/kg)*	*Cost of recycled Hg (€/kg)*	*Cost of disposed Hg waste (€/kg)*
1	40.0	1.0	10.0	0.1	0.2	150.0	15.0	10.0
2	15.0	2.0	5.0	2.0	0.0	220.0	----	4.0
3	15.0	1.0	0.0	0.0	1.0	30.0	----	----
4	8.0	0.0	4.0	0.0	0.0	----	550.0	----
5	9.0	1.0	1.0	1.0	2.0	----	----	----
6	22.0	0.0	20.0	2.3	0.0	----	----	----
7	10.0	0.0	0.0	0.0	0.0	----	----	----
8	17.0	43.0	17.0	67*	0.0	27.0	----	15.0
9	3.0	0.0	3.0	0.0	0.0	----	----	----
10	30.0	40.0	40.0	0.0	0.0	37.0	6.5	----
11	6.0	0.0	6.0	0.0	0.0	----	22.0	----
12	13.5	7.0	0.0	7.0	0.0	21.0	----	4.5

13	10.0	12.0	60.0	0.3	20.0	37.3	34.8	8.8
14	24.0	8.0	0.0	8.0	0.0	90.0	----	90.0
15	10.0	1.0	6.0	1.0	0.0	218.3	----	2.5
16	11.0	0.0	1.0	0.4	0.0	----	----	10.0
17	22.5	0.0	22.5	0.0	0.0	----	----	----
18	30.0	105.0	105.0	0.2	0.0	45	10	0.2
19	4.0	6.0	2.0	0.0	0.0	340.0	----	----
20	400*	0.0	50.0	5.0	60.0	----	----	80.0
21	50.0	0.0	15.0	1.0	20.0	----	44.0	----
22	20.0	0.0	5.0	0.0	0.5	----	8.0	----
23	16.0	12.0	4.0	12.0	1.0	38.0	----	0.5
24	3.0	0.0	95.0	5.0	0.0	----	----	----
25	20.0	2.0	0.0	0.0	0.0	30.0	----	----
26	15.0	0.5	10.0	0.0	10.0	47.1	15.1	4.6
27	40.0	0.0	30.0	0.0	0.0	----	14.0	----
28	8.0	0.0	7.0	1.0	0.0	----	----	6.9
29	173.0	0.0	14.0	1.0	0.2	----	----	3.4
30	5.0	8.8	8.8	0.0	2.5	53.0	2.0	0.0
31	10.0	40.0	40.0	0.0	0.0	37.8	10.0	----
32	27.0	1.0	54.0	1.0	0.0	47.0	----	15.0
33	4.0	20.0	16.0	0.0	0.0	40.0	7.0	----
34	10.0	0.0	5.0	1.0	0.0	----	----	3.7
35	4.0	4.0	1.0	0.0	1.0	----	----	----
36	5.0	1.0	1.0	0.0	0.0	150.0	60.0	----
37	16.0	12.0	20.0	8.0	0.0	55.0	18.0	20.0
38	6.0	9.0	0.0	9.0	0.0	76.0	----	----
39	10.0	5.0	5.0	5.0	5.0	24.2	----	----
40	5.0	0.5	0.5	0.5	0.0	----	----	----
41	6.0	1.0	0.0	1.0	0.0	79.0	----	----
42	6.5	6.5	7.0	0.4	0.0	62.0	33.0	----
43	17.5	0.5	20.0	0.1	7.5	55.0	15.0	17.0

44	40.0	10.0	0.0	0.0	0.0	87.8	----	----
45	6.0	3.0	0.0	3.0	3.0	77.0	----	3.3
46	12.0	0.0	18.0	0.0	5.0	45.7	15.1	----
47	15.0	0.5	15.0	0.5	0.0	1000*	15.1	----
48	10.0	10.0	10.0	0.0	0.0	25.0	9.0	----
49	14.0	0.0	1.0	0.0	0.0	----	----	----
50	1.5	2.5	0.0	1.5	1.0	230.0	----	----
51	4.0	6.0	0.0	6.0	0.0	484.6	----	4.0
52	39.0	0.0	20.0	0.3	0.0	----	13.0	13.0
53	18.0	0.0	18.0	0.5	0.0	0.0	61.0	----
54	0.5	5.0	20.0	0.0	0.0	150.0	1.6	----
55	6.0	0.5	0.5	0.5	0.5	----	----	----
56	10.0	0.0	0.0	0.1	0.0	----	----	----
57	6.0	0.0	0.0	0.0	0.0	----	----	----
58	3.0	36.0	36.0	0.0	0.0	33.0	6.0	----
59	10.0	0.0	9.0	1.0	5.0	37.0	6.5	----
60	10.0	3.0	7.0	3.0	0.0	137.0	----	----
61	20.0	1.0	10.0	0.0	0.0	90.0	24.0	----
62	30.0	30.0	14.0	16.5	0.0	35.0	25.0	1.2
63	1.0	0.1	0.9	0.1	0.0	----	----	----
64	10.0	10.0	10.0	0.0	0.0	37.3	6.5	4.0
65	20.0	4.0	4.0	4.0	0.0	15.0	15.0	----
66	20.0	0.0	15.0	3.0	0.0	----	15.0	17.0
67	51.0	2.0	200*	1.9	0.0	43.2	13.3	4.5
68	12.0	10.0	10.0	0.0	0.0	89.2	4.6	----
69	7.5	2.5	2.0	0.5	2.5	88.0	----	----
70	10.0	2.0	10.0	0.0	0.0	341.0	40.0	----
Average	**17.2**	**7.2**	**13.6**	**1.7**	**2.1**	**93.3**	**35.2**	**13.2**
Total	1138	479	941	114	148	not applicable	not applicable	not applicable

The values indicated by (*) were excluded from analysis (as considered to be unrepresentative)
All the price information is converted to €.
If the answer is presented as range of values, an average is reported in the table.

(II) List of material available on circa

(http://circa.europa.eu/Members/irc/enterprise/lmudsp/library?l=/thematic_folder/mercury_follow_up&vm=detailed&sb=Title)

1. ESH Guidelines for home BP, J.Hypertension (2007).
2. Minutes and presentations of the Commission Mercury Workshop (April 2009).
3. Options for reducing mercury use in products and applications, and the fate of mercury already circulating in society (COWI, 2008).
4. Alternatives to mercury-containing measuring devices (COWI 2006, EPA Denmark)
5. Mercury-free blood pressure measurement equipment (KEMI, Sweden, 2005).
6. Blood pressure monitors and sphygmomanometers. (MHRA, UK, 2005).
7. Mercury-free Health Care. Med.J.World (2008).
8. The global movement for Mercury free healthcare (HCWH, 2007).
9. Blood pressure measurement – is it good enough for accurate diagnosis of hypertension? (Current Controlled Trials in Cardiovascular Medicine, 2006).
10. Mercury in Healthcare (WHO, 2005).
11. End of an Era. The phase-out of Mercury Blood Measuring Devices. HCWH (2008).
12. Positions of (a) Member States (DE, FI, IE, IT, LA, LU, NL, PL, SE, HU, UK) and (b) associated industry (COCIR, AAMI, Russels Scientific) (c) NGOs (EEB, HCWH).
13. An Assessment of the Future Levels of Demand for Mercury in the UK. RPA (2009).
14. Report of the Independent Advisory Group on Blood Pressure Monitoring in Clinical Practice (BMP monitoring 2005)
15. Report from the EEB Conférence : EU Mercury phase-out in Measuring and Control Equipment (June, 2009).
16. The following indicative list of scientific publications:
Markandu et al. (2001); O' Brien (2000, 2003, 2005); O' Brien et al. (2005); Parati et al. (2006); Parati et al. (2008); Pickering et al. (2005); Pater (2005); Colloquit and Jones, 2002; Canzanello et al. (2001);Reinders et al. (2003) etc.

Opinion of the Scientific Panel on Contaminants in the Food Chain on a request from the Commission related to mercury and methylmercury in food

(Request N° EFSA-Q-2003-030)

(adopted on 24 February 2004)

SUMMARY

The Panel has been asked to assess the possible risks to human health from the consumption of foods contaminated with mercury and methylmercury, based on intake estimates for Europe and the provisional tolerable weekly intake (PTWI) established recently by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Mercury is an environmental contaminant that is present in fish and seafood products largely as methylmercury. Food sources other than fish and seafood products may contain mercury, but mostly in the form of inorganic mercury. Based on the available data the contribution to methylmercury exposure from these foods is considered to be insignificant. Inorganic mercury in food is considerably less toxic than methylmercury. Methylmercury is highly toxic particularly to the nervous system, and the developing brain is thought to be the most sensitive target organ for methylmercury toxicity. The JECFA established a Provisional Tolerable Weekly Intake (PTWI) of 1.6 µg/kg body weight based on two epidemiological studies that investigated the relationship between maternal exposure to mercury and impaired neurodevelopment in their children. A previous evaluation by the (U.S.) National Research Council (NRC) established an intake limit of 0.7 µg/kg body weight per week. The estimated intakes of mercury in Europe varied by country, depending on the amount and the type of fish consumed. The mean intakes were in most cases below the JECFA PTWI but the average intake in some countries exceeded the U.S.-NRC limit. High intakes may also exceed the JECFA PTWI. A probabilistic analysis of the French data indicated that children are more likely to exceed the PTWI than adults. Intake data from a recent large survey in Norway indicate that the intakes derived from the analysis of the SCOOP data (*scientific co-operation on questions relating to food*) may overestimate the true intakes of methylmercury for some countries, when the type of fish consumed consists of species with a relatively low concentration of methylmercury. There may be population-groups in Europe with a frequent consumption of large predatory fish, which are at the top of the food chain (for instance swordfish and tuna) which often have a higher concentration of methylmercury. These population-groups may therefore have higher dietary intakes than those found in populations with a high intake of fish containing low levels of methylmercury. Because the intake estimates for high consumers are close to the PTWI established by the JECFA, and exceed the limit established by the U.S.-NRC, reliable intake data should be established from studies focused on women of childbearing age. Methylmercury toxicity has been demonstrated at low exposure levels, and exposure to this compound should therefore be minimized, while recognising that fish constitutes an important part of a balanced diet.

KEYWORDS

Methylmercury, fish, seafood products, developmental neurotoxicity.

BACKGROUND

Mercury, in particular methylmercury, poses a risk to public health, for example, it can affect the development of the brain of infants and can cause neurological changes in adults. However, the extent of the possible risks to the health of EU consumers from mercury in foods is unclear. At present there is no EU scientific opinion on mercury in food. However, legislation setting maximum levels for mercury in fishery products has been in place since 1993. Originally, maximum levels were set in veterinary legislation (Decision 93/351/EEC[1]). In 2001 these provisions were consolidated via Decision 2001/182/EC[2] into Regulation (EC) No 466/2001[3] setting maximum levels for certain contaminants in food, as amended by Regulation (EC) No 221/2002[4].

In June 2003, the FAO/ WHO Joint Expert Committee on Food Additives (JECFA) revised its Provisional Tolerable Weekly Intake (PTWI) for methylmercury to 1.6 µg/kg body weight, whereas it was previously 3.3 µg/kg body weight.

The Member States have gathered data on levels of mercury in foods and have made limited estimates on dietary exposure as part of the scientific co-operation (SCOOP) task 3.2.11 (Decision 2001/773/EC[5]). The results indicate that some consumers may exceed the JECFA PTWI.

The maximum levels set for total mercury in Commission Regulation 466/2001 are under review. At present a maximum level of 0.5 mg/kg applies to fishery products, with the exception of certain listed fish species for which 1 mg/kg applies. In addition to fishery products, the data from some Member States indicate that elevated levels of mercury can be found in other foods.

With reference to the risk assessment already performed by the JECFA, an assessment of the risks from dietary exposure to mercury in the EU is necessary. This assessment would be used to support the scientific basis for reviewing the legislative measures on mercury in food, aimed to help reduce possible risks to EU consumers

[1] OJ L 144 16.6.1993 p23-24
[2] OJ L 77 16.3.2001 p22-23
[3] OJ L 77 16.3.2001 p1-12
[4] OJ L 37 7.2.2002 p4-6
[5] OJ L 290 7.11.2001 p9-11

TERMS OF REFERENCE

The European Commission requests that the European Food Safety Authority issues a scientific opinion on the assessment of the risks to EU consumers from mercury, in particular methylmercury, in food. Assessment of the contribution of different foods towards the overall human exposure should be included. Considerations on the respective risks to vulnerable groups should be made, in particular regarding pregnant women, the unborn child and children.

Interpretation of the terms of reference by the Panel

Evaluation of the hazard database on methylmercury by the Panel would be a major undertaking that appears unnecessary given the background to the Commission request, and would be incompatible with the time-frame available. The risk characterization given below relates to comparisons of European intake estimates, based on the recent SCOOP report, with the PTWI derived by the JECFA and also the value calculated by the U.S.-NRC. The latter limit has been used previously in an EC position paper prepared by an independent expert group in connection with the EU´s Fourth Daughter Directive on Air Quality (Pirrone *et al.*, 2001). Different PTWI values for methylmercury were estimated by the JECFA and the U.S.-NRC, largely because of different interpretations of the main epidemiology studies, which reported different findings and conclusions. The methylmercury database is complex and raises a number of issues that will need to be considered generically by the Panel. These are described later under hazard characterisation.

The JECFA and the U.S.-NRC evaluations were based on the effects of methylmercury exposure in epidemiology studies, while the SCOOP report describes total mercury intakes. The major source of methylmercury intake is fish and seafood products and the opinion concentrates on these sources. Considering the lack of consistent data on conversion factor to allow the fraction of mercury present as methylmercury, the intake estimates for total mercury have been considered to represent methylmercury. Other possible sources of human intake, such as might arise from the consumption of meat and meat products of animals fed methylmercury containing fishmeal, have not been considered but would need to be taken into account in any comprehensive evaluation of methylmercury intake.

ASSESSMENT

Intake Assessment

Mercury is widely distributed within food but methylmercury, its most toxic form, is found at significant levels only in fish and seafood products. Exposure to mercury from food sources other than fish and seafood products is not relevant in the present context because they contain

inorganic mercury, and would not contribute to the exposure to methylmercury, which is the subject of the JECFA and the U.S.-NRC risk assessments.

The present exposure assessment is based mainly on the scientific co-operation (SCOOP) task 3.2.11 report related to heavy metals (EC, 2003) and in particular on the chapter entitled "Dietary Intake of Mercury". In the SCOOP report, all the results are expressed as "total mercury" for the various food categories considered, because mercury speciation is not performed routinely by national control laboratories. In order to provide an intake estimate for methylmercury, only the results related to fish, crustaceans, bivalves and molluscs were considered. The highest proportion of total mercury present as methylmercury in fish and seafood products can be estimated assuming conservatively that all the mercury is methylmercury.

Assessment of the mean international dietary exposure based on the results in the SCOOP report

The SCOOP data on fish and seafood product contamination by mercury consists of 14,912 samples aggregated by the Member States into 196 analytical results. In order to generate a distribution curve for methylmercury concentrations in fish and seafood products, it was necessary to combine those data from different sources, i.e. from both individual and aggregated results from different countries (FAO/WHO Workshop – 2000). The combination of these data permits a mean contamination level to be calculated, with weighting as a function of the number of samples. In practice, the data were "disaggregated" by weighting each result by the number of single samples of which it was composed; the resulting weighted mean was 109 µg/kg food of total mercury. In addition, based on the assumption that the distribution of contaminant data follows a lognormal distribution, a log transformation of the data can provide the standard deviation and a simulated distribution including high percentiles.

The weighted mean contamination, which was based on all data for the mercury concentration in fish and seafood products submitted by the Member States, was 109 ± 845 µg/kg; the high standard deviation reflects the wide variations in the analytical results.

Because of the biological half-life of methylmercury in the human body (about 1.5 to 2 month) and considering that the toxicological endpoints are related to long term exposure, the assessment should be based on chronic dietary exposure assessment. Considering the distribution of both food ingestion and food contamination, a realistic way of expressing the exposure consists of combining the distribution of consumption with the mean (or the median) value for the level of contamination. Such an approach means that even a high consumer is very unlikely to be exposed regularly to highly contaminated food but more realistically to food for which the contamination is randomly distributed.

The mean daily consumption for fish and seafood products provided by the Member States ranged between 10g (the Netherlands) and 80g (Norway) per person (70 to 560 g/week). A simple calculation based on these values and the overall international average concentration shows that the mean estimated dietary exposure would be between 7 and 61 µg/person per week of total mercury; for a 60 kg adult this corresponds to 0.1 to 1.0 µg/kg body weight per week. The SCOOP data show that for a food item like fish the variation of mean consumption in different countries across Europe is very high and the variation in food consumption could result in exposures that vary by a factor 10.

This analysis is consistent with the range estimated by the JECFA in 1999 of 0.3-1.1 µg/kg body weight per week based on GEMS regional diet and a mean contamination level of 200 µg/kg of food.

Assessment of the high international dietary exposure based on the results in the SCOOP report

To assess the exposure of high consumers, the high percentiles for fish consumption may be combined with the international average level of contamination. The highest figure from the SCOOP was reported by Norway with consumption (at the 95th percentile) equal to 275 g/day of fish and seafood products (Table 1). Consumption of such an amount on a regular basis would result in an exposure of 3.5 µg/kg body weight per week of total mercury for a 60 kg adult. This calculation assumes that the high consumer eats fish and seafood products of a composition corresponding to the European average.

Assessments of the national dietary exposures based on the results in the SCOOP report

The data available in the SCOOP report are not suitable for a probabilistic analysis. Based on the results in the SCOOP document, national average exposures to total mercury from fish and seafood products are between 1.3 (the Netherlands) and 97.3 µg/week (Portugal), corresponding to <0.1 to 1.6 µg/kg body weight per week (assuming a 60 kg body weight for adults) (Table 1). Based on the results from the same report, the range of high exposure in Member States is estimated to be between 0.4 µg/kg body weight per week (Ireland) and 2.2 µg/kg body weight per week (Greece) of total mercury.

Table 1. Summary of the data for fish- and seafood product consumption and dietary intake of methylmercury (MeHg) from such foods according to the SCOOP task 3.2.11 for countries showing high and low intakes

	The Netherlands	Portugal	Ireland	Greece	France	Norway
Food consumption	*(g/day) Mean (High)*	*(g/day) Mean (High)*	*(g/day) Mean (High)*	*(g/day) Mean (High)*	*(g/day) Mean (High)*	*(g/day) Mean (High)*
- Fish and seafood[1]	*10 (-)*	*50 (-)*	*20 (75)*	*41 (71)*	*35 (-)*	*80 (275)*
Intake of MeHg[2]						
SCOOP: International dietary exposure[3]	*µg MeHg/kg bw/week*	*µg MeHg/kg bw/week*	*µg MeHg/kg bw/week*	*µg MeHg/kg bw/week*	*µg MeHg/kg bw/week*	*µg MeHg/kg bw/week*
- Mean	0.1	0.6	0.3	0.5	0.4	1.0
- High[4]		-	1.0	0.9	-	3.5
SCOOP: National dietary exposure[5]						
- Mean	<0.1	1.6	<0.1	0.5	0.3	0.4
- High	-	-	0.4	2.2	-	1.8

[1] *Including fish, crustaceans, bivalves and molluscs*

[2] *Assuming that all mercury is methylmercury*

[3] *Estimated intake = Consumption of fish- and seafood products x 109 µg/kg food.*

[4] *High percentile represents 95th or 97.5th percentile of the distribution depending of the country considered*

[5] *Estimated intake = Consumption of fish- and seafood products x national data for the concentration of mercury.*

The SCOOP data showed that, although the population in Norway had the highest total consumption of fish and seafood products, the estimated high intake of methylmercury from these foods was lower in Norway than, for instance, in Greece. The reason for this is probably that the type of fish consumed in Norway consists of species, such as cod and saithe, which contain relatively low levels of methylmercury. The consumption of large predatory fish, which are at the top of the food chain such as swordfish and tuna, which all contain higher levels of methylmercury, may be significantly greater in countries in southern Europe.

Refined intake assessment using national data

A probabilistic analysis of the likelihood of exceeding the PTWIs was carried out using the French contamination data as reported to SCOOP in combination with the distribution of fish and seafood product consumption in France (Table 2).

The probability for a population to reach an exposure over the JECFA-PTWI and the U.S.-NRC limit was calculated using an empirical method, in which the individual consumption of each consumer of seafood products is multiplied by the mean level of contamination. The empirical probability is calculated as the number of subjects with an intake greater than 1.6 µg/week divided by the total number of subjects in the survey.

Table 2. Exposure assessment and probability of overstepping the tolerable intakes based on the distribution of consumption and fish contamination in France (Tressou *et al.*, 2004).

Group	Number of subjects	Mean consumption (g/week)	Mean exposure (µg/kg bw/week)	50th %ile (µg/kg bw/week)	97.5th %ile (µg/kg bw/week)	Empirical probability of exceeding the PTWI (µg/kg bw/week)	
						JECFA (1.6)	U.S.-NRC (0.7)
Children 3-6 years	293	178	0.83	0.61	3.0	11.3%	44%
Adults 25-34 years	248	282	0.38	0.28	1.28	1.2%	17%

Children in the 3 to 6 year age group consume a greater amount of fish and seafood products than adults, when the consumption is expressed on a body weight basis. The calculated probabilities of exceeding the methylmercury exposure limits are therefore much higher for small children, who may then constitute a group with increased exposure.

It should be noted that these calculations were performed for a country in which fish and seafood products are consumed in relatively small amounts. For example, the consumption of fish at the 97.5th percentile intake in France is about 880 g per week/person corresponding to 125 g/day which is about one-half the amount consumed in Norway.

In addition, since the SCOOP-data were submitted, the Norwegian Food Safety Authority has made a more detailed intake calculation of mercury based on individual consumption figures for fish and seafood products and self-reported body-weight. The intake calculations were based on data on food consumption and the mean concentration of mercury in foods that were submitted to the SCOOP task. Instead of using single point estimates for food consumption (mean and 95th percentile), which was the case when assessing the mean and high intake of mercury for the SCOOP task, the new intake estimate was based on the distribution of the consumption values. This means that the individual consumption estimate for each species of fish and seafood products was multiplied with the concentration value for this particular fish species and seafood products. Subsequently, the intake of mercury from each of the fish and seafood products was totalled for each individual. The resulting distribution of the total intakes of all the participants was used to derive the mean and 95th percentile intake of mercury. The self-reported body weight of each participant was used in order to calculate the intakes expressed on a body weight basis.

Based on the distribution of the intake of mercury among the consumers of fish and seafood products (n=5696) the estimated intake of mercury was 1.0 µg/kg body weight per week (at the 95th percentile). Female participants of childbearing age (n=1565) had an estimated high intake of mercury (95th percentile), equal to the intake among the rest of the participants.

These estimates show a considerably lower high-level intake from fish and seafood products than the high international estimated exposure of 3.5 µg/kg body weight/week for Norway. This is mainly due to a lower concentration in the fish most commonly eaten in Norway (i.e. <50 µg/kg fish) than the mean concentration of 109 µg mercury/kg fish used when estimating the international intakes of the substance. However, the estimates are also lower than the SCOOP high national intake for Norway (1.8 µg/kg body weight/week). This may be explained by the methods used for estimating the exposure. As mentioned before, the SCOOP estimates were based on single points estimates for consumption (95th percentile) combined with single point estimates for concentration, which generates higher high-level intakes than when the distribution of individual intake estimates are used to derive high-level intake.

Hazard Characterisation

Evaluations of methylmercury by the JECFA and by the U.S.-NRC

In 1999, the fifty-third meeting of the JECFA reviewed information that had become available since its previous evaluation, particularly the information available on neurobehavioral development in children in the Faroe Islands and Seychelles. Because of the absence of any clear indication of a consistent risk in the epidemiology studies available at that time, the fifty-third meeting recommended that methylmercury should be re-evaluated at a subsequent meeting, in order to consider the 96-month evaluation of the Seychelles cohort and other relevant data that may have become available. The provisional tolerable weekly intake (PTWI) for methylmercury was not reconsidered and was maintained at the value established previously (200 µg of methylmercury equivalent to 3.3 µg per kg of body weight). This value was originally based on adverse effects in adults exposed during a poisoning outbreak in Iraq, and did not allow for the fact that the foetus could be more susceptible than the mature organism.

The sixty-first meeting of the JECFA in 2003 (JECFA, 2003) reviewed new data and analyses from the Seychelles Islands cohort and concluded that no adverse effects of prenatal methylmercury exposure had been detected in this cohort, in which intake occurs mainly from high levels of fish consumption. In contrast, neuropsychological deficits that correlated with the extent of methylmercury exposure have been detected consistently in a cohort of children in the Faroe Islands, in which intake occurs mainly from the consumption of whale meat. Stratifying analyses of the data from the Faroe Islands were used to allow for any confounding by possible neurotoxic effects of PCBs which are contaminants in whale blubber. The results from the two cohorts were combined in the JECFA evaluation, and the JECFA concluded that both were consistent with the absence of appreciable adverse effects in children born to mothers with hair concentrations of 14 µg mercury/g maternal hair. However, the Panel noted that this hair level was not a NOAEL in the data from the Faroe Islands. Information from other studies, including data from exposed cohorts in Iraq and New Zealand, were not incorporated quantitatively in the combined exposure-response assessment because these data were derived from smaller cohorts or differed substantially in study design.

The maternal hair concentration of 14 µg mercury/g was converted by the JECFA to a blood concentration using the average hair:blood ratio from a number of studies of Caucasian and Oriental subjects; the resulting maternal blood concentration (0.056 mg/L) was converted to a daily intake (1.5 µg/kg body weight) using an equation which incorporated the rate of elimination. Uncertainty factors were applied to allow for interindividual variability in the hair:blood ratio (2-fold) and in the rate of elimination ($10^{0.5}$ or 3.16-fold). Uncertainty factors for interindividual variability in (toxicodynamic) vulnerability or for incompleteness of the database were considered not to be necessary. Thus the PTWI was estimated as 1.6 µg/kg body weight/week ([1.5/6.32] µg/kg body weight/day). The JECFA considered that the available data

for other effects, such as cardiotoxicity, were not conclusive and could not be used as a basis for estimating the PTWI.

As directed by the U.S. Congress, the U.S. Environmental Protection Agency (EPA) asked the U.S.-NAS to perform an evaluation of the toxicological effects of methylmercury and to prepare recommendations on the establishment of a scientifically appropriate methylmercury exposure reference dose (RfD) (NRC, 2000). The U.S.-NRC used benchmark dose level from the Faroes study (12 µg mercury/g maternal hair) and used a composite uncertainty factor of 10, to take into account interindividual variability and incompleteness of the data base, to derive an exposure limit of 0.1 µg/kg body weight per day or 0.7 µg/kg body weight per week. Further probabilistic modelling including the results of the three prospective studies (Faroe Islands, New Zealand, and Seychelles Islands) led basically to the same outcome. This limit agreed with the limit calculated previously by the U.S.-EPA on the basis of marked adverse effects in children prenatally exposed to methylmercury during a poisoning incident in Iraq, but the U.S.-NRC suggested that the justification should be based on the more recent epidemiological evidence on children exposed prenatally.

These risk assessments are based on studies of internal dose, as reflected by mercury concentrations in blood or hair. They have then been translated to average daily intake levels that can be compared with intake assessment included in the present opinion.

Evaluation of methylmercury by the Scientific Panel on Contaminants in the Food Chain

The Panel agrees with the JECFA and the U.S.-NRC evaluations that the developing brain should be considered the most sensitive target organ for methylmercury toxicity. The Panel also agrees with the JECFA that human risk assessment is possible on the basis of the prospective epidemiological studies on childhood development. However, an increasing body of data is now indicating that raised methylmercury exposure may augment the risk of cardiovascular morbidity and mortality (JECFA, 2003), but the complexity of the information available precludes a conclusion at this time.

There is a very large toxicity database from animal and epidemiology studies, and substantial complexity involved in assessing dose-response relationships from the available epidemiological data. In addition, the mathematical conversion of the exposure biomarker in the different cohorts into intake estimates depends on several assumptions, each associated with some degree of uncertainty. The Panel has noted that different approaches and uncertainty factors have been used in recent evaluations (e.g. the JECFA and the U.S.-NRC).

In interpreting the JECFA evaluation, several aspects should be kept in mind, which might lead to a lower exposure limit, such as the one determined by the U.S.-NRC. First, the benchmark dose level is a statistically defined point of deviation, and whether in the case of methylmercury it is consistent with a negligible adverse effect, as was concluded by the JECFA, will require careful and detailed consideration. Second, exposure assessment in epidemiological studies is

always imprecise, since the exposure is not controlled *a priori*. In the case of methylmercury, calculation of the intake is complex because it is based on the conversion of biomarker data such as hair levels into daily intake. Imprecision in intake estimates may lead to underestimation of the true mercury effect and to an overestimation of the benchmark dose level. Third, epidemiology studies are associated with uncertainty because the effect of a single factor is ascertained in a situation where many covariates may affect the outcome. There are a large number of potential confounders in the main epidemiology studies on methylmercury, such as the source and pattern of methylmercury exposure, the nature of the populations, the influence of nutrition, and the presence of other pollutants such as PCBs, which make comparison of the studies and interpretation of the data difficult. Factors of potential relevance to the performance of children in neuropsychological tests, and that were not considered in the study reports include the possibility of an uneven distribution of parental consanguinity in isolated island populations which has been reported for the Faroe Islands and which could result in a depression of the performance of the children, and a number of other social, nutritional and environmental factors. All of these complexities need to be taken into account in evaluating the dose-response relationships and in assessing the adequacy of the uncertainty factors used in the recent evaluations.

The reduction of the PTWI for methylmercury by the JECFA at its latest meeting is justified because the new PTWI is based on the most susceptible lifestage, i.e. the developing foetus and intake during pregnancy, rather than on the general adult population, which was the basis for their previous evaluation. The recent evaluations by the JECFA and the U.S.-NRC considered several sources of uncertainties. The health based guidance values differed by a factor of two, and arose largely because of the different uncertainty factors used. Any refinement of the hazard characterisation for methylmercury will be dependent on resolution of a number of generic issues that have been raised above. The Panel recognises that this will require the establishment of working groups by the EFSA Scientific Committee.

Risk characterisation

Exposure evaluation based on the SCOOP data can be compared to the new PTWI of the JECFA. Comparison with the lower U.S.-NRC limit may offer additional guidance.

Fish and seafood products are important sources of energy, protein, and a variety of essential nutrients, such as vitamins, trace elements, and fatty acids. The nutrient contents vary between species, and dietary advice should seek to optimize the contribution of fish and seafood products to a healthy diet, while at the same time minimizing the exposure to contaminants, such as methylmercury.

Simplistic analyses of the data in the SCOOP report indicated that the international mean intake of methylmercury was below the PTWI established by the JECFA in 2003. Population-groups who frequently consume large predatory fish, such as swordfish, tuna, and halibut, may have a

considerably higher intake of methylmercury and exceed the PTWI. Based on national data the highest average intake estimates were just at the PTWI and exceeded the U.S.-NRC exposure limit.

Analyses were done on national data sets in order to assess the probability of intakes above the PTWI established by the JECFA in 2003. The limited data available indicate that proportions of young children may exceed the PTWI when expressing exposure on a body weight basis. In addition, a percentage of adult populations with higher fish consumption would be predicted to have intakes above the PTWI. Nevertheless, the quality of data at European level is not sufficient to assess the size of these population groups.

CONCLUSIONS AND RECOMMENDATIONS

The major source of methylmercury intake in humans is fish and seafood products. Specifically, large predatory fish which are at the top of the food chain, such as swordfish and tuna, which all contain higher levels of methylmercury, are significant sources of human exposure to methylmercury. Food sources other than fish and seafood products may also contribute mercury exposure, but mainly in the form of inorganic mercury that would not affect the current opinion on methylmercury.

The developing brain is the most sensitive target organ for methylmercury toxicity; *in utero* exposure is believed to be the critical period for methylmercury neurodevelopmental toxicity, although the duration of increased susceptibility may extent into postnatal development. To derive a PTWI, the JECFA used the data from two major epidemiological studies of foetal neurotoxicity performed in the Faroe Islands and the Seychelles Islands thereby basing its evaluation on the most sensitive population. The data from the SCOOP report indicate that the average intake of fish and seafood products in some countries may be close to the JECFA PTWI and, when compared to the previously established U.S.-NRC limit, some average intake levels may exceed this limit. Specific intake data for pregnant women are not available.

The data available in the SCOOP report do not allow reliable estimations of the intakes by high consumers in different populations. Because in some cases the estimated intakes based on the SCOOP report are close to or exceed the PTWI, specific intake studies, especially for women and children, should be performed on methylmercury. A more complete evaluation of exposures in Europe that includes data on internal dose levels would allow direct comparison of exposure with the dose-effect relationships, which are the basis for the hazard characterisation.

Mercury compounds serve no biological purpose in the human body. Methylmercury toxicity has been demonstrated at low exposure levels, and exposure to this compound should therefore be minimized, while recognizing that fish represents an important part of a balanced nutrition.

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European Food Safety Authority

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Mercury as undesirable substance in animal feed[1]

Scientific opinion of the Panel on Contaminants in the Food Chain

Question N° EFSA-Q-2005-288

Adopted on 20 February 2008

This opinion, published on 1 December 2008, replaces the earlier version published on 9 April 2008[2].

PANEL MEMBERS

Jan Alexander, Guðjón Atli Auðunsson, Diane Benford, Andrew Cockburn, Jean-Pierre Cravedi, Eugenia Dogliotti, Alessandro Di Domenico, Maria Luisa Férnandez-Cruz, Peter Fürst, Johanna Fink-Gremmels, Corrado Lodovico Galli, Philippe Grandjean, Jadwiga Gzyl, Gerhard Heinemeyer, Niklas Johansson, Antonio Mutti, Josef Schlatter, Rolaf van Leeuwen, Carlos Van Peteghem and Philippe Verger.

[1] For citation purposes: Opinion of the Scientific Panel on Contaminants in the Food chain on a request from the European Commission on mercury as undesirable substance in feed, *The EFSA Journal* (2008) 654, 1-76.

[2] In chapter 8 on page 50 the CONTAM Panel clarified the derivation of a no-observed-adverse effect level for cats and the possible health effects for these animals in relation to the current EU maximum levels. This clarification now takes into account a 12% water content of the feed material and consequently the respective figure in the conclusion was revised. The changes do not affect the overall conclusions of the opinion. To avoid confusion, the original version of the opinion has been removed from the website, but is available on request as is a version showing all the changes made.

SUMMARY

Mercury exists in the environment as elemental mercury (metallic), inorganic mercury and organic mercury (primarily methylmercury). Elemental and inorganic mercury released into the air from mining, smelting, industrial activities, combustion of fossil fuels, is deposited to soil, water and thereby to sediments where the mercury is transformed into methylmercury. Methylmercury bioaccumulates and biomagnifies along the food chain, particularly in the aquatic food chain; longlived carnivorous fish and marine mammals exhibiting the highest contents. The toxicity and toxicokinetics of mercury in animals and humans depends on its chemical form. Elemental mercury is volatile and mainly absorbed through the respiratory tract, whereas its absorption through the gastrointestinal tract is negligible. Gastrointestinal absorption of inorganic mercury is in the 10-30% range. Following absorption, inorganic mercury distributes mainly to the kidneys and, to a lesser extent, to the liver. The critical effect of inorganic mercury is renal damage. In animals, as in humans, methylmercury and its salts are readily absorbed in the gastrointestinal tract (>80%). Absorbed methylmercury is widely distributed to all tissues, although the largest deposition occurs in the kidney. Excretion of unchanged methylmercury occurs predominantly in the faeces through biliary excretion. The enterohepatic cycle results in a long half-life for this compound compared to inorganic mercury. Methylmercury is able to cross the blood-brain and the placental barriers. As a consequence, the nervous system is the primary site of toxicity in animals and humans. In humans, effects on neurological development have been observed in children of mothers orally exposed to methylmercury. Animal studies confirmed these neurodevelopmental effects in foetus of dams exposed to methylmercury in the diet.

A substantial number of feed materials have been analysed for total mercury in recent years within the EU Member States, and for the large majority, the concentrations were below the maximum level specified in the feedingstuffs legislation. The most common source of mercury in feed materials is fishmeal, however, in this category, no sample exceeded the maximum level of 0.5 mg/kg. In contrast, approximately 8% of the complete feedingstuffs for fish exceeded the maximum level of 0.1 mg/kg. The relatively few data available on the speciation of mercury in fishmeals indicate that it is mainly present as methylmercury. The most sensitive domestic animal species to methylmercury toxicity are cats and mink. Based on the available data on the occurrence of total mercury in feed materials and complete feedingstuffs, it is unlikely that these species will be exposed to toxic levels.

The maximum concentration reported in farmed salmonids is approximately five times lower than the EU maximum level for mercury in fish for human consumption (500 µg/kg for salmonids). This mercury concentration in salmonids would allow weekly consumption of two fish meals, as recommended by nutritionists, without appreciable health risk. The maximum level for fish feed is sufficient to ensure that contamination levels in farmed salmonids pose no appreciable risk to consumers, but the validity of the maximum level need to be ascertained for other farmed fish.

KEYWORDS: Mercury, methylmercury, organic mercury, inorganic mercury, animal feed, occurrence, toxicity, analysis, bioaccumulation, carry over, animal health, human health, human exposure.

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BACKGROUND AS PROVIDED BY THE REQUESTOR

1. General background

Directive No (EC) 2002/32 of the European Parliament and of the Council of 7 May 2002 on undesirable substances in animal feed[3] has, since 1 August 2003, replaced Council Directive No (EC) 1999/29 of 22 April 1999 on the undesirable substances and products in animal nutrition[4].

The main modifications can be summarised as follows

- extension of the scope of the Directive to include the possibility of establishing maximum limits for undesirable substances in feed additives.
- deletion of the existing possibility to dilute contaminated feed materials instead of decontamination or destruction (introduction of the principle of non-dilution).
- deletion of the possibility for derogation of the maximum limits for particular local reasons.
- introduction of the possibility of the establishment of an action threshold triggering an investigation to identify the source of contamination ("early warning system") and to take measures to reduce or eliminate the contamination ("pro-active approach").

In particular the introduction of the principle of non-dilution is an important and far- reaching measure. In order to protect public and animal health, it is important that the overall contamination of the food and feed chain is reduced to a level as low as reasonably achievable, thereby providing a high level of public health and animal health protection. The deletion of the possibility of dilution is a powerful means of stimulating all operators throughout the chain to apply the necessary prevention measures to avoid contamination as much as possible. The prohibition of dilution accompanied with the necessary control measures will effectively contribute to safer feed.

During the discussions prior to the adoption of Directive No (EC) 2002/32 the Commission made the commitment to review the provisions laid down in Annex I on the basis of updated scientific risk assessments, taking into account the prohibition of any dilution of contaminated non-complying products intended for animal feed. The Commission therefore requested the Scientific Committee on Animal Nutrition (SCAN) in March 2001 to provide these updated

[3] OJ L140, 30.5.2002, p. 10
[4] OJ L 115, 4.5.1999, p. 32

scientific risk assessments in order to enable the Commission to finalise this review as soon as possible (Question 121 on undesirable substances in feed)[5].

The opinion on undesirable substances in feed, adopted by SCAN on 20 February 2003 and updated on 25 April 2003[6] provides a comprehensive overview on the possible risks for animal and public health as the consequence of the presence of undesirable substances in animal feed.

It was nevertheless acknowledged by SCAN itself and by the Standing Committee on the Food Chain and Animal Health that for several undesirable substances additional detailed risk assessments are necessary to enable a complete review of the provisions in the Annex.

2. Specific background

Mercury in the natural environment is present in both inorganic and organic forms. The inorganic forms are less toxic, but can be converted into organic form by the micro-flora and micro-fauna in the environment. Among organic forms, the most toxic is methylmercury. Chromatographic techniques to separate organic mercury from inorganic mercury are available and validated. However they are not used routinely because of their complexity and cost. As a consequence, only total mercury content is routinely determined, mostly by atomic absorption spectrometry.

Directive No (EC) 2002/32 of the European Parliament and of the Council of 7 May 2002 on undesirable substances in animal feed establishes maximum levels for total mercury in feed materials and compound feed.

SCAN concluded[7] that the ions and elements, including mercury, listed in Council Directive No (EC) 2002/32 are commonly encountered substances with known toxicity. In each case, the contribution of food products of animal origin to the human exposure is limited and listing of these elements as undesirable substance in feed, although concomitantly contributing to an overall reduction of human exposure to toxic forms, is mainly justified by reasons of animal health.

SCAN concluded furthermore that a detailed risk assessment of the presence of mercury in animal feed and the possible effects for animal health and public health is necessary and that this detailed assessment should address the risks related to the organic forms of mercury.

[5] Summary record of the 135th SCAN Plenary meeting, Brussels, 21-22 March 2001, point 8 – New questions (http://europa.eu.int/comm/food/fs/sc/scan/out61_en.pdf)
[6] Opinion of the Scientific Committee on Animal Nutrition on Undesirable Substances in Feed, adopted on 20 February 2003, updated on 25 April 2003 (http://europa.eu.int/comm/food/fs/sc/scan/out126_bis_en.pdf)
[7] Opinion of the Scientific Committee on Animal Nutrition on Undesirable Substances in Feed, point 6.11. Conclusions and recommendations.

Indeed, methylmercury is recognised as significantly more toxic than inorganic mercury and therefore the determination of total mercury in feed may not always accurately reflect the risk posed by the organic forms.

TERMS OF REFERENCE AS PROVIDED BY THE REQUESTOR

In accordance with Article 29 (1) of Regulation (EC) No 178/2002 the European Commission asks the European Food Safety Authority requests to provide a scientific opinion on the presence of mercury in animal feed.

This detailed scientific opinion should comprise the

- determination of the toxic exposure levels (daily exposure) of organic forms of mercury (methylmercury) and, if relevant, of inorganic mercury for the different animal species (difference in sensitivity between animal species) above which
    - signs of toxicity can be observed (animal health / impact on animal health) or
    - the level of transfer/carry over of organic forms of mercury (methylmercury) and inorganic mercury from the feed to the products of animal origin results in unacceptable levels of organic forms of mercury (methylmercury) and, if relevant, of inorganic mercury in the products of animal origin in view of providing a high level of public health protection[8].
- identification of feed materials which could be considered as sources of contamination by mercury and the characterisation, insofar as is possible, of the distribution of levels of contamination, in particular the typical ratio between mercury in organic forms and mercury in inorganic forms for the different (groups of) feed materials.
- assessment of the contribution of the different identified feed materials as sources of contamination by organic forms of mercury (methylmercury) and if relevant of inorganic mercury
    - to the overall exposure of the different relevant animal species to organic forms of mercury (methylmercury) and inorganic mercury,
    - to the impact on animal health,

[8] The possible risks to human health from the consumption of foods contaminated with mercury and methyl mercury has been assessed by EFSA – Opinion of the Scientific Panel on Contaminants in the Food Chain on a request from the Commission related to mercury and methyl mercury in food (Request N° EFSA-Q-2003-030, opinion adopted on 24 February 2004), EFSA Journal (2004) 34, 1-14
http://www.efsa.eu.int/science/contam/contam_opinions/259/opinion_contam_01_en1.pdf

- to the contamination of food of animal origin (the impact on public health), taking into account the ratio between mercury in organic forms and mercury in inorganic forms, the dietary variations and variable carry over rates (bio-availability) depending on the nature of the different feed materials and the form in which mercury is present [9].

- identification of eventual gaps in the available data which need to be filled in order to complete the evaluation.

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ASSESSMENT

1. Introduction

Mercury (Hg) and its compounds are ubiquitous and persistent in the environment. Mercury is a naturally occurring element that is released from a variety of sources including human activities. Once released into the environment, mercury undergoes a series of complex chemical and physical transformations as it cycles between atmosphere, land, and water. Humans, plants, and animals are routinely exposed to mercury and accumulate it during this cycle, potentially resulting in a variety of health impacts.

Mercury may exist in elemental, inorganic or organic forms.

Elemental (or metallic) mercury is a liquid at normal ambient temperatures and pressures; it partitions strongly to air in the environment. Most of the mercury encountered in the atmosphere is elemental mercury gas, whereas in all other environmental compartments inorganic mercury salts and organomercurials predominate.

[9] Importance of the human exposure to mercury from foods of animal origin compared to overall human dietary mercury exposure can be assessed making use of the information contained in the report on a task on human exposure assessment to mercury which has been recently performed at EU level within the framework of co-operation by Member States in the scientific examination of questions related to food (SCOOP – Task 3.2.11) http://europa.eu.int/comm/food/food/chemicalsafety/contaminants/scoop_3-2-11_heavy_metals_report_en.pdf

Inorganic mercury compounds are salts and are used in numerous industrial processes. They have been extensively used in batteries and included in products such as fungicides, antiseptics or disinfectants.

There are several organic mercury compounds; however, by far the most common in the environment and in the food chain is methylmercury. Organic mercury compounds have been used as fungicides and as pharmaceutical agents (Mercurochrome as topical antiseptics; Thiomersal as a preservative in vaccines). Phenylmercury salts were used as fungicides and in pharmaceutical and cosmetic preparations to control growth of microbial organisms while the primary use of phenylmercury acetate was in latex paint as a preservative. Like the inorganic mercury compounds, methylmercury, ethylmercury and phenylmercury exist as salts such as chloride or acetate.

Although inhalation of gaseous mercury in ambient air, ingestion of drinking water contaminated with mercury, and exposure to mercury through medical treatments can contribute to the exposure to this contaminant in animals and in humans, dietary intake is considered as the most important source of non accidental and non occupational exposures to mercury (ATSDR, 1999).

1.1. Chemistry

Mercury occurs in three valence states: elemental mercury (also known as metallic mercury, Hg^0), monovalent-mercurous (Hg_2^{++}), and the divalent mercuric (Hg^{++}); the Hg^0 and Hg^{++} being the most important in nature. Elemental mercury is the most stable form and does not react readily with oxygen, although thermodynamically favoured, or water (Cotton and Wilkinson, 1988). Generally, mercuric and mercurous mercury are thermally unstable and readily decompose to elemental mercury during heat treatment, exposure to light and reducing agents. Hg^0 is only slightly water-soluble (Table 1), and is more soluble in non-polar organic solvents than water. Hg^0 is relatively volatile and vapours of elemental mercury can occur at room temperature presenting a hazard if spillages occur.

The most common and abundant mineral of mercury is the red cinnabar (mercuric sulfide), HgS. HgS precipitating in for example sediments is black, metacinnabar. HgS is water insoluble and Hg^{++} has generally high affinity for sulfur and mercaptans; even elemental mercury reacts with elemental sulfur and hydrogen sulfide (but not mercaptans) (Nowak and Singer, 2000; Wilhelm *et al.,* 2006). Hg^{++} has affinity for Group VIb elements in the order: O<<S<Se≈Te, and the affinity of Hg^{++} decreases in the order $RS^->SH^->OH^->Cl^-$ which is of general importance for speciation of Hg^{++}. Organic matter, especially humic substances, abundant in soil, water and sediments, forms very stable complexes with Hg^{++} which are relatively insensitive to pH (Jackson, 1998; Skyllberg *et al.* 2006). Mercuric chloride ($HgCl_2$) is a linear molecule in the solid state and exists almost entirely as discrete covalent and linear molecules in aqueous solutions and organic solvents (Greenwood and Earnshaw, 1997).

$HgCl_2$ is soluble in water, Table 1, but also in some organic solvents (Nowak and Singer, 2000).

Mercurous chloride (Hg_2Cl_2) contains the diatomic cation Hg_2^{++} and is very unstable in most natural environments; it forms no stable aqueous complexes and disassociates spontaneously to elemental mercury and complexed Hg^{++} in the presence of ligands that bind Hg^{++} (Jackson, 1998) or at pH > 3-4 (Lindqvist *et al.*, 1991).

Methylmercury chloride and other halides of methylmercury, together with dimethylmercury are linear molecules like $HgCl_2$. As the Hg-C bond is highly covalent, organometallic Hg^{++} compounds are resistant to oxidation and hydrolysis and are kinetically stable (but not thermodynamically) in water and O_2 (Jackson, 1998). Dimethylmercury is much more lipophilic than methylmercury and devoid of dipole moment with stable, largely covalent bonds that do not dissociate in water at pH > 5.6 (Fagerström and Jernelöv, 1972). Below pH 5, dimethylmercury is thermodynamically unstable in water and is spontaneously converted to methylmercury (Fagerström and Jernelöv, 1972; Jackson, 1998). Dimethylmercury is also very volatile, practically insoluble in water and with high Henry's law constant and therefore dimethylmercury, like Hg^0, readily escapes into the atmosphere from water surfaces, whereas methylmercury, like $HgCl_2$, has a greater tendency to be retained in water (Jackson, 1998). The chemical affinities of methylmercury for ligands, including organic matter, is analogous to Hg^{++} but the stability constants of methylmercury complexes with these ligands are consistently lower than for the corresponding Hg^{++} complexes. Furthermore, unlike Hg^{++}, methylmercury easily and rapidly exchanges one thiol group for another, a property that has been suggested to explain why methylmercury spreads more easily through internal tissues of both plants and animals than inorganic Hg^{++}, which has a greater tendency to be retained at the point of entry (Jackson, 1998; Boudou *et al.*, 1991). Due to the complex speciation chemistry of mercury compounds in aquatic systems, apparent K_{ow}, water solubility, vapour pressure, and Henry's law constant are strongly affected by pH, salinity, concentration and nature of complexing ligands, temperature, ionic strength, and redox potential.

Table 1. Physical and chemical properties of major toxicologically relevant mercury compounds (adapted from ATSDR, 1999, except noted otherwise).

Chemical name	Elemental mercury[a]	Mercuric chloride	Mercurous chloride[b]	Methylmercury chloride[c]	Dimethyl mercury
Molecular formula	Hg^0	$HgCl_2$	Hg_2Cl_2	CH_3HgCl	CH_3HgCH_3
CAS N°	7439-97-6	7487-94-7	10112-91-1	115-09-3	593-74-8
Oxidation state	0	+2	+1	+2	+2
Molecular weight	200.6	271.5	472.1	251.1	230.7
Water solubility, g/L	5.6×10^{-5} at 25°C	69 at 20°C	2.0×10^{-3} at 19°C	<0.1 at 21°C 5-6 at 25°C[g]	Practically insoluble, see text
Vapor pressure, Pa	0.27 at 25°C 0.18 at 20°C[g]	133 at 136.2°C 9×10^{-3} at 20°C[g]	$\approx10^{-5}$ at 25°C[j]	1.1 at 25°C 1.76 at 25°C[g]	7.8×10^{3} at 23.7°C[d] 8.3×10^{3} at 25°C[g]
Log K_{ow}	0.62[g]	-0.215[e] -0.30[g] 0.52[h]	No data	0.41[e] 0.23[h]	2.28
Henry's law constant, Pa m^3/mol	729 at 20°C[g]	3.69×10^{-5} at 20°C[g]	No data	3.8×10^{-2} at 15°C and pH 5.2[g]	646 at 25°C[g] 340 at 0°C[i]

[a]Also known as metallic mercury

[b]Also known as calomel

[c]Methylmercury chloride is used experimentally to investigate the effects of methylmercury

[d]Long and Cattanachi, 1961; [e]Halbach, 1985;.[f]Greenwood and Earnshaw, 1997; [g]Schroeder and Munthe 1998; [h]Mason *et al.* 1995.[i]Schlüter 2000; [j]Lindqvist *et al.* 1991.

1.2. Production, uses, and environmental fate

1.2.1. Production

The terrestrial abundance of mercury is of the order of 50 µg/kg (range of 30-1000 µg/kg) (DeVito, 2005) and mainly found in the mercuriferous belt where most of principal mercury deposits are found (Schlüter, 2000).

The world production of mercury peaked in the early 1970s at about 10,000 tons annually. In 2000, the global primary production was about 2,000 tonnes/year with additional approximately 2,000 tonnes/year from secondary production (UNEP, 2002; RPA, 2002).

Mercury compounds used as pesticides are subject to the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade, implemented in the Community by Regulation (EC) No. 304/2003[10]. This Regulation also bans the export of cosmetic soaps containing mercury, and requires notification of mercury compounds for all other uses. However, there are no Community or international restrictions on trading elemental mercury (EC, 2005).

1.2.2 Use

The current global mercury demand is around 3,600 tonnes per year. The main global uses are in batteries, gold mining, and the chlor-alkali industry, which together accounted for over 75% of the worldwide mercury consumption (EC, 2005). In 2003, the 15 EU Member States used around 300 tonnes annually (EC, 2005) as compared to estimated 448 tonnes per year in 1993 or 11.7% of the global usage (UNEP, 2002). Mercury has also been widely used in the production of dental amalgam.

Mercury compounds were widely used as pesticides and fungicides in agriculture since the beginning of the 20th century resulting in high concentrations of mercury in intensively cultivated soil. Various alkyl mercuric compounds were produced for use as disinfectants in agriculture but were banned or severely restricted in many countries around 1970. Mercury compounds are still in use for agricultural purposes in some countries, *e.g.* in Australia, Belarus, India, Benin, Burkina Faso, Yvory coast, Ghana, and Guinea (UNEP, 2002).

1.2.3 Environmental fate and levels

Atmosphere

Mercury exists in ambient air predominantly in gaseous form, *i.e.* 90-95% as monoatomic gas (Hg^0) (Schroeder and Munthe, 1998). Small amounts of mercury are in the particulate phase (Lindqvist *et al*., 1991) and minor quantities as methylmercury or up to 5% of total mercury in precipitation, usually around 1.5% (Downs *et al.*, 1998; Lindqvist *et al*., 1991; Glass and Sorensen, 1999; Grigal, 2002). Dimethylmercury has also been found in air but it is expected to be very short-lived due to rapid oxidation with a half-life of only several hours (Niki *et al.*, 1983; Lin and Pehkonen, 1999).

The main natural sources of mercury to air are degassing of mercury from mineral deposits and aquatic and terrestrial systems, volcanic emissions, and forest fires. The total natural

[10] Regulation (EC) No. 304/2003 of the European Parliament and of the Council of 28 January 2003 concerning the export and import of dangerous chemicals, OJ L 63, 6.3.2003.

emission was estimated to be about 2,500 tonnes annually in the late 20th century, where Europe accounts for 250-300 tonnes/year (Nriagu, 1989; Nriagu, 1990; Axenfeld *et al.*, 1991; Pacyna *et al.,* 2001).

The total global anthropogenic emission has been estimated to be about 2,000 tonnes in 1995-2000 where a decrease in emissions by about 60% in the last 20-30 years has been estimated (Pacyna *et al*., 2006a; Pirrone *et al.* 1996; Lamborg *et al.* 2002; Nriagu, 1989; Nriagu and Pacyna, 1988). The main source is coal combustion accounting for two thirds of the global emission. Between 1990 and 2000, the emission rates have decreased most significantly in Europe and North America but an increase of more than 50% was observed in Asia of which half originated in China (Pacyna *et al.*, 2006a and 2006b). As regards Europe, countries in the central and eastern part generate the highest emissions (Pacyna *et al*., 2006b).

Presently, the global average level of mercury in the atmosphere is 1.6 ng/m^3 (Lamborg *et al*., 2002). The total mercury levels in rain are usually in the range of 1-50 ng/L (Lindqvist *et al*., 1991; Hall, 1995; Downs *et al*., 1998), while results from unpolluted North Temperate areas indicate a volume weighted average of 5-15 ng/L (Grigal, 2002). The main form of mercury found in precipitation is Hg^{++} following oxidation of elemental mercury by mainly ozone in the aqueous phase (Munthe *et al*., 1991; Hall, 1995; Lin and Pehkonen, 1999). Several studies indicate a long-term decrease in levels of mercury in the atmosphere of Europe and North-America in the last 20-30 years (Iverfeldt *et al.,* 1995; Slemr and Schell, 1998; Kock *et al*., 2005; Steffen *et al*., 2005; Temme *et al*., 2007; Wängberg *et al.* 2007).

Soil

Reflecting deposition from air, the dominant form of mercury in soil is Hg^{++}. Recent studies by Skyllberg *et al.* (2006) show that inorganic mercury in soil is strongly complexed to organic matter. Methylmercury is typically present at 0.01-2% of the total mercury with most data <1% (Lindqvist *et al*., 1991; Davis *et al*., 1997; Grigal, 2003) with dimethylmercury levels at <1000 times the concentrations of methylmercury (Davis *et al*., 1997). Hence, mercury has a long retention time in soils, and mercury accumulated may continue to be released to surface waters and other media for long periods of time, possibly hundreds or even thousands of years (UNEP, 2002; Hissler and Probst, 2006).

Volatilisation from soils is preceded by reduction of ionic mercury to elemental mercury (biotic and abiotic) (Zhang and Lindberg, 1999; Jackson, 1998) after which Hg^0 is volatilised at rates dependent on temperature (Schlüter, 2000; Scholtz *et al*., 2003), soil water content, pH, and clay and soil organic matter content (Ericksen *et al*., 2006; Grigal, 2002; Zhang and Lindberg, 2002).

Agricultural soils, and the vegetation growing on them, usually contain very little mercury, although a considerable range of concentrations in soils has been reported. Archer and Hodgson (1987) suggested that a 'normal' range was 0.02 to 0.40 mg/kg; contents exceeding

these values should be considered contaminated from anthropogenic or other sources (Kabata-Pendias, 2001).

Urban soils contain higher and more variable levels of mercury than rural and agricultural soils, while soils close to natural or anthropogenic sources may contain very high levels (Schlüter, 2000; Tack *et al*., 2005; Rodrigues *et al*., 2006).

Vegetation

Uptake of mercury from soils by vascular plants is very limited with concentrations of mercury in plants being significantly lower than in soil where roots act as important adsorption sites and barriers for mercuric mercury transport (Grigal, 2002, 2003; Millhollen *et al.* 2006). In contrast, the atmosphere is almost the exclusive source of mercury in vegetation (Grigal, 2003; Ericksen *et al*., 2003; Rea *et al*., 2001; Millhollen *et al*, 2006). Foliage not only receives mercury from air by dry deposition but also via uptake of gaseous Hg^0 (and gaseous Hg^{++}-compounds) (Grigal, 2002). The mercury accumulated in the leaves does not transport to other parts of trees or only to a very limited extent (Lindqvist *et al*., 1991). The average ratio of methylmercury to total mercury in tree litterfall, predominantly foliage, is generally very similar to that in precipitation, indicating atmosphere as the main source (Grigal, 2002, 2003).

Total concentration of mercury in vegetation, excluding nonvascular plants, is generally less than 0.1 mg/kg dry weight in background areas (Lindqvist *et al*., 1991). Reported foliar levels of trees differ widely depending on atmospheric concentrations and differences in uptake efficiencies.

Aquatic systems and sediments, methylation

Mercury is present in various physical and chemical forms in the natural aquatic environment. The main chemical species are complexes of the mercuric ion with various organic and inorganic ligands, elemental mercury, methylmercury and dimethylmercury.

Speciation of the Hg^{++}-ion in oxygenated water is largely dominated by organic complexes, and in freshwater, more than 90% of Hg^{++} is complexed by dissolved organic matter and most methylmercury as well (>70%) (Ullrich *et al*., 2001). In anoxic waters, however, the speciation chemistry of Hg^{++} and methylmercury is governed by sulfide (Jackson, 1998).

Between 10 and 30% of dissolved mercury in oceans and lake water is elemental mercury (Ullrich *et al*., 2001) and surface waters are usually supersaturated in Hg^0 with respect to the atmosphere, especially during summer (Gårdfeldt *et al*., 2001; Anderson *et al*., 2007). Hg^0 in aquatic systems derives from various biotic and abiotic reduction processes of Hg^{++} species.

Methylmercury concentrations of up to 10% of total mercury in lake water in Sweden have been reported (Lindqvist *et al*., 1991), while dimethylmercury is normally not detected (Ullrich *et al*., 2001). In ocean water, methylmercury usually accounts for between 10 and 40% of total mercury (Leermarkers *et al*., 2001; Kotnik *et al*., 2007; Horvat *et al*., 2003;

Mason and Sullivan, 1999; Mason *et al*., 1998). Methylmercury is formed by methylation of Hg^{++}-compounds by abiotic but mostly biotic processes, both in the water column and, most actively, in the sediments. The methylation process is not fully understood and a wide variety of factors may affect the rate of methylation and demethylation (Ullrich *et al*., 2001).

Dimethylmercury is usually only found in deep ocean waters at very low levels, *e.g.* at <0.5% of total mercury in the Mediterranean Sea and only at depths below 20 to 40 m (Kotnik *et al*., 2007; Horvat *et al*., 2003). Dimethylmercury is predominantly found in some sediments, believed to be formed from methylmercury in the presence of sulfide (Quevauviller *et al.,* 1992; Baldi *et al.,* 1995; Weber *et al*., 1998; Stein *et al*., 1996).

Uncontaminated freshwaters generally contain <5 ng/L total mercury median values of 3.1 to 6.2 ng/L in 25 Swedish lakes were reported (Lindqvist *et al*., 1991), although up to 10 or 20 ng/L can be found in humic lakes or rivers rich in particulate mercury (Ullrich *et al*., 2001). Contaminated waters may, however, be in the µg/L range (Ullrich *et al*., 2001). Total mercury concentrations in the marine environment are much lower and range between 0.1 to 1 ng/L (Leermarkers *et al*., 2001; Kotnik *et al*., 2007; Horvat *et al*., 2003; Mason and Sullivan, 1999; Mason *et al*., 1998).

Since methylation of mercury occurs almost solely in aquatic systems, aquatic biota and fish eating birds and animals usually contain much higher levels of mercury than terrestrial animals. Additionally, the concentrations usually increase with trophic level and age. For example, Arctic zooplankton contains between 1 to 10 µg/kg wet weight while top predators like beluga whale (toothed whale, *Delphinapterus leucas*), polar bears (*Ursus maritimus*) and ringed seals (*Phoca hispida*) may contain >10,000 µg/kg in their livers (Dehn *et al*., 2006). However, trophic status or age is not the only factors governing the mercury level. The highest levels of mercury in marine mammals are usually found in kidneys and livers. In muscle tissue, the main form of mercury is methylmercury, while the proportion of methylmercury - particularly in livers of many marine mammals and seabirds - decreases with increased total concentration of mercury indicating demethylation in these animals (Gaskin *et al*., 1979; Falconer *et al*., 1983; Chen *et al*., 2002; Endo *et al*., 2004; Thompson and Furness, 1989; Wagemann *et al*., 1998, 2000).

1.3. Hazard assessment for humans

This chapter is not intended to be an exhaustive review of the voluminous literature published on health effects of mercury. Rather, the purpose is to present a brief survey of the available data regarding the three forms of mercury. Because organic mercury is the predominant form to which humans are exposed via food, the sections related to elemental and inorganic mercury only focus on major issues.

Mercury is highly toxic to most forms of life but its toxicity depends on its chemical form, and thus symptoms and signs are rather different after exposure to elemental mercury,

inorganic mercury compounds, or organic mercury compounds. Elemental mercury is relatively inert and not readily taken up by the gastrointestinal tract in vertebrates, but it is volatile and its vapour is toxic. Mercuric salts are also highly toxic, but of even greater concern is the ability of micro-organisms to methylate mercury and its salts to produce species, such as methylmercury (CH_3Hg^+) and dimethylmercury ($(CH_3)_2Hg$) (Rowland *et al*. 1980).

1.3.1. Elemental mercury

In animals, as in humans, effects on the nervous system appear to be the most sensitive toxicological endpoint observed following exposure to elemental mercury. Symptoms associated with elemental mercury-induced neurotoxicity include tremors, irritability, nervousness, excessive shyness, insomnia, neuromuscular changes, polyneuropathy, memory loss and performance deficits in test of cognitive function (US-EPA, 1997). At higher concentrations, adverse renal effects and pulmonary dysfunction may also be observed. However, the toxicity of elemental mercury is essentially due to the vapour, and, therefore, of limited concern in this opinion.

1.3.2. Inorganic mercury

The kidney appears to be the critical target organ for the effects of acute ingestion of inorganic mercury compounds, although there are several animal studies in which inorganic mercury-induced neurotoxicity has been reported.

Acute oral exposures of rats and mice to inorganic mercury at 2-5 mg/kg b.w. per day resulted in an increased kidney weight. Higher doses induced tubular necrosis (US-EPA, 1997). Males showed increased sensitivity, resulting in more severe histological changes than females (Fowler, 1972; NTP, 1993).

Long-term studies have also demonstrated histopathological effects affecting the tubules and glomeruli, including thickening of basement membranes and degeneration of tubular cells (Carmignani *et al.,* 1989; Jonker *et al.,* 1993; NTP, 1993). A no observed adverse effect level (NOAEL) for rat of 0.23 mg/kg b.w. per day has been identified for renal effects in a 26 week study (ATSDR, 1999). Autoimmune glomerular nephritis has been induced in genetically susceptible strains of rats and mice. When rodents are treated with mercuric chloride, they produce antibodies which attack the kidneys causing an autoimmune glomerulonephritis (NRC, 2000). Evidence exists that human exposure to inorganic mercury can trigger an autoimmune response. Tubbs *et al.* (1982) reported deposits of IgG and complement C3 were found in the glomeruli of two workers exposed to inorganic mercury.

Other commonly reported effects in rodents include signs of cardiovascular toxicity (e.g. increased blood pressure and changes in the contractility of the heart), irritation of the gastrointestinal mucosa, reproductive toxicity (e.g. changes in the estrous cycle and ovulation), and developmental toxicity (e.g. increased number of abnormal foetuses) (US-

EPA, 1997). Such effects were seen at doses of 0.3 mg/kg b.w. per day (cardiovascular toxicity, only one dose tested) and ≥2 mg/kg b.w. per day (other effects).

In a recent study, male mice were repeatedly orally dosed with mercuric chloride during the pre-mating and mating periods, whereas females were similarly exposed during pre-mating, mating, gestation and lactation periods (Khan *et al.*, 2004). The results showed that oral exposure to between 0.25 and 1 mg/kg b.w. per day of mercuric chloride produced adverse effects on reproductive performance of mice but without overt mercury toxicity in dams.

Mercuric chloride has produced some positive results for clastogenicity in a variety of *in vitro* and *in* vivo genotoxicity assays. Conflicting results regarding its mutagenic activity have been reported (WHO-IPCS, 2003)

DNA damage (single strand breaks) has been reported in rat and mouse fibroblasts as well as CHO cells and human cells. There are positive results for induction of chromosomal aberrations in mice exposed by gavage (Ghosh *et al.*, 1991) but contrasting data for chromosome aberrations and SCE induction in rodent and human cells in vitro. Mercuric chloride was not mutagenic in Salmonella typhimurium but it was positive for the induction of gene mutations in mouse lymphoma cells (NTP, 1993; IARC, 1997; US-EPA, 1995).

Studies in rats administered with mercuric chloride orally gave weakly positive results for dominant lethal mutation (Zasukhina *et al.*, 1983) and a slight reduction of the numbers of implants and living embryos in female mice admistered by intraperitoneal injection (Suter, 1975; WHO-IPCS, 2003).

There is equivocal evidence of carcinogenicity of mercuric chloride in animals. Focal papillary hyperplasia and squamous cell papillomas of the forestomach, together with thyroid follicular adenomas and carcinomas, were observed in male rats gavaged with 3.7 mg mercuric chloride/kg b.w. for 2 years (NTP, 1993). In the same study, evidence for increased incidence of squamous cell forestomach papillomas in female rats and renal adenomas and carcinomas in male mice were observed. However, the forestomach tumours did not progress to malignancy and were thought to arise from the hyperplastic response of the tissue (US-EPA, 1997). The kidney tumours observed in mice occurred at doses that were also nephrotoxic, and would be expected to arise by a non-genotoxic mechanism (ATSDR, 1999). There are no data available on the carcinogenic effects ofinorganic mercury in humans.

1.3.3. Organic mercury

Nearly all of the available toxicity studies for organic mercury compounds are for methylmercury. Toxic effects have been demonstrated in animal studies and observed in humans. Mitochondrial changes, induction of lipid peroxidation, microtubule disruption, and disrupted protein synthesis have all been proposed as possible mechanisms of methylmercury neurotoxicity (ATSDR, 1999; NRC, 2000).

The severity of the symptoms may depend on the concomittant presence of other environmental contaminants able to enhance the oxidative damage induced by organic mercury (Yoneda and Suzuki, 1997). It has been observed in experimental animals that the presence of dietary antioxidants (i.e. Vitamin E and selenium) could mitigate the toxic effects. The significance for humans is uncertain (Stohs and Bagchi, 1995).

1.3.3.1 *In vitro* and animal data

Oral exposure of laboratory animals to methylmercury levels >0.5 mg/kg b.w. resulted in damage to the kidneys, stomach and large intestine, changes in blood pressure and heart rate, as well as adverse effects on sperm, and male reproductive organs. In addition, several studies have reported an increase in embryonic lethality, decrease in foetus body weight and teratogenicity in rats (cleft palates, vertebral defects, histological abnormalities in the cerebellum, effects on lachrymal glands and ribs) (ATSDR, 1999).

Although there is emerging evidence that the cardiovascular and immune systems might also be sites of its toxicity, the critical organ for methylmercury adverse effects is the brain. Both the adult and foetal brains are susceptible to methylmercury toxicity. In adult rodents, the major clinical effects include motor disturbances, such as ataxia, tremors and paralysis, as well as signs of sensory dysfunction, such as impaired vision. The predominant neuropathological feature is degenerative changes in the cerebellum, which is likely to be the mechanism involved in many of the motor dysfunctions (US-EPA, 1997). The developing nervous system appears to be more sensitive. Animal studies provide evidence of damage to the nervous system from exposure to methylmercury during development, and these effects remain/continue to develop during aging, even after the exposure stops. Developmental neurotoxicity has been observed in offsprings of rats, mice and guinea pigs treated orally with levels of methylmercury <1 mg/kg b.w. per day during gestation, lactation and/or post weaning. Some studies suggest that cats and monkeys are more susceptible to the neurotoxic effects of organic mercury than rodents. Visual defects have been reported in monkeys (NRC, 2000).

Mutagenicity and genotoxicity of methylmercury have been investigated *in vitro* and *in vivo.* In reviews of WHO-IPCS (1990), NTP (1993), IARC (1997), US-EPA (1995), and NTP (2000), methylmercury was not found to be a weak mutagen, but appears to be capable of causing chromosomal damage and DNA strand breaks in a variety of systems including yeast, bacteria, fish cells, mammalian cells, human lymphocytes and brain cell lines. Tests for unscheduled DNA synthesis, sister chromatid exchange, chromosomal aberrations and dominant lethal mutations in mammals *in vivo* have given conflicting results. Tests for clastogenicity in fish and amphibians have provided more convincingly positive results. Strain-specific differences exist with respect to the ability of methylmercury to produce dominant lethal effects in mice (Suter *et al*., 1975). Nondisjunction and sex-linked recessive lethal mutations were reported in Drosophila melanogaster treated with methylmercury in the diet (Ramel, 1972). There are data showing induction of changes in chromosome number in

oocytes of Syrian hamsters treated by i.p. with methylmercuric chloride (Mailhes, 1983). The doses of methylmercury chloride that induced sister chromatid exchange in cultured human lymphocytes were 5-25 times lower than those needed of mercuric chloride, whereas 5-10 times lower doses of methylmercury chloride than mercuric chloride were required to induce polyploidy (NTP, 1993; IARC, 1997; US-EPA, 1995). In summary, these data indicate that methylmercury is clastogenic but not a potent mutagen.

Data from animal studies show some evidence of carcinogenicity in two strains of mice but studies in rats are negative. In ICR and B6C3F1 mice exposed orally to methylmercuric chloride, only males were observed to have an increased incidence of renal adenomas, adenocarcinomas, and carcinomas. Renal epithelial cell hyperplasia and tumours, however, were observed only in the presence of profound nephrotoxicity suggesting that the tumours may be a consequence of reparative changes to the damaged kidneys. No increase in tumor incidence was observed in studies conducted in rat and cat. Tumours were observed at a single site, in a single species and sex. Therefore they are considered to provide limited evidence of carcinogenicity (US-EPA, 1997; NRC, 2000).

1.3.3.2 Human data

Accidental methylmercury poisoning in humans has been reported on a number of occasions. From the methylmercury poisoning episodes in Japan (Minamata Bay and Niigata, 1956-1965) and Iraq (1956 and 1959-1960) it appeared that the most severe effects take place in the development of the brain and nervous system of the foetus. The reports on the Minamata outbreak described only slight symptoms in the mothers whose children had been exposed *in utero.* These children had cerebral palsy and/or microcephaly, and it was concluded that the foetus was more sensitive to the effects of methylmercury than adults (WHO-IPCS, 1976). Further analysis of the Japanese and Iraqi data revealed additional information on the effects of prenatal methylmercury exposure, such as the limitation of the growth of the foetal brain and the inhibition of the migration of neurones from the embryological generation layer to the final destination in the cortex. Clinical examination revealed behavioural changes and reduced cognitive and motor ability in children exposed *in utero*.

The primary human exposure to methylmercury is from fish consumption. Research efforts have therefore focused on individuals consuming large amounts of seafood with the aim to determine if chronic exposure from this source could present a health risk. A series of large epidemiological studies have provided evidence that methylmercury present in pregnant women's diets appears to have subtle, persistent effects on the children's mental development as observed at about the start of the school age (NRC, 2000).

In 1989-1990, a cohort of 779 children in a fish-eating population of the Seychelles Islands was enrolled to study the developmental effects of prenatal methylmercury exposure (Davidson *et al.,* 1998). The cohort was prenatally exposed to methylmercury from maternal fish consumption, and the children started consuming fish products at about 1 year of age.

Prenatal exposure was measured in maternal hair and recent postnatal exposure in the child's hair. The cohort was examined six times over 11 years using an extensive battery of age-related developmental tests. Mean maternal hair mercury concentration was 6.8 µg/g hair (range 3-26.7 µg/g hair)[11]. Analyses of a large number of developmental outcomes showed no convincing evidence for an association between prenatal exposure and child development in this fish-eating population (Myers *et al.,* 2003). More recent analyses however have suggested that latent or delayed adverse effects might be emerging at maternal exposure above 10-12 µg/g (measured in maternal hair) as the children mature. This suggests that the association between prenatal exposure and child development may be more complex than originally believed (Davidson *et al.,* 2006). A subsequent study of another Seychelles cohort showed that a negative mercury effect was present when the neurodevelopmental outcomes were adjusted for the positive effects of n-3 fatty acids (Strain *et al*., 2007).

In 1986-1987, a cohort of 1,022 births was studied in the Faroe Islands, where increased methylmercury exposure occurs from traditional seafood diets that include pilot whale meat. Cohort members underwent detailed neurobehavioral examination, and blood and hair samples obtained from the participants were analysed for mercury. The neuropsychological test battery was designed for assessing motor speed, visuospatial function, attention, language, and verbal memory. Median maternal hair mercury concentration was 4.5 µg/g hair (range 0.17-39.1 µg/g hair). At seven years of age, clear dose-response relationships were observed for deficits in attention, language, and memory. An increase in blood pressure was also associated with the prenatal exposure level (Sørensen *et al*., 1999). At the age of 14 years, methylmercury exposure was significantly associated with deficits in tests of motor, attention, and verbal ability. Postnatal methylmercury exposure had no discernible effects (Debes *et al.,* 2006), but the current exposure at age 14 years was associated with an increased latency for peak V on the brainstem auditory evoked potentials (Murata *et al*., 2004). These findings are similar to those obtained for the age of 7 years and an analysis of the test score difference between results at 7 and 14 years suggested that mercury-associated deficits had not changed between the two examinations. The most recent report from this cohort showed that, when adjusting for the beneficial effects of maternal fish intake during pregnancy, the mercury effects tended to increase, with the greatest impact on mercury-associated deficits on motor function (Budtz-Jørgensen *et al*., 2007).

A smaller prospective study in Boston showed that visual recognition memory in children aged 6 months decreased at increasing maternal hair-mercury concentrations, but this association was only statistically significant after adjustment for maternal fish consumption during pregnancy (Oken *et al*., 2005). All these observational studies confirmed that the

[11] A daily average methylmercury intake of 0.1 µg/kg b.w. per day by an adult woman is estimated to result in hair mercury concentrations of about 1 µg/g (NRC, 2000). According to research at the Center for Air Toxic Metals (CATM) there is linear relationship between intake and concentrations of methylmercury in hair http://www.undeerc.org/catm/pdf/area4/MercuryMetabolism2004.pdf

developing foetus is the most sensitive sub-population and that nervous system domains involving motor function, attention, verbal learning and memory can be affected by methylmercury exposure. Overall, the published evidence suggests that mercury toxicity may in some cases be hidden by the beneficial effects of nutrients from fish.

1.4. Evaluations and classifications

JECFA re-evaluated the PTWI for methylmercury and lowered it from 3.2 to 1.6 µg/kg b.w. per week, based on two epidemiology studies (see above, chap. 1.3.3.2.) that investigated the relationship between maternal exposure to mercury and impaired neurodevelopment in their children (FAO/WHO, 2003).

In a previous evaluation, the NRC (2000) used benchmark dose level from the Faroes study (12 µg mercury/g maternal hair) and used a composite uncertainty factor of 10, to take into account interindividual variability and incompleteness of the data base, to derive an exposure limit of 0.1 µg/kg b.w. per day or 0.7 µg/kg b.w. per week.

An International Programme on Chemical Safety (IPCS) Working Group (WHO-IPCS, 2003) recommended a TDI of 2 µg/kg b.w. for inorganic mercury, based on the NOAEL of 0.23 mg/kg b.w. per day for kidney effects in a 26-week study in rats (NTP, 1993) and applying an uncertainty factor of 100 (for inter- and intra-species variation) after adjusting for 5 days per week dosing. A similar TDI was obtained by applying an uncertainty factor of 1000 (an additional uncertainty factor of 10 for adjustment from a lowest observed adverse effect level (LOAEL) to a NOAEL) to the LOAEL for renal effects of 1.9 mg/kg b.w. per day in a 2-year study in rats (NTP, 1993).

Mercuric chloride was classified by IARC in group 3 (not classifiable as carcinogenic to humans), based on limited evidence in experimental animals, and by US-EPA in group C (possible human carcinogen), based on the absence of data in humans and limited evidence of carcinogenicity in rats and mice. Methylmercury was classified by US-EPA in group C and by IARC in group 2B (possibly carcinogenic to humans) (IARC, 1993; US-EPA, 1995).

The available human data are inconclusive regarding the carcinogenicity of methylmercury in humans exposed by the oral route (US-EPA, 1997).

2. Methods of analyses

No analytical methods are prescribed by the European Commission for the determination of mercury in animal feed.

2.1. Determination of total mercury

Most data regarding mercury in feed relate to total mercury. Total mercury is most frequently analysed by cold vapour atomic absorption spectrometry (CV-AAS) after acidic digestion of the biological samples as described by Hatch and Ott (1968). The sensitivity is about 1 ng mercury (corresponding to a limit of quantification (LOQ) of less than about 0.030 mg/kg dry weight in compound feedingstuffs and biological samples) where further sensitivity enhancement may be obtained by amalgamation. However, sensitivity enhancement is usually not necessary for feeds. A further enhancement of sensitivity by two orders of magnitude and better selectivity may be obtained by cold vapour atomic fluoresence (CV-AFS) instead of atomic absorption (Sánchez Uria and Sanz-Medel, 1998).

The main advantage of the cold vapour technique is the separation of the analyte from the potentially interfering sample matrix. The most frequently occurring interference in CV-AAS is that of nitrites and nitric oxides reducing the signal of mercury (Jones, 1997; Nunes *et al.,* 2005) requiring either stripping the sample digest with inert gas or treating it with reducing agents. Samples rich in iodine, like kelp, may require removal or sequestering of iodine to prevent it from interfering with the analysis.

Another technique, offering somewhat better sensitivity than CV-AAS (by a factor of about 3) and greater selectivity, is direct analysis of the sample digest by inductively coupled plasma mass spectrometry (ICP-MS) (Krata and Bulska, 2005; Palmer *et al.,* 2006), a technique that is increasingly being used. Recently, a interlaboratory study was reported by the Nordic Committee on Food Analysis (NMKL) where ICP-MS was used for total mercury in foodstuffs after pressure digestion of the samples in nitric acid (Julshamn *et al*., 2007). However, it has been shown that nitric acid may suppress the signal of mercury during analysis by ICP-MS (Quevauviller *et al.,* 1993; Jian *et al.,* 2000; Krata and Bulska, 2005). The method gave very satisfactory results for total mercury down to 40 μg/kg dry weight, while the LOQ was at 10 μg/kg dry weight.

CV-AAS and CV-AFS and increasingly ICP-MS have been used for a wide variety of organic and inorganic samples with good results although some modifications or care may be required for certain types of samples. Since maximum levels of the current EU-legislation (see Chapter 3) are well above the limits of detection (LODs) and LOQs of these techniques, the data obtained must be considered as satisfactory. However, participation in proficiency testing programmes and intercomparison exercises of appropriate sample matrices is highly recommended for laboratories producing results for mercury in feed materials as an integral part of their quality control schemes.

2.2. Determination of organic mercury compounds

Gas chromatography (GC) with both packed and capillary columns has been the most widely used technique for the separation of mercury species while high performance liquid

chromatography (HPLC) is increasingly being applied (Sánchez Uria and Sanz-Medel, 1998; Carro and Mejuto, 2000; Harrington, 2000). The detection of mercury species by GC has mainly been carried out by electron capture detector (ECD) which is, however, not specific to mercury. Cold vapour atomic absorption spectrometry (CV-AAS) and cold vapour atomic fluorescence spectrometry (CV-AFS) are therefore more appropriate for detection, together with microwave induced plasma atomic emission spectrometry (MIP-AES), inductively coupled plasma atomic emission spectrometry (ICP-AES), mass spectrometry, and increasingly ICP-MS (Sánchez Uria and Sanz-Medel, 1998; Carro and Mejuto, 2000; Willoud *et al.,* 2004).

Extraction procedures vary but most are based on the initial work of Westöö (1966, 1967, 1968) where the sample is treated with hydrochloric acid to release methylmercury from sulfhydryl groups and sodium chloride to enable its recovery into the organic phase (benzene or toluene). Inorganic mercury remains in the aqueous phase. The organic phase is further back extracted to aqueous cysteine solutions to purify the extract. Modifications have included other organic phases, thiosulfate instead of cysteine, application of copper(II) to release methylmercury from proteins, use of bromide or chelating agents to improve extraction, further purification by back-extraction into organic phase, and defatting the samples prior to digestion to prevent emulsifications (Carro and Mejuto, 2000; Sánchez Uria and Sanz-Medel, 1998).

Some workers have analysed the extracted mercury species as for total mercury, denoting it as organic mercury, and the aqueous phase of the sample for Hg^{++}. Other workers differentiate between inorganic and organic mercury compounds by selective reduction where the samples are treated with stannous chloride, reducing Hg^{++} to Hg^{0} and leaving Hg-C bonds intact. After complete purging of Hg^{0} it is analysed by CV-AAS or CV-AFS, while the remaining sample, assumed to contain only organic mercury, is analysed as for total mercury.

Instead of extraction, biological samples treated with sulfuric acid and iodoacetic acid have been subjected to steam distillation where volatile methylmercuryiodide is distilled off. The distillate is usually derivatised with sodium tetraethylborate (forming methylethylmercury) to improve sensitivity and performance of the GC-analysis. However, the steam distillation may produce methylmercury from Hg^{++} as an artefact (Bloom *et al.,* 1997).

Alkaline digestions, usually in the presence of cysteine to avoid losses of methylmercury hydroxides and to stabilise the Hg-C bond, with subsequent acidification and extraction of methylmercury as above, have also been used. The hydroxide releases methylmercury quantitatively from proteins. This procedure is often followed by derivatisation with sodium tetraethylborate prior to GC-analysis. However, in the presence of high levels of inorganic mercury, Hg^{++} may be converted to methylmercury during derivatisastion (Delgado *et al.* 2007).

By using HPLC instead of GC for separation, the derivatisation procedure may be omitted and the cleanup becomes less critical. Digestion may be carried out in aqueous cysteine hydrochloride directly at 60°C and the solution analysed for methylmercury and Hg^{++} with reversed-phase HPLC after simple filtration (Hight and Cheng, 2006; Chiou *et al.,* 2001; Percy *et al.,* 2007). Precision and accuracy in single-laboratory validations have been shown to be satisfactory, but validation by way of intercomparison and/or interlaboratory studies is required. Although these methods appear promising, they have only recently been introduced and are therefore currently not in widespread use. Detection by CV-AAS, CV-AFS, MS or ICP-MS methods are all suitable as regards sensitivity for samples of feeds. The advantage of MS and ICP-MS are their multi-element and multi-isotope capabilities, whereas CV-AAS and CV-AFS have the advantage of being comparatively low cost and simple operations (Armstrong *et al.,* 1999; Cai *et al.,* 2000; Krata and Bulska, 2005).

Once in solution, methylmercury may decompose when exposed to light. pH, ionic strength, acidity, temperature, type of containers etc. may also affect the stability (Yu and Yan, 2003; Hight and Cheng, 2006; Delgado *et al.,* 2007; Devai *et al.,* 2001).

Dimethylmercury is, for several reasons, not reliably determined by most of the methods above (Puk and Weber, 1994; Leermakers *et al*., 2005).

3. Statutory limits

Mercury is listed in the Annex to Directive No (EC) 2002/32 on undesirable substances in animal feed[12]. The maximum levels (MLs) are shown in Table 2 below.

Table 2. EU legislation on total mercury in feed materials.

Product intended for animal feed	**Maximum content in mg/kg relative to a feedingstuff with a moisture content of 12%**
Feed materials with the exception of: - feedingstuffs produced by the processing of fish or other marine animals - calcium carbonate	0.1 mg/kg 0.5 mg/kg 0.3 mg/kg
Complete feedingstuffs with the exception of: - complete feedingstuffs for dogs and cats	0.1 mg/kg 0.4 mg/kg
Complementary feedingstuffs except - complementary feedingstuffs for dogs and cats (Article 6 of 2002/32)	0.2 mg/kg

[12] OJ L140, 30.5.2002, p. 10

No information on national or international standards for mercury in feed outside the EU has been identified.

4. Occurrence in feed and animal dietary exposure

As described above, mercury exists in elemental, organic and inorganic forms. The determination of mercury concentrations in feed materials are undertaken by Member States as part of routine surveillance programmes. Because legislation specifies MLs of total mercury, differentiation into the different forms of mercury are not normally undertaken. Therefore, data provided by Member States and presented in this section refer to total mercury.

4.1. Occurrence in feeding materials

SCAN (EC, 2003) concluded that mercury uptake by plants from soil is low, and that levels of mercury in plant material is independent of the soil mercury concentration. Studies by Ericksen *et al.* (2003) confirmed that nearly all of the mercury found in the foliage originated from the atmosphere. In general, therefore, it appears that mercury levels in plants are more likely to be related to atmospheric levels than soil concentrations. For non-plant feed materials, SCAN identified fishmeal to be the most common source of mercury for farmed animals under normal farming conditions .

In order to estimate levels of exposure to mercury by farmed livestock and fish within Europe, European countries were invited to provide information on levels of mercury in feedingstuffs acquired as part of routine surveillance programmes. Data on levels of mercury in 3,253 samples of feed were received from 13 European countries (Table 3) for the period 2002-2006.

Table 3. Number of samples of animal feedingstuffs analysed for mercury in the period 2002-2005 as reported by Member States, Iceland and Norway.

Country	Number of samples analysed in year						
	2002	2003	2004	2005	2006	Total	% of samples received
Belgium			25	183	75	283	8.7
Cyprus			3		2	5	<1
Czech Republic				69	184	253	7.8
Denmark	21	10	51	52	55	189	5.8
Finland				18	75	93	2.9
France		82	84	139		305	9.4
Hungary			265	270	257	792	24.3
Iceland	21	36	8			65	2.0
Ireland	101	99	67	88		355	10.9
Norway	33	58	68	60	82	301	9.3
Slovak Republic					451	451	13.9
Slovenia		4	13	28	8	53	1.6
Spain					108	108	3.3
Total	176	289	584	907	1,297	3,253	

Qualitative information (compliant/non-compliant) was provided by the UK, but the data could not be included in the above analysis. FEDIAF, The European Pet Food Industry Federation, also provided data on concentrations of mercury in samples of pet food; these data are not included in the table above but are discussed in the section on pet food (below).

There was a significant increase in the number of samples analysed for mercury over the period 2002-2006. However, the data are not evenly distributed across the EU; almost 25% originated from Hungary, while a further 20% came from the Nordic countries. In contrast, relatively few data originated from southern European/Mediterranean region.

Data were provided for a wide range of feed materials. Table 4 provides a summary of the total levels of mercury (average, median and MLs) reported in each of the main commodity groups. For many of the samples analysed, levels of mercury were reported as being less than the LOD or of LOQ for the particular method of analysis employed. In addition to the absolute values reported, the European countries were requested to provide information on the LOD or LOQ; where concentrations were reported as <LOD or <LOQ, these were considered equal to LOD/2 or LOQ/2 respectively.

Table 4 also provides information on the number of samples (total and as a percentage) that exceeded the ML for each particular commodity group.

Table 4. Levels of mercury reported in feedingstuffs (moisture content of 12%), categorised by feed commodity, and the number and percentage of samples analysed in each category in the period 2002-2006 that exceeded the maximum levels (MLs).

	No. of samples	Mercury concentration (mg/kg)			ML (mg/kg)	Samples exceeding ML	
Food commodity		**Average**	**Median**	**Max**		**n**	**%**
Additives and premixtures	290	0.03	0.01	1.3	0.1	5	1.7
Complete feed	539	0.03	0.04	0.12	0.1	11	2.0
Forage crops	368	0.02	0.002	0.19	0.1	2	0.5
Minerals and mineral feedingstuff	530	0.02	0.005	0.59	0.1	7	1.3
Other feedingstuffs	319	0.01	0.005	0.13	0.1	2	0.6
Unspecified feeds and raw materials	238	0.03	0.01	0.22	0.1	26	10.9
Complementary feed	228	0.02	0.01	0.34	0.2	1	0.4
Calcium carbonate	42	0.01	0.01	0.03	0.3	0	0
Complete feed for dogs and cats	126	0.02	0.01	0.18	0.4	0	0
Fish meal	193	0.10	0.10	0.26	0.5	0	0
Fish and bone meal	13	0.15	0.15	0.22	0.5	0	0
Fish oil	63	0.03	0.03	0.21	0.5	0	0
Fish silage	23	0.06	0.05	0.17	0.5	0	0
Complementary feed for fish	1	0.01	0.01	0.01	0.2	0	0
Complete feedingstuff for fish	280	0.06	0.05	0.4	0.1	23	8.2
Total	3253	0.03	0.01	1.3		86	2.6

Although the total number of samples that exceeded the ML tended to increase over time (detailed data not reported here), this was a reflection of the greater number of samples

analysed. Over the period 2002-2006 there was no apparent trend, with the percentage of samples that exceeded the ML ranging from 1.3 (2006) to 4.7 (2005). For the period as a whole, 2.6% of all samples exceeded the maximum level.

Average values for complete feedingstuffs for fish in each of the years 2002-2006 were 0.044, 0.061, 0.065, 0.062 and 0.051 mg/kg, respectively, suggesting that there was no trend in this particular category.

Additives and premixtures

Almost half (42%) of all samples in this category were described as premixtures. Although some authorities specified the livestock category for which the premixture was intended, the majority did not, and therefore it has not been possible to identify livestock species that have been exposed to the highest concentrations.

Complete feedingstuffs other than for pets and fish

Of the 11 complete feeds that exceeded the ML (0.1 mg/kg) for this category, two were for mink while the target species for others were unspecified. For 366 of the feeds in this category (68%), it was possible to identify the target species, and the data for the main species are summarised in Table 5.

Table 5. Average and maximum concentrations of total mercury in complete feedingstuffs for terrestrial animal categories.

Target species	Number of samples	Average (mg/kg)	Median (mg/kg)	Maximum (mg/kg)
Pigs	123	0.032	0.050	0.050
Poultry	96	0.039	0.050	0.10
Ruminants[13]	56	0.012	0.004	0.10
Horses	9	0.022	0.010	0.10
Mink	39	0.053	0.054	0.12
Rabbits	18	0.031	0.050	0.10
Rodents	25	0.050	0.050	0.10

Forage crops

Although data on 368 samples of forage crops were provided, they generally lacked information with which to further classify them, with the majority being variously described as ‘green feed’, ‘pasture crops’, ‘plant raw material’ etc. Only two samples exceeded the ML (0.1 mg/kg), with the highest concentration (0.19 mg/kg) in a sample described as ‘various

[13] Includes both complete and complementary feedingstuffs

fodder'. For 28 samples of alfalfa (lucerne), the average and maximum mercury concentrations were 0.005 and 0.02 mg/kg, respectively, while for forage maize (n=42) they were 0.007 and 0.05 mg/kg, respectively. In general the concentrations of mercury in forages appear to be low, and similar to the values reported by SCAN (EC, 2003). Since the diet of many ruminants consists almost entirely of forages, it seems reasonable to assume that their exposure to mercury is low.

Minerals and mineral feedingstuff

Data on 530 samples of minerals were provided. In only seven samples did mercury concentrations exceed the ML (0.1 mg/kg), with the highest concentration of 0.59 mg mercury/kg in a sample of manganese oxide. Very few authorities provided information on the type of mineral, feedingstuff or target livestock species, and so it has not been possible to establish risks for particular livestock types resulting from the consumption of these feedingstuffs.

Other feedingstuffs

This category consisted of named feed materials, e.g. wheat, rapeseed meal, vegetable oil etc. For the major feed materials, the average, median, and maximum concentrations are given in Table 6. Overall, mercury concentrations were low, with only two samples in this category exceeding the ML (0.1 mg/kg). The highest concentrations of mercury were reported in a sample of distillers dried grain (0.13 mg/kg) and a sample of shrimp meal (0.12 mg/kg).

Table 6. The average, median and maximum total mercury concentrations (mg/kg) in a number of common feed materials.

Feedingstuffs	Number of samples	Average mercury concentration (mg/kg)	Median mercury concentration (mg/kg)	Maximum mg/kg
Barley	29	0.006	0.001	0.078
Wheat	48	0.003	0.001	0.030
Oil seed rape	42	0.007	0.002	0.100
Sunflower meal	13	0.003	0.001	0.010
Soya bean meal	13	0.022	0.011	0.050
Distillers dried grains	8	0.047	0.020	0.130
Maize gluten feed	15	0.026	0.015	0.100
Vegetable oils	16	0.021	0.020	0.050

Unspecified feeds and raw materials

The greatest number of data (238) and highest proportion of non-compliant samples (10.9%) was in this category. The returns from the European countries described these as 'raw materials', 'animal feed' etc., and therefore it is not possible to further characterise the specific feeds or livestock that might be at risk from consuming them.

Complementary feed

A complementary feed will not, on its own, provide all the nutrients required on a daily basis but is intended to be fed with other feed materials. For this reason, the ML can be higher than for complete feedingstuffs. The ML for mercury in complementary feed is 0.2 mg/kg. In one sample (target species unspecified) analysed in 2005, the concentration of mercury was 0.34 mg/kg; in the remaining 227 samples levels were all <0.2 mg/kg. For 160 samples, the target species was indicated. The average concentrations of mercury in complementary feeds for pigs (n=44), poultry (n=23) and cattle (n=80) were 0.006, 0.007 and 0.011 mg/kg, respectively.

Calcium carbonate

The average and median mercury concentrations of the 42 samples of calcium carbonate analysed in 2002-2006 were 0.01 and 0.005 mg/kg, respectively, and in none of the samples did mercury concentrations exceed the ML of 0.3 mg/kg

Complete feed for dogs and cats

Mercury concentrations in 126 samples of pet food were provided. The highest reported concentration in this category was 0.18 mg/kg in a sample of compound feedingstuff for cats. This was well below the maximum permitted level of 0.4 mg/kg in this category. The majority of samples were simply designated "Complete feed – dogs and cats" and so it was not possible to calculate average and median values for each species. Furthermore, since 80% of the samples analysed originated from one country (Hungary), it is not clear to what extent these results are representative of the EU as a whole. In addition to the information obtained from the European feed authorities, FEDIAF also provided data on 78 samples of canned pet food and 119 of dried pet food analysed in the period 2003-2006. The average (and maximum) concentrations were 0.021 (0.026) and 0.033 (0.110) mg/kg for the canned and dry pet foods, respectively (12% moisture basis).

Feed for fur-producing animals

Denmark provided data on 25 samples of complete feedingstuffs for mink. The average, median and maximum concentration of these samples was 0.053, 0.054 and 0.12 mg/kg, respectively.

Fishmeal

As discussed elsewhere in this report, mercury accumulates in the food chain, particularly in fish, and in recognition of this the ML for fishmeal is higher (0.5 mg/kg) than in other feed materials. The average and median concentrations in the samples analysed between 2002 and

2006 were 0.10 mg/kg, with the highest concentration reported of 0.26 mg/kg. Information on samples in this category were provided, predominantly (but not exclusively) by the Nordic countries (Denmark, Iceland and Norway).

Fish and fish bone meal

Information on mercury concentrations in 13 samples of fish and bone meal were provided by Iceland. The average and highest concentrations were 0.15 and 0.22 mg/kg, respectively, which were well below the maximum permitted concentration (0.5 mg/kg).

Fish oil

The highest reported concentration of mercury in fish oil was 0.21 mg/kg, although the average for the 63 samples was 0.03 mg/kg,

Fish silage

Fish residues and unwanted fish may be ensiled – rather than dried – for storage before being used as livestock feed. Data for fish silage analysed in this period were provided by the Danish (n=7) and Norwegian (n=16) Food Authorities. The highest concentration reported was 0.17 mg/kg, with an average concentration for all samples of 0.06.

Complete feedingstuff for fish

Fishmeal constitutes the major ingredient in most complete feeds for fish, and therefore concentrations of mercury in this category tend to be higher than in complete feeds for land animals and birds. Information on 280 samples of complete feedingstuffs for fish was provided. The average and median concentrations were 0.06 and 0.05 mg/kg, respectively, which compares with the ML of 0.1 mg/kg aproximately 8% of fish feeds exceeded the ML. Twenty three samples exceeded the ML, with the highest concentration being 0.4 mg/kg. The highest concentration of mercury found in fish feed for marine larvae which typically contain high inclusion levels of fishmeal.

Few data were provided on the proportion of methylmercury in fish feed. In Norway, the average concentration of methylmercury in fish feed analysed in 2004 was 0.044 mg/kg (and ranged between 0.03-0.06 mg/kg, n=49) representing approximately 81% of the total mercury. In 2005 methylmercury represented approximately 86% of the total mercury in fish feed (n=19). The average concentrations of total mercury and methylmercury in fish feed in 2006 were 0.06 mg/kg and 0.05 mg/kg respectively (concentrations of total mercury and methylmercury ranged between 0.02-0.18 mg/kg (n=49) and 0.03-0.13 mg/kg (n=17) respectively), the proportion of methylmercury representing approximately 89% of total mercury (Måge *et al.*, 2005, 2006, 2007).

Protein hydrolysates from feathers

Hair and feathers can accumulate a large amount of methylmercury. The practice of recycling poultry (chicken, turkey) feathers as feather meal (as protein hydrolysate) to feed back to farmed animals could represent an additional source of methylmercury contamination (Plummer and Bartlett, 1975; Soares *et al.*, 1973). According to Regulation No (EU)

1774/2002 and Regulation No (EU) 1292/2005, only feathers originating from animals that are slaughtered in a slaughterhouse, after undergoing ante-mortem inspection, can be used to produce protein hydrolysate with a molecular weight of <10,000 daltons. Protein hydrolysate from feather meal can be used in animal feeding with the following indicative figures for maximum amounts used in complete feeds: pigs 3%, chickens for fattening 5%, ruminants 6%, fish 15% (Animal Feed Resources Information System[14]).

Water

In addition to mercury in feed materials, livestock and poultry may also be exposed to mercury in drinking water. Although no information was provided by Member States on mercury in drinking water for livestock, IPCS (WHO-IPCS, 1990) suggest that the concentration range for mercury in drinking water is the same as in rain, with an average of approximately 25 ng/L. Therefore, water does not make a significant contribution to the exposure of livestock except in highly polluted areas.

Summary

A substantial number of feed materials have been analysed for total mercury in recent years, and for the large majority the concentrations of mercury were below the MLs specified in feedingstuffs legislation. Less than 3% exceeded the MLs, including additives and premixtures. In the category of feedingstuffs produced by the processing of fish or other marine animals, which normally contain higher mercury concentrations, no sample exceeded the maximum level. However, approximately 8% of the complete feedingstuffs for fish exceeded the ML.

For a large proportion of all the samples for which data were provided by European countries, however, there was insufficient information to allow the data to be usefully used. For example, 10% of all samples were categorised as "Other feedingstuffs" without any meaningful description. Even in well defined categories, information was frequently lacking; for the 288 sample described as "Complementary feeds", for example, only 158 included information on the target species. Given the considerable amount of effort associated with collecting and analysing the samples, it is unfortunate that a full description of the sample is not available.

4.2 Animal exposure

Land animals and poultry

The extent to which land animals and poultry are exposed to mercury is a function of the concentration in feed and the amount of feed consumed. In an attempt to estimate levels of exposure by different categories of livestock, a number of assumptions have had to be made

[14] http://www.fao.org/ag/AGA/AGAP/FRG/afris/

regarding the level of feed intake and concentrations in different dietary ingredients. Even within livestock categories, the amount of feed consumed can vary considerably as a result of a wide range of animal, environmental and management factors. In the estimates of exposure, the assumptions made for each category have been given in Annex Tables 2 and 3. Similarly, concentrations of mercury in feedingstuffs vary widely; in the calculations that follow both the average and maximum concentrations in feedingstuffs described above have been used provide an indication of 'typical' and 'worst case' levels of exposure. This method of estimating exposure by land animals and poultry is similar to that used for other opinions of the CONTAM panel.

Ruminants

Ruminant rations consist predominantly of forages, supplemented where necessary by concentrate feeds e.g. cereals, oilseed meals and minerals, vitamins etc. Concentrations of mercury in forages vary considerably. Flachovsky (2006) reported values that range from 0.005-0.03, while data provided by Member States for this report had a range of 0.0002 to 0.19 mg/kg. In estimating likely exposure from forages (Table 7), the average and maximum levels from Table 4 have been used. The non-forage component of the diet consists of feedingstuffs within the categories other feedingstuffs, unspecified feeds and raw materials or complementary feeds, which may be fed as individual feeds separately, given as a loose mix of ingredients – either separately or mixed with the forage – or provided in a compound feed. Where concentrate feeds are fed separately or are mixed on-farm, the choice of feed, and the proportions used varies considerably thoroughout the EU, making it difficult to describe a 'typical' ration. On many farms, however, forages are supplemented with complete feedingstuffs – usually as compound feeds – and therefore the data presented in Table 5 have been used to estimate the exposure to mercury from the concentrate component of the ration. The animal and feed intake data used to calculate these exposures are given in Annex Table A2.

For comparison, levels of exposure by livestock consuming feeds with the maximum permitted concentrations (see Table 2) are also given. Since the highest mercury concentration in forages (0.19 mg/kg) exceeded the ML (0.1 mg/kg), estimates of mercury intake by ruminants consuming forages with this concentration exceed the regulatory maximum. However, the likelihood of this occurring in practice is extremely small; only two (of 368) samples exceed the ML, while the average for all samples was 0.02 mg/kg.

Table 7. Likely intake of mercury, as mg/day or mg/kg body weight, by different classes of ruminant livestock, when consuming forages and concentrates containing the average or maximum concentrations of mercury calculated from data provided by European countries (see Tables 5 and 6) or the maximum levels (MLs).

Livestock type	Mercury intake average[a]		Mercury intake max[b]		Mercury intake ML[c]	
	mg/d	mg/kg LW[d]	mg/d	mg/kg LW[d]	mg/d	mg/kg LW[d]
Growing cattle	0.051	0.0006	0.391	0.0043	0.240	0.0027
Growing cattle	0.103	0.0005	0.883	0.0044	0.500	0.0025
Growing cattle	0.178	0.0005	1.632	0.0047	0.880	0.0025
Dairy cow-dry	0.280	0.0004	2.660	0.0043	1.400	0.0022
Dairy cow-lactating (20 kg/d)	0.378	0.0006	3.015	0.0048	1.800	0.0029
Dairy cow-lactating (40 kg/d)	0.497	0.0008	3.542	0.0057	2.300	0.0037
Sheep-growing lamb	0.016	0.0005	0.152	0.0051	0.080	0.0027
Sheep-lactating ewe	0.049	0.0007	0.299	0.0043	0.220	0.0031
Goats-lactating	0.060	0.0008	0.307	0.0038	0.260	0.0033

[a] forage = 0.02 mg Hg/kg, concentrate = 0.024 mg Hg/kg

[b] forage = 0.19 mg Hg/kg, concentrate = 0.10 mg Hg/kg

[c] forage = 0.10 mg Hg/kg, concentrates = 0.10 mg Hg/kg

[d] life weight

As discussed above, concentrations of mercury in fishmeal and other fish products are often higher than in feeds derived from vegetable material. The period for which data for this report have been provided (2002-2006) cover the period during which it has been illegal to feed fishmeal to ruminants[15]. The lifting of the ban, were it to occur, might result in higher concentrations of mercury in the diets of ruminant livestock, but in practice the extent to which this is likely to occur would be determined by the cost of fishmeal relative to other feed ingredients and the demands of consumers.

Non-ruminants and fish

In contrast to ruminants, rations for pigs and poultry consist almost entirely of concentrate feeds. These are normally fed in the form of compound feeds, but individual feed materials may be fed, separately or in a loose mix. For all poultry and most pigs the concentrate is fed in a dry form, either as meal or in pellets. In some areas pigs are given feed in liquid form, but since no data were provided on concentrations of mercury in liquid feeds, no attempt has been made to estimate exposure of pigs given these feed in this way.

Complete feed consist of a range of feed materials, selected on the basis of price, availability, and the contribution that they may make to the supply the nutrients required by the target

[15] The prohibition on feeding fishmeal to ruminants was introduced in December 2001 as part of the European Commission's programme to control BSE, as laid down in regulation 999/2001. OJ L 147 31.5.2001 p 1-40.

animals. Fishmeal may be included in rations for non-ruminants, largely because of its superior amino acid profile relative to other feed materials. Estimates of the average or maximum mercury concentrations (from Table 5) have been used to estimate the likely intakes of mercury (mg/day or mg/kg body weight) by pigs and poultry consuming complete feeds (Table 8). It is acknowledged that the composition of compound feeds differ for different types of livestock within the same category. For example, there will be differences in formulation and composition between feeds for broilers and layers or young and old pigs. In practice, however, the differences are generally relatively small, and variation in the use of raw materials is likely to be greater between manufacturer and between regions of the EU. In the information provided by Member States, the descriptions of the feeds were generally insufficient to permit further differentiation of the data.

The relative contribution of methyl mercury from food versus water to rainbow trout in controlled laboratory conditions was examined by Phillips and Buhler (1978). Nearly 70% of the methylmercury ingested was assimilated while approximately 10% of the methylmercury that passes over the gills was assimilated. The main source of mercury in fish is from the diet, waterborne exposure does not contribute significantly under normal farming conditions. Fishmeal is currently the main source of protein in fish feed, however the inclusion level depends on the species farmed and marine predatory fish species have a particularly high requirement for fishmeal for normal development. Considering that the protein content may be as high as 56% in salmon feed (Måge *et al.,* 2006) and assuming inclusion of fish meal with a maximum mercury concentration of 0.26 mg/kg (Table 4) the resulting feed would contain 0.12 mg mercury/kg. Consequently the ML in fish feed of 0.1 mg/kg (88% dry matter) and the ML of 0.5 mg/kg (88% dry matter) in feedingstuffs produced by the processing of fish or other marine animals are not harmonized. This is supported by the data submitted to EFSA, that the exceedence of the maximum level of 0.1 mg mercury/kg is most frequently reported for fish feed (see Table 4).

Table 8. The intake of mercury, as mg/day or mg/kg body weight (bw), of different classes of pigs and poultry when complete feedingstuffs containing the average or maximum concentrations of mercury calculated from data provided by Member States (see Table 5), or the maximum level (ML) (Table 2)*.

Livestock type	Hg concentrations in complete feedingstuffs average		Hg concentrations in complete feedingstuffs maximum		Hg concentrations in complete feedingstuffs ML	
	mg/day	mg/kg b.w.	mg/day	mg/kg b.w.	mg/day	mg/kg b.w.
Growing pigs	0.0480	0.0016	0.0750	0.0025	0.1500	0.0050
Growing pigs	0.0928	0.0015	0.1450	0.0024	0.2900	0.0048
Growing/ fattening pigs	0.1056	0.0012	0.1650	0.0018	0.3300	0.0037
Growing/ fattening pigs	0.1088	0.0009	0.1700	0.0014	0.3400	0.0028
Dry sow	0.0864	0.0004	0.1350	0.0007	0.2700	0.0014
Lactating sow	0.2080	0.0010	0.3250	0.0016	0.6500	0.0033
Broilers (finishing)	0.0059	0.0023	0.0150	0.0060	0.0150	0.0060
Laying hens	0.0041	0.0012	0.0115	0.0033	0.0115	0.0033
Turkeys	0.0234	0.0015	0.0650	0.0041	0.0650	0.0041

* The animal and feed intake data used to calculate these exposures are given in Annex Table A3.

Pets

The average, median and maximum concentrations of mercury in complete feeds for dogs and cats were 0.02, 0.01 and 0.18 mg/kg, respectively. Unfortunately, information on the target animal was provided for only 29 of the 126 samples. The average, median and maximum mercury concentrations in 13 samples of complete feed that were clearly identified as being for cats were 0.037, 0.010 and 0.18 mg/kg, respectively. For 16 samples of dog food, the average, median and maximum concentrations were 0.037 0.010 and 0.02 mg/kg, respectively. The reasons for the higher concentrations in cat feed are not clear, but it may be unwise to draw any conclusions from this relatively small population of samples, the majority of which originated from one country.

Fur-producing animals

Based on the feed concentration data provided by Denmark, exposure of mink consuming feed containing either the average or maximum mercury concentrations are given in Table 9.

Table 9. The intake of mercury by mink consuming feed containing average and maximum concentrations of mercury observed in 25 samples of mink feed .

	Age (weeks)	Body weight (g)	Feed intake (g/day)	Hg exposure at average dietary concentrations (0.053 mg /kg)		Hg exposure at maximum dietary concentrations (0.12 mg/kg)	
				mg/day	mg/kg b.w.	mg/day	mg/kg b.w.
Male	7	630	40	0.002	0.003	0.005	0.008
	31	2400	130	0.007	0.003	0.016	0.007
Female	7	450	30	0.002	0.004	0.004	0.008
	31	1300	85	0.005	0.003	0.010	0.008
	Lactating	1300	200	0.011	0.008	0.024	0.018

5. Adverse effects on fish, livestock and pets, and exposure-response relationship

While there is a large amount of data on mercury dose-response effects in laboratory animals, few and rather old data are available for farmed animals, mostly focused on clinical signs of toxicity observed in acute situations.

Toxicological data for inorganic and organic mercury are summarised for the different species in Table A1 in the Annex.

5.1. Fish

A four month study was conducted with triplicate groups of Atlantic salmon (*Salmon salar*) exposed to methylmercury chloride at levels of 0.03, 0.12, 0.63, 4.4 and 8.5 mg mercury (expressed as total mercury)/kg feed (dry weight). Metallothionein levels were elevated and adverse effects in terms of monoamine oxidase activity, brain pathology and altered blood parameters were evident in fish exposed for four months to 4.4 mg methylmercury/kg feed, equivalent to 1.2 mg of methylmercury (as total mercury)/kg body weight. Growth appeared to be an insensitive parameter, and was not affected in Atlantic salmon parr exposed to a dietary concentration of 8.5 mg methylmercury/kg feed for four months (Berntssen *et al.*, 2004a). Elevated blood packed cell volume and hyperplasia of gill epithelium was seen in rainbow trout (*Oncorhynchus mykiss*) exposed to 16 mg/kg feed for 3.5 months (Wobeser, 1975). A NOAEL of 0.17 mg methylmercury (expressed as total mercury)/kg b.w. can be established for salmonids corresponding to 0.63 mg methylmercury (expressed as total mercury/kg feed (dry weight).

5.2. Ruminants

Goats experimentally exposed to mercuric chloride added to drinking water (average 150 mg mercury/head per day (7 – 7.5 kg b.w.)) developed signs of toxicity after 43 days, such as gastrointestinal disturbances and renal dysfunction (Pathak and Bhowmik, 1998).

Palmer *et al.* (1973) produced acute mercury toxicosis in yearling cattle and sheep with an ethyl-mercury fungicide, administered in capsules at 0.48 mg/kg b.w. (equivalent to 0.15 mg/kg elemental mercury), with deaths recorded between 7 and 27 days.

Chronic methylmercury intoxications were experimentally achieved in 4 week old calves (Herigtad *et al*., 1972), cattle and sheep (Wright *et al.*, 1973; D'Itri, 1971). Main manifestations were dysfunction of the central nervous system (CNS) (incoordination and unsteady gait) and of the digestive and genito-urinary systems, as well as skin and visual problems (Annex, Table A1). Young animals are more susceptible to methylmercury intoxication as compared to adults.

The NOEL values (Annex, Table A1), usually expressed as mg/kg feed were estimated on the basis of a dry matter intake corresponding to 2% of the body weight in non lactating ruminants. They range from 5 (calves) to 12 mg/kg feed (yearlings) for exposures that cover 10-30% of the expected economic life in meat producing animals.

5.3. Pigs

Weanling pigs exposed to methylmercury and ethylmercury salts via feed at doses of 0.19, 0.38 and 0.76 mg total mercury/kg b.w. (equivalent to 20 mg total mercury/kg feed) for 60-90 days showed anorexia, incoordination and liver degeneration (Tryphonas and Nielsen, 1970, 1973). The NOAEL based on liver failure, the most sensitive endpoint, was 0.19 mg/kg b.w. per day corresponding to 3.4 mg total mercury/kg feed.

5.4. Poultry

Fifty percent of one day old chicks exposed to methylmercury at 5.0 mg/kg feed died within 33 days, while 2.2 mg/kg feed resulted in no appreciable signs of intoxication (Soares, 1973).

Scott (1975) observed reduced weight gains, a drop in egg production and infertility in hens fed methylmercury at 10 mg/kg diet. More recently, Lundholm (1995) reported a significant drop in egg production of hens exposed for 50 days to methylmercury at 0.75 mg/kg b.w. (corresponding approximately to 10 mg/kg feed for a 3 kg hen, eating daily 200 g feed containing 12% moisture).

Gardiner (1972) reported that 5 day-old ducks fed on a diet containing 3.3 mg methylmercury/kg feed showed a reduced growth rate. At the same concentration level, Heinz

(1979) reported embryo toxicity associated to methylmercury exposure over two breeding seasons. More recently, in mallard duck, Heinz and Hoffmann (2003) derived a LOAEL of 5 mg total mercury/kg feed, based on embryo deformations resulting from the carry-over of methylmercury into eggs. Considerable differences in the sensitivity of mallard embryos, especially from different parents, were recorded.

Incoordination and weakness were provoked in 16 week-old turkeys, fed a feed containing a ethylmercury fungicide at a 5 mg/kg b.w. for 13-42 days (Palmer *et al.,* 1972) equivalent to a 0.16 mg/kg total mercury/kg b.w. and to 24 mg total mercury/kg feeds.

5.5. Cats

Over a period of two years, Charbonneau *et al.* (1976), exposed groups of adult cats (male/female ratio 1:1; control, n =10; exposed n=8 for each dose) to diets based on natural methylmercury in fish at doses of 0.05 (control), 0.14, 0.33, 0.76, 1.23 and 2.95 mg total mercury/kg (methylmercury was not measured), corresponding to 3.0 (control), 8.4, 20.0, 46.0, 74.0, and 176.0 µg total mercury/kg b.w. per day. During the same period other groups of cats were fed the control feed (containing 0.05 mg methylmercury/kg feed) contaminated with exogenous methylmercury chloride, at the same levels reported above. The feeding rate was 60 g feed/kg b.w. per day, with selenium present at 0.13 mg/kg in the diet. Haematological, and biochemical investigations, together with neurological and clinical examinations were performed at regular intervals. At 1.23 mg/kg feed marked signs of methylmercury neurotoxicity were recorded after 40 weeks of exposure in all animals (loss of balance, ataxia, impaired hopping, hypalgesia, motor incoordination, muscle weakness). At 0.76 mg/kg feed (46 µg methylmercury/kg b.w. per day) one animal out of eight developed neurological signs of toxicity and was sacrificed after 38 weeks of exposure. Another died due to acute renal failure after 68 weeks of treatment. The remaining animals all showed slight neurological damage (mild impairment of the hopping reactions and hypalgesia) after 60 weeks of treatment, and their condition did not deteriorate in the remaining period of the study. No treatment–related effects were noted in the groups exposed to 0.14 and 0.33 mg/kg feeds. No difference in toxicity was observed between methylmercury naturally present in fish and methylmercury added in pure form to the diet. Therefore the NOAEL was 0.33 mg methylmercury (expressed as total mercury)/kg feed.

Cats fed tuna fish showed a modified behaviour: they were less active, vocalized less, and spent more time on the floor and more time eating than cats fed commercial beef cat food (Houpt *et al.,* 1988). In this study, possible additive effects between mercury and thiaminase present in raw fish cannot be excluded. Several types of raw fish, including carp and herring, contain thiaminase that cause thiamine (vitamin B1) deficiency in cats. Clinical cases of thiamine deficiency (anorexia, ataxia, vomiting, dilation of the pupils, ventroflexion of the neck and convulsions have been reported in cats and mink fed raw fish (i.e. herring and carp) containing thiaminase (Davidson, 1992). The presence of a sulfur atom in the thiamine

structure determines interaction with divalent mercury and possibly methylmercury, thus causing the denaturation and the subsequent loss of vitamin B1 activity.

5.6. Dogs

Mongrel dogs (estimated body weight around 30 kg) were orally exposed to different doses of methylmercury (1.2 (n=1), 12 (n=1), 60 (n=1), 120 (n=1), 430 (n=4), 640 (n=4) µg/kg b.w. expressed as total mercury) for 385 days (Davies *et al.,* 1977). The dose of 430 µg/kg b.w. per day resulted in neurological signs of toxicity in all animals within 60 days of exposure, and disseminated cerebral lesions. No clinical signs were observed up to 120 µg/kg b.w. although histological examination revealed degeneration of brain tissues at 120 µg/kg b.w.. Due to the weakness of the toxicological database and only single animal experiments no NOAEL could be derived for dogs. The LOAEL was 0.12 mg methylmercury (expressed as total mercury)/kg b.w. corresponding to 8 mg/kg feed.

5.7. Horses

The acute toxic dose of inorganic mercury (calomel) in horses is 8-10 grams. Chronic toxicity was observed following ingestion of 0.4 mg inorganic mercury (calomel)/kg b.w. per day over a period of several weeks (Guglick *et al.,* 1995). The main clinical signs were renal failure and ulceration of the digestive apparatus.

No relevant information is available for methylmercury toxicity.

5.8. Fur animals

Woebeser *et al.* (1976) exposed four groups of adult mink (5 animals/group) to methylmercury chloride at levels of 0.1 (control), 1.1, 1.8, 4.8, 8.3 and 15 mg/kg feed (expressed as total mercury), for 93 days (corresponding to around 30% of the production cycle). Mink exposed to feed contaminated at 0.1 mg/kg did not show appreciable clinical symptoms, whereas in the 1.1 mg/kg group (equivalent to 0.18 mg/kg b.w. per day) a tendency to ataxia was noted in two animals on the last three days of the experiment. Small necrosis foci were noted during the histological investigation in brain. Since the nature of the mercury species in the control feed (0.1 mg/kg) is not known, the NOAEL for methylmercury cannot be derived from this experiment. The LOAEL was 1.1 mg methylmercury (expressed as total mercury)/kg feed.

As mentioned for cats, also for mink a possible additive effect of thiaminase and methylmercury present in raw fish offals cannot be excluded if the diet is based on fish.

It is worth noting that fur animals are excluded from the restrictions in the use of processed animal protein in feedingstuffs, including fishmeal, to prevent the spread of Transmissible Spongiform Encephalopathies (TSE) (Regulation No (EC) 1774/2002) [16].

5.9. Rabbits

Limited data are reported concerning mercury exposure via feedingstuffs in rabbits under farming practices. Most of the experiments deal with the rabbit as a laboratory animal model to study inorganic and organic mercury toxicity on target organs such as kidney, brain and the immune system following non-oral routes of exposure (Petersson, 1991; Dock, 1994; Moszczynski, 1997).

Abdelhamid (1988) studied the effects of $HgSO_4$ administered via feed to rabbits for 7 weeks at concentrations of 0, 150, and 300 mg total mercury/ kg feed (6 animals/group). Diarrhoea, haemorrhage, oedema, liver and stomach necrosis and mortality were observed in the treated groups. The contaminated diets significantly increased feed intake, drinking water consumption and body weight gain. The most affected organ was the liver, which showed a slight dry weight increase, as well a severe reduction in vitamin A and iron content for the animals fed the 300 mg total mercury/kg diet. The highest level of mercury also caused a significant rise in glycemia and an increase in bone magnesium.

Ultrastructural changes were described by Jacobs *et al.* (1977) in different districts of the nervous system of rabbits administered methylmercury at an oral daily dose of 7.5 mg total mercury/kg b.w. within 1-4 days.

No NOAEL or LOAEL for mercury after oral exposure could be established for rabbits.

Conclusions

The toxicological database for farmed animals is limited in terms of proper dose-reponse experiments, toxicological endpoints (reproductive toxicity studies (except for poultry), immunotoxicity, length of study, type of mercury species, etc.). Some observational studies may have been affected by the presence of confounding factors (i.e. the simultaneous exposure to metals other than mercury, and/or to persistent organic pollutants), and the exposure time has not always encompassed the full production cycle of the animals.

The most sensitive domestic animal species to methylmercury toxicity are cats and mink.

New-born animals (calves, chickens) are more susceptible to methylmercury intoxication as compared to adults (Annex, Table A1).

[16] OJ L 273, 10.10.2002, p. 1–95.

6. Toxicokinetics and tissue disposition

The knowledge of the toxicokinetics of mercury is mainly based on experimental studies carried out in humans and laboratory animals 20 to 30 years ago. These data have been assessed by a number of national (US-EPA, 1997; ATSDR, 1999; NRC 2000) and international (WHO-IPCS, 1990, 1991, 2000) bodies. A summary of these data is given below, completed with either more recent studies (e.g. carried out on marine mammals or seabirds) or data obtained on farmed animals, including fish, that were not taken into consideration in these assessments.

The absorption, distribution, metabolism and excretion of mercury are largely dependent on its chemical form, i.e. elemental mercury, inorganic mercury and organic mercury.

6.1. Absorption

Elemental mercury (Hg^0) in vapour phase is absorbed to a large extent (80%) through inhalation. Hg^0 and mercurous salts (Hg_2^{++}, e.g. Hg_2Cl_2) are poorly absorbed (<0.10%) following oral exposure or contact with the gills.

Mercuric salts (Hg^{++}, e.g. $HgCl_2$) are absorbed to a limited extent in the gastrointestinal tract. The extent to which inorganic mercury is transported across the intestinal tract is largely dependent on its solubility and its dissociation in the lumen. Mercuric compounds are more readily absorbed than mercurous forms because of their solubility. Their absorption varies according to the species (e.g. 20% for the adult mice, 30% for the goat, 7% for humans), age (38% in the 1 week-old mice), individuals, nutritional factors (organic ligands such as phytate, proteins/aminoacids, micronutrients like selenium) and physiological factors (feed intake, gut passage time and physiology).

Organic mercurials are absorbed much more extensively and rapidly after oral intake than are inorganic forms. More than 80% methylmercury and phenylmercury have been shown to be absorbed by humans, laboratory animals and farmed animals (poultry, ruminants and fish) following oral exposure. Feed composition has a major influence on the digestion and release of mercury from feed components in the intestinal lumen and subsequently bioavailability. Association with organic ligands such as phytates or proteins and/or amino acids can affect the absorption of mercury over the intestinal tract. Other factors such as feed intake, gut passage time and gut physiology also contribute to the large inter- and intraspecies differences in bioavailability of mercury (Schlekat *et al.*, 2005). In fish (trout) absorption of methylmercury dissolved in water through the gills occurs at a limited extent as compared with digestive absorption following ingestion of contaminated feed and was shown to be dependent on the metabolic rate (e.g. related to water temperature) (de Freitas and Hart, 1975). Evidence of reduced bioavailability of inorganic mercury for fish with increasing salinity has been given, which cannot be attributed unequivocally to either the decrease of the

bioproduction of methylmercury from inorganic mercury and/or the intrinsic decrease of fish absorption.

6.2. Distribution

Absorbed elemental mercury vapor readily distributes through the body and crosses the blood-brain and placental barriers. However, the distribution of the very small amounts absorbed through the intestine is limited primarily by the oxidation of Hg^0 to Hg^{++} that occurs in tissues.

Inorganic mercury does not easily cross the blood-brain or placenta membranes. Kidneys exhibit the greatest concentration of mercury (bound to metallothioneins) following exposure to inorganic mercury salts (50-90% of the body burden in the rat). Liver and carcass, in decreasing order, contain lower amounts whereas brain harbours very limited quantities (about 1%). It has been shown in mice, goats and humans that Hg^{++} crosses the mammary barrier.

Organic mercury absorbed through the intestine or the gills is distributed throughout the animal body. In blood, most of methylmercury is found within the red blood cells, bound to hemoglobin, whereas a minor part is largely bound to plasma proteins and thiol compounds, L-cysteine and reduced glutathione (GSH). Mercury in blood only reflects recent exposure to methylmercury and inorganic mercury.

In mammals, methylmercury has been shown to cross the blood-brain and placental barriers, the mammary gland and the pilous follicle (hair, feathers). For example, the whole body retention in mice, 14 days after methylmercury oral administration, is inversely proportional to the dose applied and the mercury is distributed as follows: carcass 65-75% (including the hair which represents the major deposit), liver 8-10%, kidneys 5-20% and brain 10%. In similar conditions in the rat, it has been established that methylmercury represented 97% and 92% of the whole mercury in brain and liver respectively, whereas inorganic mercury amounted for 65 to 80% in the kidney. In human milk, 16% of total mercury was found to be methylmercury. Mercury in hair is approximately 90% methylmercury. Hair measurements provide a record of methylmercury exposure but do not accurately reflect exposure to inorganic mercury (ATSDR, 1999).

In fish, a link exists between mercury distribution in tissues and water/food regimes and contamination, with comparatively high Hg concentration ratios between gills and muscle for the periphytophagous and benthivorous species and, in contrast, ratios less than 1 for the piscivorous and omnivorous species. Methylmercury is mainly deposited (99%) in muscle of piscivorous/carnivorous species that ingest fish. In benthivorous species that ingest biofilms and small benthic vertebrates with quite low methylmercury burden (18-52% of total mercury), the highest mercury levels are observed in the liver and kidneys, the two principal

organs for the deposition of inorganic mercury in fish (Régine *et al.*, 2006). Another study on inorganic mercury accumulation in salmon showed concentrations in intestine, kidney, liver, gill, and brain in decreasing order (Berntssen *et al*., 2004a).

In chickens, organic mercury is distributed in tissues, crosses the oviduct of the laying hen to the egg and is deposited in the feathers (March *et al*., 1974 and 1983). Female mallards (*Anas platyrhynchos*) fed diets containing high levels of methylmercury (5 to 20 mg/kg) laid eggs containing 7 to 55 mg total mercury/kg of which 95 to 100% was methylmercury, which is preferentially deposited in the egg albumen rather than the yolk (Heinz and Hoffman, 2004). In laying hens fed diets contaminated with high levels of phenylmercury, methylmercury represented about 95% of the residues found in the egg white and 15% of those found in the yolk (Cappon and Smith, 1981).

6.3. Metabolism

The metabolism of mercury and mercury compounds appears to be similar for animals and humans and involves an oxidation-reduction cycle. Moreover, bacteria (rumen and gut flora) harbour an organomercurial resistance system based on an organomercurial lyase which catalyses the demethylation of methylmercury to Hg^{++}. Some seabirds may be capable of demethylating organic mercury in a species dependent way (Thompson and Furness, 1989), while animal and human studies have provided data suggesting that Hg^{++} may be further reduced to elemental mercury by a mercuric catalase. There is no evidence in the literature for the synthesis of organomercury compounds in human and mammalian tissues. It appears that methylation of inorganic mercury does not occur in fish (trout) (Huckabee *et al.,* 1979), but may do so to a very limited extent (0.17% the administered dose) in the rumen of the cow (Neathery *et al*., 1974).

Organic mercury contaminants entering the animal body are converted to Hg^{++} by cleavage of the carbon-mercury bond, with subsequent metabolism occurring via the oxidation/reduction cycle. This occurs in the rumen and the intestine, where it involves the bacterial flora, but also in red blood cells and tissues. The rate of demethylation is generally very slow. Aryl mercury compounds (e.g. phenylmercury) undergo this conversion more readily than do the short-chain (methyl) mercury compounds. For example, the rat rapidly converts phenylmercury to phenol and Hg^{++}, a reaction involving *p*- or *o*-hydroxyphenylmercury as an intermediary compound (Daniel *et al*., 1972). The conversion of phenylmercury to methylmercury has been observed in the laying hen, where the latter represents the main metabolite excreted in the egg (Cappon and Smith, 1981). Once absorbed, methylmercury undergoes a first pass metabolism in the liver and is excreted into the bile as a methylmercury-glutathione complex (CH_3Hg-SG). It has been shown that GSH is involved in the disposition and excretion of methylmercury (Strange *et al.,* 2001). Higher levels of mercury contamination in the hair have been found in human populations harbouring a null glutathione S-transferase (GST) genotype (GSTM1 0/0) (26% frequency) when compared with the counterpart population for which the

null genotype frequency was 0%. This study and others (Klautau-Guimarães *et al.,* 2005; Gundacker *et al*., 2007) suggests that GSTs polymorphism plays an important role in the disposition of mercury in humans.

The chemical identity of mercury species in skeletal muscle of wild fish has been partly established (Harris *et al.,* 2003). Linear bonds between mercury, methyl groups and sulfur donors have been identified. Among sulfur donors cysteine is the most likely candidate as the predominant biological thiol, either in the free form or as a constituent of glutathione or proteins. More than 99% of methylmercury in both salmon and cod muscle was found in the protein fraction (Amlund *et al*., 2007). The most commonly used "model" of methylmercury species in fish experiments is aqueous methylmercury chloride, where the Hg-Cl bond is highly covalent (see chapter 1.1). Moreover, methylmercury chloride is relatively hydrophobic and therefore expected to exhibit membrane crossing properties superior to many other methylmercury species. However, the affinity of methylmercury for sulfhydryl groups is much stronger than for the chloride (see chapter 1.1), and is therefore more likely to survive in this form in, for example, the intestinal tract, or is less effectively absorbed. The higher toxicity of methylmercury chloride compared with thiol bonded species is consistent with the physicochemical differences between these methylmercury species, and could partly explain the toxicological differences observed (Harris *et al.*, 2003; Oyama *et al.*, 2000; Berntssen *et al.*, 2004b).

The selenium dose, form (oxidation state, organic or inorganic) and exposure route may affect tissue deposition of methylmercury in the body and consequently modulate mercury toxicity in animals. The mechanism by which selenium influences the deposition of mercury has not been established. Proposed mechanisms include the formation of seleno-methylmercury complexes, a selenium-induced release of methylmercury from sulfydryl bonds in the blood, and tissue-specific mechanisms that influence intracellular intake (Glynn and Lind, 1995). It has been shown that in marine mammals (i.e. ringed seal) about 50% of the mercury deposited in the liver is in the form of insoluble mercury selenide (HgSe), with inorganic mercury and methylmercury representing about 40% and only 2%, respectively (Wagemann *et al*., 2000).

6.4 Excretion

The main pathway of excretion of inorganic mercury is via the urine and faeces. Due to the poor absorption of orally administered inorganic mercury, the majority (in the order of 80%) of the ingested dose in humans is excreted in the feces. The half-life of the absorbed Hg^{++} is approximately 40 days (humans) (Clarkson *et al*., 1988). Elimination of inorganic mercury from the blood and brain is a biphasic process encompassing an initial rapid elimination phase followed by a slower phase. Inorganic mercury may also be reduced to form elemental mercury which is exhaled as elemental mercury vapour or excreted in the breast milk. Inorganic mercury is also excreted in milk during lactation, as shown in mice, guinea-pigs and

humans. In ruminants (goat), following intraruminal administration of $^{203}HgCl_2$ for 9 days, the half-time retention (carcass measurement) was 78 days (Sell and Davison, 1975).

Berlin *et al*. (2007) recently reviewed the fate of organic mercury compounds in mammals. The major part of the excretion is by the fecal route (about 90%). Much of the methylmercury excreted in the bile is absorbed in the gut, producing an enterohepatic circulation of methylmercury. In the rat, methylmercury in the bile is bound to glutathione and cysteine. A part of the mercury in the bile (approximately 30-80%) of the monkey is inorganic mercury derived from the demethylation of methylmercury in the body. This part, less effectively absorbed in the gut, is excreted. In the gut, methylmercury can be decomposed by the microflora to inorganic mercury. As inorganic mercury is absorbed to approximately 5-10%, this factor contributes to an increased excretion.

The elimination of organic mercury compounds generally follows first-order kinetics, with whole body clearance times and blood clearance times being longer than for inorganic mercury. The biological half-life of methylmercury in the human is about 1.5 – 2 months (EFSA, 2004). Milk, egg, saliva, sweat, hair and feathers have been identified as other elimination routes of mercury compounds. It has been shown that after injection of equivalent doses of inorganic and methylmercury, the concentration of total mercury in milk was 5 times higher when in the inorganic form in lactating mice and 2.5 times higher in guinea-pigs (Sundberg *et al.,* 1998). In ruminants, following a single intraruminal administration of $CH_3{}^{203}HgCl_2$ to a milking cow and a milking goat, the cumulative secretion of ^{203}Hg over a 13-day period was negligible in the cow and amounted 0.28% in the goat. The half-time retention (carcass measurement) was 22 days in the goat (Sell and Davison, 1975). Another study performed on milking cows which received a single dose of ^{203}Hg-methylmercury (Neathery *et al*., 1974), confirmed that the excretion of radioactivity in milk was very limited (0.17% of the administered dose over the 15-day milk collection period).

Total mercury accumulates in bird tissue following methylmercury administration in feeds, and is excreted when the source is removed. In chickens for fattening receiving 0.05, 0.15, 0.45 and 1.35 mg methylmercury/kg feed for 8 weeks, the elimination half-times of total mercury in tissues after withdrawal increased in proportion to the amounts of mercury retained, i.e. of the dose applied in the diet. The values were similar for the liver and pectoral muscle (4 to 8 days) but higher for kidneys (7 to 23 days). In comparison to the chicken for fattening, the elimination half-time of total mercury in tissues of laying hens that received the same range of concentrations in feed was similar for the lowest dose and proportionally higher for increasing dosages. The elimination half-times were much higher (27, 14 and 49 days for the kidneys, liver and pectoral muscle, respectively) for the lowest dose, but proportionally lower for the increasing doses (March *et al.,* 1983).

In fish, the elimination half-life of methylmercury from muscle was found to be 377 days in the Atlantic cod (Amlund *et al.*, 2007) and between 202 and 516 days in the rainbow trout

(*Oncorhynchus mykiss*), depending on dose and water temperature (Rouhtula and Miettinen, 1975).

7. Carry-over and tissue/products concentration

The carry-over of an orally administered compound to animal tissues and products (milk, eggs) is dependent on the absorption, distribution, metabolism and excretion/deposition of the compound (and its eventual metabolites). These biological phenomena are dose and/or time-dependent, but are also influenced by other factors such as the interaction with other compounds (e.g. selenium contents in the case of mercury). No dose-response studies are available concerning the transfer of inorganic or methylmercury into target species. In general, very limited or only partial data are available.

7.1 Transfer into animal products

In laying hens fed diets containing 0.05, 0.15, 0.45 and 1.35 mg methylmercury/kg feed for 28 weeks, total mercury concentration in the eggs reflected dietary concentrations and reached a plateau after 4 weeks, with the exception of the highest dose for which the concentration in the eggs increased at a much slower rate until week 28. On the basis of approximate values taken from a graph, the following linear relationship for the carry-over of methylmercury to whole egg at plateau has been established: y (mg mercury/kg egg) = 0.133 x (mg mercury/kg feed) covering the range of doses 0.05 to 0.45 mg methylmercury/kg feed (March *et al.,* 1983).

In chickens for fattening given the same range of methylmercury concentrations in feeds (see above) for 8 weeks, total mercury retention in tissues reached a steady state after 1 week. The transfer ratio for the pectorial muscle (concentration in the tissue relative to the concentration in the diet) was between 4.1 (for 1.35 mg/kg feed) and 13.8 (0.05 mg/kg feed). Transfer ratios calculated for kidneys and liver were similar and varied from about 5 to 33 according to the mercury contents of feeds (March *et al.,* 1983).

The only data available for ruminants concerns the comparative carry-over of $[^{203}Hg]Cl_2$ and $CH_3[^{203}Hg]Cl$ in goat, following intraruminal administration of 0.5 mg mercury/kg b.w. equivalent for 9 days to a single animal. Cumulative excretion (36-day period) into milk represented 0.22% and 1.12% of the intake, respectively. However, as the dose applied represents 20 to 50 times the maximum level in complementary feed, no conclusion can be drawn concerning normal levels of exposure (Sell and Davison, 1975).

7.2 Tissue levels and bioaccumulation

Terrestrial domestic animals

Experimental data available in the literature indicate that the highest mercury levels are present in the skin, nails, hair and feathers. Among the internal organs, kidneys generally contain the highest mercury concentrations, usually at approximately 100-fold the levels found in other tissues including liver or muscle (Clarkson, 1992).

A number of biomonitoring studies have been carried out during the last decades in farm species from relatively unpolluted areas, mainly associated with cattle, pig and poultry production (Korsrud *et al.,* 1985; Vos *et al.,* 1986; Jorhem *et al.,* 1991; Niemi *et al*., 1991; Salisbury *et al.*, 1991; Kluge-Berge *et al.*, 1992; Falandysz, 1993a,b; Raszyk *et al.*, 1996; Ulrich *et al.*, 2001; López-Alonso *et al.,* 2003, 2007). The results show that total mercury concentrations in meat and meat products are generally below 10-20 μg/kg wet weight, being below the LOQ (generally 1-5 μg/kg wet weight) in many liver and muscle samples. In addition, a tendency for declining total mercury content in meat products has been observed in recent decades, largely reflecting the decrease in environmental burden (Jorhem *et al.,* 1991; Falandysz, 1993a).

Data on mercury accumulation from experimental studies in domestic animals given diets with known mercury concentrations are sparse. A large number of studies have been published (e.g. Wright *et al.*, 1973; Kacmar *et al.,* 1992; Raszyk *et al.*, 1992; Krupicer *et al.,* 1996; Pathak and Bhowmik, 1998) but the information was inappropriate for inclusion in this opinion due to either the lack of information on mercury sources or because exposure doses were much too high.

Dórea (2006) has recently reviewed the transfer of methylmercury from fishmeal to animals. Depending on the concentration of methylmercury in fishmeal, feathers concentrate four to seven times more methylmercury than in breast muscle (Plummer and Barlett, 1975). In laying hens, the incorporation in complete feed of 5, 10 and 17% fish (herring) meal containing 0.17 or 0.22 mg mercury/kg resulted in total mercury concentrations in feathers that increased proportionally to the mercury content of the diet. The transfer ratio (concentration in feathers *vs* concentration in the diet) was 22. The maximum value measured (17% incorporation) was 0.85 mg mercury/kg feathers, compared to 0.09 mg for the control (soybean) diet (March *et al.,* 1974).

Fish

Estimates for whole body assimilation efficiency of dietary methylmercury in fish vary considerably among studies (from 10 – 95% of the fraction of methylmercury ingested absorbed) and depends on source (natural prey versus formulated feed), fish species, fish size (Phillips and Gregory, 1979; Leaner and Mason, 2002; Wang and Wong, 2003), dose and exposure duration (Lock, 1975; Houck and Cech, 2004).

In juvenile Atlantic salmon, whole body assimilation efficiencies for inorganic mercury chloride varied between 6 – 27% depending on whether the mercury was in live prey or formulated feed (Berntssen *et al.*, 2004a; Wang and Wong, 2003). The variability in assimilation efficiencies of mercury may possibly be due to increased bioavailability of inorganic mercury in prey species compared to inorganic mercury salts.

Transfer of methylmercury into flesh of Atlantic cod (*Gadus morhua L.*) administered a dose of 0.95 mg/kg feed (i.e. equivalent to about 10 times the maximum level in complete feed) showed a linear increase during the 3-month experiment at a rate of 0.005 mg/day; the fraction of methylmercury deposited in flesh to methylmercury ingested was approximately 38% (Amlund *et al*., 2007). This supports earlier findings that methylmercury preferentially accumulates in fish muscle (Giblin and Massaro, 1973; Julshamn *et al.*, 1982; Boudou and Ribeyre, 1985; Berntssen *et al.,* 2004a; Houck and Cech, 2004; Leaner and Mason, 2004). Mean muscle mercury concentrations in Atlantic salmon fed methylmercury (0.1, 0.5, 5 or 10 mg methylmercury/kg feed) for four months were 0.05, 0.14, 1.1 and 3.1 mg total mercury/kg wet weight. In comparison, mean muscle mercury concentration in Atlantic salmon fed inorganic mercury chloride (0.1, 1, 10 or 100 mg inorganic mercury/kg feed) for four months were 0.04, 0.03, 0.06 and 0.31 mg total mercury/kg wet weight (Berntssen *et al*., 2004a).

Since experimental feeding trials do not last for the duration of an entire production cycle, mercury concentration in fish fillets was modelled using one-compartment first-order rate kinetics (Sijm *et al.*, 1993; Berntssen *et al*., 2007). Uptake (assimilation efficiency of 38 ± 1% and elimination rate constant (0.18 ± 0.08 10^{-2}/d) described by Amlund *et al.* (2007) for mercury in Atlantic cod were used to predict the mercury concentration in farmed fish. Fish raised on feed containing 0.1 mg mercury/kg feed would contain approximately 0.05 mg mercury/kg cod fillet assuming a growth rate of 0.006 body weight/per day and a production cycle of 2.5 years. In comparison, the mercury concentration measured in farmed cod has been found to be in the range of 0.003-0.35 mg/kg wet weight (mean concentration 0.1 mg/kg wet weight, n=24[17]).

The calculation above indicates that the current maximum level of total mercury in fish feed would result in a mercury concentration in farmed cod approximately ten fold below the EU maximum level for mercury in fish (0.5 mg/kg in most species and 1 mg/kg in a limited list of fish species). The maximum mercury concentrations reported to date in farmed salmonids raised on commercial feed contain approximately 0.1 mg/kg, i.e. about 20% of the EU maximum level for mercury in fish for human consumption. The maximum mercury level measured in farmed cod represents approximately 70% of the maximum level; however limited data are available for cod and other farmed species since salmonids are currently the only major category of farmed fish in the EU.

[17] http://www.nifes.no

8. Animal risk assessment

The present limit for total mercury in complete feedingstuffs is 0.1 mg/kg feed (containing 12% moisture) for all animal species, except cats and dogs (0.4 mg/kg feed). Among pets, cats and dogs have been identified as the most sensitive species, based on longterm studies (>1 year). For cat, a NOAEL of 0.33 mg/kg feed (corresponding to 20.0 µg total mercury/kg b.w. per day) based on neurobehavioral effects has been identified. Although not clearly indicated in the study from which the NOAEL was derived (Charbonneau *et al.*, 1976), the Panel considered that the water content of the diet was 41%. Accordingly, a NOAEL of 0.5 mg/kg feed (12% moisture), can be extrapolated. In dogs, no NOAEL was identified, and the LOAEL was 0.12 mg/kg b.w., which corresponds to about 8 mg/kg feed. Taking into account an uncertainty factor of 10 for extrapolation from LOAEL to NOAEL, a chronic oral maximum feed concentration of 0.8 mg/kg feed can be derived, which should not cause adverse effects in dogs. The current ML for pets seems to be protective for dogs, but for cats the margin between the NOAEL and the ML is very small. However, based on the available data on the occurrence of total mercury in complete feedingstuffs, it is unlikely that cats and dogs will be exposed to toxic levels from feed.

For pets, the consumption of raw fish and fish based home-made feeds may represent a relevant source of exposure when given over an extended period of time (i.e. more than just occasional meals).

Whilst mink will be able to tolerate the maximum level set for total mercury in complete animal feedingstuffs, it cannot be excluded that the extensive use of offal from fish or other marine animals could result in neurotoxic effects in this species. However, these effects are highly improbable in animals fed on commercial feedingstuffs owing to the relatively low average concentration of total mercury found in such commodities in Europe.

For other land animal species and poultry the maximum levels are well below the risk level for clinical toxicity.

For fish, only data regarding salmonids were identified. A NOAEL 0.17 mg methylmercury (expressed as total mercury)/kg b.w. corresponding to 0.63 mg methylmercury (expressed as total mercury/kg feed (dry weight) was estimated. The current maximum level for complete feed for fish (0.1 mg/kg feed) is considered sufficiently protective.

In terrestrial livestocks, the margin of safety for methylmercury, (as the ratio between the NOAELs and the maximum limits of contamination in feedingstuffs in place within the EU) is sufficient and may buffer possible changes in risk scenario, i.e. as a result of the withdrawal of the ban on the feeding of fishmeal to ruminants, and/or an increased use of hydrolysates from feather meals in feed formula.

9. Human dietary exposure

In the period 2004-2007, several opinions concerning human dietary exposure to mercury were issued (EFSA, 2004, 2005; UK-COT, 2004, 2007; Japan-FSC, 2005; Canada-BCS, 2007). All these documents indicate that fish (marine and freshwater) and seafood are the major source of mercury intake in humans. Depending on species, methylmercury accounts for 70-100% total mercury in fish (EFSA, 2005). However, for conservative assessment purposes, it is generally assumed that 100% of the mercury found in fish and shellfish is methylmercury.

Wild fish species that are low in the food-chain, such as herring and sardines (plankton eaters) typically have total mercury concentrations less than 100 µg/kg wet weight, whereas predatory fish such as tuna, dogfish, halibut and shark contain considerably more mercury (typically 500-1000 µg/kg wet weight). Mercury levels are also dependent on the size and age of the fish (e.g. Boudou and Ribeyre, 1985).

Farmed salmonids have been shown to contain total mercury levels of up to approximately 100 µg/kg (Knowles *et al.*, 2003). The mercury content of 274 farmed Atlantic salmon (*Salmo salar*) fillets has been shown to vary from between <4 and 52 µg/kg wet weight[18] to up to 103 µg/kg (Knowles *et al*., 2003). The average total mercury concentration found in farmed rainbow trout (*Oncorhynchus mykiss*) fillets was 44 µg/kg (range 10-80 µg/kg, n=21). The average mercury content in farmed cod (*Gadus morhua*) fillet and liver were 100 µg/kg (range 3-350 µg/kg, n=24) and 10 µg/kg (range 1-30 µg/kg, n=21), respectively. The mean total mercury level in farmed Atlantic halibut (*Hippoglossus hippoglossus*) fillets was 50 µg/kg (range 3-90 µg/kg, n=15)[19]. The very limited data on farmed tuna fed on defrosted herring and sardines indicate that contamination levels in fillets exceed those reported for other farmed fish (490-1809 µg/kg, n=29) (Srebocan *et al.,* 2007).

The average value reported for total mercury contamination of fish in Europe was 109 ±845 µg/kg (EFSA, 2004), the high standard deviation reflecting the wide variations in the analytical results. More recent data obtained in France and Catalonia (Leblanc *et al.,* 2005, Bocio *et al*. 2005) indicated that average concentration of total mercury in fish of 62 and 97 µg/kg, respectively, which confirms former data.

According to EFSA (2004), the range of average fish consumption is from 10 to 80 g per day for six European countries, corresponding to a mercury weekly intake from 1.3 to 92 µg, per person. This is markedly lower than the values reported for Faroe Islands (average 252 µg/week), while in the Seychelles the daily mercury intake was estimated to be 103 µg, assuming a per capita consumption of fish of 75 kg per year (205 g per day) (Robinson and Shroff, 2004).

[18] Nifes, seafood data on undesirable substances: http://www.nifes.no/index.php?page_id=137&lang_id=2
[19] Nifes, seafood data on undesirable substances: http://www.nifes.no/index.php?page_id=137&lang_id=2

Some additional data on intake of mercury have recently been published. The estimated average weekly intake of mercury by the French population is 68 µg for adults aged 15 years or more (corresponding to 1.1 µg/kg b.w. per week for a 60 kg person) and 55 µg for children aged 3-4 years (Leblanc *at al.,* 2005). Estimated weekly intake of total mercury in the population from Catalonia (Bocio *et al*., 2005) is 148 µg, corresponding to 2.1 µg/kg b.w. per week, and is due principally to the high consumption of fish in this region.

The JECFA (2003) established a Provisional Tolerable Weekly Intake (PTWI) of 1.6 µg methylmercury/kg b.w. based on epidemiological studies that investigated the relationship between maternal exposure to mercury and inpaired neurodevelopment in their children. This PTWI was used along with the Reference Dose by EFSA (2004).

Several recent European risk assessments (UK-COT, 2004; EFSA, 2005; Leblanc *et al.,* 2005) concluded that for the general adult population the calculated intake of methylmercury does not exceed the PTWI. Regular consumption of top predatory fish such as tuna could result in the methylmercury PTWI being exceeded. The data examined in this opinion indicate that the maximum concentration reported to date in farmed salmonids is approximately five times lower than the EU maximum level for mercury in fish for human consumption (0.5 mg/kg in most species including salmonids and 1 mg/kg in a limited list of fish species). However, this mercury concentration in salmonids would allow weekly consumption of two fish meals, as recommended by nutritionists, without appreciable health risk. Therefore, the current level of total mercury in fish feed does not pose a threat to consumer's health, confirming that fish farming offers the possibility of managing the contaminant levels in fish in order to minimize the risks while maintaining the benefits (EFSA, 2005).

CONCLUSIONS

Chemistry and environmental fate

- Mercury is a naturally occurring element in the environment and may occur as elemental, inorganic and organic mercury. In the majority of cases, analyses of feed or animal tissues involve the measurement of the sum of all mercury (or "total mercury") in the sample, regardless of the chemical form in which it is present.
- Human activities have contributed significantly to the contamination of the environment. Currently, coal combustion is the main source. Anthropogenic emissions to air have decreased globally over the last decades and are lower in the atmosphere of Europe and North-America.
- Mercury compounds are still in use for agricultural purposes in some non-European countries.
- Methylmercury is the prevalent form in aquatic organisms and bioaccumulates in the food chain, particularly in aquatic animals.
- Analytical methods for total mercury are satisfactory and routine methods for methylmercury in feed are emerging.

Occurrence in feed

- The most common source of mercury in feed materials for farmed animals is fishmeal. Relatively few data are available on the speciation of mercury in fish feed, nevertheless the available data showed that it is mainly present as methylmercury.
- In feed materials derived from plants, average mercury concentrations are generally low (between 0.03 and 0.047 mg/kg dry matter). For all complete feedingstuffs, except those for fish and pets, the average value is 0.03 mg mercury/kg feed.
- For pets, the average concentration in complete feedingstuffs is 0.02 mg mercury/kg feed.
- Less than 3% of all feedingstuffs analysed exceeded total mercury MLs.
- Complete feedingstuffs for fish generally have the highest mercury content compared with feeds for other food producing animals. The average value was 0.06 mg mercury/kg feed, with approximately 8 % exceeding the ML. In the category of feedingstuffs produced by the processing of fish or other marine animals, no samples exceeded the ML. This indicates that the current MLs for complete feedingstuffs for fish

and feedingstuffs produced by the processing of fish or other marine animals are not harmonized.

General toxicological effects

- The three forms of mercury, namely elemental, inorganic and organic mercury, have different toxicological properties.
- Effects on the nervous system appear to be the most sensitive endpoints following inhalation, not oral (negligible absorption), exposure to elemental mercury.
- Nephrotoxicity is the most sensitive endpoint following chronic ingestion of inorganic mercury.
- Methylmercury is the form of greatest toxicological concern. Development of the central nervous system is affected by the chronic oral exposure to methylmercury. The cardiovascular, immune and reproductive systems are also affected at higher doses.

Adverse effects in target animals

- Following chronic oral exposure, the most sensitive species are cats (NOAEL for methylmercury: 0.5 mg/kg feed expressed as total mercury) and mink (LOAEL for methylmercury: 1.1 mg/kg feed expressed as total mercury).
- Due to the weakness of the toxicological database and only single animal experiments, no NOAEL could be derived for dogs. Only a LOAEL of 8 mg/kg feed expressed as total mercury) could be derived.
- For young chickens, young pigs and young calves, the NOAELs were 2.2, 3.4 and 5.0 mg/kg feed, respectively. For sheep, turkeys and ducks LOAELs of 7.7, 1.7 and 5 mg/kg feed, respectively, were established. For rabbit and horses no NOAEL or LOAEL could be derived.
- For cats on the basis on the available data on the occurrence of total mercury in complete feedingstuffs, no effects are expected. However, when cats are fed continuously with feedingstuffs containing a high proportion of top predatory fish, the current ML for complete feed for cats and dogs (0.4 mg/kg feed) appear as not sufficiently protective.
- For salmonids, the NOAEL for methylmercury is 170 µg (expressed as total mercury)/kg b.w. corresponding to 630 µg/kg feed (dry weight). The current ML for complete feed for fish (0.1 mg/kg feed) is considered sufficiently protective.

Fate in animals and carry-over to animal products

- The absorption, distribution, metabolism and excretion of mercury are largely dependent on its chemical form. Inorganic mercury is absorbed to a limited extent (10-30%) while methylmercury is absorbed extensively (typically 80%) following oral exposure.
- Inorganic mercury does not easily cross membranes, but concentrates in the kidney. Methylmercury distributes in all tissues (preferentially muscle in carnivorous fish), crosses blood-brain and placental barriers, and concentrates in hair and feathers.
- The metabolic fate of inorganic and organic mercury, which is similar for animals and humans, involves the bacterial (rumen, gut flora) demethylation of methylmercury and the oxidation-reduction cycle of Hg^{++} and Hg^{0}. Inorganic and methylmercury are mainly excreted in the faeces as Hg^{++} which is less effectively absorbed in the gut than organic mercury.
- Transfer of of organic and inorganic mercury to milk is about 1.2 and 0.2% of the dose respectively. It is limited to eggs (below 1%).
- Due to the lack of appropriate experimental data on mercury accumulation in domestic animals, it is not possible to calculate a transfer ratio of mercury into animal tissues, except for chicken meat.

Human exposure

- Fish and seafood are the main sources of human dietary exposure to mercury, and this is predominantly as methylmercury.
- Wild fish species that are low in the food chain have usually total mercury concentrations of less than 100 µg/kg wet weight, whereas predatory fish may contain more than 1000 µg/kg wet weight. Farmed fish fed pellets typically contain total mercury levels in the range of 8-100 µg/kg flesh. Higher levels have been found in farmed tuna.
- The maximum concentration reported in farmed salmonids is approximately five times lower than the EU maximum level for mercury in fish (500 µg/kg for salmonids). This mercury concentration in salmonids would allow weekly consumption of two fish meals, as recommended by nutritionists, without appreciable health risk. The ML for fish feed is sufficient to ensure that contamination levels in farmed salmonids pose no appreciable risk to consumers, but the validity of the ML need to be ascertained for other farmed fish.

RECOMMENDATIONS AND DATA NEEDS

- Although appropriate analytical methods are available for total mercury in feeds, definition of their quality performance criteria are needed.
- The analysis of methylmercury in feeds should be encouraged. Furthermore, intercomparison exercises on the analysis of methylmercury are required as well as the quality performance criteria for their use.
- Monitoring programmes should be more informative with respect to feed composition, and more systematic monitoring in terms of feed categories in the EU is needed. More data on occurrence of mercury in feed materials originating from Mediterranean countries should be made available.
- The Member States should be encouraged to report mercury levels as methylmercury and total mercury along with their respective concentrations rather than report the results as compliant or non-compliant for total mercury.
- There is a lack of data on contamination of farmed fish, except salmonids. Additional data on farmed carnivorous species, as compared with equivalent wild animals could help in estimating the capability of fish farming to reduce contamination of fish for consumption.

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Occurrence data

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France. Ministry of Agriculture and Fisheries. Bureau de la pharmacie vétérinaire et de l'alimentation animale.

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Faroe Islands. Food-, Veterinary- and Environmental Agency.

Finland. Finnish Food Safety Authority Evira.

Hungary. Ministry of Agriculture and Rural Development.

Iceland. The Icelandic Food and Veterinary Authority

Ireland. Department of Agriculture,

Norway. Norwegian Food Safety Authority.

Slovak Republic. Central Control and Testing Institute of Agriculture.

Slovenia. Veterinary Administration of Republic of Slovenia and University of Ljubljana.

Spain. Catalan Agency of Food Safety.

UK. Animal Feed Unit, Food Standards Agency.

EMFEMA. International Association of the European Manufacturers of Major, Trace and Specific Feed Mineral Materials. Belgium.

FEDIAF. The European Pet Food Industry Federation. Belgium.

FEFAC. The European Feed Manufacturers' Federation. Belgium.

Vereinigte Kreidewerke Dammann KG. Germany.

Ecosyl Products Ltd. UK.

Magnesitas de Rubián, S.A. Spain.

LIST OF ABBREVIATIONS

AAS	Atomic absorption spectrometry
AES	Atomic emission spectrometry
AFS	Atomic fluoresence spectrometry
ATSDR	Agency for Toxic Substances and Disease Registry
CNS	central nervous system
CV	Cold vapour
EC	Electron capture
EC	European Commission
EPA	Environmental Protection Agency
FEDIAF	European Pet Food Industry Federation
GC	Gas chromatography
GST	Glutathione S-transferase
HPLC	High performance liquid chromatography
IARC	International Agency for Research on Cancer
ICP	Inductively coupled plasma
IPCS	International Programme on Chemical Safety
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOAEL	Lowest observed adverse effect level
LOD	Level of detection
LOQ	Level of quantitation
MIP	Microwave induced plasma
ML	Maximum level
MS	Mass spectrometry
NMKL	Nordic Committee on Food Analysis
NMR	Nuclear magnetic resonance
NOAEL	No observed adverse effect level
PTWI	Provisional tolerable weekly intake
RPA	Risk and Policy Analysts Limited
SCAN	Scientific Committee on Animal Nutrition
SCOOP	Scientific co-operation on questions relating to food
UNEP	United Nations Environment Programme
US	United States (of America)
WHO	World Health Organization

ANNEX

Table A1. Estimates of mercury NOAELs and LOAELs in farm animals, pets and fish

Species	Age/ weight	Mercury species	NOAEL mg/kg b.w. (mg/kg feed)*	LOAEL mg/kg b.w. (mg/kg feed)*	Exposure in days	Clinical symptoms. Biochemical and histological findings	Reference
Calves	4 week old 45-57 kg	MeHg	0.1 (5)	0.2 (10)	90	Ataxia, prostration Nephrosis, cerebellar cells atrophy	Herigstad, 1972
Cattle	Yearlings	MeHg	0.225 (11)		56-65	Incoordination,stiffness, insteady gait	Wright *et al.*, 1973
Cattle	Yearlings 172-254 kg	EtHg		0.48 (24)	27	Weakness, incoordination Enlarged kidneys, congestion of cerebral vessels	Palmer *et al.*, 1973
Sheep	Yearling	MeHg		0.225 (7.7)	42-59	Incoordination, stiffness, insteady gait	Wright *et al.*, 1973
	Yearling 30-37 kg	EtHg		0.48 (17)	12	Anorexia, diarrhea Liver, kidney, cranial vessels and intestine mucosa congested	Palmer *et al.*, 1973
Pigs	5 weeks old	MeHg	0.19 (3.4)	0.38(6.8)	60	Liver degeneration	Tryphonas *et al.*, 1973
		MeHg		0.78 (8)	41-46	Anorexia, incoordination Liver degeneration	Tryphonas *et al.*, 1973
		MeHg		0.5	27	Liver degeneration	Chang *et al*., 1977
		$HgCl_2$	(5)	(50)	27	Liver degeneration	Chang *et al.*, 1977
Chickens	Day old	MeHg	(2.2)	(5)	33-49	50% death	Soares, 1973
	Adult	MeHg		(10)		Decreased weight gain, drop in eggs production and fertility	Scott, 1975
	Hens	MeHg		3.3 (44)	50	Drop in eggs production.	Lundholm, 1995

Species	Age/ weight	Mercury species	NOAEL mg/kg b.w. (mg/kg feed)*	LOAEL mg/kg b.w. (mg/kg feed)*	Exposure in days	Clinical symptoms. Biochemical and histological findings	Reference
	1.4 -1.6 kg					Alteration in egg shell	
Turkeys	16 week 6-9 kg	EtHg		0.16 (1.7-2.4)	13-42	Incoordination, weakness	Palmer *et al.*, 1973
Duck	Adult	MeHg		0.8 (11.2)		Reproductive impairment	Heinz, 1979
	Adult	MeHg		(5)		Deformities in ducklings	Heinz and Hoffman, 2003
Mink	Adult	MeHg		(1.1)	59-93	Anorexia, ataxia	Woebeser, 1976
Dogs	Adult	MeHg		0.12 (8)	385	No clinical signs; neuronal damage at histological examination	Davies *et al.*, 1977
				0.43 (28)	41-46	Anorexia, gait unsteady Neuronal, kidney and intestinal damages	Davies *et al.*, 1977
Cats		MeHg	0.020 (0.33)	0.046 (0.76)	420	Impaired hopping, ataxia, renal failure	Charbonneau *et al.*, 1976
Fish Atlantic Salmon (*S. salar*)	Parr	MeHgCl	0.17 (0.63)	1.2 (4.4)	112	Increased cell proliferation and elevated metallothionein, altered haematology	Berntssen *et al.*, 2004a
Rainbow trout (*O. mykiss*)			1.04 (21.6)		84	No effects on growth	Lock, 1975
Rainbow trout (*O. mykiss*)			(8)	(16)	105	Elevated blood packed cell volume and hyperplasia of gill epithelium	Wobeser, 1975

* expressed as mg/kg b.w. if figure is given without brackets and mg/kg feed if the figure is in brackets.

Table A2. Animal, intake and diet values used to calculate ruminant exposure levels in Table 9.

Livestock type	Live weight (kg)	Dry matter intake (kg/day)	% forage	% concentrates
Growing cattle	90	2.4	70	30
Growing cattle	200	5	85	15
Growing cattle	350	8.8	95	5
Dairy cow-dry	625	14	100	0
Dairy cow-lactating (20 kg milk/day)	625	18	75	25
Dairy cow-lactating (40 kg milk/day)	625	23	60	40
Sheep-growing lamb	30	0.8	100	0
Sheep-lactating ewe	70	2.2	40	60
Goats-lactating	80	2.6	20	80

Table A3. Animal and intake values used to calculate pig and poultry exposure levels in Table 10.

Livestock type	Body weight (kg)	Feed intake (fresh weight)(kg/day)
Growing pigs	30	1.5
Growing pigs	60	2.9
Growing/fattening pigs	90	3.3
Growing/fattening pigs	120	3.4
Dry sow	200	2.7
Lactating sow	200	6.5
Broilers (finishing stage)	2.5	0.15
Laying hens	3.5	0.115
Turkeys	16	0.65

SCIENTIFIC OPINION

Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food[1]

EFSA Panel on Contaminants in the Food Chain (CONTAM)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

This output, published on 10 April 2018, replaces the previous version published on 20 December 2012.*

ABSTRACT

EFSA was asked by the European Commission to consider new developments regarding inorganic mercury and methylmercury toxicity and evaluate whether the Joint FAO/WHO Expert Committee on Food Additives (JECFA) provisional tolerable weekly intakes for methylmercury of 1.6 µg/kg body weight (b.w.) and of 4 µg/kg b.w. for inorganic mercury were still appropriate. In line with JECFA, the CONTAM Panel established a tolerable weekly intake (TWI) for inorganic mercury of 4 µg/kg b.w., expressed as mercury. For methylmercury, new developments in epidemiological studies from the Seychelles Child Developmental Study Nutrition Cohort have indicated that n-3 long-chain polyunsaturated fatty acids in fish may counteract negative effects from methylmercury exposure. Together with the information that beneficial nutrients in fish may have confounded previous adverse outcomes in child cohort studies from the Faroe Islands, the Panel established a TWI for methylmercury of 1.3 µg/kg b.w., expressed as mercury. The mean dietary exposure across age groups does not exceed the TWI for methylmercury, with the exception of toddlers and other children in some surveys. The 95th percentile dietary exposure is close to or above the TWI for all age groups. High fish consumers, which might include pregnant women, may exceed the TWI by up to approximately six-fold. Unborn children constitute the most vulnerable group. Biomonitoring data from blood and hair indicate that methylmercury exposure is generally below the TWI in Europe, but higher levels are also observed. Exposure to methylmercury above the TWI is of concern. If measures to reduce methylmercury exposure are considered, the potential beneficial effects of fish consumption should also be taken into account. Dietary inorganic mercury exposure in Europe does not exceed the TWI, but inhalation exposure of elemental mercury from dental amalgam is likely to increase the internal inorganic mercury exposure; thus the TWI might be exceeded.

KEY WORDS

total mercury, methylmercury, inorganic mercury, tolerable weekly intake, risk assessment, fish, food

[1] On request from the European Commission, Question No EFSA-Q-2011-00923, adopted on 22 November 2012.

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* Corrections have been applied on p. 69 where the year of reference Bourdineaud et al. (2011) has been replaced with 2012, and in the reference list where the correct reference has been inserted.

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SUMMARY

Following a request from the European Commission, the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) was asked to deliver a scientific opinion on the risks to human health related to the presence of inorganic mercury and methylmercury in food. The Panel was asked to consider new developments regarding the toxicity of inorganic mercury and methylmercury since the last opinion of the European Food Safety Authority (EFSA) of 24 February 2004 and to evaluate whether the provisional tolerable weekly intakes (PTWIs) established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) of 1.6 µg/kg body weight (b.w.) for methylmercury and of 4 µg/kg b.w. for inorganic mercury were considered appropriate. The CONTAM Panel was also asked to assess human dietary exposure, taking into account specific sensitive groups and to consider the non-dietary sources of exposure to mercury species.

Mercury is a metal that is released into the environment from both natural and anthropogenic sources. Once released, mercury undergoes a series of complex transformations and cycles between atmosphere, ocean and land. The three chemical forms of mercury are (i) elemental or metallic mercury (Hg^0), (ii) inorganic mercury (mercurous (Hg_2^{2+}) and mercuric (Hg^{2+}) cations) and (iii) organic mercury. Methylmercury is by far the most common form of organic mercury in the food chain.

This opinion focuses only on the risks related to dietary inorganic mercury and methylmercury exposure and does not assess the nutritional benefits linked to certain foods (e.g. fish and other seafood).

A call for annual collection of chemical contaminant occurrence data in food and feed, including mercury, was issued by EFSA in December 2010. In response, EFSA received 59 820 results on mercury in food from 20 European countries, mainly covering the period from 2004 to 2011. A total number of 59 650 results were described with sufficient detail to be used in the statistical analysis of the respective food groups; 98.2 % of the samples were for total mercury, 1.8 % for methylmercury and three samples for inorganic mercury.

All the 20 food groups available at the first level of FoodEx were covered in the current data collection. The food groups 'Fish and other seafood' and 'Meat and meat products' dominated the food product coverage with 36.8 % and 17.6 % respectively. These were followed by 'Grain and grain-based products' at 7.8 % and 'Vegetables and vegetable products (including fungi)' at 7.3 %. More than 60 % of the data were below the limit of detection (LOD) or the limit of quantification (LOQ) (left-censored (LC)) in 11 of the food groups. However, 12 % of the results for 'Fish and other seafood', which had the highest values of total mercury in comparison to all other food categories, were LC. The mercury content varied widely among different fish species, and was highest in predatory fish.

Because of the lack of specific information on methylmercury and inorganic mercury data in the database, the exposure assessment (except for human milk) was based on the data submitted for total mercury. The analysed total mercury was converted to methylmercury and inorganic mercury by applying conversion factors based on the methylmercury/total mercury proportion derived from literature data, using a conservative approach. For fish meat, fish products, fish offal and unspecified fish and seafood a conversion factor of 1.0 was used for methylmercury and 0.2 for inorganic mercury. For crustaceans, molluscs and amphibians the conversion factor was 0.8 for methylmercury and 0.5 for inorganic mercury. For all other food categories apart from 'Fish and other seafood', total mercury was regarded as inorganic mercury. Because this approach was chosen, total mercury dietary exposure cannot be derived by adding inorganic and methylmercury dietary exposure together. In order to estimate dietary exposure, the consumption data of each individual within the surveys were multiplied by the mean occurrence data for the relevant food categories, resulting in a distribution of exposure, from which the mean and 95th percentile were identified for each survey and age class. For

human milk, the mean concentrations of methylmercury and inorganic mercury in a limited number of European studies were used for exposure assessment.

The dietary exposure to methylmercury was based only on the food group 'Fish and other seafood' and since there was little difference between the lower bound (LB) and upper bound (UB) exposure estimates, the middle bound (MB) exposures were used. The mean MB methylmercury dietary exposure varied from the lowest minimum of 0.06 µg/kg b.w. per week seen in elderly and very elderly to the highest maximum of 1.57 µg/kg b.w. per week in toddlers. The 95th percentile MB dietary exposure ranged from the lowest minimum of 0.14 µg/kg b.w. per week in very elderly to the highest maximum of 5.05 µg/kg b.w. per week in adolescents. Based on mean concentrations of methylmercury in human milk, the dietary exposure to methylmercury for infants with an average human milk consumption ranged from 0.09 to 0.62 µg/kg b.w. per week and for infants with high milk consumption the dietary exposure ranged from 0.14 to 0.94 µg/kg b.w. per week.

Fish meat was the dominating contributor to methylmercury dietary exposure for all age classes, followed by fish products. In particular tuna, swordfish, cod, whiting and pike were major contributors to methylmercury dietary exposure in the adult age groups, while the same species, with the addition of hake, were the most important contributors in the child age groups. Dietary exposure in women of child-bearing age was especially considered and found not to be different from adults in general. The dietary exposure estimations in high and frequent consumers of fish meat (95th percentile, consumers only) was in general approximately two-fold higher in comparison to the total population and varied from a minimum MB of 0.54 µg/kg b.w. per week in elderly to a maximum MB of 7.48 µg/kg b.w. per week in other children.

The estimation of dietary exposure to inorganic mercury was based on minimum LB and maximum UB data due to the high proportion of LC data and the large difference between LB and UB concentrations. The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.13 µg/kg b.w. per week in elderly to the highest maximum UB of 2.16 µg/kg b.w. per week in toddlers. The 95th percentile dietary exposure was estimated to be from the lowest minimum LB of 0.25 µg/kg b.w. per week in elderly and very elderly to the highest maximum UB of 4.06 µg/kg b.w. per week in toddlers. Based on mean concentrations of inorganic mercury in human milk, the dietary exposure for infants with an average milk consumption ranges from 0.17 to 1.29 µg/kg b.w. per week and from 0.25 to 1.94 µg/kg b.w. per week for infants with a high milk consumption.

At FoodEx Level 1, 'Fish and other seafood', 'Non-alcoholic beverages' and 'Composite food' were the most important contributors to inorganic mercury dietary exposure in the European population. Dietary exposure to inorganic mercury was driven by high concentrations in the case of fish and other seafood and composite food (where a high proportion of the data were LC), but was more likely driven by high consumption in the case of non-alcoholic beverages.

Non-dietary exposure to methylmercury is likely to be of minor importance for the general population in Europe, but exposure to elemental mercury via the outgassing of dental amalgam is believed to strongly contribute to the internal inorganic mercury exposure.

After oral intake, methylmercury is much more extensively and rapidly absorbed than mercuric and mercurous mercury. In human blood mercuric mercury is divided between plasma and erythrocytes, with more being present in plasma, whereas methylmercury is accumulated to a large extent (> 90 %) in the erythrocytes. In contrast to mercuric mercury, methylmercury is able to enter the hair follicle, and to cross the placenta as well as the blood-brain and blood-cerebrospinal fluid barriers, allowing accumulation in hair, the fetus and the brain. Mercuric mercury in the brain is generally the result of either in situ demethylation of organic mercury species or oxidation of elemental mercury. Excretion of absorbed mercuric mercury occurs mainly via urine, whereas the main pathway of excretion of absorbed methylmercury is via faeces in the form of mercuric mercury. Urinary total mercury might be a suitable biomarker of inorganic (and elemental) mercury, but not for methylmercury exposure. Total mercury in hair and blood are routinely used as biomarkers to assess long term methylmercury

exposure. A frequently cited total mercury blood to hair ratio is 1:250, however large variations exist, especially in people with infrequent fish consumption.

A recent developmental study of methylmercury in mice, applying only one low dose, indicated effects on body weight gain, locomotor function and auditory function. A large study in rats showed developmental immunotoxic effects at low doses, and the lower 95 % confidence limit for a benchmark response of 5 % ($BMDL_{05}$) of 0.01 mg/kg b.w. per day, expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day, expressed as mercury) for the specific antibody response in rats was the lowest BMDL. While bearing this in mind, the Panel concluded that experimental animal studies on methylmercury did not provide a better primary basis than the human data for a health-based guidance value.

New data from the Faroe Islands Cohort 1 at children's age 14 years indicated that the association between prenatal exposure and neurological auditory function was still present at 14 years, but with a smaller impact than at seven years. Reassessment of the data from the Faroese Cohort 1 participants at age seven years indicated that beneficial effects of fish consumption together with imprecision in the measurements of fish consumption and determination of mercury in hair might underestimate the effects of methylmercury.

Reassessments of the 4.5 years results and the 10.5 and 17 years follow up studies from the Main Cohort in the Seychelles Child Developmental Study have not revealed any consistent association between prenatal mercury exposure and neurodevelopmental endpoints. Results from the smaller Nutrition Cohort in the Seychelles Child Developmental Study indicated an association between prenatal mercury exposure and decreased scores on neurodevelopmental indices at 9 and 30 months after adjustment for prenatal blood maternal n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFAs). An apparent no-observed-effect level (NOEL) at a mercury level of approximately 11 mg/kg maternal hair was observed. No statistically significant associations between prenatal mercury exposure and developmental endpoints were found at the five years follow up of the study. However, a positive association between maternal prenatal n-3 LCPUFAs, in particular docosahexaenoic acid, and preschool language scores was reported from the five years follow up.

The reported associations between methylmercury exposure and cardiovascular disease were addressed by JECFA in their update in 2006 (FAO/WHO, 2007), and additional studies have become available. The importance of taking the beneficial effects of fish consumption into account when studying cardiovascular outcomes of methylmercury has become evident. Although the observations related to myocardial infarction, heart rate variability and possibly blood pressure are of potential importance, they are still not conclusive. Consequently, after carefully considering other endpoints than neurodevelopmental outcomes, and in particular cardiovascular disease, the CONTAM Panel concludes that associations between methylmercury exposure and neurodevelopmental outcomes after prenatal exposure still form the best basis for derivation of a health-based guidance value for methylmercury.

The mean of the apparent NOEL from the Seychelles nutrition cohort at 9 and 30 months (11 mg/kg maternal hair) and the $BMDL_{05}$ from the Faroese cohort 1 at age seven years (12 mg/kg in maternal hair), resulting in 11.5 mg/kg maternal hair, was used as the basis for derivation of a health-based guidance value. By application of a maternal hair to maternal blood ratio of 250, the maternal hair mercury concentration with no appreciable adverse effect was converted into a maternal blood mercury concentration of 46 µg/L. Using a one-compartment toxicokinetic model, the value of 46 µg/L in maternal blood was converted to a daily dietary mercury intake of 1.2 µg/kg b.w. A data-derived uncertainty factor of 2 was applied to account for variation in the hair to blood ratio. In addition, a standard factor of 3.2 was applied to account for interindividual variation in toxicokinetics, resulting in a total uncertainty factor of 6.4. A tolerable weekly intake (TWI) for methylmercury of 1.3 µg/kg b.w. expressed as mercury, was established. The Panel noted that this TWI provides a margin of about 40 compared to the $BMDL_{05}$ for the reduction in antibody response in rats.

The mean dietary exposure across age groups does not exceed the TWI for methylmercury, with the exception of toddlers and other children in some surveys. The medians of 95th percentile dietary exposures across surveys are close to or above the TWI for all age groups. High consumers of fish meat may exceed the TWI by up to approximately six-fold. Unborn children constitute the most vulnerable group for developmental effects of methylmercury exposure, and pregnant women can be present in the group of high and frequent fish consumers. Biomonitoring data on blood and hair concentrations indicate that in the general European population, methylmercury exposure is generally below the TWI. However, higher concentrations in blood and hair are also observed, confirming higher dietary exposure in some population groups. Exposure to methylmercury above the TWI is of concern, but if measures to reduce methylmercury exposure are considered, the potential beneficial effects of fish consumption should also be taken into account.

The critical target for toxicity of inorganic mercury is the kidney. Other targets include the liver, nervous system, immune system, reproductive and developmental systems. Having considered the experimental animal data on inorganic mercury, including some recent studies not reviewed by JECFA in its evaluation of 2010, the Panel agrees with the rationale of JECFA in setting a health-based guidance value using kidney weight changes in male rats as the pivotal effect. Based on the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury and an uncertainty factor of 100 to account for inter and intra species differences, with conversion to a weekly basis and rounding to one significant figure, the Panel established a TWI for inorganic mercury of 4 µg/kg b.w., expressed as mercury.

The estimated exposure to inorganic mercury in Europe from the diet alone does not exceed the TWI. Inhaled elemental mercury vapour from dental amalgam, which after absorption is converted to inorganic mercury, is an additional source that is likely to increase the internal inorganic mercury exposure; thus the TWI might be exceeded.

The CONTAM Panel recommends to develop certified reference materials and proficiency testing schemes for inorganic mercury in foodstuffs other than fish and seafood. Further effort should be made to increase the number of methylmercury and inorganic mercury data in all food groups that contribute significantly to overall exposure. In order to decrease the uncertainty in the point of departure derived from the epidemiological studies, more reliable definition of the dose response taking confounding factors into account is needed. Future studies should elucidate the relevance of additional endpoints, such as immunological and cardiovascular endpoints.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

The EFSA Scientific Panel on Contaminants in the Food Chain (CONTAM Panel) issued a scientific opinion on mercury and methylmercury in food on 24 February 2004[4]. The scientific opinion focussed mainly on methylmercury. The Panel concluded that in some countries the exposure resulting from average intake of fish and seafood products may be close to the provisional tolerable weekly intake (PTWI) of 1.6 µg/kg b.w. for methylmercury established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Some population groups who frequently consume large predatory fish may have a considerably higher intake of methylmercury and exceed the PTWI. The Panel also concluded that the occurrence data available at that time did not allow reliable estimations of the intakes by high consumers in different populations.

Regulation (EC) No. 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs[5] contains maximum levels for mercury in fish and seafood. In order to decide whether a review of these levels is appropriate, an updated scientific opinion is needed. New occurrence data on mercury as well as more detailed consumption data have become available since the EFSA opinion of 2004 and should be taken into account for more reliable intake estimations.

The updated scientific opinion should cover both forms of mercury: organic mercury (methylmercury) as the most toxic form that is prevalent in fish and seafood, as well as inorganic mercury, prevalent in most other foodstuffs. The evaluation of mercury carried out by JECFA at its 72nd meeting in February 2010[6] should be taken into account.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002 the European Commission asks the European Food Safety Authority for a scientific opinion on the risks to human health related to the presence of mercury and methylmercury in food.

The opinion should address both inorganic mercury and organic forms of mercury (in particular methylmercury).

In particular, the opinion should

- consider any new developments regarding the toxicity of inorganic mercury and methylmercury since the last EFSA opinion of 24 February 2004. This should comprise an evaluation whether the JECFA PTWIs for methylmercury of 1.6 µg/kg b.w. and of 4 µg/kg b.w. for inorganic mercury are considered appropriate,

- contain an updated exposure assessment for inorganic mercury and methylmercury in food (incl. drinking water) and outline those food groups that are main contributors to exposure for inorganic mercury and methylmercury, respectively,

- address the exposure to methylmercury for specific sensitive groups of the population (e.g. the unborn child, children, high consumers of fish and seafood) and give an indication of the age group in which children would be most exposed to the toxic effects of methylmercury,

- highlight the population groups most exposed to inorganic mercury and give an indication of the age group in which children would be most exposed to inorganic mercury,

- give a rough estimation of other non-dietary sources of exposure to mercury.

[4] The EFSA Journal (2004) 34, 1-14.
[5] OJ L 364, 20.12.2006, p. 5.
[6] WHO TRS 959, Seventy-second report of the Joint FAO/WHO Expert Committee on Food Additives, 16-25 February 2010.

ASSESSMENT

1. INTRODUCTION

1.1. General information

Mercury (Hg) is a metal that is released into the environment from both natural and anthropogenic sources. After release into the environment, it undergoes complex transformations and cycles between atmosphere, land and aquatic systems. During this biogeochemical cycle, humans, plants, and animals are exposed to mercury, potentially resulting in a variety of health impacts (EFSA, 2008).

The three chemical forms of mercury are (i) elemental or metallic mercury (Hg^0), (ii) inorganic mercury (mercurous (Hg_2^{2+}) and mercuric (Hg^{2+}) cations) and (iii) organic mercury.

In its elemental form, mercury is a liquid at ambient temperatures and pressures and it volatilises strongly. In general, elemental mercury is the predominant form of mercury in the atmosphere (Selin, 2009).

Inorganic mercury (IHg) compounds are salts of Hg_2^{2+} and Hg^{2+}, which are used in several industrial processes and can be found in batteries, fungicides, antiseptics or disinfectants (US-EPA, 2007; EFSA, 2008).

Organic mercury compounds have at least one carbon atom covalently bound to the mercury atom (WHO, 1991). Methylmercury (MeHg) is by far the most common form in the food chain (EFSA, 2008). Other organic mercury compounds like phenylmercury, thiomersal and merbromin (also known as Mercurochrome) have been used as fungicides and in pharmaceutical products (EFSA, 2008).

The largest source of mercury exposure for most people in developed countries is inhalation of mercury vapour due to the continuous release of elemental mercury from dental amalgam. Exposure to methylmercury mostly occurs via the diet. Methylmercury collects and concentrates especially in the aquatic food chain, making populations with a high intake of fish and seafood particularly vulnerable (European Commission, 2005a; Richardson et al., 2011).

The European Commission asked the European Food Safety Authority (EFSA) to provide an updated scientific opinion on the risks for public health related to the presence of mercury and methylmercury in food. Therefore, this opinion focuses only on the risks related to dietary mercury and methylmercury exposure and does not assess the nutritional benefits linked to certain foods (e.g. fish and other seafood).

1.2. Previous risk assessments

Mercury, particularly methylmercury, has been the subject of many previous risk assessments. The most relevant and recent of these are described below.

In 1999, the United States Environmental Protection Agency (US-EPA) asked the National Research Council (NRC) of the National Academy of Sciences (NAS) to provide recommendations on derivation of an appropriate reference dose (RfD) for methylmercury. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The NRC concluded that the RfD should be based on a benchmark dose (BMD) for a reliable neurobehavioural endpoint from the study conducted in the Faroe Islands. The NRC considered that dose-response data for the Boston Naming Test should be modelled based on mercury concentrations in cord blood as a reasonable point of departure for deriving the RfD. A benchmark response (BMR) of 5 % was selected, which would result in a doubling of the number of children with a response at the 5th percentile of the population, and considered significantly developmentally

compromised. That approach estimated a lower 95 % confidence limit for a benchmark response of 5 % ($BMDL_{05}$) of 58 µg/kg of mercury in cord blood (corresponding to a $BMDL_{05}$ of 12 mg/kg of mercury in hair). To calculate the RfD, the BMDL should be divided by uncertainty factors of at least 10 to take into consideration biological variability when estimating dose and methylmercury database insufficiencies. On this basis, the NRC concluded that the value of EPA's previously established RfD for methylmercury, 0.1 µg/kg body weight (b.w.) per day, was a scientifically justifiable level for the protection of public health but that the basis for this value required revision (NRC, 2000).

The US-EPA subsequently revised its risk assessment (US-EPA, 2001a). BMD analyses, in terms of cord-blood mercury, were performed for a number of endpoints from the Faroe Islands study, and also from studies conducted in the Seychelles and New Zealand. The US-EPA based its RfD of 0.1 µg/kg b.w. per day on an integrative analysis of the $BMDL_{05}$s from these three studies, which were expressed as mercury in cord blood, by converting to an ingested dose using a pharmacokinetic model and applying an uncertainty factor of 10. This factor of 10 comprised a factor of 3 to allow for pharmacokinetic variability and uncertainty in estimating an ingested dose from cord-blood mercury and a factor of 3 for pharmacodynamic variability and uncertainty.

In 1972, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a provisional tolerable weekly intake (PTWI) of 5 µg/kg b.w. for total mercury (THg) of which no more than 3.3 µg/kg b.w. should be in the form of methylmercury (FAO/WHO, 1972). This was based primarily on the relationship between the intake of mercury from fish and mercury levels in blood and hair associated with the onset of clinical disease. The JECFA maintained the PTWI of 3.3 µg/kg b.w. for methylmercury throughout a number of subsequent evaluations, whilst noting that fetuses and infants might be more sensitive than adults to its toxic effects. In 2003, the JECFA revised the PTWI to 1.6 µg/kg b.w. based on the results of the epidemiological studies in the Faroe Islands and the Seychelles (FAO/WHO, 2004). The JECFA selected the $BMDL_{05}$ of 12 mg/kg mercury in maternal hair from the Faroe Islands and the no-observed-effect level (NOEL) of 15.3 mg/kg mercury in maternal hair from the Seychelles as the basis for its revised PTWI. The average of these two values, 14 mg/kg, was considered to be an estimate of the concentration of mercury in maternal hair reflecting exposure that would have no appreciable adverse effects in these two study populations. The maternal hair concentration was extrapolated to a blood concentration of 56 µg/L by dividing by the average reported ratio of mercury in hair to mercury in blood (250:1). This blood concentration was then converted to a steady-state intake of 1.5 µg/kg b.w. per day using a similar pharmacokinetic model as used by NRC and US-EPA, incorporating values for body weight and blood volume for pregnant women. A composite uncertainty factor of 6.4 was applied, incorporating a data-derived factor of 2 for variation in hair to blood ratio, and a default factor of 3.2 for toxicokinetic variability in the relationship between blood mercury and steady state dietary intake, resulting in the PTWI of 1.6 µg/kg b.w. The JECFA considered that a factor for toxicodynamic variability was not needed because the data were derived from sensitive subgroups representing diverse populations (FAO/WHO, 2004). Hence, the key difference between the US-EPA and JECFA evaluations is that US-EPA took a more conservative view in deciding that a factor was required for toxicodynamic variability.

In 2006, the JECFA was asked to clarify the relevance of the PTWI for different subgroups of the population, taking into account that guidance values based on developmental endpoints may be overly conservative for some parts of the population. The JECFA confirmed that the methylmercury PTWI of 1.6 µg/kg b.w. was based on the most sensitive toxicological endpoint (developmental neurotoxicity) in the most susceptible species (humans). Intakes of up to about twice the PTWI would not pose a risk of neurotoxicity to adults except potentially for women of childbearing age because of the effects on the embryo and fetus. However, whilst infants and children up to about 17 years of age are not more sensitive than the embryo or fetus the data did not allow firm conclusions regarding sensitivity compared with adults (FAO/WHO, 2007).

The FAO and WHO convened a Joint Expert Consultation on the Risks and Benefits of Fish Consumption in 2010, which considered nutrients (n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFAs)) and specific chemical contaminants (methylmercury and dioxin-like compounds) in

a range of fish species. The consultation concluded that among women of childbearing age, pregnant women and nursing mothers, considering the benefits of docosahexaenoic acid (DHA) versus the risks of methylmercury, fish consumption lowers the risk of suboptimal neurodevelopment in their offspring compared with not eating fish in most circumstances evaluated. Among infants, young children and adolescents, the evidence was insufficient to derive a quantitative framework of health risks and benefits (FAO/WHO, 2011a).

In 2004, the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) published an opinion on mercury and methylmercury in food (EFSA, 2004). In view of the terms of reference and timescale of the request from the European Commission, the CONTAM Panel did not conduct a hazard characterisation, and based its risk characterisation on comparison of mercury dietary exposure with both the RfD established by the NRC and US-EPA and the JECFA PTWI. The CONTAM Panel concluded that estimates of dietary exposure to methylmercury of average consumers of fish and seafood products in some countries were close to the PTWI and exceeded the RfD. However, the available data did not allow reliable estimates of the intakes of high consumers in different populations. Therefore, there was a need for reliable intake data from studies focused on women of childbearing age.

In 2010, the JECFA reviewed the PTWI for total mercury. It was assumed that the predominant form of mercury in foods other than fish and shellfish is inorganic mercury, and that the toxicological database for mercuric chloride was relevant for assessing the health risk of foodborne inorganic mercury. An increase in relative kidney weight in male rats was identified as the appropriate basis for establishing a PTWI. The lowest $BMDL_{10}$ for mercuric chloride was equivalent to 0.06 mg/kg b.w. per day of mercury. After application of a 100-fold uncertainty factor and converting to a weekly basis, the JECFA established a PTWI of 4 µg/kg b.w for inorganic mercury. In the absence of evidence to the contrary, this PTWI was considered applicable to dietary exposure to total mercury from foods other than fish and shellfish. The estimates of average dietary exposure were at or below the PTWI (FAO/WHO, 2011b).

1.3. Chemistry

Mercury is a metal that occurs naturally in the earth's crust and in the environment. Mercury belongs to Group IIB of the periodic table and has an atomic number of 80 and molecular mass of 200.59 g/mol. There are seven stable isotopes of mercury, with ^{202}Hg being the most abundant (29.86 %). In pure form, it is known alternatively as 'elemental' or 'metallic' mercury (also expressed as Hg(0) or Hg^0). Elemental mercury is a odourless, shiny, silver-white metal and is the only common metal to be liquid at ordinary temperatures and pressures (density = 13.534 g/cm^3).

The three chemical forms of mercury known to be present in the environment (see Table 1 adapted from Kuban et al. (2007) are (i) elemental mercury (Hg^0), which has high vapour pressure and relatively low solubility in water; (ii) mercurous (Hg_2^{2+} or Hg(I)) and mercuric (Hg^{2+} or Hg(II)) inorganic cations, which can be far more soluble and which have a strong affinity for many inorganic and organic ligands, especially those containing sulphur, and (iii) organometallic compounds with one or two alkyl-/aryl- substituents are bound to the mercury atom, forming (mono-/di-) alkylated and/or arylated RHgX or RHgR' mercury species, where R and R' represent alkyl and/or aryl substituents (CH_3–, C_2H_5–, C_6H_5–) and X is an anion (halide, nitrate or sulphate). Many inorganic and organic compounds of mercury can be formed from Hg^{2+}. Inorganic mercury salts are usually found in the forms of mercuric sulphide (HgS), mercuric oxide (HgO) and mercuric chloride ($HgCl_2$). There are several organic mercury compounds; by far the most common in the environment and in the aquatic food chain is methylmercury (FAO/WHO 2011b). Because methylmercury is strongly bound to muscle, methylmercury does accumulate appreciably with increased muscle mass and increased duration of exposure.

Table 1: Elemental mercury and major mercury ions/species in environmental and biological samples (adapted from Kuban et al. (2007)).

			CAS number
Elemental mercury		Hg^0	92786-62-4
Inorganic mercury ions	Mercurous ion	Hg_2^{2+}	n/a
	Mercuric ion	Hg^{2+}	7439-97-6
Organic mercury ions/species	Methylmercury	CH_3Hg^+	22967-92-6
	Dimethylmercury	$(CH_3)_2Hg$	593-74-8
	Ethylmercury	$CH_3CH_2Hg^+$	627-44-1
	Phenylmercury	$C_6H_5Hg^+$	23172-37-4

n/a: not available.

In summary, mercury exists in the following main states under natural conditions (UNEP, 2002):

- as metallic vapour and liquid/elemental mercury;
- bound in mercury-containing minerals (solid);
- as ions in solution or bound in ionic compounds (inorganic and organic salts);
- as soluble ion complexes;
- as gaseous or dissolved non-ionic organic compounds;
- bound to inorganic or organic particles/matter by ionic, electrophilic or lipophilic adsorption.

1.4. Production, use and environmental fate

1.4.1. Production

The mercury available on the world market is supplied from a number of different sources, of which the main sources are primary production (mercury mining); secondary production (where mercury is a by-product, for example in zinc production); recycling (from fluorescent lamps, etc.); and reuse of surpluses (for example from the chloralkali industry). The total global mercury supply was estimated in 2007 at about 3 100 - 3 900 tonnes per year (Maxson, 2009).

1.4.2. Use

Batteries, gold mining and the chloralkali industry are the most important global uses, accounting for over 75 % of worldwide mercury consumption (European Commission, 2005a).

In order to reduce the mercury levels in the environment and the human exposure, the European Commission launched the European Union (EU) mercury strategy in 2005. It is a comprehensive plan that includes 20 measures to reduce mercury emissions, to reduce the supply and demand of mercury and protect against exposure.[7] In 2010 the European Commission reviewed the mercury strategy and concluded that the implementation of the strategy is in an advanced stage and almost all actions are delivered.[8] The implementation of these policies is expected to reduce the emissions, although data are not yet available.

Mercury is used in the form of thiomersal in vaccines. Thiomersal (synonyms sodium 2-ethylmercurothio-benzoate, thimerosal, merthiolate, mercurothiolate, merfamin, mertorgan, merzonin, $C_9H_9HgNaO_2S$, CAS No 54-64-8) is used to prevent bacterial and fungal growth in vaccines, especially in vaccines formulated in multidose vials.

The following global past and present mercury applications and sources have been identified (based on UNEP, 2002; Fauser et al., 2011):

[7] http://ec.europa.eu/environment/chemicals/mercury/
[8] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:52010DC0723:EN:NOT

- chloralkali production (chlorine and caustic soda);
- dental amalgam;
- artisanal gold and silver mining;
- batteries;
- measuring and control equipment (e.g. thermometers, manometers);
- electric and electronic switches (e.g. switches in sports shoes with lights in soles, thermo-switches);
- discharge lamps (e.g. fluorescent lamps);
- laboratory chemicals, electrodes and apparatus for analysis;
- pesticides (seed dressing and/or others);
- biocides for different products and processes (e.g. paints);
- slimicides for paper production;
- pharmaceuticals (e.g. preservatives in vaccines, preservatives in eye drops);
- catalytic mercury compounds;
- cosmetics (creams, soaps);
- lighthouses (marine use; for establishing lenses);
- production of counterfeit money;
- mercury metal use in religious rituals and folklore medicine;
- pigments;
- tanning;
- browning and etching steel;
- colour photograph paper;
- explosives, fireworks;
- airbag activators and anti-lock braking system mechanisms in cars;
- artisanal diamond production;
- recoil softeners for rifles;
- arm and leg bands;
- executive toys;
- surfacing material used in running tracks in sports stadiums;
- ammunition;
- hardeners and resins in plastics, fillers;
- liquid crystal displays (LCDs).

1.4.3. Environmental fate and levels

Mercury is released into the environment by both natural and anthropogenic sources. The most important natural sources of mercury are the degassing of the earth's crust, emissions from volcanoes and evaporation from water. Anthropogenic emissions such as coal burning, mining and other industrial activities add to the overall mercury release. It has been estimated that the amounts of mercury resulting from this may be quite small relative to the global emissions. However, it was stressed that there are considerable uncertainties in the estimated mercury emissions (WHO, 1991). Mercury is continuously mobilised, deposited and re-mobilised in the atmosphere, ocean and land, and a recent review by Selin (2009) describes the current understanding of this biogeochemical cycle.

Atmosphere

Mercury is naturally emitted from land and ocean surfaces as elemental mercury. Anthropogenic sources result in the emission of elemental mercury, mercuric mercury and particle-bound mercury. In general, elemental mercury is the predominant form of mercury in the atmosphere (Selin, 2009; Sprovieri et al., 2010). The global background concentration of airborne mercury is considered to be in the range 1.5 - 1.7 ng/m^3 in the Northern Hemisphere and 1.1 - 1.3 ng/m^3 in the Southern Hemisphere (Lindberg et al., 2007).

The global anthropogenic emission of mercury was estimated for 2000 to be ca. 2 190 tonnes (Pacyna et al., 2006). A similar estimation was performed for 2005 but included additional sources that had not been included previously, such as emissions from human cremation and artisanal and small-scale gold mining, and showed a total emission of 1 930 tonnes (Pacyna et al., 2010). UNEP is currently updating the estimation of mercury emissions and new data should be available in 2013.[9] Asia is the highest contributor (about 67 %) to the global anthropogenic emission of mercury, followed by North America and Europe. The main source of mercury emission is the combustion of fossil fuels, mainly coal in power plants and industrial and residential boilers (Pacyna et al., 2010). Crematoria are in relative terms not a large source, but the emissions from crematoria are significant in some countries (European Commission, 2005b). It was estimated that crematoria will be the single biggest contributor to national mercury emissions in the United Kingdom (UK) by 2020 (Wood et al., 2008).

Soil

Mercury is present in geologically enriched areas in the earth, but can be deposited from the atmosphere to the soil as mercuric mercury (Morel et al., 1998). A portion of this newly deposited mercury will be reduced to elemental mercury, which will rapidly evaporate again to the atmosphere (Selin, 2009). Newly deposited mercury that is not immediately reduced and evaporated can accumulate in vegetation, and Boening (2000) describes the factors influencing accumulation in terrestrial plants. The remaining mercury will be incorporated into a soil mercury pool, which shows slow transformation and which will be slowly released to the atmosphere, during a process that can take centuries or millennia (Schlüter, 2000; Selin, 2009).

Aquatic systems and sediments

The CONTAM Panel refers to Ullrich et al. (2001) for a comprehensive review on the occurrence of mercury in aquatic systems and sediments and discusses this topic briefly below.

The main chemical forms in which mercury occurs in water are elemental mercury, complexes of mercuric mercury with various inorganic and organic ligands, and organic mercury forms, mainly methylmercury and dimethylmercury. The occurrence of these chemical forms depends on the pH, redox potential and the concentration of inorganic and organic complexing agents (Ullrich et al., 2001). The contribution of methylmercury to total mercury is typically less than 5 % in estuarine and marine waters, but can be up to 30 % in fresh water (Ullrich et al., 2001).

Total mercury concentrations in marine systems have been reported between 0.2 and 0.5 ng/L (Cossa et al., 1997; Mason et al., 1998; Laurier et al., 2004). However, higher concentrations in the range of 1.0 - 20.1 ng/L are reported in fresh water (Morel et al., 1998).

The levels of mercury in uncontaminated sediments are comparable to levels in uncontaminated soils. The contribution of methylmercury to total mercury in sediments is typically about 1 - 1.5 % and < 0.5 % in estuarine and marine waters (Ullrich et al., 2001).

The methylation of mercury takes place mostly on sediments in fresh and ocean water but also in the water columns (WHO, 1990). The biological methylation is performed by both sulphate-reducing bacteria and iron-reducing bacteria (Kerin et al., 2006; Slowey and Brown, 2007; Yu et al., 2012). Abiotic methylation is a pure chemical process, which is also possible when suitable methyl donors are available (Ullrich et al., 2001). The methylation is influenced by several factors that often interact. It depends in the first place on microbial activity and the concentration of bioavailable mercury. However, these factors are influenced by temperature, pH, redox potential and the presence on inorganic and organic complexing agents (Ullrich et al., 2001). The results of this process are mercury species with higher solubility, bioavailability and toxicity to animals and humans (Stein et al., 1996).

9 http://www.unep.org/hazardoussubstances/Mercury/MercuryPublications/GlobalAtmosphericMercuryAssessmentSourcesEm/tabid/3618/language/en-US/Default.aspx

2. LEGISLATION

In order to protect public health, Article 2 of Council Regulation (EEC) No 315/93[10] stipulates that, where necessary, maximum tolerances for specific contaminants shall be established. The current maximum levels (MLs) for mercury are laid down in the Annex, Section 3, of Commission Regulation (EC) No 1881/2006,[11] amended by Commission Regulation (EC) No 629/2008.[12] The MLs established for mercury reflect the results of a dietary exposure assessment carried out in the SCOOP-task 3.2.11[13] and the outcome of the EFSA opinion on mercury and methylmercury in food (EFSA, 2004).

Currently, MLs are established for mercury in fishery products and muscle meat of fish and in food supplements. An ML of 0.5 mg/kg wet weight (w.w.) applies to fishery products and muscle meat of fish (including crustaceans, excluding the brown meat of crab and excluding head and thorax meat of lobster and similar large crustaceans (*Nephropidae* and *Palinuridae*). An exception is made for muscle meat of some specific fish,[14] and an ML of 1.0 mg/kg w.w. applies. Performance characteristics for the analytical determination of mercury are set in Regulation (EC) No 333/2007,[15] amended by Commission Regulation (EU) No 836/2011.[16]

Harmonised levels for mercury in drinking water are set by Council Directive 98/83/EC.[17] The Directive stipulates that Member States set limit values of 1 µg/L for mercury in water intended for human consumption. Commission Directive 2003/40/EC[18] also sets a maximum limit for mercury in natural mineral water of 1 µg/L. Performance characteristics for the analytical determination of mercury in water are set both in Council Directive 98/83/EC[17] and in Commission Directive 2003/40/EC.[18]

Commission Directive 2008/84/EC,[19] amended by Commission Directive 2009/10/EC,[20] and Commission Directive 2008/128/EC,[21] amended by Commission Directive 2011/3/EC,[22] all provide MLs between 0.1 and 3 mg/kg for mercury as an impurity in numerous food additives.

[10] Council Regulation (EEC) No 315/93 of 8 February 1993 laying down Community procedures for contaminants in food. OJ L 37, 13.02.1993 p. 1-3.
[11] Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. OJ L 364, 20.12.2006, p. 5-24.
[12] Commission Regulation (EC) No 629/2008 of 2 July 2008 amending Regulation (EC) No 1881/2006 setting maximum levels for certain contaminants in foodstuffs. OJ L 173, 3.7.2008, p. 6-9.
[13] Reports on tasks for scientific co-operation, Task 3.2.11 'Assessment of dietary exposure to arsenic, cadmium, lead and mercury of the population of the EU Member States'. http://ec.europa.eu/food/food/chemicalsafety/contaminants/scoop_3-2-11_heavy_metals_report_en.pdf
[14] Anglerfish (*Lophius* species), Atlantic catfish (*Anarhichas lupus*), bonito (*Sarda sarda*), eel (*Anguilla* species), emperor, orange roughy, rosy soldierfish (*Hoplostethus* species), grenadier (*Coryphaenoides rupestris*), halibut (*Hippoglossus hippoglossus*), marlin (*Makaira* species), megrim (*Lepidorhombus* species), mullet (*Mullus* species), pike (*Esox lucius*), plain bonito (*Orcynopsis unicolor*), poor cod (*Tricopterus minutes*), Portuguese dogfish (*Centroscymnus coelolepis*), rays (*Raja* species), redfish (*Sebastes marinus*, *S. mentella, S. viviparus*), sail fish (*Istiophorus platypterus*), scabbard fish (*Lepidopus caudatus*, *Aphanopus carbo*), seabream, pandora (*Pagellus* species), shark (all species), snake mackerel or butterfish (*Lepidocybium flavobrunneum*, *Ruvettus pretiosus*, *Gempylus serpens*), sturgeon (*Acipenser* species), swordfish (*Xiphias gladius*) and tuna (*Thunnus* species, *Euthynnus* species, *Katsuwonus pelamis*)
[15] Commission Regulation (EC) No 333/2007 of 28 March 2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs OJ L 88, 29.3.2007, p.29-38.
[16] Commission Regulation (EU) No 836/2011 of 19 August 2011 amending Regulation (EC) No 333/2007 laying down the methods of sampling and analysis for the official control of the levels of lead, cadmium, mercury, inorganic tin, 3-MCPD and benzo(a)pyrene in foodstuffs. by OJ L 215, 20.8.2011, p. 9-16.
[17] Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption OJ L 330, 5.12.1998, p.32-54.
[18] Commission Directive 2003/40/EC of 16 May 2003 establishing the list, concentration limits and labelling requirements for the constituents of natural mineral waters and the conditions for using ozone-enriched air for the treatment of natural mineral waters and spring waters OJ L126, 22.5.2003, p. 34-39.
[19] Commission Directive 2008/84/EC of 27 August 2008 laying down specific purity criteria on food additives other than colours and sweeteners. OJ L253, 20.9.2008, p.1-175.
[20] Commission Directive 2009/10/EC of 13 February 2009 amending Directive 2008/84/EC laying down specific purity criteria on food additives other than colours and sweeteners.OJ L44, 14.2.2009, p. 62-78.

Mercury compounds have been used in the past as pesticides but are no longer authorised in the EU (Council Directive 79/117/EEC).[23] Commission Regulation 149/2008[24] provides maximum residue levels (MRLs) for mercury compounds in various food types of 0.01 and 0.02 mg/kg (sum of mercury compounds expressed as mercury). These MRLs are default values used for unauthorised substances.

Codex Alimentarius[25] has also set a number of guidelines for mercury (total) and methylmercury, namely for natural mineral waters (total mercury: 0.001 mg/kg), food grade salt (total mercury: 0.1 mg/kg), fish except predatory fish (methylmercury: 0.5 mg/kg) and predatory fish such as shark, swordfish, tuna and pike (methylmercury: 1 mg/kg). The guideline levels for methylmercury are intended for fresh or processed fish and fish products moving in international trade.

Directive 2009/48/EC[26] sets migration limits, from toys or components of toys that shall not be exceeded. For mercury the migration limits range from 1.9 mg/kg in liquid or sticky toy material to 94 mg/kg in scraped-off toy material.

Directive 2002/32/EC[27] amended by Directive 2010/6/EU[28] sets maximum contents for mercury in a number of feed commodities (see Table 2). All levels are based on a product with a moisture content of 12 %.

Table 2: EU legislation on mercury in products intended for animal feed.

Products intended for animal feed	Maximum content in mg/kg relative to a feedingstuff with a moisture content of 12 %
Feed materials with the exception of:	0.1
- feedingstuffs produced from fish or by the processing of fish or other aquatic animals,	0.5
- calcium carbonate.	0.3
Compound (complementary and complete) feedingstuffs with the exception of:	0.1
- mineral feed,	0.2
- compound feedingstuffs for fish,	0.2
- compound feedingstuffs for dogs, cats and fur animals	0.3

[21] Commission Directive 2008/128/EC of 22 December 2008 laying down specific purity criteria concerning colours for use in foodstuffs OJ L6, 10.1.2009, p. 20-63.
[22] Commission Directive 2011/3/EU of 17 January 2011 amending Directive 2008/128/EC laying down specific purity criteria on colours for use in foodstuffs. OJ L13, 18.1.2011, p. 59-63.
[23] Council Directive of 21 December 1978 prohibiting the placing on the market and use of plant protection products containing certain active substances (79/117/EEC). OJ L33, 8.2.1979, p. 36-40.
[24] Commission Regulation (EC) No 149/2008 of 29 January 2008 amending Regulation (EC) No 396/2005 of the European Parliament and of the Council by establishing Annexes II, III and IV setting maximum residue levels for products covered by Annex I thereto. OJ L58, 1.3.2008, p. 1-398.
[25] Codex general standard for contaminants and toxins in food and feed. CODEX STAN 193-1995, p. 1-41.
[26] Directive 2009/48/EC of the European Parliament and of the Council of 18 June 2009 on the safety of toys. OJ L170, 30.6.2009, p. 1-37.
[27] Directive 2002/32/EC of the European Parliament and of the Council of 7 May 2002 on undesirable substances in animal feed. OJ L140, 30.5.2002, p. 10-21.
[28] Commission Directive 2010/6/EU of 9 February 2010 amending Annex I to Directive 2002/32/EC of the European Parliament and of the Council as regards mercury, free gossypol, nitrites and Mowrah, Bassia, Madhuca. OJ L37, 10.2.2010, p. 29-32.

3. SAMPLING AND METHODS OF ANALYSIS

3.1. Sample collection and storage

Sampling as well as analytical quality play a crucial role in the accuracy and precision of the determination of mercury in food commodities.

The sampling of food for mercury analysis requires specific precautions in order to avoid contamination or losses during handling, storage and transport to the laboratory. Samples must be collected so that the sample integrity and traceability are maintained. Sample handling is generally critical only for water samples. The best materials for water sample storage and processing are polytetrafluoroethylene (PTFE) and fluorinated ethylene-propylene. Fresh samples are usually stored deep-frozen, lyophilised in darkness or sometimes sterilised. It has been reported that methylmercury may be decomposed in some food matrices with repeated freezing and unfreezing (particularly in bivalves). However, relatively little is known about the effect of storage on the stability of methylmercury in food samples (FAO/WHO 2011b).

In the EU, methods of sampling for the official control of levels of mercury in foodstuffs have to fulfil the sampling methods described in Commission Regulation (EC) No 333/2007,[15] amended by Commission Regulation (EU) No 836/2011.[16]

3.2. Methods of analysis

3.2.1. Sample preparation

The analyst must ensure that samples do not become contaminated during sample preparation. Wherever possible, apparatus and equipment that comes into contact with the sample should not contain those metals to be determined and should be made of inert materials e.g. plastics such as polypropylene or PTFE. In speciation analysis the use of dark Pyrex glass containers is recommended for mercury species. These should be acid cleaned to minimise the risk of contamination. High quality stainless steel or ceramic knives may be used for cutting edges. According to Commission Regulation (EC) No 333/2007,[15] amended by Commission Regulation (EU) No 836/2011,[16] there are many satisfactory specific sample preparation procedures that can be used for the products under consideration. Those described in the European Committee for Standardisation (CEN, 2002 modified by CEN, 2012) have been found to be satisfactory, but others may be equally valid. According to CEN (2012), samples intended for speciation purposes should be stored at 4 °C or lower in darkness. Dilution shall be done only immediately before the analysis. Some considerations shall be kept in mind when storing samples for speciation purposes. Parameters with a strong influence in speciation analysis are:

a) temperature: storage shall be done at –20 °C to prevent microbial activity resulting in reactions e.g. methylation and biodegradation. Generally storage should be kept as short as possible.

b) pH: the pH of the media may strongly affect the stability of the inorganic species. Samples intended for species analysis shall not be changed in their acidity for preservation purposes.

c) light: light may cause instability of organometallic compounds by photodegrading. When analysing organometallic compounds storage shall be done in the dark or in opaque containers.

3.2.2. Instrumental techniques

3.2.2.1. For total mercury analysis

The methods of analysis of total mercury have been reviewed by Evans et al. (2006), Bolann et al. (2007) and Sardans et al. (2010). The methods that have become the most established ones will be briefly summarised below.

Following acidic digestion of samples (Evans et al. 2006), cold vapour atomic absorption spectrometry (CV-AAS; Torres et al., 2009; Mousavi et al., 2010; Jarzynska and Falandysz, 2011) or cold vapour atomic fluorescence spectrometry (CV-AFS; Cava-Montesinos et al., 2004; da Silva et al., 2010; Xia et al., 2010; Senila et al., 2011) has been widely used for the determination of total mercury in several food matrices. Similar limits of quantification (LOQ) may be obtained by CV-AFS (LOQ of about 2 - 10 µg/kg) and CV-AAS (about 3 ng/L in water and 4 - 30 µg/kg in foods). The main advantages of the cold vapour (CV) technique are the separation of the analyte from the potentially interfering sample matrix and its comparatively low cost. However, to avoid interferences by CV-AFS, special precautions must be taken to completely remove vapours when nitric acid is used for digestion. Elemental mercury analysers, also known as automated or direct mercury analysers, with atomic absorption spectrometry (AAS) or atomic fluorescence spectrometry (AFS) detection are also commonly used with the main advantages that they are designed for the direct mercury determination in solid and liquid samples without the need for sample chemical pre-treatment (no digestion step) and have a high sensitivity (LOQ < 1 µg/kg; Carbonell et al., 2009).

After pressure digestion of the samples, inductively coupled plasma-mass spectrometry (ICP-MS) is increasingly being used even if its cost is slightly higher, due to its multielement capacity, sensitivity (LOQ of about 10 µg/kg) and its greater selectivity (Nardi et al., 2009; Rose et al., 2010; Millour et al., 2011a). To limit the memory effects of mercury in the sample delivery system, which may influence the results of samples analysed after measurement of high concentrations and need prolonged washout times, gold chloride is added to the internal standard solution to stabilise mercury in the solution.

3.2.2.2. For mercury speciation analysis

The methods of analysis of mercury species have been reviewed by several authors and can be classified into two general approaches: chromatographic methods (including gas chromatography (GC), liquid chromatography and capillary electrophoresis) and non-chromatographic methods based on the chemical and physical properties of different mercury species (Pereiro and Diaz, 2002; Evans et al., 2006; Diez and Bayona, 2008; Chen and Belzile, 2010; Leopold et al., 2010; Sanchez-Rodas et al., 2010; Amouroux et al., 2011; Clémens et al., 2012). This section will focus on chromatographic separation techniques. The separation of the mercury species can be achieved either by GC or by high-performance liquid chromatography (HPLC), although GC is preferred. Although capillary electrophoresis has not yet been extensively used for mercury speciation (Evans et al., 2006), there is a growing interest, as evidenced in the reviews of Kuban et al. (2007, 2009). Owing to the greater complexity of these hyphenated techniques, it should be noted that the cost of mercury speciation analysis is higher than that of total mercury. The methods that have become the most established ones are briefly summarised below.

Mercury speciation analysis in food is influenced by the nature of the matrix and by the analytical method used. Consequently, the main difficulty is to preserve the initial distribution of mercury species in the sample because of losses and/or cross-species transformations that may occur. Extraction is one of the most critical steps, because two conflicting issues need to be addressed: obtaining high extraction efficiency and minimising losses. Extraction of the mercury species from its matrix requires an aggressive treatment, such as acid digestion, distillation or alkaline extraction, with the option of applying ultrasonic or microwave energy to assist in the procedure (Abrankó et al., 2007; Hajeb et al., 2009a). Methylmercury appears to be more stable in alkaline media than in acid media, with proteins being easily hydrolysed. Once in solution, methylmercury may decompose when

exposed to light, low pH and high storage temperatures. Other factors, such as the type of storage container, may also affect the stability.

Gas chromatography techniques

Speciation of organomercury compounds is most commonly performed by GC with both packed and capillary columns, coupled to several detectors such as mass spectrometry (MS), AAS, AFS, CV-AFS, ICP-MS, microwave-induced plasma atomic emission spectroscopy or furnace atomisation plasma emission spectrometry, and with excellent sensitivity and selectivity (Pereiro and Diaz, 2002; Landaluze et al., 2004; Evans et al., 2006; Abrankó et al., 2007; Diez and Bayona, 2008; Hippler et al., 2009; Jackson et al., 2009; Sanchez-Rodas et al., 2010; Clémens et al., 2011). Following aqueous ethylation with sodium tetraethylborate ($NaBEt_4$), advantages and disadvantages of three hyphenated techniques for mercury speciation analysis in different sample matrices using GC with mass spectrometry (GC-MS), ICP-MS (GC-ICP-MS) and pyrolysis atomic fluorescence (GC-pyro-AFS) detection were recently evaluated by Nevado et al. (2011). Absolute detection and quantification limits were in the range of 2 - 6 pg for GC-pyro-AFS, 1 - 4 pg for GC-MS, with 0.05 - 0.21 pg for GC-ICP-MS, the latter showing the best limits of detection of the three systems employed. However, all systems are sufficiently sensitive for mercury speciation in food samples, with GC-MS and GC-ICP-MS offering isotope analysis capabilities for the use of species-specific isotope dilution analysis, and GC-pyro-AFS being the most cost-effective alternative.

The recent developments in species-specific isotope dilution procedures (i.e. spiking the samples with isotopically enriched species) with GC-MS and GC-ICP-MS techniques has drastically improved the quality and accuracy of the data on mercury speciation analysis (Jackson et al., 2009; Leopold et al., 2010; Amouroux et al., 2011; Clémens et al., 2012). Indeed, the use of isotopically enriched species (i.e. spikes) as tracers overcame the traditional problems related to non-quantitative recoveries and the formation of mercury artefacts that can occur during the extraction and derivatisation steps. The main extraction method used is microwave-assisted extraction because of its speed, efficiency and low occurrence of methylation and demethylation reactions. For the derivatisation of mercury species, alkylating reagents such as sodium tetrapropylborate ($NaBPr_4$) and $NaBEt_4$ are mainly used because derivation takes place in an aqueous medium, the natural environment of most biological samples. Such derivatisation procedures avoid additional solvent extraction steps needed, for example, when Grignard reagents are used (Clémens et al., 2012).

In the last few years, several methodologies, based on the use of multiple spiking species-specific isotope dilution analysis have been developed to overcome abiotic artificial transformations of mercury species (i.e. methylation and demethylation). In the case of mercury speciation analysis, the addition of two isotopically enriched species to the sample (double spiking) provides the quantification of the extent of both methylation and demethylation processes and, therefore, the correction of the final mercury species concentrations (Amouroux et al., 2011; Clémens et al., 2011, 2012). Advantages and limitations of isotopic dilution analysis have also been discussed recently (Clémens et al., 2012).

High-performance liquid chromatography techniques

HPLC is increasingly being applied instead of GC for the separation of mercury species because the mercury species do not need to be derivatised to volatile compounds before HPLC separation. The main methods of analysis have been reviewed (Evans et al., 2006; Chen and Belzile, 2010; Leopold et al., 2010; Sanchez-Rodas et al., 2010; Amouroux et al., 2011; Clémens et al., 2012).

A mild extraction method may be carried out by acid leaching or enzymatic extraction, with the option of applying ultrasonic (Lopez et al., 2010; Rodrigues et al., 2010a; Batista et al., 2011; Guzman-Mar et al., 2011) or microwave energy (Jagtap et al., 2011) to assist in the procedure. The digest is then analysed for methylmercury and the mercuric cation with reversed-phase HPLC after simple filtration.

Separation with a reversed phase column based on alkyl-silica and a mobile phase containing an organic modifier, together with a chelating or ion pair reagent (and in some cases a pH buffer) is usually used. ICP-MS has the highest sensitivity for the detection of mercury species in the HPLC eluent, which is directly injected to the nebuliser of the ICP-MS without splitting or dilution (Lopez et al., 2010; Rodrigues et al., 2010a; Batista et al., 2011; Jagtap et al., 2011). The use of CV generation after HPLC separation coupled to AFS detection is the most common approach to lower the detection limit (Bramanti et al., 2005; Guzman-Mar et al., 2011). However, an extra step for the conversion of mercury species to inorganic mercuric mercury prior to CV generation is necessary, or else the magnitude of the response would be dependent on the species present. Recently, a novel solution cathode glow discharge induced vapour generation was developed as interface to on-line couple HPLC-AFS (He et al., 2011). Alternatively, pre-concentration on a suitable microcolumn prior to HPLC separation coupled to ICP-MS or CV-AAS detection, or the use of micro-HPLC coupled through a micronebuliser to ICP-MS, achieves detection limits in the low ng/L range. The advantage of MS and ICP-MS is their multielement and multi-isotope capabilities offering isotope dilution analysis capabilities (Amouroux et al., 2011; Clémens et al., 2012), whereas CV-AAS and CV-AFS have the advantage of being comparatively low-cost and simple operations.

3.2.3. Analytical quality assurance: performance criteria, reference materials, validation and proficiency testing

The performance criteria for methods of analysis for official control are also laid down in Commission Regulation (EC) No 333/2007[15] amended by Commission Regulation (EU) No 836/2011.[16] The Regulation follows the 'criteria approach'. This means that no prescribed fixed official methods have to be followed, but laboratories can use any method of analysis, provided it can be demonstrated in a traceable manner that it strictly fulfils the analytical requirements laid down in the relevant legislation. The methods used for the determination should be applicable to those foodstuffs specified in Commission Regulation (EC) No 1881/2006,[11] amended by Commission Regulation (EC) No 629/2008.[12] The limit of detection (LOD) is required to be less than one-tenth of the ML (see Section 2) and the LOQ to be less than one-fifth of the ML. The LOD and LOQ will vary with the analytical technique, the sample mass, the laboratory and the food matrix.

When no extraction step is applied in the analytical method (e.g. in the case of metals), the result may be reported uncorrected for recovery if evidence is provided by ideally making use of suitable certified reference material that the certified concentration allowing for the measurement uncertainty is achieved (i.e. high accuracy of the measurement), and thus that the method is not biased. If the result is reported uncorrected for recovery this shall be mentioned. Concerning precision, it is required that the $HORRAT_r$[29] and $HORRAT_R$[30] values are less than 2. The requirement for specificity is given as 'free from matrix or spectral interferences'.

Finally, Commission Regulation (EC) No 333/2007[15] amended by Commission Regulation (EU) No 836/2011[16] sets requirements for reporting results and for the assessment of compliance of the lot or sublots. For this, the analytical result corrected for recovery, if necessary, should be used for checking compliance. The analytical result shall be reported as $x \pm U$, whereby x is the analytical result and U is the expanded measurement uncertainty, using a coverage factor of 2, which gives a level of confidence of approximately 95 %. The lot or sublot is accepted if the analytical result of the laboratory sample does not exceed the respective ML as laid down in Regulation (EC) No 1881/2006,[11] modified by Regulation (EC) No 629/2008,[12] taking into account the expanded measurement uncertainty and correction of the result for recovery, if an extraction step has been applied in the analytical method used.

[29] $HORRAT_r$: The observed relative standard deviation calculated from results generated under repeatability conditions (RSD_r) divided by the RSD_r value estimated from the (modified) Horwitz equation using the assumption that the repeatability r = 0.66R (reproducibility). The Horwitz equation and the modified Horwitz are generalised precision equations which are independent of analyte and matrix but solely dependent on concentration for most routine methods of analysis.

[30] $HORRAT_R$: The observed relative standard deviation calculated from results generated under reproducibility conditions (RSD_R) divided by the RSD_R value calculated from the (modified) Horwitz equation.

To demonstrate the trueness (i.e. systematic error) and precision (i.e. random error) of trace element data, one of the important criteria is the reporting of correct (and precise) data for the mercury content of certified reference materials that closely match the matrix of the samples under investigation (Jorhem, 2004). Several standard or certified reference materials (SRMs and CRMs) are available for both total mercury and methylmercury (Table 3). However, there is a current need for CRMs in other foodstuffs certified in inorganic mercury. The status of certification of the new reference materials can be found on the web sites of the reference material providers.

Table 3: Some standards or certified reference materials relevant to mercury food analysis (in mg Hg/kg dry mass).

Food type	Descriptor (supplier)[a]	Total mercury	Methylmercury
Fish and other seafood			
Fish protein	DORM-3 (NRCC)	0.382 ± 0.060[b]	0.355 ± 0.056
Dogfish liver	DOLT-4 (NRCC)	2.58 ± 0.22	1.33 ± 0.12
Tuna fish	BCR 463 (IRMM)	2.85 ± 0.16	3.04 ± 0.16
Fish muscle	IAEA 407 (IAEA)	0.222 ± 0.006	0.200 ± 0.012
Oyster tissue	SRM 1566b (NIST)	0.0371 ± 0.0013	0.0132 ± 0.0007
Mussel tissue	SRM 2976 (NIST)	0.0610 ± 0.0036	0.02809 ± 0.00031
Lobster hepatopancreas	TORT-2 (NRCC)	0.27 ± 0.06	0.152 ± 0.013
Mussel tissue	ERM-CE278 (IRMM)	0.196 ± 0.009	
Crab	LGC 7160 (LGC)	0.096 ± 0.034	
Other foodstuffs			
Cabbage	GBW 10014 (IGGE)	0.0109 ± 0.0016	
Chicken	GBW 10018 (IGGE)	0.0036 ± 0.0015	
Rice flour	SRM 1568a (NIST)	0.0058 ± 0.0005	
Spinach leaves	SRM 1570a (NIST)	0.030 ± 0.003	
Skimmed milk powder	BCR 150 (IRMM)	0.0094 ± 0.0017	
White cabbage	BCR 679 (IRMM)	0.0063 ± 0.0014	

(a): NRCC: National Research Council of Canada (Canada); IRMM: Institute for Reference Materials and Measurements (Belgium); IAEA: International Atomic Energy Agency (Austria); NIST: National Institute of Standards and Technology (USA); LGC: LGC (UK); IGGE: Institute of Geophysical Exploration (China).
(b): The uncertainty is usually given as the 95 % confidence interval.

Most of analytical methods published in the literature are to a certain extent in-house validated for total mercury (Cava-Montesinos et al., 2004; Carbonell et al., 2009; Nardi et al., 2009; Torres et al., 2009; da Silva et al., 2010; Xia et al., 2010; Jarzynska and Falandysz, 2011; Millour et al., 2011a; Senila et al., 2011; Djedjibegovic et al., 2012) and methylmercury (Landaluze et al., 2004; Abrankó et al., 2007; Diez and Bayona 2008; Hippler et al., 2009; Jackson et al., 2009; Clémens et al., 2011; Guzman-Mar et al., 2011; He et al., 2011; Nevado et al., 2011). Two fully validated, European standardised methods for determination of total mercury by CV-AAS and ICP-MS detection are available (CEN, 2003, 2010). No standardised methods are available for determination of methylmercury and inorganic mercury, but the European Commission has mandated the European Committee for Standardization (CEN) to establish a standardised method of analysis by isotopic dilution for the determination of methylmercury in food of marine origin (including seaweed).

Some proficiency testing schemes are regularly organised by several providers for both total mercury and methylmercury to demonstrate and maintain analytical quality assurance. In 2010-2011, a proficiency testing on the determination of total mercury in frozen fish was organised by the European Union Reference Laboratory for Chemical Elements in Food of Animal Origin (EURL-CEFAO, ISS, Rome, Italy). All the results of the 28 European National Reference Laboratories (NRLs) were considered satisfactory (EURL-CEFAO, 2011). In 2010, two proficiency tests on the determination of total mercury and methylmercury in seafood and of total mercury in vegetable food were organised for the European NRLs by the European Union Reference Laboratory for Heavy Metals in Feed and Food (Institute for Reference Materials and Measurements (IRMM), Joint Research Centre, Geel, Belgium). Twenty-one out of the 28 participants performed satisfactorily for total mercury in vegetable food

(IMEP 110).[31] Thirty-four out of 35 participants scored satisfactorily for total mercury in the dogfish liver and four out of five results were considered satisfactory for methylmercury (IMEP 109). A parallel proficiency test (IMEP 30) open to all laboratories willing to take part in the exercise was also organised using the same test material. Of the 57 participants (45 from EU), 90 % of the 52 results for total mercury and 89 % of the nine results for methylmercury were considered satisfactory.

Between March and December 2011, the Food Analysis Performance Assessment Scheme (FAPAS) organised seven different proficiency tests: six on the determination of total mercury in canned fish (FAPAS® reports 07156 and 07164), canned crab meat (FAPAS® report 07160), infant cereal (FAPAS® report 07165), milk powder (FAPAS® report 07154) and soy flour (FAPAS® report 07166) and one on the determination of total mercury and methylmercury in canned fish (FAPAS® report 07153). The results indicate that most of the participating laboratories, although applying different methods, are capable of reliably analysing total mercury (range 82 - 98 % satisfactory results, 45 to 98 participants) and methylmercury (100 % satisfactory results, 17 participants) at the level of interest.

Finally, a world-wide proficiency test was conducted by the International Atomic Energy Agency (IAEA) in 2009 to determine total mercury and methylmercury in marine biota (scallop) (IAEA, 2010). Out of the 80 and 20 participating laboratories, 62 showed satisfactory analytical results for total mercury (assigned value 0.15 mg/kg) and 15 laboratories for methylmercury (assigned value 0.0217 mg Hg/kg), respectively.

3.3. Concluding comments

In summary, several analytical techniques are suitable for the determination of mercury in foods. For total mercury, CV-AAS, CV-AFS and increasingly ICP-MS have been used for a wide variety of foodstuffs and two European standardised methods by CV-AAS and ICP-MS detection are available (CEN, 2003, 2010).

GC coupled to MS or ICP-MS are the most widely used techniques for the separation and detection of mercury species. This is due to their multi-element and multi-isotope capabilities which allow for more accurate and precise results by speciated isotope dilution MS, which can also check for species transformations and extraction recoveries. More recently, HPLC techniques are also increasingly being used but, usually, GC methods have higher sensitivity than liquid chromatography. For the moment, no fully validated or standardised methods are available for the separation and detection of mercury species.

Several SRMs and CRMs are available for both total mercury and methylmercury. Regular proficiency testing schemes are organised by several providers for both total mercury and methylmercury in foodstuffs to demonstrate and maintain analytical quality assurance. However, there is a current need to develop CRMs and proficiency testing schemes for inorganic mercury in foodstuffs other than fish and seafood.

4. OCCURRENCE OF METHYLMERCURY AND INORGANIC MERCURY IN FOOD

4.1. Background

Total mercury concentrations in foods, other than fish and other seafood, are in the range < LOD/LOQ – 50 µg/kg. Higher concentrations are observed in fish and other seafood and concentrations up to 11 400 µg/kg were reported by JECFA in 2011 (FAO/WHO, 2011b). The amount of mercury is related to the age of the fish and the position of the fish species within the food chain; predatory fish and older fish having higher concentrations than others. Unlike some contaminants, mercury content is not related to the fat content of the fish and, as such, mercury is not considered a problem associated especially with oily fish. Some fish species that usually have higher concentrations of mercury include

[31] IMEP reports are available from http://irmm.jrc.ec.europa.eu/interlaboratory_comparisons/imep/Pages/index.aspx

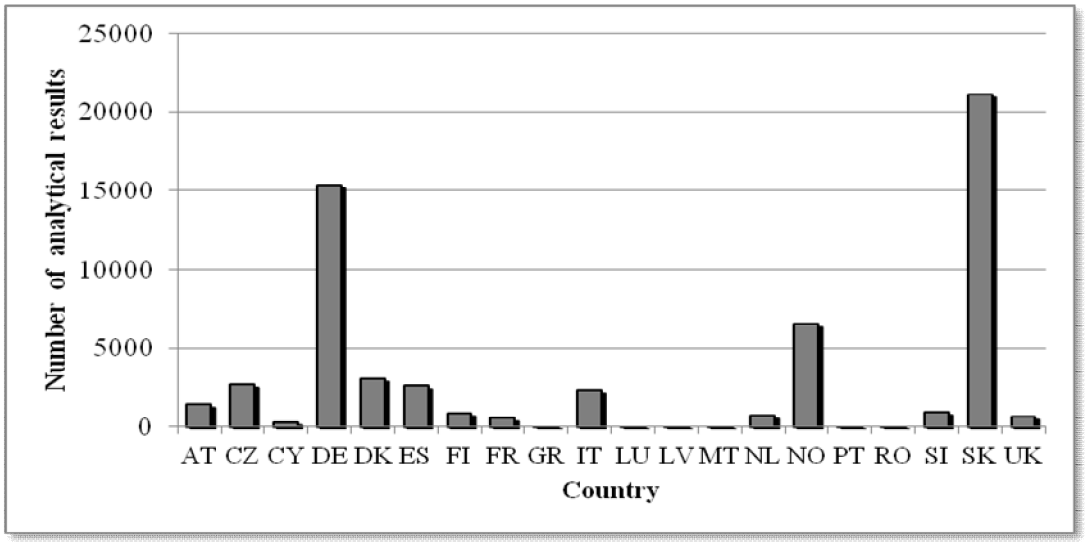
shark, swordfish and marlin. Mercury in these fish species may exceed 1 000 µg/kg. Fresh tuna often contains mercury concentrations between about 100 and 1 500 µg/kg. Predatory freshwater fish are also a source of mercury dietary exposure. Specific ecosystem characteristics contribute to the variability in mercury concentration (Munthe et al., 2007). A table listing mean content of mercury (plus certain nutrients and dioxins) of 103 species of fish is presented as Appendix A of the report of the WHO risk benefit assessment for fish consumption (FAO/WHO, 2011a).

4.2. Occurrence results reported to EFSA

Since the exposure assessment in the previous EFSA opinion on mercury and methylmercury of 2004 (EFSA, 2004) was based on a very limited number of data from a SCOOP exercise,[13] it was decided that there was a need for a new data collection, covering the years from 2006. Following a European Commission mandate to EFSA, a call for annual collection of chemical contaminant occurrence data in food and feed, including mercury, was issued by EFSA in December 2010 with a closing date of 1 October of each year. In response EFSA has received a total of 59 820 results from testing of the presence of mercury in food from 20 European countries. The data reported represent the period from 2002 to 2011, although the call for data was originally limited to the period from 2006 to 2011.

4.2.1. Data collection summary

The source of 59 820 analytical results for mercury submitted by 20 European countries is illustrated in Figure 1. Slovakia reported 35.4 % of the data followed by Germany (25.8 %) and Norway (11 %).



Legend: AT: Austria; CY: Cyprus; CZ: Czech Republic; DE: Germany; DK: Denmark; ES: Spain; FI: Finland; FR: France; GR: Greece; IT: Italy; LV: Latvia; LU: Luxembourg; MT: Malta; NL: the Netherlands; NO: Norway; PT: Portugal; RO: Romania; SI: Slovenia; SK: Slovakia; UK: United Kingdom.

Figure 1: The number of reported analytical results for mercury across European countries.

Overall, 58 730 (98.2 %) of the analytical results were reported for total mercury, 1 087 (1.8 %) for methylmercury and only three samples were reported for inorganic mercury. Data on methylmercury were provided by four countries: Germany (788 results), Spain (206 results), Czech Republic (90 results) and Slovakia (three results).

The data provided were sampled in the period 2002 - 2011, with only 55 results covering the period before 2004. The distribution of the results over the years of sampling is shown in Figure 2.

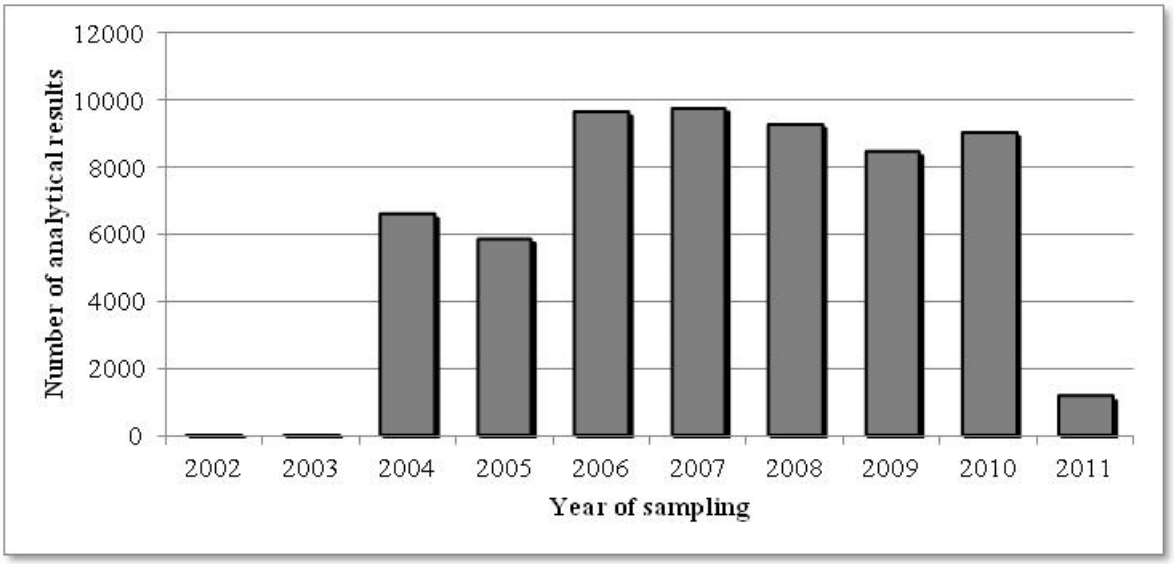


Figure 2: The number of reported analytical results for mercury over years of sampling (note that 2011 was not a complete year of sampling).

A total of 170 samples were excluded from further analysis during the data cleaning steps as they provided incomplete or incorrect description of food type or unit of measure. Some data from fish were excluded because they showed insufficient sensitivity of the analytical method (a LOD of more than 50 µg/kg or a LOQ of more than 100 µg/kg). The cut-off value of left-censored (LC) data was determined according to the criteria defined in Commission Regulation (EC) No 836/2011,[16] amending Commission Regulation (EC) No 333/2007,[15] which defines that the LOD for mercury should be equal to or less than one-tenth of the ML and the LOQ should be equal to or less than one-fifth of the ML. The ML of 0.5 mg/kg w.w. for a range of fishery products and muscle meat of fish set by Commission regulation (EC) No 629/2008,[12] amending Commission Regulation (EC) No 1881/2006,[11] was used.

A total number of 59 650 results were described with sufficient detail to be used in the statistical analysis of the respective food groups; 58 560 samples were analysed for total mercury (98.2 %), 1 087 samples (1.8 %) for methylmercury and three samples for inorganic mercury.

4.2.2. Distribution of samples across food categories

The data providers were asked to codify all food descriptors according to the EFSA FoodEx 1 Classification system (EFSA, 2011a).

FoodEx 1 (hereinafter referred to as 'FoodEx') is a provisional food classification system developed by the EFSA Dietary and Chemical Monitoring Unit (DCM, formerly DATEX) in 2009 with the objective of simplifying the linkage between occurrence and food consumption data when assessing dietary exposure to hazardous substances.[32] It contains 20 main food categories (FoodEx Level 1), which are further divided into subgroups having 140 items at the FoodEx Level 2, 1 260 items at the FoodEx Level 3 and reaching about 1 800 endpoints (food names or generic food names) at the FoodEx Level 4. It is based on a hierarchical coding for an easier cross-checking and it is structured in a child-parent relationship, as illustrated in Figure 3.

The distribution of analytical results across the different food groups for total mercury and methylmercury is illustrated in Figure 4.

[32] Recently, the FoodEx 2 classification system has been developed and is available now for future applications, but for this opinion the previous version (FoodEx 1) was used. Further information on FoodEx 2 is available at http://www.efsa.europa.eu/en/supporting/doc/215e.pdf

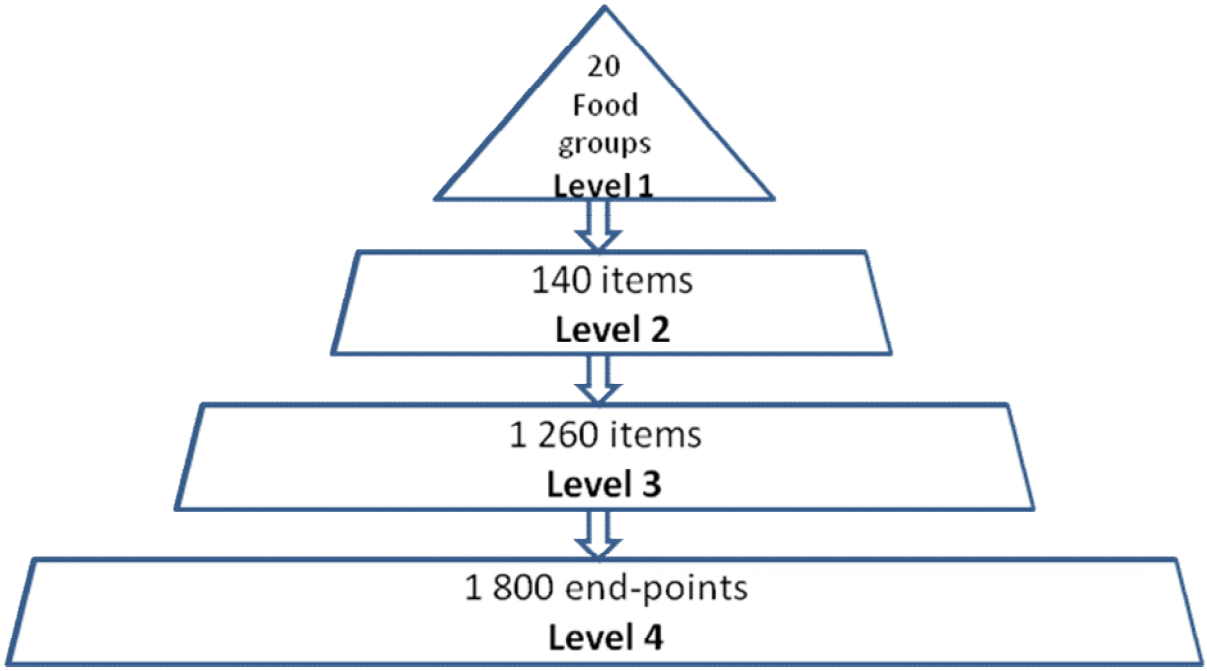


Figure 3: Hierarchy of the FoodEx food classification system.

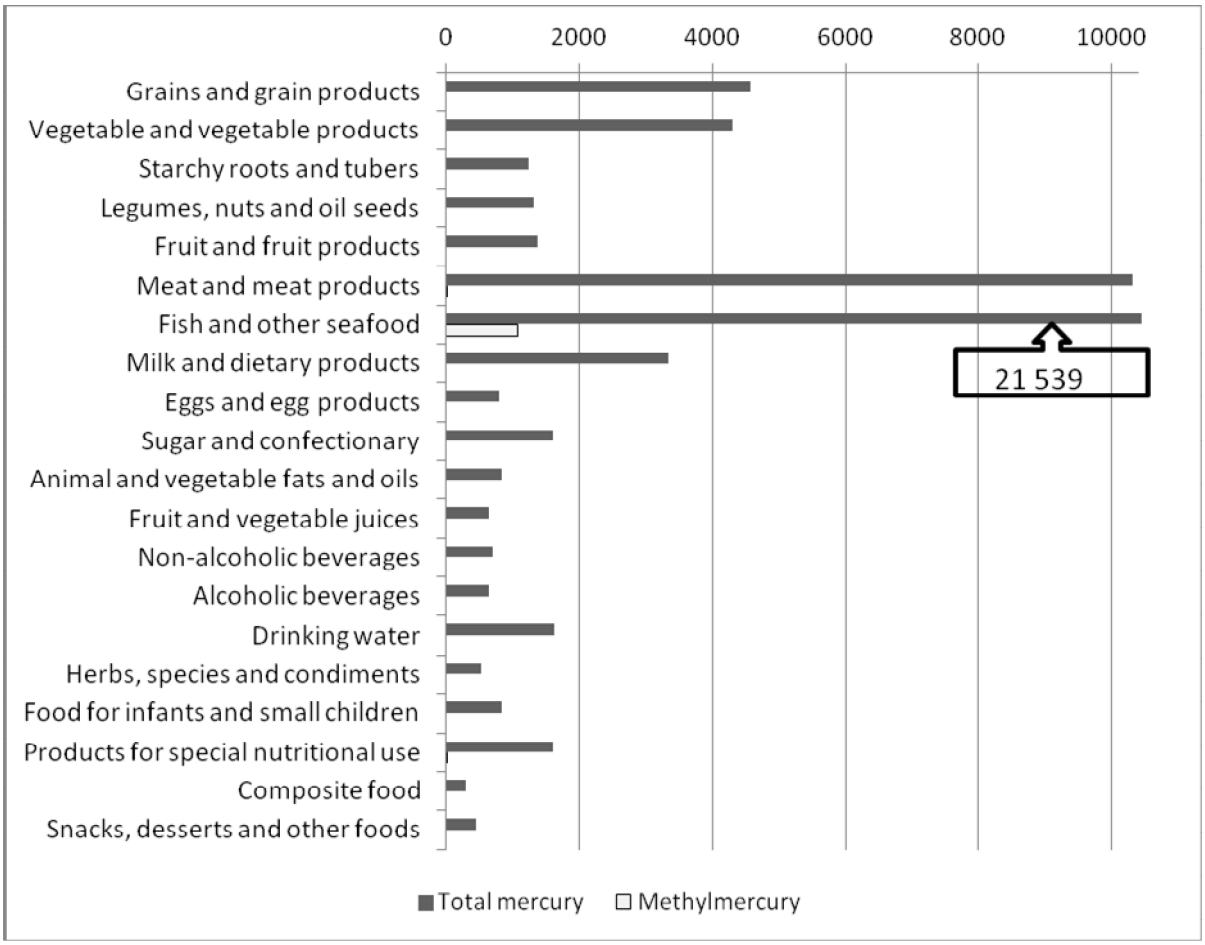


Figure 4: The number of mercury analytical results reported for food groups according to the FoodEx Level 1 (the arrow indicates the number of mercury analytical results for fish and other seafood).

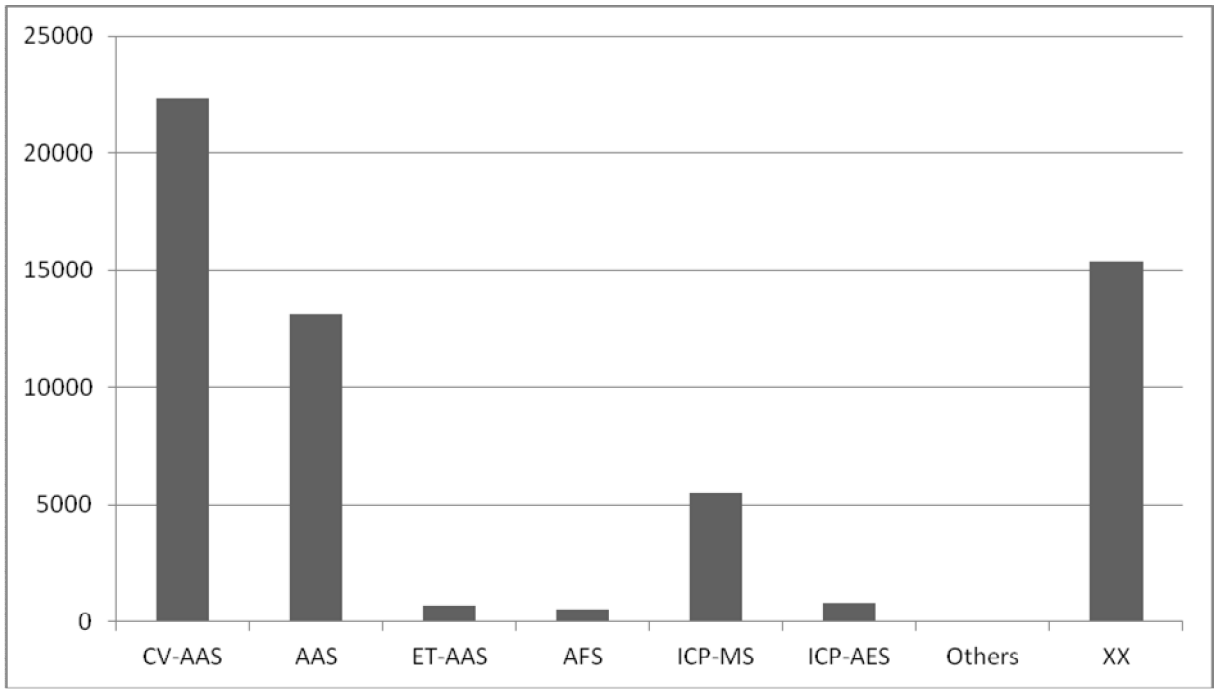
Regarding total mercury analyses, all the 20 food groups available at the first level of FoodEx were covered in the current data collection. The food groups 'Fish and other seafood (including amphibians, reptiles, snails and insects)' (hereinafter referred to as 'Fish and other seafood') and 'Meat and meat products' dominated the food product coverage, with 36.8 % and 17.6 % respectively. These were followed by 'Grain and grain-based products' at 7.8 % and 'Vegetables and vegetable products (including fungi)' at 7.3 %. Regarding more detailed levels of the FoodEx classification for 'Fish and other seafood', the most analysed food category at Level 2 was 'Fish meat' (13 737 results). Salmon and trout[33] (1 741 results) and halibut (1 713 results) were the most reported fish species at FoodEx Level 3.

The lowest number of samples (fewer than 500) of total mercury was reported for the food groups 'Composite food (including frozen products)' and 'Snacks, desserts and other food'.

All analytical results were reported on a wet weight basis.

4.2.3. Analytical methods used

The original results were reported in mg/kg (95 %), in mg/L (3 %), in µg/kg (1.9 %), in µg/L (0.7 %), in ng/g (0.025 %) and one result in mg/100 g. All the measurements were converted to µg/kg. For the measurements expressed as a volume unit, the approximate equivalence of 1 kg = 1 L has been used. As demonstrated in Figure 5, the most commonly used method for total mercury analysis was CV-AAS with 38 %, followed by unspecified AAS technique(s) with 22 %. In 26 % of the cases, no information was provided on the analytical method used. Since so many of the results lacked a description of the analytical method, it was not meaningful to cross-tabulate the food matrix results with the analytical method.



Legend: AAS – atomic absorption spectrometry (unspecified); AFS - atomic fluorescence spectrometry (unspecified); CV-AAS - cold vapour - atomic absorption spectrometry; ET-AAS – electrothermal atomic absorption spectrometry; ICP-AES - inductively coupled plasma atomic emission spectrometry; ICP-MS - inductively coupled plasma mass spectrometry; XX: analytical method not specified.

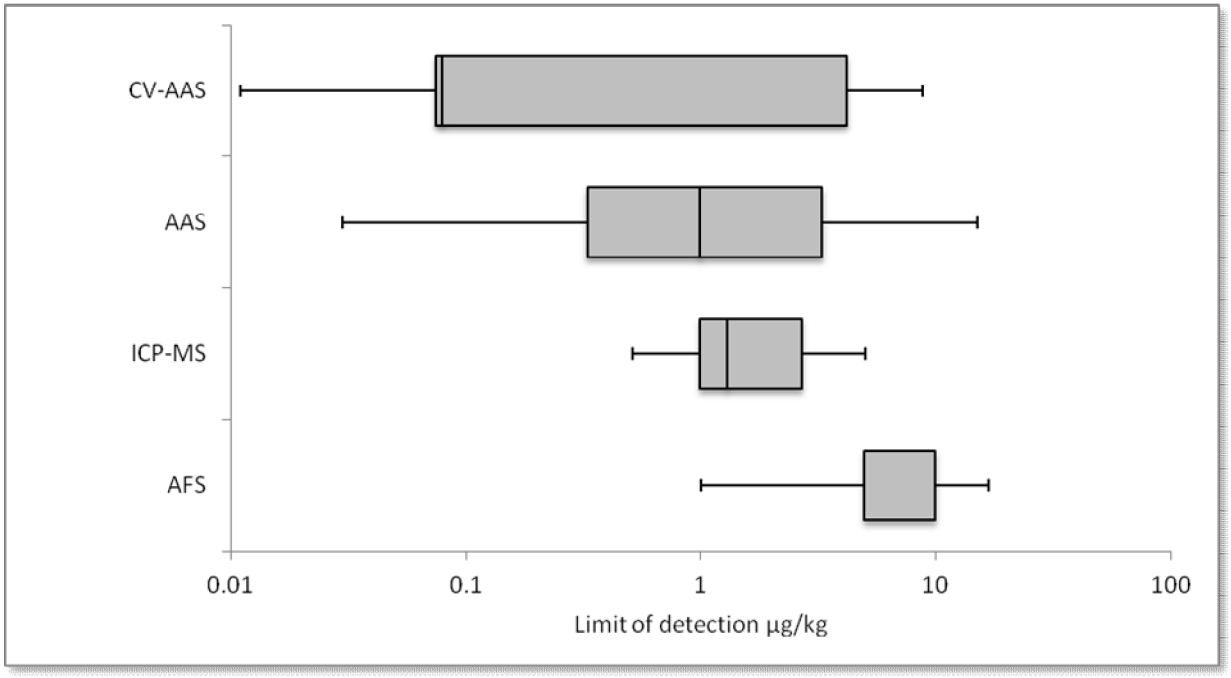
Figure 5: Distribution of analytical methods used for total mercury analysis.

[33] These species are reported as one category at FoodEx Level 3.

Regarding methylmercury, complete information on the separation technique was not always obtained. For 73 % of analytical results the analytical method was not specified, while in 16 % AAS and in 9 % ICP-MS were reported as the detection method used, but the separation technique was not given. For 30 methylmercury results HPLC was indicated as a separation technique hyphenated with an unspecified detector.

Overall, 44 % of the results for total mercury and 14 % of the results for methylmercury were LC, meaning below LOD or LOQ. For 17 % of the LC data, the LOD was not reported; in these cases the LOD was replaced by the reported LOQs divided by a conversion factor of two in accordance with Commission Regulation (EC) No 836/2011[16] amending Regulation (EC) No 333/2007.[15] Since it is not mandatory to report LOD or LOQ when the value is quantified, 7 218 results were not included in the analysis of LODs (Figures 6 and 7).

The LODs varied with the analytical technique (Figure 6), the laboratory (not shown) and the food group (Figure 7). As mentioned above, according to the performance criteria defined in legislation, the LOD for mercury should be equal to or less than one-tenth of specified MLs. However, performance characteristics for the analytical quantification of mercury are set by legislation only for the analysis of fish and some other seafood for human consumption. There is no current legislation defining the performance characteristics for analytical methods applied to any other food group; laboratories are therefore free to modify the analytical methods to be fit for purpose for the particular set of samples tested. This may be a reason for some of the differences observed.



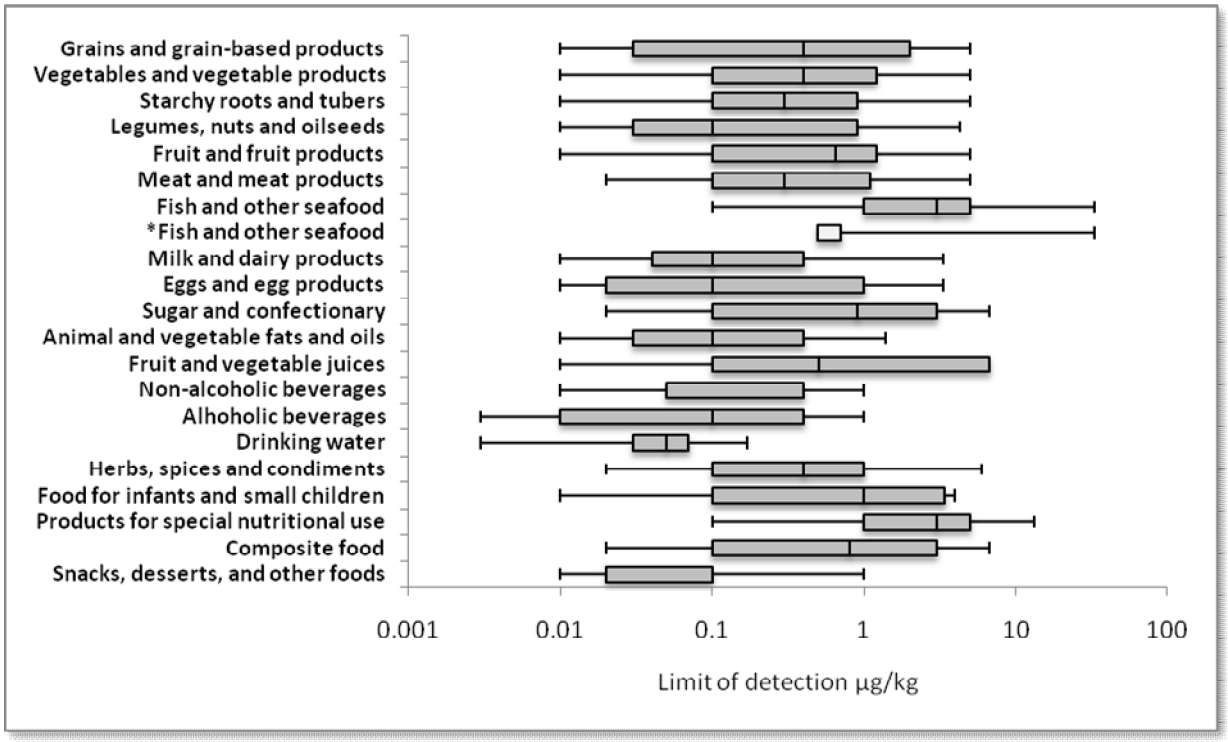
Legend: AAS – atomic absorption spectrometry (unspecified); AFS - atomic fluorescence spectrometry (unspecified); CV-AAS - cold vapour - atomic absorption spectrometry; ICP-MS - inductively coupled plasma mass spectrometry. Number of missing results = 24 878; Box-plot: whiskers at P5 and P95, box at P25 and P75 with line at P50

Figure 6: Distribution of the LOD for total mercury according to the most commonly used analytical methods as reported by laboratories.

Concerning the analytical methods for total mercury, the laboratories using CV-AAS reported the lowest LODs with a median of 0.08 µg/kg (Figure 6). On the other hand, higher LODs were shown in the samples analysed by unspecified AFS (median of 10 µg/kg). A limited number of data on LOD were obtained for electrothermal atomic absorption spectrometry (ET-AAS) and inductively coupled plasma atomic emission spectroscopy (ICP-AES). The LOD range for the ET-AAS was

0.5 - 33.3 µg/kg. The LOD for the ICP-AES was reported for all results at a concentration of 6.6 µg/kg.

Concerning methylmercury analyses, lower LODs were achieved by ICP-MS (median of 0.66 µg/kg) while higher LODs were observed for AAS (median of LOD of 33.3 µg/kg). The sensitivity of the method is often set by the laboratory to fulfil legislative requirements for mercury in fish. The extra cost and time to fine-tune the method to achieve optimally low LODs may not be warranted. This is satisfactory for routine monitoring purposes, but does cause slight problems when results are used also to calculate human dietary exposure since high LODs for LC data might increase the upper bound (UB) exposure estimates.



Legend: *: data on methylmercury; box-plot: whiskers at P5 and P95, box at P25 and P75 with line at P50.

Figure 7: Distribution of the LOD for total mercury and methylmercury according to the FoodEx Level 1.

The lowest LODs were shown for the food group 'Drinking water' with a median of 0.05 µg/kg followed by 'Legumes, nuts and oilseeds', 'Milk and dairy products', 'Eggs and egg products', 'Animal and vegetable fats and oils', 'Alcoholic beverages' and 'Snacks, desserts, and other foods' with a median of 0.1 µg/kg. On the other hand, the highest LOD is observed in 'Fish and other seafood' with a median of 3 µg/kg for total mercury and 0.5 µg/kg for methylmercury.

4.2.4. Occurrence data on total mercury by food category

The proportions of LC and quantified results in the 20 food groups at FoodEx Level 1 are shown in Figure 8.

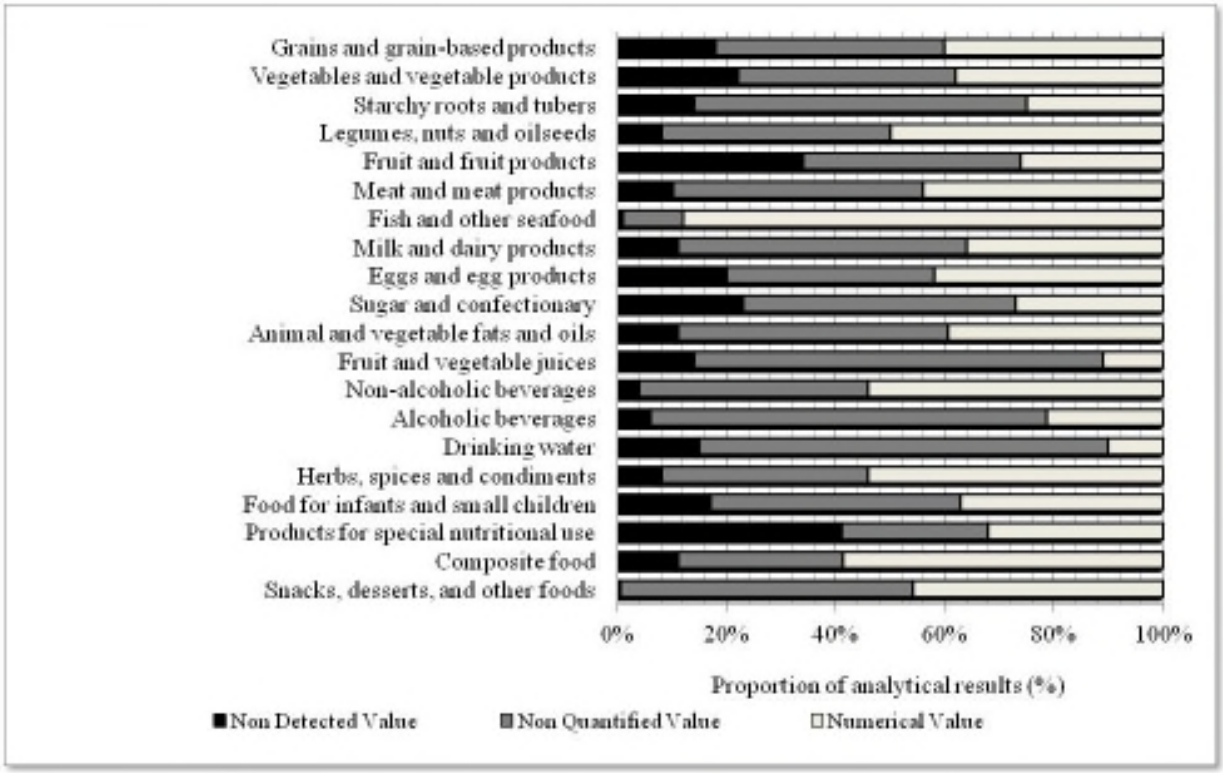


Figure 8: Proportion of quantified results and results below the limits of detection or quantification for total mercury reported for individual food groups according FoodEx Level 1.

Since the proportion of quantified results was below 40 % in 11 food groups (Figure 8), the handling of the LC data was carefully considered. As recommended in the 'Principles and Methods for the Risk Assessment of Chemicals in Food' (WHO, 2009) and in the EFSA scientific report 'Management of LC data in dietary exposure assessment of chemical substances' (EFSA, 2010) the substitution method was applied for the treatment of LC data. The lower bound (LB) was obtained by assigning a value of zero to all the samples reported as less than the LC limit, the middle bound (MB) by assigning half of the LC limit and the UB by assigning the LC limit as the sample result.

Table 4 provides a summary of occurrence data on total mercury including the number of results reported and statistical descriptors of the results (proportion of LC data in %, mean, and 95th percentile for LB, MB and UB results). More details on statistical description are reported in Appendix A, Table A1-A24.

Table 4: Summary of the total mercury occurrence data by food group (µg/kg).

Food category, Level 1	N	% LC	Mean			P95		
			LB	MB	UB	LB	MB	UB
Grains and grain-based products	4 545	60	0.9	2.0	3.1	4.0	5.3	10
Vegetables and vegetable products	4 299	62	6.0	7.0	7.8	8.3	10	11
Starchy roots and tubers	1 234	75	0.2	0.8	1.4	0.8	2.5	5.0
Legumes, nuts and oilseeds	1 311	51	2.3	2.8	3.3	9.6	10	10
Fruit and fruit products	1 368	74	0.3	1.2	2.1	1.0	5.0	9.6
Meat and meat products	10 304	56	1.9	2.7	3.5	9.0	10	11
Fish and other seafood	21 539	12	131	133	136	540	540	540
Milk and dairy products	3 345	64	0.9	1.5	2.1	4.3	8.0	11
Eggs and egg products	798	58	0.6	1.2	1.8	3.2	4.6	6.3
Sugar and confectionery	1 617	73	0.6	2.6	4.7	2.9	10	20
Animal and vegetable fats and oils	835	61	1.1	1.6	2.0	6.0	6.0	6.0
Fruit and vegetable juices	651	89	0.1	3.2	6.2	0.4	10	20
Non-alcoholic beverages	699	46	3.4	4.0	4.5	16	16	20
Alcoholic beverages	652	79	0.1	0.4	0.7	0.3	1.0	2.0
Drinking water	1 637	90	0.0	0.1	0.2	0.1	0.3	0.5
Herbs, spices and condiments	529	47	3.1	4.3	5.5	10	13	20
Food for infants and small children	834	63	0.6	1.6	2.5	3.0	5.0	6.0
Products for special nutritional use[(a)]	1 608	68	96	99	102	35	38	43
Composite food	304	41	16	18	19	59	59	59
Snacks, desserts, and other foods	451	54	1.2	1.5	1.9	3.0	4.7	5.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a): Note that mean values are higher than P95 values because of a heavily right-skewed distribution of the data.

Tables 5 and 6 provide summaries of occurrence data for the 'Fish and other seafood' category split into the FoodEx Level 2 and Level 3, respectively, with the number of results reported and statistical descriptors of the results (proportion of LC data in %, mean and 95th percentile for LB, MB and UB results). In cases where the number of results is less than 60, the 95th percentile descriptor should be considered indicative only, owing to the limited number of data (EFSA, 2011b).

Since a few very high values heavily influenced the estimated mean value a specific analysis of such values was carried out. Those very high results did not show a uniform trend and were spread across reporting countries and food groups. When the mercury concentration was ten times higher than the second highest value within the same subcategory and influenced significantly the mean, the result was considered as an outlier and excluded from the calculation. Moreover, several extremely high values were considered as erroneously reported, a view supported by literature data on mercury concentration (WHO, 2008; Spada et al., 2012), and therefore excluded. In total, nine samples have been eliminated following these criteria. Four samples in the food group 'Fish and other seafood' were excluded because of extremely high concentrations: three samples of swordfish reported to contain mercury at 1.5 g/kg, 1.2 g/kg and 1.2 g/kg, and one sample of shark reported to contain mercury at 14 600 µg/kg. It was considered unlikely from a biological point of view to be real data and therefore with a high probability of having been erroneously reported. Another five samples excluded from other food groups because of extremely high concentrations and because of significant influence on the mean were: (i) two samples of products for special nutritional use, with reported mercury content of 2.3 g/kg and 0.52 g/kg, originating from India, (ii) one sample of lettuce reported to contain 10 001 µg/kg, (iii) one sample of confectionery (not-chocolate) reported to contain 1 000 µg/kg, and (iv) one sample of poultry mixed meat reported to contain 498 µg/kg. Since some genuine or occasional causes may lead to high mercury contamination, for example in old large predatory fish, in specific species of wild mushrooms and in herbal dietary supplements some moderately high results were kept in the database.

The 'Fish and other seafood' category comprises a total of 21 539 analytical results on total mercury divided into six subcategories at FoodEx Level 2 (Table 5). Two groups of unspecified fish and seafood samples were identified in the dataset: (i) within the FoodEx Level 1, in a group of 1 968 samples for which the specification at FoodEx Level 2 was missing (these results were for dietary exposure calculation matched to consumption data at FoodEx Level 1, Table 5); (ii) within the FoodEx Level 2 a group of 1 502 samples for which the specification at FoodEx Level 3 was missing and these data were replaced by overall concentration reported in specified fish species, as explained later (Table 6 and Section 6.1).

Table 5: Statistical description of concentrations of total mercury for the six FoodEx Level 2 subgroups of the food group 'Fish and other seafood' in µg/kg.

Food category Level 2	N	% LC	Mean			P95[(b)]		
			LB	MB	UB	LB	MB	UB
Fish and other seafood, unspecified (FoodEx1[(a)])	1 968	3	100	100	101	273	273	273
Fish meat	13 737	7	177	178	180	710	710	710
Fish products	241	8	37	38	38	109	109	109
Fish offal	158	58	12	19	26	67	67	70
Crustaceans	1 478	21	43	47	50	189	189	189
Molluscs	3 926	26	31	36	41	100	100	100
Amphibians, reptiles, snails, insects	31	48	19	20	21	140	140	140

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a): Data available only on FoodEx Level 1.
(b): The 95th percentile obtained on occurrence data with fewer than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore is considered only indicative.

As shown in Table 4 the 'Fish and other seafood' category was the one that recorded the highest values of total mercury in comparison to all other food categories. This is very much driven by high mean values in the fish meat category, as can be seen in Table 5. The LB, MB and UB mean values of total mercury content in 'Fish meat' were all around 180 µg/kg, with the 95th percentile at 710 µg/kg. The maximum value recorded in this category was for a sample of unspecified fish meat with a total mercury concentration of 6 890 µg/kg (Appendix A, Table A8). Further descriptive statistics of concentration of total mercury for the food group 'Fish and other seafood' at FoodEx Level 2 are presented in more detail in Appendix A, Table A8.

The food category 'Fish meat' split at FoodEx Level 3 is described in more detail in Table 6.

Table 6: Statistical description of concentrations of total mercury in the FoodEx Level 3 food categories of 'Fish meat' in µg/kg.

Fish species[(a)], FoodEx Level 3	N	% LC	Mean			P95[(b)]		
			LB	MB	UB	LB	MB	UB
Anchovy	110	33	73	83	92	200	200	200
Angler fish	61	30	186	195	204	551	551	551
Barbel	10	0	211	211	211	n/a	n/a	n/a
Barracuda	1	0	340	340	340	n/a	n/a	n/a
Bass	78	10	199	203	206	698	698	698
Bonito	25	8	580	583	586	1 920	1 920	1 920
Bream	253	11	224	225	226	883	833	883
Capelin	11	82	2.0	5.0	8.0	n/a	n/a	n/a
Carp	338	5	55	55	55	194	194	194
Char	8	0	32	32	32	n/a	n/a	n/a

Fish species[a], FoodEx Level 3	N	% LC	Mean			P95[b]		
			LB	MB	UB	LB	MB	UB
Cod and whiting	1 308	18	91	94	96	340	340	340

Table 6: Continued.

Fish species[a], FoodEx Level 3	N	% LC	Mean			P95[b]		
			LB	MB	UB	LB	MB	UB
Dentex	3	0	2 019	2 019	2 019	n/a	n/a	n/a
Eel	487	2	177	178	178	461	461	461
Flounder	23	17	85	91	97	185	185	185
Garfish	3	0	1 180	1 180	1 180	n/a	n/a	n/a
Grenadier	3	0	104	104	104	n/a	n/a	n/a
Grey mullet	52	23	152	159	167	566	566	566
Grouper	2	0	195	195	195	n/a	n/a	n/a
Gurnard	4	25	103	109	116	n/a	n/a	n/a
Hake	131	16	130	136	142	420	420	420
Halibut	1 713	0	209	209	209	610	610	610
Herring	1 272	0	36	36	36	78	78	78
Jack mackerel	3	0	127	127	127	n/a	n/a	n/a
John Dory	6	0	302	302	302	n/a	n/a	n/a
Lizardfish	2	0	611	611	611	n/a	n/a	n/a
Luvarus	1	0	590	590	590	n/a	n/a	n/a
Mackerel	1 348	5	106	108	109	520	520	520
Meagre	2	50	145	170	195	n/a	n/a	n/a
Perch	423	0	165	165	165	370	370	370
Pike	267	0	394	394	394	979	979	979
Plaice	194	2	64	64	65	160	160	160
Ray	32	3	229	229	230	1 170	1 170	1 170
Redfish	221	0	189	189	189	676	676	676
Roach	17	0	122	122	122	n/a	n/a	n/a
Salmon and trout	1 741	7	31	33	35	57	57	70
Sardine and pilchard	399	18	32	38	44	116	116	116
Scorpion fish	1	0	422	422	422	n/a	n/a	n/a
Sea bass	10	0	300	300	300	n/a	n/a	n/a
Sea catfish and wolf-fish	67	54	103	109	114	770	770	770
Shad	1	0	173	173	173	n/a	n/a	n/a
Shark	272	11	688	691	695	1 900	1 900	1 900
Smelt	2	0	325	325	325	n/a	n/a	n/a
Sole	49	24	69	77	84	180	180	180
Sprat	107	1	21	21	21	50	50	50
Sturgeon	4	50	40	52	65	n/a	n/a	n/a
Swordfish	264	5	1 210	1 212	1 214	3 300	3 300	3 300
Tuna	849	5	286	290	291	850	850	850
Turbot	4	0	62	62	62	n/a	n/a	n/a
Weever	11	0	763	763	763	n/a	n/a	n/a
Whitefish	37	16	77	85	93	250	250	250
Wrasse	12	0	511	511	511	n/a	n/a	n/a
Fish meat,	1 502	10	279	280	280	1 194	1 194	1

Fish species[a], FoodEx Level 3	N	% LC	Mean			P95[b]		
			LB	MB	UB	LB	MB	UB
unspecified[c]								194
Fish meat, overall[d]	12 235	10	164	166	168	499	500	501

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): Common names and Latin names reported in the Glossary
(b): The 95th percentile obtained on occurrence data with fewer than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore is considered only indicative.
(c): Data reported as fish meat without further specification.
(d): Data calculated on overall concentrations of individual specified fish species.

As shown in Table 6, the mercury content varied widely among different fish species, depending on the size and feeding habits, and as expected, was higher in predatory fish. This is in line with the results from other studies showing a higher mercury concentration in older predatory fish species (WHO, 2008). Considering only fish species with a sufficient number of results reported (N ≥ 25), the highest mean concentrations were found in swordfish (MB mean = 1 212 µg/kg) and in shark (MB mean = 691 µg/kg). Very high mean values were also recorded in dentex, garfish and weever, but because of the very low number of samples analysed for these species, the results may be considered only as indicative. Further descriptive statistics of the concentration of total mercury across the fish species and in unspecified fish meat is presented in more detail in Appendix A, Table A9.

4.2.5. Occurrence data on methylmercury

Methylmercury was analysed in 1 083 samples for 'Fish and other seafood' category in five subcategories of FoodEx Level 2 (Appendix A, Table A10).

Similarly to total mercury, for FoodEx Level 2 the highest methylmercury concentration was reported in 'Fish meat' (MB mean = 135 µg/kg), followed by 'Crustaceans' (MB mean = 102 µg/kg). Owing to the low number of reported results, especially for the most important contributing fish species, it was not possible to clearly identify the fish species with the highest content of methylmercury. The statistical description of reported results is summarised in Appendix A, Table A11.

4.2.6. Relationship between concentrations of total mercury and methylmercury in data reported to EFSA

A total of 377 samples from the dataset submitted to EFSA were analysed both for total mercury and methylmercury. In order to assess whether the contribution of methylmercury to total mercury is in line with the literature data, the mean (± standard deviation (SD)) and the range of the contributions were calculated in 239 samples reported as quantified data. The summary from these calculations covering various fish species, crustaceans, molluscs and fish products are reported in Table 7.

Table 7: Description of the contribution of methylmercury to total mercury for quantified results.

Food category	N	Mean	SD	Range
Angler fish	2	0.89	0.01	0.88-0.89
Anchovy	1	0.85	-	-
Bass	2	0.91	0.37	0.61-1.00
Bream	2	0.90	0.14	0.81-1.00
Carp	26	0.71	0.24	0.28-1.00
Cod and whiting	1	0.67	-	-
Eel	3	1.23	0.30	0.95-1.55
Grey mullet	1	0.81	-	-
Hake	3	0.92	0.13	0.77-1.00
Halibut	9	0.95	0.37	0.58-1.88
Mackerel	29	1.04	0.28	0.50-2.05

Salmon and trout	14	0.87	0.26	0.41-1.33
Sardine and pilchard	2	0.92	0.00	0.91-0.92
Shark	4	0.81	0.04	0.79-0.87
Tuna	45	0.80	0.31	0.27-1.73
Fish meat, unspecified	53	0.89	0.38	0.03-1.92
Crustaceans	10	0.95	0.09	0.74-1.00
Fish products	29	0.78	0.17	0.39-1.17
Molluscs	2	0.85	0.21	0.69-1.00

N: number of results; SD: standard deviation.

Taking into account the individual measurement uncertainties of total mercury and methylmercury results, it is expected that some contributions of methylmercury to total mercury exceeded 100 %, but a contribution above 130 - 140 % is considered inaccurate. This may have influenced the mean contributions calculated at species level (e.g. for eel) but since a low number of samples were affected overall (n = 15), this was not investigated further.

4.3. Previously reported occurrence results

There is an extensive quantity of data in the literature as regards total mercury in food, although there is less for methylmercury. All the analytical results are reported on a wet weight basis unless otherwise specified.

4.3.1. Occurrence in fish and other seafood

There are many publications giving results for only total mercury in fish and seafood. These papers are in general agreement with each other as regards occurrence, and they are also in agreement with the data reported above in Section 4.2. Selected studies are summarised below to reflect a broad overview of previously reported data from different fish species and from different geographical locations.

In Bosnia and Herzegovina, total mercury concentrations in muscle of six fresh fish species decreased in the following order: mullet > chub > brown trout > common carp > rudd > Prussian carp and were in the range 6 - 611 µg/kg (mean ranges 50 - 401 µg/kg) (Djedjibegovic et al., 2012).

In Italy, total mercury concentrations were measured in edible marine species (18 fish, five cephalopod molluscs, three crustaceans) collected in the Adriatic Sea (Storelli, 2008). Maximum concentrations corresponded to fish (70 - 1 560 µg/kg), followed by cephalopod molluscs (100 - 550 µg/kg) and crustaceans (270 - 330 µg/kg). In 2010, the analysis of total mercury in the flesh and hepatopancreas of 320 cephalopod molluscs sampled in the southern Adriatic Sea indicated that mercury concentrations were equally distributed in the two tissues, hepatopancreas and flesh (Storelli et al., 2010a). Regarding the edible portion (flesh), the highest concentrations were in Octopodidae (440 µg/kg) and Sepiidae (270 µg/kg), while Loliginidae tended to accumulate less mercury (110 µg/kg). Total mercury concentrations in 20 fresh bluefin tuna (*T. thynnus*) and in 45 popular brands of canned tuna were also determined by Storelli et al. (2010b) and ranged from 70 to 1 760 µg/kg (average 610 µg/kg) in fresh tuna and from 40 to 1 790 µg/kg (average 410 µg/kg) in canned tuna. In 32 samples of the most popular brands of salted anchovies (*Engraulis encrasicolus*) from the Mediterranean Sea (n = 20) and Atlantic Ocean (n = 12), total mercury concentrations ranged from 50 to 510 µg/kg (average 240 µg/kg) and from 50 to 350 µg/kg (average 170 µg/kg), respectively (Storelli et al., 2011).

In France, of the 1 319 food samples analysed for the second total diet study (TDS) (Millour et al., 2011b), only 5 % of total mercury values were quantified (LOQ of 10 µg/kg). The highest mean concentration (45 µg/kg) was found in the group 'Fish and fish products'. In fish, the mean content was 65 µg/kg and oven cooked tuna was found to have the highest concentrations on average (476 µg/kg, maximum 702 µg/kg). 'Shellfish' had a mean concentration of 19 µg/kg with highest concentrations found in shrimps (mean 26 µg/kg, maximum 40 µg/kg) and mussels (mean 15 µg/kg and maximum 32 µg/kg). For oysters and scallops, the mean concentrations were close to the LOQ

(12 µg/kg and 10 µg/kg, respectively). Total mercury contents were quantified in 97 % of samples (LOQ of 40 µg/kg) in white and brown meat of 108 batches of crustaceans (lobsters, spider crabs, common crabs, swimming crabs and king crabs) from France (Noël et al., 2011a). In white meat, the mean mercury concentrations ranged from 76 µg/kg for king crabs to 151 µg/kg for swimming crabs. The concentration obtained was within the range of typical concentrations found in crustacean muscle (20 - 200 µg/kg) (Francesconi, 2007). The highest concentrations were found in common crabs in both white meat (465 µg/kg) and brown meat (331 µg/kg). Among 118 batches of marine gastropods, echinoderms and tunicates, 94 % were below the LOQ of 40 µg/kg (Noël et al., 2011b). Mercury was quantified only in marine gastropods. Mean mercury concentrations ranged from 40 µg/kg in common winkles and abalone to 71 µg/kg in murex where the highest concentration was found (185 µg/kg). Another French study of total mercury in eight shark species indicated that 5 out of 91 samples exceeded the ML of 1 000 µg/kg, ranging from 2 430 to 4 780 µg/kg (Velge et al., 2010). In 67 fish (Artic charr) from four lakes located in the French Alps, total mercury muscle concentrations did not exceed 500 µg/kg (Marusczak et al., 2011).

In the UK TDS (Rose et al., 2010), the highest mean total mercury was found in fish (56 µg/kg).

In Alaska, United States of America (USA), mercury concentrations were overall ≤ 1 000 µg/kg in 17 freshwater fish species and 24 anadromous and marine fish species, for a total of 2 692 specimens (Jewett and Duffy, 2007). Northern pike contained the highest muscle mercury values, whereas Pacific salmon had low mercury concentrations (≤ 100 µg/kg) and Pacific halibut contained less than 300 µg/kg. The amount of mercury present in canned tuna purchased in Las Vegas, Nevada, USA indicated that chunk white tuna (619 ± 212 µg/kg) and solid white tuna (576 ± 178 µg/kg) were both statistically significantly ($p < 0.001$) higher in mean mercury than chunk light tuna (137 ± 63 µg/kg) (Gerstenberger et al., 2010).

Most of the methylmercury occurrence data available in the literature concern fish and sometimes other seafood products. Some of the previously reported methylmercury data quantified in fish and other seafood since 2000 and the percentage of methylmercury are summarised in Table 8 and at a fish species level in Appendix B (Tables B1 and B2).

Table 8: Comparison of the range (mean) and percentage of methylmercury quantified in fish and shellfish (µg Hg/kg wet weight).

Group	Origin	Number species	Number samples	MeHg	THg or ∑Hg species	% MeHg	References
Fish							
	Belgium	15[b]	170	43-598	39-613	91-98	Baeyens et al. (2003)
	Czech Republic	1[a]	96	33-362	39-384 (128)	76-90 (82)	Kružíková et al. (2008)
	France	3[b]	28	28-588 (90)	30-642 (97)	84-97 (93)	Clémens et al. (2011)
	France	41[b]	108	10-944 (169)	-	70-100	Sirot et al. (2008)
	Germany	32[b]	536[c]	6-567 (38)	-	14-100 (70)	Kuballa et al. (2011)
	Italy	9[b]	1081	170-16 060	170-18 290	43-100	Storelli et al. (2002a)
	Italy	3[b]	15	400-4 560	670-5 160	51-97	Storelli et al. (2002b)
	Italy	15[b]	2 880	0-1 740 (314)	0-1 870 (356)	52-100 (88)	Storelli et al. (2003)
	Italy	2[b]	n.r.	ND-1 740	ND-1 740	60-100	Storelli et al. (2005)
	Poland	1[a]	4	18-2 630	25-2950	72-98 (87)	Baralkiewicz et al. (2006)
	Portugal	1[a]	45	70-200	63-240	85-97	Mieiro et al. (2009)
	Slovenia	27[b]	52	2-1 120 (127)	3-1 110 (150)	40-110 (80)	Miklavčič et al. (2011a)
	Spain	14[b]	25	54-596	-	-	Sahuquillo et al. (2007)
	Canada	9[b]	112	9-2 346 (342)	20-2 729 (542)	30-94 (64)	Forsyth et al. (2004)
	Caspian sea	1[a]	12	10-107	10-108 (40)	97-100	Agah et al. (2007)
	China	13[b]	148	40-590 (260)	10-660 (180)	59-84 (74)	Cheng et al. (2009)
	China	1[a]	12	24-98 (60)	61-680 (292)	7-93 (28)	Qiu et al. (2009)
	China	4[a]	40	5-499	24-1 199	18-85	Jin et al. (2006)
	Ghana	24[a]	-	9-107	-	-	Voegborlo et al. (2011)
	Hong-Kong	89[a,b]	280	3-1 010 (72)	3-1 370 (91)	-	Tang et al. (2009)
	India	7[b]	-	8.0-16 (13)	8.7-17 (15)	71-95	Mishra et al. (2007)

	Malaysia	3(b)	17	20-100	41-120	50-89	Hajeb et al. (2009b)
	Malaysia	2(b)	69	(378)	(459)	70-82 (77)	Hajeb et al. (2010)
	Papua New Guinea	7(a)	95	26-458	48-500	54-94	Bowles et al. (2001)
	Persian gulf	6(b)	63	11-100	12-87 (37)	63-100	Agah et al. (2007)
	USA	9(b)	-	(13-278)	(16-292)	93-98 (96)	Hight and Cheng (2006)
Shellfish							
	France	4	34	1.9-33 (16)	3.9-34 (20)	28-98 (75)	Clémens et al. (2011)
	France	18	47	3-219 (54)	-	-	Sirot et al. (2008)
	Italy	1	10	66-155 (110)	236-559 (386)	17-49 (32)	Di Leo et al. (2010)
	Italy(d)	1	10	17-116	40-830	33-91	Ipolyi et al. (2004)
	Italy(e)	1	10	15-51	35-115	14-98	Ipolyi et al. (2004)
	Brazil	4	14	3.8-37 (15)	3.8-40 (16)	-	Batista et al. (2011)

Table 8: Continued.

Group	Origin	Number species	Number samples	MeHg	THg or ∑Hg species	% MeHg	References
	China	3	-	11-25	-	-	Xiong and Hu (2007)
	India	3	-	(34)	(48)	-	Mishra et al. (2007)

n.r.: not reported; ND: not detected; MeHg: methylmercury; THg: total mercury; ∑Hg species: some of mercury species.
(a): freshwater fish;
(b): marine fish;
(c): for fish and shellfish;
(d): Sardinian coast campaign 1;
(e): Sardinian coast campaign 2.

Table 8 indicates a range of concentrations of methylmercury or total mercury in freshwater fish (methylmercury: 5 - 2 630 µg/kg; total mercury: 10 - 2 950 µg/kg), in shellfish (methylmercury: 2 - 220 µg/kg; total mercury: 40 - 830 µg/kg) and in marine fish (methylmercury: 0 - 16 000 µg/kg; total mercury: 0 - 18 000 µg/kg). These concentrations of total mercury and methylmercury are similar to those reported to EFSA and are in good agreement with the general conclusions of the JECFA (FAO/WHO, 2011b), which indicated that:

- Total mercury concentrations in 6 114 fish samples ranged from 1 to 11 400 µg/kg, with the maximum concentration found in marlin. About 5 % exceeded 1 000 µg/kg, particularly for lamprey, Portuguese dogfish, swordfish, shark, marlin, splendid alfonsino, picked dogfish, tuna, catshark, scabbardfish, ling, pike and ray.

- Total mercury concentrations in 1 892 shellfish samples (80 % above LOQ) ranged from 2 to 860 µg/kg. No shellfish species contained methylmercury at concentrations greater than 500 µg/kg (range 2 - 451 µg/kg), with the maximum concentration found in edible crab.

4.3.2. Occurrence in other food

Of the 1 319 food samples analysed for the second French TDS (Millour et al., 2011b), only 5 % of total mercury values were quantified (LOQ of 10 µg/kg). The highest mean concentration for foods other than fish and seafood were found in 'sweeteners, honey and confectionery' (12 µg/kg) where the product group 'chocolate' contained on average 17 µg/kg of mercury with a maximum concentration of 50 µg/kg found in a dark chocolate while the mean concentration in sugars and sugar-based products was lower than LOD (5 µg/kg). For the other food groups, the mean content was lower than the LOQ but high concentrations (243 µg/kg) were found in a merguez sausage in the food group 'meat and offal'. In the first French TDS (Leblanc et al., 2005), the food groups apart from fish and seafood containing the highest concentrations of mercury were 'sweeteners, honey and confectionery' (13 µg/kg). The other food groups had contents lower than the LOQ of 10 µg/kg.

The means of mercury content in mushrooms in Poland (LOQ of 5 µg Hg/kg dry weight (d.w.)) varied between 95 and 280 µg/kg d.w. in caps and between 45 and 130 µg/kg d.w. in stipes in 120 composite samples of 383 Slippery Jack, *Suillus luteus*, mushroom (Chudzynski et al., 2011).

In Spain, the concentration of total mercury found in 24 natural rice samples from four different origin ranged between 1.3 and 7.8 µg/kg (LOQ of 0.9 µg/kg) (da Silva et al., 2010). Mercury has also been found in rice from close to a former mining area in China (see Section 4.4 below).

In the UK TDS (Rose et al., 2010), total mercury was detected in the 'Offal' (4 µg/kg), and 'Other vegetables' food groups (0.7 µg/kg); the concentration was below the LODs (0.5 - 3 µg/kg[34] depending on food group in all other categories (apart from fish and seafood).

Also in the UK, mercury was detected at concentrations at or above the LOD (0.2 – 1.0 µg/kg depending on sample weight taken) in only about one quarter of the samples in a wide range of commercial weaning foods and formulae, usually in those containing fish (FSA, 2006). The mean mercury concentration was 1 µg/kg, slightly lower than the mean value from a previous survey where the mean was 3 µg/kg (FSA, 2003).

The general conclusions of the JECFA (FAO/WHO, 2011b) indicated that total mercury concentrations in foods other than fish products were generally low (range 0.1 - 50 µg/kg), with about 80 % of the 6 183 samples containing concentrations below the LOQs. The highest concentrations were found in fungi. Mean methylmercury concentrations reported by China in non-fish samples ranged from 1 to 23 µg/kg, with a maximum concentration found in poultry. No other information on methylmercury in non-fish samples was received from other countries. In water, total mercury concentrations in 98 % of 90 545 samples analysed in France were below the LOQ of 0.02 µg/L, with a maximum of 4.3 µg/ L.

In summary, the published data since 2000 on total mercury and methylmercury in fish and other seafood and on total mercury in other food are in the same range as those reported to EFSA and support the findings and evaluation reported above in Section 4.2.

4.3.3. Occurrence in human milk

Mercury can be transferred into human milk as inorganic and methylmercury. This section gives an overview of concentrations in human milk in Europe sampled since 2000 or during a period that started earlier but included the year 2000 (Table 9).

Three studies were identified in which both total and methylmercury were measured in the same human milk samples. Valent et al. (2011) studied mother-infant pairs living in the region Friuli Venezia Giulia (Italy). Total mercury was measured in 77 samples of human milk with a mean concentration of 0.70 µg/kg and methylmercury in 79 samples with a mean concentration of 0.20 µg/kg. For the 77 human milk samples in which both methylmercury and total mercury were measured, the mean contribution of methylmercury to total mercury was 0.31 (median: 0.25; P75: 0.42; P100: 1.00). A statistically significant, but weak correlation was observed between methylmercury in human milk and the total fish consumption (Spearman correlation coefficient (r_s) = 0.29, p = 0.085, n = 79) and fresh fish consumption (r_s = 0.31, p = 0.0054, n = 79).

Miklavčič et al. (2011b) analysed in Slovenia total mercury in human milk and found a mean concentration of 0.3 µg/kg. Human milk samples (n = 11) from mothers with a concentration of total mercury in hair of at least 1.0 mg/kg were also analysed for methylmercury and a mean concentration of 0.68 µg/kg was reported. For nine human milk samples, both methylmercury and total mercury concentrations were determined and the mean contribution of methylmercury to total mercury was 0.39 (Miklavčič, personal communication, 2012). No correlation was observed between total mercury concentrations in human milk and the frequency of fish consumption (r_s = 0.08, 95 % confidence

[34] LOD errorounously reported as 0.005-0.003 in the paper (M.Rose, 2012, personal communication).

interval (CI): -0.04 - 0.20), but a weak correlation was observed between total mercury in human milk and calculated methylmercury concentrations in the most frequently eaten fish species (r_s = 0.14; 95 % CI: 0.02 - 0.25).

The third study analysed total mercury in human milk from Italian, Croatian and Greek women and compared the data on human milk with a subset of the results reported by Miklavčič et al. (2011b). When the total mercury concentration in the mother's hair was at least 1.0 mg/kg, methylmercury was analysed as well. The highest concentrations of total mercury in human milk were reported in Greek women (n = 44) with a median concentration of 0.6 µg/kg (range: < LOD - 12 µg/kg). Statistically significant lower concentrations were reported for Italian (n = 605), Slovenian (n = 284) and Croatian (n = 125) women, all with a median concentration of 0.2 µg/kg (Miklavčič et al., in press). The mean contributions of methylmercury to total mercury were 0.59 in Italian women (n = 224), 0.63 in Croatian women (n = 26) and 0.26 in Greek women (n = 21) (Miklavčič, personal communication, 2012), so the highest median methylmercury concentration (0.17 µg/kg) among women with hair mercury of at least 1 mg/kg was found in Croatian women. The authors reported a statistically significant but weak correlation for total and methylmercury in human milk from Mediterranean women (Italy, Slovenia, Croatia and Greece) and frequency of total fish consumption (total mercury: r_s = 0.0977, p = 0.002, n = 1 005; methylmercury: r_s = 0.1377, p = 0.027, n = 259)

Garcia-Esquinas et al. (2011) reported a geometric mean total mercury concentration of 0.53 µg/L (n = 100) in human milk in Spain. Total mercury in human milk was not statistically significant correlated with the presence of dental amalgam fillings and fish and shellfish consumption. A mean concentration of 0.94 µg/L was reported by Ursinyova and Masanova (2005) in Slovakia republic (n = 158) and Björnberg et al. (2005) reported a median concentration of 0.29 µg/L, 4 days postpartum and 0.14 µg/L, 6 weeks postpartum in human milk from Sweden.

In contrast to the above-mentioned studies, Aballe et al. (2008) reported mean concentrations of total mercury between 2.63 (n = 13) and 3.53 µg/L (n = 10). However, the concentrations did not appear to be related to the amount of fish and fishery products consumed.

One study was identified that analysed inorganic mercury in 21 human milk samples from Austria and reported a median concentration of 0.2 µg/L (Gundacker et al., 2010a).

A limited number of studies report concentrations of mercury (total, methyl- or inorganic) in human milk. Mean concentrations of total mercury between 0.3 and 3.53 µg/L were reported. The mean contribution of methylmercury to total mercury ranged from 26 to 63 %. Inconsistent results regarding the correlation between total mercury or methylmercury in human milk and fish consumption were observed.

Table 9: Overview of mercury concentrations in the European population in human milk.

Country	Additional information	Human milk (µg Hg/L) N	mean	SD	P50	Variation (specified by footnotes)	Reference
Sweden	Day 4 postpartum	20			T:0.29	T:0.06-2.1[(b)]	Björnberg et al. (2005)
	6 weeks postpartum	20			T:0.14	T:0.07-0.37[(b)]	
Slovak Republic		158	T:0.94[(e)]		T:0.72[(e)]	T:<LOD-4.74[(b,e)]	Ursinyova and Masanova (2005)
Italy	Mothers from Venice with low consumption of local fish and fishery products (region Veneto)	10	T:2.68				Abballe et al. (2008)
	Mothers from Venice with medium consumption of local fish and fishery products (region Veneto)	13	T:2.63				
	Mothers from Venice with high consumption of local fish and fishery products (region Veneto)	6	T:2.99				
	Mothers from Rome (region Lazio)	10	T:3.53				
Austria		21			I:0.2	I:0.1-2.0[(b)] I:0.1-0.3[(d)]	Gundacker et al. (2010a)
Spain		100	T:0.53[(a)]		T:0.61	T:0.22-1.17[(c)]	García-Esquinas et al. (2011)
Slovenia	All mothers	284	T:0.3[(e)]		T:0.2[(e)]	T:0.06-0.6[(c,e)]	Miklavčič et al. (2011)
	Mothers of which the T in hair ≥ 1 mg/kg	11	M:0.68[(e)]	M:1.8[(e)]	M:0.07[(e)]	M:0.03-6.2[(c,e)]	
Italy	Mothers from the region Friuli Venezia Giulia	77	T:0.7[(e)]	T:1.29[(e)]	T:0.4 [(e)]	T:10.29[(e,f)] T:0.66[(e,g)]	Valent et al. (2011)
		79	M:0.2[(e)]	M:0.4[(e)]	M:0.08[(e)]	M:2.43[(e,f)] M:0.15[(e,g)]	
Italy	All mothers	605			T:0.2[(e)]	T:<0.045-28[(b,e)]	Miklavčič et al. (in press); Miklavčič, personal communication (2012)
	Mothers of which the T in hair ≥ 1 mg/kg	224	M:0.17[(e)]	M:0.14[(e)]	M:0.13[(e)]	M:0.01-1.09[(b,e)]	
Croatia	All mothers	125			T:0.2[(e)]	T:<0.045-2.4[(b,e)]	
	Mothers of which the T in hair ≥ 1 mg/kg	26	M:0.18[(e)]	M:0.11[(e)]	M:0.17[(e)]	M:0.04-0.55[(b,e)]	
Greece	All mothers	44			T:0.6[(e)]	T:<0.045-12[(b,e)]	
	Mothers of which the T in hair ≥ 1 mg/kg	21	M:0.1[(e)]	M:0.08[(e)]	M:0.08[(e)]	M:0.01-0.23[(b,e)]	

N: number of samples; SD: standard deviation; PX: X^{th} percentile; T: total mercury; M: methylmercury; I: inorganic mercury; Hg: mercury.
(a): Geometric mean
(b): Minimum-maximum
(c): P10-P90
(d): P25-P75
(e): µg/kg
(f): Maximum
(g): P75

4.4. Relationship between concentrations of total mercury and methylmercury

In order to assess the relationship between total mercury and methylmercury in foods, the data discussed above (see Section 4.2.6) together with the available scientific literature (Appendix B, Tables B1 and B2) was evaluated and the amounts found are described below.

Fish

It is generally found that about 80 - 100 % of total mercury in fish muscle is methylmercury; details from specific studies are shown in Table 8. However, studies in which methylmercury was also determined in fish lower in the food chain showed that not only was the total mercury content lower, but the percentage of methylmercury may be quite variable and even down to around 50 % of total mercury. This is in agreement with the conclusion of the JECFA, which indicated that in fish, the contribution of methylmercury to total mercury generally ranged between 30 % and 100 %, depending on species of fish, size, age and diet (FAO/WHO, 2011b). Furthermore, in about 80 % of these data, methylmercury accounted for more than 80 % of total mercury. However, a few submitted data showed contributions of methylmercury to total mercury of about 10 % or less.

The CONTAM Panel used a conservative approach to calculate methylmercury dietary exposure by assuming that 100 % of mercury in fish is in the form of methylmercury. However, in order to ensure that dietary exposure to inorganic mercury was not underestimated, 20 % of total mercury in fish was simultaneously assumed to be inorganic mercury when calculating inorganic mercury dietary exposure.

Other seafood

In seafood other than fish, methylmercury typically comprises 50 - 80 % of total mercury. In order to be conservative and to avoid underestimating methylmercury, the Panel assumed 80 % methylmercury for this type of food. Again, in order to ensure that dietary exposure to inorganic mercury was not underestimated, for shellfish a figure of 50 % inorganic mercury was assumed for dietary exposure estimates.

Other foods

There are data in the literature about mercury in rice originating from close to a former mercury mining area in China. In this area, methylmercury was reported to be around 20 - 40 % of the total mercury present in the rice, but this was associated with this particular contamination incident (Qiu et al., 2008). The contribution of methylmercury to total mercury in rice from non-contaminated areas is unknown and therefore not taken into consideration.

In other foods, mercury is presumed to be present as inorganic mercury. Because of this and since the number of data for other foods is low, a contribution of methylmercury to total mercury was not proposed for other foods, and a figure of 100 % inorganic mercury was assumed for dietary exposure estimates.

Human milk

Three European studies were identified in which both methylmercury and total mercury were analysed in human milk and the mean contribution of methylmercury to total mercury reported in these studies ranged from 26 to 63 % (See Section 4.3.3.).

The limited available data on the contribution of methylmercury to total mercury in human milk showed a wide variation, and the mean contribution was not considered sufficiently robust to form a basis for exposure assessment. Therefore, mean concentrations of methylmercury in human milk were used for methylmercury exposure assessment and the difference between total mercury and

methylmercury concentrations in human milk was used to calculate mean inorganic mercury concentrations for use in the exposure assessment.

4.5. Food processing

Mercury when present in food is stable and resistant to the effects generally encountered during processing. WHO (2008) stated that methylmercury in fish is bound to tissue protein rather than with fatty deposits, therefore trimming and skinning of fish does not reduce the mercury content of the fillet portion. Moreover, the mercury concentration in fish is not changed when cooked. However, because some moisture is usually lost during cooking, mercury concentrations are often slightly higher in cooked fish than in raw wet tissue. In addition, some preparation methods, such as deep frying, can actually increase the weight of the fish, potentially resulting in slightly lower concentrations of mercury. However, the total amount of mercury in fish remains relatively unchanged after cooking, and the slight changes in mercury concentrations due to cooking methods are relatively insignificant and generally do not need to be considered when estimating dietary exposures.

There have been a few studies that have specifically looked at the impact of processing and these are summarised below.

Frying and baking were found not to affect the mercury content of blue shark in a study by Chicourel et al. (2001). Deep frying was found to increase concentrations of mercury in fish in a study by Burger et al. (2003), but the increase was probably accounted for by weight loss combined with breading and absorption of oil. A small increase in mercury concentrations in fish after cooking was also found by Perelló et al. (2008), probably also accounted for by changes in weight. Fish cooked in rice was found to have an increased mercury content in a study by Musaiger and D'Souza (2008) and this was attributed to spices used with the rice, which are reported to be an additional source of heavy metals.

Farias et al. (2010) looked at the impact of different cooking processes on mercury consumed in a community in the Amazon region and concluded that up to 30 % of mercury may be lost during cooking. It was suggested that the volatility of methylmercury could be a contributory factor.

Some studies used *in vitro* gastrointestinal digestion techniques to make preliminary assessments with respect to mercury bioavailability and these are discussed below. Torres-Escribano et al. (2011) found that mercury bioaccessibility decreases after cooking by up to around half of the original concentration. It was proposed that the change in bioaccessibility after cooking might be attributable to alterations in the structural conformation of the fish muscle proteins produced by temperature, which could cause the loss of the native protein structure. These changes might impede the access of the enzymes used in *in vitro* gastrointestinal digestion to the structures to which mercury is bound in the muscle low-molecular-weight thiols, i.e. sulphydryl groups containing molecules such as cysteine. Maulvault et al. (2011) also found reductions of up to 40 % in the bioaccessible fraction of mercury in fish after it was cooked. Ouédraogo and Amyot (2011) found that mercury concentrations (dry weight) were slightly higher in boiled fish but that boiling or frying reduced bioaccessibility by 40 - 50 % and that the reduction was greater, 50 - 60 %, in the presence of tea or coffee.

In general, there is a consensus from both the *in vitro* studies discussed above and the studies conducted on cooking and processing described earlier that there is little impact of cooking or processing on the content of mercury in foods and so data for mercury in raw foods are suitable to use for dietary exposure estimates.

5. FOOD CONSUMPTION

5.1. EFSA's Comprehensive European Food Consumption Database

During 2010, the EFSA Comprehensive European Food Consumption Database (hereinafter Comprehensive Database) was built from existing national information on food consumption at a detailed level. Competent organisations in the EU Member States provided EFSA with data from the

most recent national dietary survey in their country at the level of consumption by the individual consumer. Survey results for children were mainly obtained through the EFSA Article 36 project 'Individual food consumption data and exposure assessment studies for children' through the EXPOCHI consortium (EFSA, 2011b). Results from a total of 32 different dietary surveys carried out in 22 different Member States covering more than 67 000 individuals are included in the Comprehensive Database version 1 as published (EFSA, 2011b; Merten et al., 2011).

Individuals were categorised into seven age groups covering infants (< 1 year), toddlers (1-< 3 years), other children (3-< 10 years), adolescents (10-< 18 years), adults (18-< 65 years), elderly (65 - < 75 years) and the very elderly (≥ 75 years) (EFSA, 2011b). There are two surveys available for infants, nine surveys available for toddlers, 17 surveys available for other children, 12 surveys available for adolescents, 15 surveys available for adults, seven surveys available for elderly and six surveys available for very elderly.

For each survey, food consumption data are presented according to the FoodEx classification system at FoodEx Level 1 (including 20 categories) and Level 2 (including around 160 categories). The FoodEx Level 1 food category 'Fish and other seafood ' is split in six subcategories at FoodEx Level 2, including 'Fish meat', 'Fish products', 'Fish offal', 'Crustaceans', 'Molluscs' and 'Amphibians, reptiles, snails, insects'. The 'Fish meat' category contains 32 fish species to be merged with occurrence data for calculating dietary exposure.

Although the food consumption data in the Comprehensive Database are the most complete and detailed currently available in the EU, it should be pointed out that different methodologies were used between surveys to collect the data and thus direct country-to-country comparisons can be misleading (Merten et al., 2011). Only surveys covering more than one day as described in Table 10, and thus appropriate for calculating chronic dietary exposure, were selected.

Table 10: Surveys included from the Comprehensive Database version 1 for calculating dietary exposure.

Country	Survey	N	Method	Days	Age	Year
Belgium	Regional Flanders	661	Dietary record	3	2-6	2003
Belgium	Diet National 2004	3 245	24-h dietary recall	2	15-105	2004
Bulgaria	NUTRICHILD	1 723	24-h dietary recall	2	0.1-5	2007
Cyprus	Childhealth	303	Dietary record	3	11-18	2003
Czech Republic	SISP04	1 751	24-h dietary recall	2	4-64	2004
Germany	DONALD 2006	303	Dietary record	3	1-10	2006
Germany	DONALD 2007	311	Dietary record	3	1-10	2007
Germany	DONALD 2008	307	Dietary record	3	1-10	2008
Germany	National Nutrition Survey II	13 926	24-h dietary recall	2	14-80	2006
Denmark	Danish Dietary Survey	4 118	Food record	7	4-75	2001
Spain	enKid	382	24-h dietary recall	2	1-14	2000
Spain	NUT INK05	760	24-h dietary recall	2	4-18	2005
Spain	AESAN	418	24-h dietary recall	2	18-60	2009
Spain	AESAN FIAB	1 068	Dietary record	3	17-60	2001
Finland	DIPP	1 448	Dietary record	3	1-6	2005
Finland	STRIP	250	Dietary record	4	7-8	2000
Finland	FINDIET 2007	2 038	48-h dietary recall	2	25-74	2007
France	INCA2	4 079	Dietary record	7	3-79	2006
United Kingdom	NDNS	1 724	Dietary record	7	19-64	2001
Greece	Regional Crete	874	Dietary record	3	4-6	2005
Hungary	National Representative Survey	1 360	Dietary record	3	18-96	2003
Ireland	NSIFCS	958	Dietary record	7	18-64	1998
Italy	INRAN SCAI 2005/06	3 323	Dietary record	3	0.1-98	2006
Latvia	EFSA TEST	2 070	24-h dietary recall	2	7-66	2008
the Netherlands	VCP kids	1 279	Dietary record	3	2-6	2006

Table 10: Continued.

Country	Survey	N	Method	Days	Age	Year
the Netherlands	DNFCS 2003	750	24-h dietary recall	2	19-30	2003
Sweden	NFA	2 495	24-h dietary recall	4	3-18	2003
Sweden	Riksmaten 1997/98	1 210	Dietary record	7	18-74	1997

N: number of participants.

5.2. Food consumption data for different age and consumer groups

5.2.1. Specific consumption patterns of 'Fish and other seafood' in the total population and in consumers only in European countries

Consumption data for 'Fish and other seafood' were analysed in all dietary studies specified in Table 10 for both the total population (meaning all participants in the surveys) and the consumers only.

The median of the mean consumption levels for this food group in the total population across all countries and dietary surveys was highest in the group elderly followed by adults and very elderly and lowest in child age groups (Appendix C, Table C1). A similar pattern was seen for 95th percentile fish and other seafood consumption.

The elderly and adults age groups also had the highest consumption among consumers only of fish and other seafood both for the median of mean and 95th percentile consumption (Appendix C, Table C2).

5.2.2. Specific consumption patterns of 'Fish meat' in the total population and in consumers only in European countries

Consumption data for fish meat were analysed in all dietary studies specified in Table 10 for both the total population (meaning all participants in the surveys) and the consumers only.

The highest consumption level for fish meat in the total population across all countries and dietary surveys was seen in the group elderly and very elderly (Appendix C Table C3). On the other hand, lower consumption levels of fish meat were found in other children, toddlers and in infants.

The highest median values of the 95th percentile fish meat consumption in the total population were observed in elderly followed by adults. The highest maximum consumption across the dietary surveys was reported in adults, adolescents and elderly.

The highest consumption level for fish meat in consumers only across all countries and dietary surveys was seen in the group elderly followed by adults and very elderly (Appendix C Table C4). Lower consumption levels were seen in other children, infants and in toddlers.

The 95th percentile fish meat consumption in the consumers only followed a similar pattern to the mean consumption. The highest values were observed in adults followed by elderly. The highest maximum consumption across the dietary surveys was reported in elderly, adults and adolescents.

6. EXPOSURE ASSESSMENT IN HUMANS

6.1. Occurrence data used for exposure assessment

In order to ensure quality and representativeness of the data, specific adjustments to 'Fish and other seafood' results were carried out as described in this section.

Most of the data reported to EFSA were for total mercury, and since the low number of results reported for methylmercury was difficult to combine with data for total mercury, the methylmercury data were excluded from further analyses.

It was assumed that the group of unspecified fish meat probably reflected fish species that are not covered by the FoodEx classification and, because of the high mercury mean concentration, the CONTAM Panel believed that large predatory fish might be overrepresented in this group. For this reason, the unspecified fish meat entry was replaced by the mean of all individually specified fish species to be matched with consumption of unspecified fish meat for the dietary exposure calculation (Table 6).

Fish species with insufficient numbers of samples ($n < 25$) were merged into three groups for calculating dietary exposure: (i) freshwater fish (containing sturgeon, barbel, char, meagre, roach and smelt); (ii) lower concentration marine fish (containing capelin, Jack mackerel, flounder, grouper, gurnard, shad and turbot); and (iii) higher concentration marine fish (containing barracuda, dentex, garfish, lizardfish, luvarus, scorpion fish, sea bass, weever, wrasse and John Dory).

Because of the lack of specific information on methylmercury and inorganic mercury data in the database, with the exception of human milk, the exposure assessment was based on the data submitted for total mercury. The analysed total mercury was converted to methylmercury and inorganic mercury by applying conversion factors based on the contribution of methylmercury to total mercury derived from literature data (Section 4.3 and Section 4.4). The following conversion factors for different food categories were proposed and used for dietary exposure calculation:

- fish meat, fish products, fish offal and unspecified fish and seafood: 1.0 for methylmercury and 0.2 for inorganic mercury;
- crustaceans, molluscs and amphibians, reptiles, snails, insects: 0.8 for methylmercury and 0.5 for inorganic mercury;
- all other food categories apart from 'Fish and other seafood': 1.0 for inorganic mercury and 0 for methylmercury;

Because this approach was chosen, total mercury dietary exposure cannot be derived by adding inorganic and methylmercury dietary exposure together for these foods.

For human milk, the dietary exposures were calculated using measured data for methylmercury. The concentration of inorganic mercury in human milk was estimated from the difference between the total mercury and methylmercury concentration.

6.2. Exposure assessment to methylmercury based on data reported to EFSA

Mean occurrence results are used by EFSA to calculate chronic dietary exposure. This is also the most common input used internationally for contaminant data since, in the case of datasets in which LC data constitute more than half of the results, the median will not be influenced at all by the magnitude of the positive results. Thus, dietary exposure was calculated by multiplying the mean mercury concentration for each food or food group by the corresponding consumption amount per kg b.w. separately for each individual in the database, calculating the sum of exposure for each survey day for the individual and then deriving the daily mean for the survey period. The mean and 95th percentile

dietary exposures were calculated for the total survey population separately for each survey and age class.

The CONTAM Panel focused the calculation of dietary exposure to methylmercury only on the food group 'Fish and other seafood' since it was assumed that in foods other than fish and other seafood mercury is present in inorganic form.

For this opinion, exposure estimates were calculated for 28 different dietary surveys carried out in 17 European countries (denoted the total population). The estimation of the dietary exposure to methylmercury in the text below is based on MB data since there was virtually no difference between LB and UB. The MB mean methylmercury concentration data of the food group 'Fish and other seafood' described in Section 4.2.4. were combined with the consumption and body weight data at the individual level to express methylmercury dietary exposure in µg/kg b.w. per week.

The minimum, median and maximum of the mean and the 95th percentile dietary exposure to methylmercury for all age groups across the surveys are summarised in Table 11. The MB mean methylmercury dietary exposure varied between 0.06 µg/kg b.w. per week seen in the elderly and very elderly groups to 1.57 µg/kg b.w. per week in toddlers. The MB 95th percentile dietary exposure ranged from 0.14 µg/kg b.w. per week in very elderly to 5.05 µg/kg b.w. per week in adolescents. The detailed results of the exposure calculation are presented in Appendix D, Table D1-D6 for the different surveys and age groups.

Table 11: Summary statistics of the chronic dietary exposure to methylmercury (µg Hg/kg b.w. per week) by age class. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown (further details are shown in Appendix D, Tables D1-D6).

	Minimum			Median			Maximum		
	LB	MB	UB	LB	MB	UB	LB	MB	UB
Mean dietary exposure in total population									
Toddlers	0.09	0.09	0.09	0.26	0.27	0.28	1.49	1.57	1.65
Other children	0.13	0.14	0.14	0.31	0.32	0.32	1.45	1.49	1.54
Adolescents	0.07	0.08	0.08	0.31	0.31	0.32	1.06	1.09	1.12
Adults	0.07	0.07	0.07	0.24	0.24	0.25	1.04	1.08	1.12
Elderly	0.06	0.06	0.07	0.25	0.26	0.26	0.61	0.63	0.65
Very elderly	0.05	0.06	0.06	0.24	0.25	0.25	0.37	0.38	0.39
P95 dietary exposure in total population									
Toddlers	0.66	0.68	0.70	1.57	1.59	1.62	2.70	2.72	2.74
Other children	0.73	0.75	0.76	1.59	1.60	1.62	4.60	4.96	5.04
Adolescents	0.41	0.42	0.42	1.32	1.38	1.48	5.04	5.05	5.06
Adults	0.50	0.51	0.53	1.11	1.13	1.14	3.00	3.04	3.08
Elderly	0.34	0.34	0.35	1.23	1.24	1.26	2.49	2.49	2.49
Very elderly	0.13	0.14	0.16	1.15	1.17	1.19	1.40	1.42	1.42

b.w.: body weight; Hg: mercury; LB: lower bound; MB: middle bound; P95: 95th percentile; UB; upper bound.

6.2.1. Infants (less than one year old)

Breast-fed infants

For the exposure assessment of infants below six months of age, a value of three months was selected, assuming a body weight of 6.1 kg, with an estimated average daily consumption of 800 mL and a high consumption of 1 200 mL of human milk (Table 12). For the occurrence data, mean occurrence levels of methylmercury reported in the literature were used (see Section 4.3.3.). The CONTAM Panel noted that in two of these studies, methylmercury was not analysed in milk from mothers with total mercury

concentrations in hair below 1 mg/kg, but concluded that this was unlikely to have a major impact on the data.

Based on the reported mean concentrations of methylmercury in human milk, the mean dietary exposure to methylmercury for infants with an average milk consumption ranged from 0.09 to 0.62 µg/kg b.w. per week (Table 12). For infants with a high milk consumption the dietary exposure ranged from 0.14 to 0.94 µg/kg b.w. per week.

Table 12: Exposure scenario to methylmercury based on average and high human milk consumption for infants below 6 months based on the mean occurrence data reported in literature (see Section 4.3.3.).

Country	Dietary exposure to methylmercury (µg Hg/kg b.w. per week)		Reference
	Average human milk consumption	High human milk consumption	
Slovenia[(a)]	0.62	0.94	Miklavčič et al. (2011b)
Italy	0.18	0.28	Valent et al. (2011)
Italy[(a)]	0.16	0.23	Miklavčič et al. (in press) and Miklavčič, personal communication, 2012
Croatia[(a)]	0.17	0.25	
Greece[(a)]	0.09	0.14	

b.w.: body weight; Hg: mercury.
(a): methylmercury was only analysed in human milk from mothers with total mercury concentrations in hair above 1 mg/kg.

This exposure assessment was based on a low number of studies reporting concentrations of methylmercury in human milk. The contribution of methylmercury to total mercury in human milk shows high variation. A study reporting only total mercury in human milk has shown higher concentrations than the studies that also provided speciation analyses (Table 9). Therefore, the possibility of higher dietary exposures to methylmercury from human milk in Europe cannot be excluded.

Total dietary intake for infants

Only two dietary surveys reported consumption data for infants, therefore the dietary exposure calculation should not be considered as representative of the European infant population. Moreover, only 16 participants were included in one of these surveys. Therefore, these data were not included in Table 11. Taking into account these limitations, the mean methylmercury dietary exposure was for the MB 0.02 and 0.08 µg/kg b.w. per week.

6.2.2. Children and adolescents (≥ 1 to < 18 years old)

There were nine surveys available reporting food consumption for toddlers, covering a total of 1 597 survey participants (Appendix D, Table D1). The MB methylmercury dietary exposure varied for the mean between 0.09 and 1.57 µg/kg b.w. per week with a median of 0.27 µg/kg b.w. per week and for the 95th percentile between 0.68 and 2.72 µg/kg b.w. per week with a median of 1.59 µg/kg b.w. per week (Table 11).

There were 17 surveys available reporting food consumption for other children covering a total of 8 468 survey participants (Appendix D, Table D2). The MB methylmercury dietary exposure varied for the mean between 0.14 and 1.49 µg/kg b.w. per week, with a median of 0.32 µg/kg b.w. per week, and for the 95th percentile between 0.75 and 4.96 µg/kg b.w. per week, with a median of 1.60 µg/kg b.w. per week (Table 11).

There were 12 surveys available reporting food consumption for adolescents, covering a total of 6 329 survey participants (Appendix D, Table D3). The MB methylmercury dietary exposure varied for the mean between 0.08 and 1.09 µg/kg b.w. per week, with a median of 0.31 µg/kg b.w. per week, and for the 95th percentile between 0.42 and 5.05 µg/kg b.w. per week, with a median of 1.38 µg/kg b.w. per week (Table 11).

Of the reported age groups, other children and adolescents were those with the highest median of mean methylmercury dietary exposure (0.32 and 0.31 µg/kg b.w. per week for MB, respectively). toddlers and other children were those with the highest median of 95th percentile dietary exposure (1.59 and 1.60 µg/kg b.w. per week for MB, respectively). This outcome may be influenced by the higher consumption of fish relative to body weight. This was observed in most surveys included in the Comprehensive Database when children and adolescents versus adults were compared.

6.2.3. Adults (≥ 18 to < 65 years old)

There were 15 surveys available reporting food consumption for adults covering a total of 30 788 survey participants (Appendix D, Table D4). The MB methylmercury dietary exposure varied for the mean between 0.07 and 1.08 µg/kg b.w. per week, with a median of 0.24 µg/kg b.w. per week, and the MB 95th percentile ranged between 0.51 and 3.04 µg/kg b.w. per week, with a median of 1.13 µg/kg b.w. per week (Table 11).

6.2.4. Elderly (≥ 65 to < 75 years old) and very elderly (≥ 75 years old)

There were seven surveys available reporting food consumption for the elderly covering a total of 4 056 survey participants (Appendix D, Table D5). The MB methylmercury dietary exposure varied for the mean between 0.06 and 0.63 µg/kg b.w. per week, with a median of 0.26 µg/kg b.w. per week, and the MB 95th percentile ranged between 0.34 and 2.49 µg/kg b.w. per week, with a median of 1.24 µg/kg b.w. per week (Table 11).

There were six surveys available reporting food consumption for the very elderly covering a total of 1 614 survey participants (Appendix D, Table D6). The MB methylmercury dietary exposure varied for the mean between 0.06 and 0.38 µg/kg b.w. per week, with a median of 0.25 µg/kg b.w. per week, and the MB 95th percentile ranged between 0.14 and 1.42 µg/kg b.w. per week, with a median of 1.17 µg/kg b.w. per week (Table 11).

The highest dietary exposure was seen in surveys carried out in Mediterranean countries (Italy, Spain and France). The higher exposure seems to be more related to type of fish consumed rather than amounts consumed. In fact, the consumption of bass and mullet, which contain a considerable amount of methylmercury, is reported in Italy, France, Spain and Greece and not in northern Europe, where the more preferred fish species are cod, herring and salmon. Moreover, consumption of other fish species with typically high methylmercury concentrations reported by southern European countries only are swordfish (Italy, Spain and Greece) and shark (Italy, France and Spain), but this could be survey related (Welch et al., 2002).

6.2.5. Contributions of different food groups to methylmercury exposure

The contribution to methylmercury dietary exposure for each of the six subcategories at FoodEx Level 2 in the food category 'Fish and other seafood' was assessed separately for each survey and age group with a summary presented in Table 13. Dietary exposure was calculated based on MB mean methylmercury concentration combined with individual consumption in the total population and presented as the range of mean contribution as calculated for different surveys.

Table 13: Contribution (%) of 'Fish and other seafood' at FoodEx Level 2 to chronic dietary exposure of methylmercury using middle bound concentrations. Range of the mean contribution for each age class and food category is shown.

Food category	Lowest mean contribution – highest mean contribution (%)					
	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Fish meat	59-100	69-100	74-97	81-100	92-100	90-100
Fish products	0-40	0-29	0-22	0-13	0-2.2	0-1.5
Molluscs	0-5.3	0-8.2	0-9.7	0-7.2	0-6.3	0-6.9
Crustaceans	0-5.1	0-3.2	0-12	0.0-6.4	0-3.5	0-2.8
Fish offal	0	0-1.9	0-0.9	0-1.0	0-0.6	0-0.7
Amphibians, reptiles, snails, insects	0	0-0.1	0-0.1	0-0.1	0-0.1	0-0.1

Fish meat is the dominating contributor to methylmercury dietary exposure for all age classes followed by fish products, the latter particularly in the younger but not the older age groups. Fish offal as well as amphibians, reptiles, snails and insects each contribute to less than 1 % of methylmercury exposure except in the other children age group with slightly higher fish offal consumption.

'Fish meat' was further split into individual fish species at FoodEx Level 3. The results are reported as a number of surveys for the following contribution ranges: 0 - 5 %, 5 - 10 %, 10 - 25 %, 25 - 50 %, 50 - 75 %, 75 - 90 %, higher than 90 % (Table 14). The number of surveys reported for the same contribution ranges at FoodEx Level 2 is shown in Appendix D, Table D7.

Contributions of individual fish species to methylmercury dietary exposure varied considerably between the surveys and age groups, reflecting different food consumption habits across European countries. In particular tuna, swordfish, cod and whiting and pike were major contributors to methylmercury dietary exposure in the adult age groups, while the same species and hake were the most important contributors in the child age groups. Unfortunately, in some surveys a large part of the fish consumption was not broken down into individual fish species and thus the 'Fish meat, unspecified' category has a high mean contribution.

Table 14: Number of surveys split according to their percentage contribution to chronic dietary exposure of methylmercury using middle bound concentrations across age groups and fish species at FoodEx Level 3.

	Toddlers							Other children							Adolescents						
	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %
Fish meat (unspecified)	3	-	2	4	-	-	-	4	-	3	6	3	-	1	4	-	2	5	-	1	-
Tuna	5	3	1	-	-	-	-	4	4	8	-	1	-	-	2	1	4	3	2	-	-
Swordfish	9	-	-	-	-	-	-	15	-	1	1	-	-	-	10	-	1	1	-	-	-
Cod and whiting	5	1	1	2	-	-	-	9	2	4	2	-	-	-	4	6	2	-	-	-	-
Pike	7	-	1	1	-	-	-	14	-	3	-	-	-	-	11	-	1	-	-	-	-
Hake	7	-	1	1	-	-	-	14	-	-	3	-	-	-	9	-	1	2	-	-	-
Carp	9	-	-	-	-	-	-	16	-	1	-	-	-	-	12	-	-	-	-	-	-
Salmon and trout	5	2	2	-	-	-	-	11	5	1	-	-	-	-	11	1	-	-	-	-	-
Plaice	9	-	-	-	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Perch	8	-	1	-	-	-	-	14	3	-	-	-	-	-	12	-	-	-	-	-	-
Bream	9	-	-	-	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Herring	9	-	-	-	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Bass	8	1	-	-	-	-	-	15	2	-	-	-	-	-	11	1	-	-	-	-	-
Fish meat, marine, high	9	-	-	-	-	-	-	16	-	-	1	-	-	-	12	-	-	-	-	-	-
Angler fish	8	-	-	1	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Mackerel	8	-	1	-	-	-	-	15	1	1	-	-	-	-	11	1	-	-	-	-	-
Sole	7	-	-	2	-	-	-	16	1	-	-	-	-	-	11	1	-	-	-	-	-
Anchovy	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Whitefish	8	-	1	-	-	-	-	16	-	-	1	-	-	-	12	-	-	-	-	-	-
Sardine and pilchard	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Eel	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Ray	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Halibut	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Fish meat, freshwater	9	-	-	-	-	-	-	15	1	1	-	-	-	-	12	-	-	-	-	-	-
Fish meat, marine, low	9	-	-	-	-	-	-	16	1	-	-	-	-	-	12	-	-	-	-	-	-
Sea catfish, wolf-fish	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Grey mullet	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Shark	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Sprat	9	-	-	-	-	-	-	17	-	-	-	-	-	-	12	-	-	-	-	-	-
Redfish	6	1	2	-	-	-	-	14	-	3	-	-	-	-	12	-	-	-	-	-	-

Table 14: Continued.

	Adults							Elderly							Very elderly						
	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	75-90 %	>90 %
Fish meat (unspecified)	3	2	4	3	1	2	-	2	1	1	3	-	-	-	3	-	-	3	-	-	-
Tuna	2	1	4	7	1	-	-	2	1	3	-	1	-	-	1	-	2	3	-	-	-
Swordfish	11	2	1	1	-	-	-	4	1	1	1	-	-	-	4	2	-	-	-	-	-
Cod and whiting	5	4	5	1	-	-	-	1	-	6	-	-	-	-	-	3	2	1	-	-	-
Pike	13	1	-	1	-	-	-	6	-	-	-	1	-	-	6	-	-	-	-	-	-
Hake	13	-	2	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Carp	14	-	1	-	-	-	-	6	-	1	-	-	-	-	6	-	-	-	-	-	-
Salmon and trout	9	6	-	-	-	-	-	4	3	-	-	-	-	-	5	1	-	-	-	-	-
Plaice	14	1	-	-	-	-	-	6	-	1	-	-	-	-	5	-	1	-	-	-	-
Perch	14	1	-	-	-	-	-	5	1	1	-	-	-	-	5	1	-	-	-	-	-
Bream	14	1	-	-	-	-	-	6	1	-	-	-	-	-	5	1	-	-	-	-	-
Herring	14	1	-	-	-	-	-	5	1	1	-	-	-	-	4	1	1	-	-	-	-
Bass	14	1	-	-	-	-	-	6	1	-	-	-	-	-	6	-	-	-	-	-	-
Fish meat, marine, high	14	1	-	-	-	-	-	6	-	1	-	-	-	-	6	-	-	-	-	-	-
Angler fish	14	1	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Mackerel	14	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Sole	15	-	-	-	-	-	-	5	2	-	-	-	-	-	5	-	1	-	-	-	-
Anchovy	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Whitefish	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Sardine and pilchard	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Eel	15	-	-	-	-	-	-	6	1	-	-	-	-	-	5	1	-	-	-	-	-
Ray	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Halibut	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Fish meat, freshwater	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Fish meat, marine, low	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Sea catfish, wolf-fish	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Grey mullet	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Shark	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Sprat	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-
Redfish	15	-	-	-	-	-	-	7	-	-	-	-	-	-	6	-	-	-	-	-	-

6.2.6. Dietary exposure to methylmercury for specific groups

6.2.6.1. Women in child-bearing age

Since the prenatal period is the most sensitive stage of the life cycle for the neurodevelopmental effects of methylmercury, dietary exposure was calculated separately for women of child-bearing age. Consumption data for women aged 18 - 45 years available in 15 surveys in the Comprehensive Database were combined with methylmercury concentration levels. No appreciable differences were detected in this subpopulation compared with adults in general.

6.2.6.2. High and frequent fish consumers

There is a concern that high and frequent consumers of fish meat might have elevated levels of methylmercury dietary exposure. To test such a hypothesis, the 95th percentile dietary exposure from the daily consumption of fish meat among consumers only was retrieved from the Comprehensive Database for surveys in which the number of selected participants exceeded 60.

Results calculated for the 25 surveys that included the minimum, median and maximum of 95th percentile methylmercury dietary exposure are shown in Table 15. The dietary exposure estimations in high and frequent consumers varied from a minimum MB of 0.54 µg/kg b.w. per week in elderly to a maximum MB of 7.48 µg/kg b.w. per week in other children.

The methylmercury dietary exposure in high and frequent consumers of fish meat was higher in the child age groups than in adult population groups. This is explained by the higher food consumption of children in relation to their body weight.

The dietary exposure to methylmercury in high and frequent consumers is approximately two-fold higher than in the total population, but the increase ranged from one-fold to seven-fold. For further details see Appendix D, Table D8.

Table 15: Minimum, median and maximum of the 95th percentile dietary exposure to methylmercury among fish meat consumers only by age class (µg Hg/kg b.w. per week) (further details are shown in Appendix D, Table D8).

Age group	P95 dietary exposure in the fish meat consumers only								
	Minimum			Median			Maximum		
	LB	MB	UB	LB	MB	UB	LB	MB	UB
Toddlers	4.60	4.66	4.72	4.73	4.88	5.02	4.87	5.10	5.32
Other children	1.39	1.41	1.43	3.51	3.88	4.09	7.47	7.48	7.49
Adolescents	0.80	0.80	0.81	2.53	2.56	2.58	7.22	7.25	7.29
Adults	0.56	0.57	0.58	2.05	2.08	2.10	6.15	6.16	6.17
Elderly	0.54	0.54	0.55	2.03	2.05	2.06	4.52	4.52	4.52
Very elderly	1.07	1.10	1.12	1.63	1.64	1.65	2.29	2.31	2.33

b.w.: body weight; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound; Hg: mercury.

6.3. Exposure assessment to inorganic mercury based on data reported to EFSA

Similarly to methylmercury exposure estimation, the mean and the 95th percentile inorganic dietary exposures were calculated separately for each country and age class for all participants in the surveys (the total population) using consumption data at individual level from the Comprehensive Database. The LB and UB mean total mercury results for each food group described in Section 4.2 and Appendix A, transformed into inorganic mercury by applying the conversion factors as described in Section 6.1, were used as occurrence values and combined with consumption data for the exposure assessment.

The estimation of dietary exposure to inorganic mercury was based on minimum LB and maximum UB data due to the high proportion of LC data and the large difference between LB and UB concentrations.

Table 16 provides an overview of the results of the surveys that included the minimum, median and maximum of mean and 95th percentile dietary exposure to inorganic mercury for different age groups. The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.13 µg/kg b.w. per week in elderly to the highest maximum UB of 2.16 µg/kg b.w. per week in toddlers. The 95th percentile dietary exposure was estimated to range from 0.25 µg/kg b.w. per week in elderly and very elderly to 4.06 µg/kg b.w. per week in toddlers. The detailed results of the dietary exposure calculation are presented in Appendix D, Tables D9-D14 for the different surveys and age group.

Table 16: Summary statistics of the chronic dietary exposure to inorganic mercury (µg Hg/kg b.w. per week) by age class. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown (further details are shown in Appendix D, Tables D9-D14).

Age group	Minimum			Median			Maximum		
	LB	MB	UB	LB	MB	UB	LB	MB	UB
Mean dietary exposure in total population									
Toddlers	0.27	0.79	1.31	0.37	1.13	1.71	0.59	1.36	2.16
Other children	0.24	0.59	0.89	0.38	0.84	1.24	0.76	1.13	1.75
Adolescents	0.16	0.39	0.59	0.25	0.44	0.68	0.51	0.73	0.94
Adults	0.14	0.26	0.38	0.23	0.41	0.55	0.40	0.53	0.70
Elderly	0.13	0.23	0.33	0.22	0.35	0.48	0.30	0.42	0.55
Very elderly	0.14	0.25	0.35	0.19	0.33	0.47	0.24	0.38	0.52
P95 dietary exposure in total population									
Toddlers	0.67	1.35	2.18	0.84	1.77	2.83	1.07	2.30	4.06
Other children	0.50	1.12	1.66	0.86	1.62	2.20	1.85	2.27	3.37
Adolescents	0.31	0.71	1.00	0.62	0.88	1.26	1.70	1.85	2.33
Adults	0.36	0.53	0.72	0.59	0.78	1.02	1.52	1.66	1.83
Elderly	0.25	0.40	0.55	0.54	0.72	0.92	0.77	0.94	1.12
Very elderly	0.25	0.40	0.54	0.47	0.62	0.82	0.64	0.81	1.01

b.w.: body weight; Hg: mercury; LB: lower bound; MB: middle bound; P95: 95th percentile; UB: upper bound.

There is considerable uncertainty associated with the calculation of dietary exposure to inorganic mercury. The number of sample results reported is low for some of the FoodEx Level 1 food groups. The proportion of LC data is 60 % or more in 11 of the food groups. Finally the assumptions made in relation to the contribution of inorganic mercury to total mercury in the fish and other seafood categories are conservative. The results should be interpreted with these caveats in mind.

6.3.1. Infants (less than one year old)

Breast-fed infants

The dietary exposure of infants below six months of age to inorganic mercury was calculated as described in Section 6.2.1. For the occurrence data, inorganic mercury concentrations were calculated as the difference between total mercury and methylmercury (see Section 4.3.3.). The CONTAM Panel noted that in two of these studies, methylmercury was not analysed in milk of mothers with total mercury concentrations in hair below 1 mg/kg, but concluded that this was unlikely to have a major impact on the data.

Based on mean concentrations of inorganic mercury in human milk, the mean weekly exposure for infants with an average milk consumption ranges from 0.17 to 1.29 µg/kg b.w. per week (Table 17). For infants with a high milk consumption the dietary exposure ranges from 0.25 to 1.94 µg/kg b.w. per week.

Table 17: Exposure scenario to inorganic mercury based on average and high human milk consumption for infants below 6 months based on the mean occurrence data reported in literature (see Section 4.3.3).

Country	Dietary exposure to inorganic mercury (µg Hg/kg b.w. per week)		Reference
	Average human milk consumption	High human milk consumption	
Slovenia[(a)]	0.39	0.59	Miklavčič et al. (2011b)
Italy	0.44	0.67	Valent et al. (2011)
Italy[(a)]	0.28	0.41	Miklavčič et al. (in press); Miklavčič, personal communication (2012)
Croatia[(a)]	0.17	0.25	
Greece[(a)]	1.29	1.94	

b.w.: body weight; Hg: mercury.
(a): methylmercury was only analysed in human milk from mothers with total mercury concentrations in hair above 1 mg/kg.

This exposure assessment was based on a low number of studies reporting concentrations of methylmercury and total mercury in human milk. The concentrations of inorganic mercury were calculated as the difference between total and methylmercury. The contribution of inorganic mercury to total mercury in human milk shows a high variation. A study reporting only total mercury in human milk has shown higher concentrations of total mercury in human milk than the studies that provided speciation analyses (Table 9). Therefore, the possibility of higher dietary exposure to inorganic mercury from human milk in Europe cannot be excluded.

Total dietary intake for infants

Only two dietary surveys reported consumption data for infants, therefore the exposure calculation should not be considered as representative of the European infant population. Moreover, only 16 participants were included in one of these surveys. Therefore, these data were not included in Table 16. Taking into account these limitations, mean MB dietary exposure to inorganic mercury was estimated to be 0.74 and 0.80 µg/kg b.w. per week in these two survey populations.

6.3.2. Children and adolescents (≥ 1 to < 18 years old)

There were nine surveys available reporting food consumption for toddlers, covering a total of 1 597 survey participants (Appendix D, Table D9). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.27 µg/kg b.w. per week to the highest maximum UB of 2.16 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.67 µg/kg b.w. per week to 4.06 µg/kg b.w. per week (Table 16).

There were 17 surveys available reporting food consumption for other children covering a total of 8 468 survey participants (Appendix D, Table D10). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.24 µg/kg b.w. per week to the highest maximum UB of 1.75 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.50 µg/kg b.w. per week to 3.37 µg/kg b.w. per week (Table 16).

There were 12 surveys available reporting food consumption for adolescents covering a total of 6 329 survey participants (Appendix D, Table D11). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.16 µg/kg b.w. per week to the highest maximum UB of 0.94 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.31 µg/kg b.w. per week to 2.33 µg/kg b.w. per week (Table 16).

6.3.3. Adults (≥ 18 to < 65 years old)

There were 15 surveys available reporting food consumption for adults covering a total of 30 788 survey participants (Appendix D, Table D12). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.14 µg/kg b.w. per week to the highest maximum UB of 0.70 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.36 µg/kg b.w. per week to 1.83 µg/kg b.w. per week (Table 16).

6.3.4. Elderly (≥ 65 to < 75 years old) and very elderly (≥ 75 years old)

There were seven surveys available reporting food consumption for the elderly covering a total of 4 056 survey participants (Appendix D, Table D13). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.13 µg/kg b.w. per week to the highest maximum UB of 0.55 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.25 µg/kg b.w. per week to 1.12 µg/kg b.w. per week (Table 16).

There were six surveys available reporting food consumption for very elderly, covering a total of 1 614 survey participants (Appendix D, Table D14). The mean dietary exposure to inorganic mercury varied from the lowest minimum LB of 0.14 µg/kg b.w. per week to the highest maximum UB of 0.52 µg/kg b.w. per week. The 95th percentile dietary exposure was estimated to be from 0.25 µg/kg b.w. per week to 1.01 µg/kg b.w. per week (Table 16).

6.3.5. Contributions of different food groups to inorganic mercury exposure

The contribution to inorganic mercury dietary exposure for each of the 20 main food groups of the FoodEx classification system, FoodEx Level 1, was assessed separately for each survey and age group. Dietary exposure was calculated based on mean inorganic mercury concentration combined with individual consumption and is presented in Appendix D, Table D15 as the range of mean contributions as calculated for the different surveys. An overview of the results reported as the number of surveys for the contribution ranges: 0 - 5 %, 5 - 10 %, 10 - 25 %, 25 - 50 % and 50 - 75 % is presented in Table 18.

The main contributors to inorganic mercury dietary exposure varied between age groups reflecting different consumption patterns at different ages. The food group 'Fish and other seafood' contributed more than 25 % of inorganic mercury dietary exposure in 15 surveys. In nine surveys, mainly covering other children, 'Composite food', and in eight surveys, mainly covering adults, 'Non-alcoholic beverages' contributed more than 25 %. Dietary exposure seemed to be driven by high mercury concentration for 'Fish and other seafood' and 'Composite food' that might include fish as an ingredient, while it seemed to be consumption driven for 'Non-alcoholic beverages'. In the case of 'Composite food', a high percentage of LC data in some food categories also influenced the dietary exposure estimation outcome.

Other food groups that were important for inorganic mercury dietary exposure included 'Vegetable and vegetable products', 'Fruit and vegetable juices', 'Grains and grain products' and 'Milk and dairy products', 'Meat and meat products' in all cases driven by a high percentage of LC data (≥ 60 % of LC data within the main food group or within the food categories at lower FoodEx levels).

Table 18: Number of surveys split according to their percentage contribution to chronic dietary exposure of inorganic mercury using middle bound concentrations across age groups for the main food groups at FoodEx Level 1.

	Toddlers					Other children					Adolescents				
	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %
Fish and other seafood	4	2	1	2	-	2	8	4	3	-	2	1	5	4	-
Non-alcoholic beverages	7	2	-	-	-	7	9	1	-	-	5	3	4	-	-
Composite food	5	3	1	-	-	7	3	3	4	-	5	4	-	3	-
Vegetables and vegetable products	3	4	2	-	-	7	8	2	-	-	7	4	1	-	-
Fruit and vegetable juices	-	1	7	1	-	1	4	9	3	-	1	6	4	1	-
Grains and grain-based products	-	4	5	-	-	-	3	14	-	-	-	3	9	-	-
Milk and dairy products	-	-	7	2	-	-	2	15	-	-	-	5	7	-	-
Meat and meat products	6	3	-	-	-	10	7	-	-	-	5	5	2	-	-
Starchy roots and tubers	8	1	-	-	-	17	-	-	-	-	12	-	-	-	-
Alcoholic beverages	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Fruit and fruit products	5	4	-	-	-	12	5	-	-	-	11	1	-	-	-
Drinking water	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Products for special nutritional use	9	-	-	-	-	17	-	-	-	-	11	1	-	-	-
Animal and vegetable fats and oils	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Legumes, nuts and oilseeds	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Herbs, spices and condiments	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Sugar and confectionery	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Eggs and egg products	9	-	-	-	-	17	-	-	-	-	12	-	-	-	-
Snacks, desserts, and other foods	8	1	-	-	-	16	1	-	-	-	12	-	-	-	-
Food for infants and small children	4	2	3	-	-	17	-	-	-	-	12	-	-	-	-

Table 18: Continued.

	Adults					Elderly					Very elderly				
	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %	0-5 %	5-10 %	10-25 %	25-50 %	50-75 %
Fish and other seafood	1	4	7	2	1	-	1	4	2	-	1	-	4	1	-
Non-alcoholic beverages	4	-	7	4	-	1	-	5	1	-	-	2	1	3	-
Composite food	9	4	-	2	-	6	1	-	-	-	4	2	-	-	-
Vegetables and vegetable products	5	8	1	1	-	1	4	2	-	-	2	2	2	-	-
Fruit and vegetable juices	6	4	5	-	-	3	3	1	-	-	4	2	-	-	-
Grains and grain-based products	-	9	6	-	-	-	1	6	-	-	-	2	4	-	-
Milk and dairy products	1	11	3	-	-	-	4	3	-	-	-	5	1	-	-
Meat and meat products	3	10	2	-	-	2	4	1	-	-	1	4	1	-	-
Starchy roots and tubers	14	1	-	-	-	7	-	-	-	-	4	2	-	-	-
Alcoholic beverages	14	1	-	-	-	7	-	-	-	-	6	-	-	-	-
Fruit and fruit products	14	1	-	-	-	1	6	-	-	-	-	6	-	-	-
Drinking water	14	1	-	-	-	7	-	-	-	-	6	-	-	-	-
Products for special nutritional use	15	-	-	-	-	7	-	-	-	-	5	1	-	-	-
Animal and vegetable fats and oils	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Legumes, nuts and oilseeds	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Herbs, spices and condiments	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Sugar and confectionery	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Eggs and egg products	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Snacks, desserts, and other foods	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-
Food for infants and small children	15	-	-	-	-	7	-	-	-	-	6	-	-	-	-

The major contributors, defined as the food groups contributing to 5 % or more of inorganic mercury exposure at FoodEx Level 2, reported for individual age groups are listed in Table 19. The number of surveys and the highest recorded contribution (%) is reported.

Table 19: Major contributors to mean middle bound chronic dietary inorganic mercury exposure for the food groups at FoodEx Level 2 contributing to 5 % or more of total exposure. Number of surveys and the highest mean contribution are shown.

Food category	Toddlers		Other children		Adolescents		Adults		Elderly		Very elderly	
	N	%	N	%	N	%	N	%	N	%	N	%
Non alcoholic beverages												
Tea (infusion)[35]	2	6	3	19	3	19	11	40	6	28	6	30
Soft drinks	-	-	5	7	4	10	2	7	-	-	-	-
Fish and other seafood												
Fish meat	6	26	15	28	10	34	14	39	7	27	5	23
Molluscs	-	-	1	7	3	8	3	7	1	6	-	-
Crustaceans	-	-	-	-	1	10	2	7	-	-	-	-
Composite food												
Cereal-based dishes	-	-	5	20	3	25	2	11	-	-	-	-
Prepared salads	-	-	2	17	2	18	1	22	-	-	-	-
Ready to eat soups	-	-	3	9	1	9	2	11	1	7	1	8
Fish and seafood based meals	-	-	1	10	-	-	-	-	-	-	-	-
Meat-based meals	-	-	4	7	1	7	1	7	-	-	-	-
Mushroom-based meals	-	-	-	-	-	-	1	6	-	-	-	-
Vegetables and vegetable products												
Fungi, wild, edible	-	-	1	15	1	11	1	15	2	10	1	9
Fungi, cultivated	1	11	-	-	1	6	1	6	1	7	1	5
Vegetable products	1	5	1	5	-	-	-	-	-	-	-	-
Fruit and vegetable juices												
Fruit juice	8	16	15	20	9	20	4	13	3	9	2	8
Concentrated fruit juice	1	15	3	15	2	16	2	7	-	-	-	-
Mixed fruit juice	3	7	4	21	1	11	1	6	-	-	-	-
Fruit nectar	-	-	-	-	-	-	1	6	-	-	-	-
Grains and grain based products												
Bread and rolls	6	7	10	9	9	8	9	10	6	10	6	10
Pasta (raw)	1	5	-	-	-	-	-	-	-	-	-	-
Grain milling products	1	5	-	-	-	-	1	5	1	5	-	-
Breakfast cereals	-	-	1	5	-	-	-	-	-	-	-	-
Fine bakery wares	-	-	1	5	2	5	-	-	-	-	-	-
Milk and dairy products												
Fermented milk products	7	17	13	13	2	6	2	6	1	6	-	-
Liquid milk	8	15	12	11	6	8	2	5	2	5	1	5
Milk and dairy products	1	7	-	-	-	-	-	-	-	-	-	-
Milk and milk products imitates	1	6	-	-	-	-	-	-	-	-	-	-
Concentrated milk	-	-	1	5	-	-	-	-	-	-	-	-

N: number of surveys; %: highest mean contribution.

'Tea (infusion)' and 'Soft drinks' contributed to inorganic mercury dietary exposure in the food group 'Non-alcoholic beverages' at levels of up to 40 % and 10 %, respectively, mainly driven by high consumption amounts of black tea in particular in the first case.

[35] Includes black tea and others prepared as for consumption

The food category 'Fish meat' was also an important contributor (up to 39 % in adults) to inorganic mercury dietary exposure in all age groups at FoodEx Level 2, mainly through consumption of 'Fish meat, unspecified' (up to 18 %), 'Tuna' (up to 15 %), 'Swordfish' (up to 13 %) and 'Cod and whiting' (up to 11 %) at FoodEx Level 3 (data not shown).

The dietary exposure to inorganic mercury from the 'Composite food' category was mainly due to high occurrence levels in 'Cereal–based dishes' and in 'Prepared salads', with contributions of up to 25 % and 22 %, respectively, but was true for only a few surveys. Within the food group 'Cereal-based dishes' the major contributors were 'Pasta cooked' (up to 18 %) and 'Pizza and pizza-like pies' (up to 8 %) at FoodEx Level 3. Within the food group 'Prepared salads' the major contributor was 'Prepared mixed vegetable salads' (up to 14 %) in FoodEx Level 3 (data not shown).

Other important individual food categories at FoodEx Level 3 contributing to inorganic mercury dietary exposure in one or more age groups include mixed fruit juice (up to 21 %), cow's milk yoghurt (up to 16 %), boletus and unspecified concentrated fruit juice (each up to 15 %), apple juice and cow milk (each up to 14 %), orange juice and orange juice concentrate (each up to 13 %), unspecified fermented milk products (up to 9 %), multi-fruit juice and wheat bread and rolls (each up to 8 %) and mixed wheat and rye bread and rolls (up to 6 %).

The contribution to inorganic mercury dietary exposure from rice was considered negligible at a maximum of 2 %.

6.3.6. Dietary exposure to inorganic mercury for specific groups

6.3.6.1. Dietary supplements consumers

There is a concern that the consumers of dietary supplements might have elevated levels of inorganic mercury dietary exposure. Particularly, traditional herbal preparations used in Asian traditional medicine usually purchased at the European market, may contain significant amounts of mercury (Martena et al., 2010). Since the consumption of dietary supplements in total population is rare, for this opinion the exposure assessment to inorganic mercury from dietary supplements was carried out separately for consumers only. Two groups of dietary supplements with significantly different inorganic mercury concentration levels were identified: (i) a group with high levels (LB mean = 504 µg/kg, UB mean = 513 µg/kg), including unspecified dietary supplements and plant extract formula, and (ii) a group of other dietary supplements with lower levels (LB mean = 5.58 µg/kg, UB mean = 11.7 µg/kg). The exposure to inorganic mercury from dietary supplements was calculated separately with respect to these two groups for every individual using his/her own consumption data.

Results calculated for the eight European surveys included with the minimum, median and maximum of the mean and the 95th percentile inorganic mercury dietary exposure are shown in Table 20. The mean dietary exposure estimations in dietary supplements consumers varied from a minimum LB of 0.00 µg/kg b.w. per week seen almost in all age groups to a maximum UB of 0.19 µg/kg b.w. per week in very elderly. The 95th percentile dietary exposure estimations in dietary supplements consumers varied from a minimum LB of 0.00 µg/kg b.w. per week to a maximum UB of 0.24 µg/kg b.w. per week in adults, but this results could not be obtained for all age groups due to a low number of participants.

The inorganic mercury dietary exposure in consumers of dietary supplements seems to be highest in very elderly. However, only one survey for this age group was available and therefore this outcome needs to take into account a considerable limitation when interpreted.

Table 20: Summary statistics of the chronic dietary exposure to inorganic mercury (µg Hg/kg b.w. per week) from dietary supplements in consumers only by age class. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown.

	N	Minimum			Median			Maximum		
		LB	MB	UB	LB	MB	UB	LB	MB	UB
	Mean dietary exposure in the dietary supplements consumers only									
Infants[a]	4	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Toddlers	446	0.00	0.00	0.00	0.01	0.01	0.01	0.02	0.03	0.04
Other children	742	0.00	0.00	0.00	0.01	0.02	0.02	0.06	0.06	0.07
Adolescents	182	0.00	0.00	0.01	0.00	0.01	0.01	0.01	0.01	0.01
Adults	1 426	0.00	0.00	0.00	0.03	0.03	0.04	0.06	0.06	0.06
Elderly	227	0.00	0.00	0.00	0.02	0.02	0.02	0.03	0.03	0.03
Very elderly[a]	17	0.18	0.18	0.19	0.18	0.18	0.19	0.18	0.18	0.19
	P95 dietary exposure in the dietary supplements consumers only									
Infants[a]	4	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]
Toddlers	446	0.00	0.00	0.00	0.02	0.02	0.03	0.02	0.03	0.05
Other children	742	0.00	0.00	0.00	0.01	0.02	0.02	0.09	0.09	0.09
Adolescents	182	0.00	0.00	0.01	0.00	0.01	0.01	0.01	0.01	0.01
Adults	1 426	0.01	0.01	0.01	0.10	0.11	0.11	0.23	0.24	0.24
Elderly	227	0.01	0.01	0.02	0.07	0.07	0.07	0.13	0.13	0.13
Very elderly[a]	17	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]

b.w. body weight; Hg: mercury; LB: lower bound; MB: middle bound; N: number of participants; P95: 95th percentile; UB: upper bound.
(a): Minimum, median and maximum calculation not possible since only one survey was available.
(b): Calculation of P95 not possible due to a low number of participants.

6.4. Previously reported human exposure assessments

Recently reported exposure assessments were summarised by Arnich et al. (2012). The data in Table 21 are based on Arnich et al. (2012), updated with more recent data, and exposure is expressed on a weekly basis in order to allow comparison.

Table 21: Summary of dietary exposure assessments to mercury in various countries.

Country	Mean adult exposure µg/kg b.w. per week	Mean children's exposure[a] µg/kg b.w. per week	Reference
Total mercury			
Australia	0.07-0.63 [b]	0.07-1.4 [b]	FSANZ (2003)
Australia	0.21-0.35 [b]	0.42-0.56 [b]	FSANZ (2011)
Chile	0.49 [b]		Muñoz et al. (2005)
China	0.63 [b]		Sun et al., 2011
France	0.16-1.39 [b]	0.26-1.94 [b]	Arnich et al. (2012)
Korea	0.21* [b]		Lee et al. (2006)
Lebanon	0.28 [b]		Nasreddine et al., (2006)
Norway	0.35		Jenssen et al., (2012)
Spain	2.1** [b] in men		Falcó et al. (2005)
	1.96** [b] in women		Rubio et al. (2008)
	0.63* [b]		Domingo et al. (2012)
	4.69* [b]		
UK	0.14-0.55 [b]	0.21-0.56 [b]	Rose et al. (2010)
USA	0.28-0.56 [b]		Dougherty et al. (2000)

Table 21: Continued.

Country	Mean adult exposure µg/kg b.w. per week	Mean children's exposure[(a)] µg/kg b.w. per week	Reference
Methylmercury			
Australia	0.43	0.43	FSANZ (2011)
France	0.12-0.13	0.15	Arnich et al. (2012)
Japan	0.71* in pregnant women		Yaginuma-Sakurai et al. (2009)
Spain	0.88 in pregnant women 0.98 in women of child-bearing age		Ortega-Garcia et al. (2009)
Sweden	0.42 in women in child-bearing age [(b)]		Ström et al. (2011)
Germany	0.13*		Kuballa et al. (2011)

b.w.: body weight
(a): children generally from 3 to < 10 years,
(b): reported by the authors as µg/kg b.w. per day.
* Assuming a 60 kg b.w.
** Assuming a 60 kg b.w. for women and 70 kg b.w. for men.

Most previously reported dietary exposure estimates are for total mercury, and results from France, UK, USA and Australia were all in broad agreement with each other on a LB and MB basis. The French population's mean dietary exposure to total mercury was estimated at 0.16 µg/kg b.w. per week in adults for the LB and 1.39 µg/kg b.w. per week for the UB assumption and mean dietary exposure for children was estimated at 0.26 (LB) and 1.94 (UB) µg/kg b.w. per week (Arnich et al 2012). The last UK TDS reported a mean total mercury intake between 0.14 and 0.35 µg/kg b.w. per week for adults and 0.21 and 0.56 µg/kg b.w. per week for children (LB and UB, Rose et al., 2010). Dougherty et al. (2000), reported a mean US dietary exposure of between 0.28 and 0.56 µg/kg b.w. per week (LB and UB). In Australia, mean dietary exposure ranged from 0.07 to 0.63 µg/kg b.w. per day for adults and from 0.07 to 1.4 µg/kg b.w. per week for children in 2003 (FSANZ, 2003) and in 2011 from 0.21 to 0.35 µg/kg b.w. per week for adults and from 0.42 to 0.56 µg/kg b.w. per week for children (FSANZ, 2011). Mean adult intake estimates are also available for Chile (0.49 µg/kg b.w. per week, Muñoz et al., 2005), China (0.63 µg/kg b.w. per week, Sun et al., 2011), Lebanon (0.28 µg/kg b.w. per week, Nasreddine et al., 2006) and Norway (0.35 µg/kg b.w. per week; Jenssen et al., 2012). In Korea, Lee et al. (2006) estimated the mean adult intake at 11.3 µg per day (ca. 0.21 µg/kg b.w. per week assuming a 60 kg default body weight). The highest levels have been reported by Domingo et al. (2012) in Spanish adults, with a mean at 282.8 µg per week (ca. 4.69 µg/kg b.w. per week). In a previous study from Spain (Falcó et al., 2005), mean adult exposure was estimated at 151.9 and 116.9 µg per week for men and women, respectively (ca. 2.10 and 1.96 µg/kg b.w. per week assuming a 70 kg default b.w. for men and 60 kg for women). The authors noted that fish and cereals were the major contributors to total mercury intake in their study. The mean mercury concentration was 97 µg/kg in fish and seafood and 30 µg/kg in cereals. Lower levels have also been reported by Rubio et al. (2008) for Canary Islands (Spain) with a mean estimated total mercury intake at 39.9 µg per week. However, these lower levels can be explained by the differences in assumptions regarding levels below the LOD. Rubio et al. (2008) used a LB assumption where measurements were below the LOD whereas Falcó et al. (2005) and Domingo et al. (2012) used a MB approach, i.e. non-detected values were assumed to be LOD/2.

For methylmercury dietary exposure calculations, it has been assumed that 100 % of mercury in fish and other seafood products is present as methylmercury. The French population's mean dietary exposure to methylmercury through the consumption of fish and seafood products was estimated to be 0.12 µg/kg b.w. per week for adults and 0.15 µg/kg b.w. per week for children (Arnich et al., 2012). In Australia, results from a TDS reported a mean dietary exposure of 0.43 µg/kg b.w. per week both for adults and children aged between 6 and 12 years (FSANZ, 2011). A mean dietary exposure level for

women in Spain is reported at 0.98 µg/kg b.w. per week for women of child-bearing age and 0.88 µg/kg b.w. per week for pregnant women (Ortega-Garcia et al., 2009), a mean and 95th percentile methylmercury exposure for women in child-bearing age in Sweden is reported at 0.42 and 1.05 µg/kg b.w. per week respectively (Ström et al., 2011) and a mean value of 0.70 µg/kg b.w. per week is reported for pregnant Japanese women (Yaginuma-Sakurai et al., 2009). In Germany, methylmercury exposure from fish and other seafood was estimated for adults and showed a mean exposure of 8 µg per week, which corresponds to 0.13 µg/kg b.w per week for a 60 kg adult (Kuballa et al., 2011).

The French population mean dietary exposure to inorganic mercury through the consumption of foods other than seafood products was estimated at 0.04 µg/kg b.w. per week in adults (LB) and 1.26 µg/kg b.w. per week (UB). For children, mean dietary exposure was estimated to be 0.10 µg/kg b.w. per week (LB) and 1.82 µg/kg b.w. per week (UB) (Arnich et al., 2012). It was assumed in this study that 100 % of mercury in foods other than seafood products is present as inorganic mercury. The Australian TDS estimated mean exposure for adults to be between 0.21 and 0.35 µg/kg b.w. per week for adults and between 0.42 and 0.56 µg/kg b.w. per week for children.

Comparison between previously reported data and estimates of dietary exposure made in this opinion

Several factors make a direct comparison between data reported in the literature and that presented in this opinion difficult. This is mostly because it is not always clear which method is used for dietary exposure calculations, it is not always clear in which way the data was handled (e.g. treatment of LC data) and different categories are used for age groups. There are also different approaches used to estimate total mercury and methylmercury. The approach used by EFSA for exposure assessments is conservative and may result in some higher values. A qualitative inspection of the data above supports the detailed exposure assessment presented in Section 6.2.

6.5. Non-dietary exposure

In addition to food, inorganic mercury exposure occurs through medicinal products and the use of alternative medicine and some religious practices (summarised in FAO/WHO, 2011b). Although medicinal uses of mercurous and mercuric species have virtually disappeared in industrial countries, and inorganic mercury is banned as an active ingredient in cosmetics in the EU, it is still used in skin-lightening creams predominantly in less developed countries (Chan, 2011). A recent population-based inorganic mercury biomonitoring in New York identified skin care products as a possible source of high exposure even in industrial countries (McKelvey et al., 2011).

Exposure to elemental mercury (with a special focus on children) has recently been summarised by the Agency for Toxic Substances and Disease Registry (ATSDR) and includes breakage of mercury-containing instruments (e.g. thermometers) and fluorescent light bulbs, off-gassing from flooring materials containing a mercury catalyst and outgassing of mercury vapour from dental amalgams (ATSDR, 2009). Mercury vapour is readily taken up by the lungs, with up to 80 % of the inhaled elemental mercury being retained in human tissues (ATSDR, 1999) and rapidly being oxidised to mercuric mercury. Assessment of exposure from dental amalgam amounts to 0.2 to 0.4 µg/day per amalgam-filled tooth surface or 0.5 to 1 µg/day per amalgam filled tooth (e.g. Health Canada 1995; Richardson et al., 2011); each amalgam-filled surface results in an increase of mercury in urine of 0.1 µg Hg/L or 0.06 to 0.07 µg Hg/g creatinine (summarised in Richardson et al., 2011). Based on an estimated daily absorption of total mercury from diet, water and air of 2.6 µg (WHO 1990, 1991), and the estimated daily absorption of elemental mercury from dental amalgam of 3 – 17 µg (WHO 1990, 1991), in case of individuals with a large number of amalgam fillings, amalgam fillings may account for 87 % (17 µg out of 19) of the absorbed total mercury. In individuals with only a few amalgam fillings, this source may account for about 50 % (3 µg out of 5.6 µg) of the absorbed total mercury (summarised in ATSDR, 1999). It is known that in the human body elemental mercury is oxidised to mercuric mercury. However to date no reliable factor exists for the extent to which elemental mercury contributes to the internal mercuric mercury exposure.

In general, mercury vapour in the ambient atmosphere is low and thus human exposure is negligible; typical outdoor-air mercury concentrations are within the 1 - 4 ng/m^3 range (e.g., Pacyna et al., 2009; Watras et al., 2009; Cairns et al., 2011). However, elemental mercury still has many industrial applications, including for example, the manufacturing of fluorescent lamps and the production of caustic soda and chlorine, which might result in the escape of mercury vapour in the working atmosphere (Berlin et al., 2007). Owing to breakage of mercury-containing thermometers or compact fluorescent light lamps indoor mercury concentrations in the high ng to µg/m³ range can transiently occur (e.g. Smart 1986; Fromme et al., 2011; Salthammer et al., 2012). After breakage of a fluorescent lamp, rapid reduction in mercury concentration in air can be obtained by ventilation (Salthammer et al., 2012). Several institutions, including the WHO, the Californian OEHHA, the US-EPA and the German Federal Ministry for Environment, Nature Conservation and Nuclear Safety (Umweltbundesamt, UBA), have published inhalation-based guideline values for indoor and ambient air not related to the workplace[36,37] (Link, 1999; WHO, 2000, 2003).

Thiomersal is used as a preservative in multidose vials of some vaccines (thiomersal concentrations between 0.001 – 0.01 % (US-FDA, 2009)) as well as in several cosmetic products and cleaning solutions for contact lenses (Aschner et al., 2010). A vaccine containing 0.01 % Thiomersal contains 50 µg thiomersal per 0.5 mL dose, which equates to approximately 25 µg mercury per dose.

7. HAZARD IDENTIFICATION AND CHARACTERISATION

7.1. Toxicokinetics

Toxicokinetics of mercuric, mercurous and methylmercury species are discussed based on the reports of ATSDR (ATSDR 1999), EFSA (EFSA 2008a) and JECFA (FAO/WHO, 2007, 2011b), a number of reviews (Clarkson and Magos, 2006; Berlin et al., 2007; Mutter et al., 2007; Bridges and Zalups, 2010; Ceccatelli et al., 2010; Hirner and Rettenmeier, 2010; Bernhoft, 2012; Syversen and Kaur, 2012) and recent original papers.

7.1.1. Absorption

Absorption of mercuric and mercurous salts in the gastrointestinal tract is in general low, with mercuric species being more readily absorbed than mercurous species because of higher water solubility. In experimental animals absorption of mercuric mercury salts ranges from 2 – 38 %, depending upon the form and the test conditions. Old experimental human data indicate that approximately 2 % of ingested mercuric chloride is absorbed. In case of high intake, the corrosive action of mercuric chloride might disturb permeability of the gastrointestinal tract, thereby increasing the absorption rate. Absorption of mercuric salts is higher in experimental animals, including mice, rats and goats, and is strongly influenced by nutritional factors (e.g. selenium, sulphydryl-containing molecules, organic ligands such as phytate). It has been suggested that the means by which mercuric mercury is absorbed via the intestine strongly depend on the existence of ligands in the intestinal lumen to which mercuric mercury can bind and form specific mercuric species. Thus, mercuric thio S-conjugates formed within the gastrointestinal tract have been discussed to act as structural and/or functional homologues of endogenous molecules such as amino acids and peptides that are absorbed by specific enterocytic transporters along the small intestine.

Methylmercury species are much more extensively and rapidly absorbed after oral intake than inorganic mercuric and mercurous salts. Absorption rates are higher than 80 % and do not greatly vary between humans and experimental animals. Whether the acidic, high chlorine conditions in the human stomach convert methylmercury cysteine or other S-conjugates of methylmercury present in seafood to methylmercuric chloride is still to be elucidated. Similarly to elemental mercury, methylmercury most likely crosses cell membranes by passive diffusion. The methylmercury L-cysteine complex (MeHgCys) is believed to be transported via the respective amino acid transporters by mimicking L-

[36] http://www.oehha.ca.gov/air/allrels.html
[37] http://www.epa.gov/iris/subst/0370.htm#inhalrfc

methionine. Methylmercury L-cysteine and glutathione complexes might also be transported by organic anion transporters. In humans methylmercury is recycled through the enterohepatic system and nutritional factors seem to influence methylmercury reabsorption rate rather than its primary absorption (Chapman and Chan, 2000). During reabsorption methylmercury comes in contact with the intestinal microflora, which is able to convert methylmercury to mercuric mercury. Additionally, the contribution of genetic background to individual differences in methylmercury absorption has been recently discussed (Gundacker et al., 2010b).

7.1.2. Distribution

In blood mercuric mercury is divided between plasma and erythrocytes, with somewhat more mercuric mercury being present in plasma. In erythrocytes, mercuric mercury is bound to sulphydrylgroups of hemoglobin, probably to metallothionein and to glutathione; in plasma it is distributed in different plasma protein fractions. Based on limited lipophilicity, neither mercurous nor mercuric mercury readily crosses the placental or the blood-brain barrier. Mercuric mercury distribution in the body is strongly differentiated to specific organs and within the respective organs to specific cells. The highest proportion of the body burden is located in the kidney, where mercuric mercury is located in the proximal convoluted renal tubule. Mercuric mercury accumulation in the kidney has been related to induction of binding to metallothionein and the formation of mercuric glutathione conjugates. The next largest deposition occurs in the liver, with highest concentrations to be found in the periportal areas. Additionally, the mucous membranes of the intestinal tract, the epithelium of the skin, the interstitial cells of the testes as well as the choroid plexus in the brain are likely to accumulate mercuric mercury.

In contrast to mercuric mercury, in human blood methylmercury is accumulated to a large extent (> 90 %) in the erythrocytes, where it is bound to the cysteinyl residues of hemoglobin. Interestingly, the fraction of methylmercury bound to red blood cells strongly depends on the species; in humans, the erythrocytes to plasma ratio is about 20, in mice and monkeys about 10 and in rats about 300. The accumulation of methylmercury in rat erythrocytes might also result from the fact that, in comparison with human hemoglobin, rat hemoglobin exhibits almost twice as many free thiol groups. Thus, hemoglobin of rats has recently been shown to bind significantly more ethylmercury units than human hemoglobin, which is most likely the similar case for methylmercury (Janzen et al., 2011). In plasma, most methylmercury (about 99 %) is bound to albumin, which has a free sulphydryl group in a terminal cysteinyl residue. By complex ligand exchange mechanisms, methylmercury is transferred from plasma proteins to the low molecular weight thiols glutathione and cysteine.

The amphiphilic methylmercury crosses the mammary gland, is excreted in milk and thus can reach the child during breastfeeding. In human milk, a mean of 26 - 63 % of total mercury was found to be methylmercury, however the proportion can rise with increased methylmercury intake (Miklavčič et al., 2011b), see also Section 4.4. Moreover, methylmercury is able to cross the hair follicle, the placenta and the blood-brain barrier, allowing accumulation in hair, the fetus and the brain. Fetal distribution is similar to maternal distribution, although fetal methylmercury levels in erythrocytes (Sakamoto et al., 2004, 2008, 2010) and total mercury levels in brain may be higher. The exact mechanisms, by which methylmercury crosses barriers are not fully understood. Due to structural similarities to methionine, methylmercury L-cysteine has been proposed to cross membranes via specific amino acid transporters. Probably because the binding of methylmercury to the erythrocytes retards its entry into the brain, the erythrocytes to plasma ratios correlate with the blood to brain ratios. Thus rats have a much higher blood to brain ratio than humans, which has to be taken into account when using rats to study methylmercury neurotoxicity.

In humans, after absorption into the blood, equilibrium between the blood and body is reached within 30 hours to three days, with about 5 and 10 % ending up in blood and brain, respectively (Kershaw et al., 1980; Clarkson, 2002). Since methylmercury is able to penetrate all membranes and to cross barriers, its tissue distribution is generally uniform and tissue concentrations tend to be constant relative to blood levels. Transport across cell membranes into cells is believed to occur by a

methylmercury complex with cysteine or homocysteine and, exit from cells by a glutathione complex via endogenous glutathione carriers. The highest total mercury concentrations are found in the kidneys.

7.1.3. Metabolism

The metabolism of mercury species involves an oxidation/reduction cycle and the conjugation with glutathione, and seems to be similar in humans and experimental animals. From mice studies some limited evidence exists suggesting that a small amount of mercuric mercury can be reduced to elemental mercury and eliminated as elemental mercury vapour. In contrast, elemental mercury can be readily oxidised by hydrogen peroxide and catalase to mercuric mercury. There is no evidence in literature for the synthesis of methylated mercury species in human tissue. In mammals, methylmercury is partly demethylated to mercuric mercury in the presence of reactive oxygen species (e.g. the hydroxyl radical), which in liver may be formed through the involvement of nicotinamide adenine dinucleotide phosphate (NADPH) cytochrome P450 reductase (Suda and Hirayama, 1992). Besides the liver, demethylation occurs predominantly in the intestinal tract, the spleen, and to a lesser extent in phagocytic cells and slowly in the brain. Thus, mercuric mercury in the brain is generally the result of either in situ dealkylation of organic mercury species, including methylmercury and thiomersal (Rodrigues et al., 2010b), or oxidation of elemental mercury. Demethylation also can not be excluded in other tissues, including the kidney and the gallbladder.

7.1.4. Excretion

The main pathway of excretion of absorbed mercuric mercury is via the urine and, to a lesser extent, via faeces. Excretion via faeces most likely involves formation of glutathione complexes prior to secretion into bile. The half-life of absorbed mercuric mercury in the human body is approximately 40 days.

Methylmercury has a half-life of approximately 70 - 80 days in the human body, with approximately 90 % being excreted by the faecal route as mercuric mercury. The half-life strongly varies in different animal species, e.g. being only 8 and 16 days in mice and rats, respectively. Methylmercury elimination in humans mainly occurs via the biliary route after conjugation with liver glutathione S-transferases (GSTs), which produce a stable glutathione–metal conjugate which is then, eliminated mainly via feces (Ballatori and Clarkson, 1985). GSTs are highly polymorphic in humans and an association between certain GST genotypes (e.g. GSTM1∗0/GSTT1∗0) and the retention of the metal has been established (Mazzaron Barcelos et al., 2012). Methylmercury undergoes enterohepatic cycling, and is thereby partly converted by the intestinal microflora to mercuric mercury, which is less effectively absorbed in the gut and therefore excreted via faeces.

7.1.5. Biomarkers of exposure

In numerous studies fish consumption is positively correlated with total mercury in blood (e.g. Schober et al., 2003; Mahaffey et al., 2004), red blood cells (e.g. Sanzo et al., 2001) and hair, and thus these parameters have often been used as a proxy for methylmercury exposure in individuals. Total blood mercury is closely correlated with ingested methylmercury and generally reflects short-term exposure (giving an estimate of exposure over the most recent two to five months). However, in populations with frequent regular patterns of fish consumption, total blood mercury might reflect a steady-state concentration and could be an accurate measure of average intake over time (NRC, 2000; Roman et al., 2011).

Although total blood mercury is well correlated with methylmercury exposure among populations with regular fish consumption, it is generally known that total blood mercury also comprises inorganic mercury, arising from elemental mercury in dental amalgams and demethylation of methylmercury as well as from other sources of inorganic mercury exposure. Thus depending on the degree of inorganic mercury exposure, total mercury in whole blood is known to give rise to an overestimation of the methylmercury exposure. For these reasons, mercury speciation can be helpful.

Since more than 90 % of methylmercury in the blood is located in the red blood cells and inorganic mercury is more evenly distributed between red blood cells and plasma, total mercury in red blood cells and plasma is sometimes used as a biomarker for methylmercury exposure and inorganic mercury exposure respectively (in the case of low methylmercury exposure in populations with no or low fish consumption) (NRC, 2000). Total mercury in red blood cells seems to be a suitable and even more precise biomarker (compared with total blood mercury) for methylmercury exposure, but has been less commonly reported (Berglund et al., 2005; Roman et al., 2011). In the general population consuming fish, total mercury in plasma is not a reliable biomarker of inorganic mercury exposure, since total mercury in plasma has been shown to be associated with both inorganic and organic mercury (Berglund et al., 2005).

Urinary total mercury (adjusted to specific gravity or creatinine) might be a suitable biomarker of inorganic (and elemental) mercury exposure (also at very low exposure levels), as nearly all mercury in urine is inorganic. Inorganic mercury in urine has been reported not to be strongly associated with fish consumption whereas it is strongly associated with dental amalgam fillings (Berglund et al., 2005) and occupational inorganic/elemental mercury exposure (Morton et al., 2004). In case of frequent tuna consumption (1 - 7 meals per week) (Carta et al., 2003) or high fish consumption (> 4 carnivorous fish meals per week) (Passos et al., 2007) and the absence of occupational inorganic mercury exposure and dental amalgams, urinary total mercury has been related to carnivorous fish consumption. This might result from both absorption of inorganic mercury from fish and demethylation of methylmercury (Passos et al., 2007).

Total mercury in hair is believed to reflect methylmercury exposure at all exposure levels (e.g. Cernichiari et al., 1995; Lindberg et al., 2004; Berglund et al., 2005; Hsiao et al., 2011) and seems to provide the best measure of long term average methylmercury exposure. Measuring total mercury in 1-cm segments of mothers' hair can be used to assess the monthly maternal methylmercury exposure throughout pregnancy (e.g. Boischio and Cernichiari, 1998; Sakamoto et al., 2012). Methylmercury in hair is quite stable over time, indicating that demethylation within the hair is minimal (al-Shahristani and Shihab, 1974; Phelps et al., 1980; Berglund et al., 2005). However, it has to be taken into account that hair treatment as well as inter-individual variability in the toxicokinetics of mercury uptake from blood to hair shaft and hair growth rate may affect mercury hair content. A frequently cited total mercury blood to hair ratio of 1:250 was also used by JECFA (FAO/WHO, 2004). It is well known, that large inter-study and inter-individual variations exist, especially in populations with infrequent fish consumption (WHO, 1990; FAO/WHO, 2004; Berglund et al., 2005; Mergler et al., 2007) and there are some indications that the total mercury blood to hair ratio is lower (e.g. Sakamoto et al., 2007; Yaginuma-Sakurai et al., 2012); however, the Panel considered the evidence insufficient to identify a more appropriate ratio; Appendix E, Table E1 gives an overview of reported blood to hair ratios.

Similarly to hair mercury, total toenail and fingernail mercury are used as indicators of average methylmercury exposure over time, serving as a biomarker for long term methylmercury and most likely not inorganic mercury exposure (Wickre et al., 2004; Björkman et al., 2007; Ohno et al., 2007; Rees et al., 2007; Mozaffarian et al., 2011). Reported hair to toenail ratios for total mercury are in the range 2.38 - 3 (Appendix E, Table E4); reported blood to toenail ratios are summarised in Appendix E, Table E3.

Cord tissue and cord blood are extensively discussed and summarised in a previous evaluation (FAO/WHO, 2007). In summary, total mercury and methylmercury are in general higher (by a factor of 1.7 – 2.2) in cord blood than in maternal blood at parturition (e.g. Björnberg et al., 2005; Kim et al., 2011; Sakamoto et al., 2012). Total mercury in cord tissue correlates with methylmercury in cord tissue, and total mercury and methylmercury in cord tissue correlate with total mercury in cord blood. A significant relationship was reported between fish consumption during pregnancy and total mercury in cord blood (FAO/WHO, 2007). Recently, total mercury in cord blood has been shown to correlate with maternal hair total mercury; the strongest correlation was observed with maternal hair in the first

1 cm-segment from the scalp at parturition (Sakomoto et al., 2012). Appendix E, Table E2 gives an overview of reported ratios for cord blood to maternal biomarkers.

7.1.6. Toxicokinetic models for conversion between chronic dietary exposure and concentration in blood

The concentration of mercury in blood can be related to steady state dietary exposure by a one-compartment toxicokinetic model expressed by the following equation (WHO, 1990; US-EPA 2001b):

$$d = C*b*V/(A*f*b.w.)$$

where

d = dietary exposure (µg/kg b.w. per day)
C = concentration in blood (µg/L)
b = elimination constant (ln 2 / half-life in blood = 0.014 per day)
V = blood volume (L)
A = gastrointestinal absorption factor (0.95)
f = fraction of absorbed dose distributed to blood
b.w. = body weight (kg)

Slightly different values for two of the parameters in this model have been used in different risk assessments of mercury. A blood volume of 5 L (corresponding to 7.1 % of the b.w.) was used both for a 70 kg b.w. by WHO (WHO, 1990) and for a 60 kg b.w. (corresponding to 8.3 % of the b.w.) by US-EPA (US-EPA 2001b). WHO used a fraction of absorbed dose distributed to blood of 0.05, whereas EPA used 0.059. JECFA later refined the model in order to take into account pregnant women, and used a blood volume of 9 % of the b.w. (which corresponds to 6.3 L for a 70 kg pregnant woman), and a fraction of absorbed dose distributed to blood of 0.05 (FAO/WHO, 2004). A thorough discussion of the variabilities and uncertainties associated with the parameters in a similar toxicokinetic model was provided by Stern (Stern, 2005). No new information about the parameters has been indentified by the Panel, except for a longer half-life of mercury in blood reported recently from an intervention study where participants consumed mercury in fish at 3.4 µg/kg b.w. per day for 14 weeks, followed by a 15-weeks washout period (Yaginuma-Sakurai et al., 2012). However, after correcting for background exposure, the half-life was in the same range as the 50 days previously used by WHO and EPA.

Section 7.5.1 gives an overview of the values for the parameters that were used in the current risk assessment.

7.2. Toxicity of mercury in experimental animals

The toxicity of inorganic and organic mercury in experimental animals is discussed below. The toxicity of elemental mercury and thiomersal is not discussed in this opinion since mercury is not present in that form in food in toxicologically significant amounts, unless there is accidental or deliberate contamination with elemental mercury. There are considerable differences in the toxicokinetics between elemental and mercuric mercury. Elemental mercury vapour is readily taken up through the lungs and subsequently easily penetrates membranes and physiological barriers due to its lipophilicity (ATSDR, 1999). On the other hand, lifetime of elemental mercury in the body is rather short, because of the rapid oxidation of elemental mercury to mercuric mercury. Effects on the nervous system seem to be the most sensitive toxicological endpoint following elemental mercury exposure (WHO, 2008), and there is some evidence that the ultimate neurotoxic mercury species after elemental mercury vapour exposure is mercuric mercury (Warfvinge, 2000).

7.2.1. Methylmercury

In all experiments described below, the test substance was given as methylmercuric chloride.

There are extensive toxicological data on the effects of organic mercury, particularly methylmercury, in laboratory animal species. These have been reviewed elsewhere (US-EPA, 1997; ATSDR, 1999; NRC, 2000; WHO, 2000, FAO/WHO, 2004, 2007). A report of an EFSA contractor (Hassauer et al., 2012) was used as a starting point and further details of animal toxicity studies on organic mercury, published since 2002 in addition to those summarised below, can be found in that report. Since the critical toxicological information for establishing a health-based guidance value for methylmercury is derived from the human epidemiological data, the animal data are only briefly discussed here.

As summarised in the CONTAM Panel's earlier opinion (EFSA, 2008), oral exposure of laboratory animals to methylmercuric chloride at doses of > 0.5 mg /kg b.w. per day, expressed as mercury, has resulted in damage to the kidneys, stomach and large intestine, changes in blood pressure and heart rate, as well as adverse effects on sperm and male reproductive organs. In addition, several studies have reported an increase in embryonic lethality, decrease in fetal body weight and teratogenicity in rats (cleft palate, vertebral defects, histological abnormalities in the cerebellum, effects on lachrymal glands and ribs) (ATSDR, 1999).

7.2.1.1. Cardiovascular toxicity

There is evidence in experimental animals that the cardiovascular system might be adversely affected by organic mercury. Grotto et al. (2009b) reported statistically significant increases in systolic blood pressure in adult male rats given methylmercuric chloride by oral gavage for 100 days at 0.1 mg/kg b.w. per day, equivalent to 0.08 mg/kg b.w. per day expressed as mercury. Jin et al. (2012) also found that treatment of adult rats with methylmercury for 14 days by oral gavage at 3 mg/kg b.w. per day (dose said to be expressed as methylmercury) caused changes in several biomarkers that indicate it may increase the risk of cardiovascular disease; methylmercury increased urinary F2-isoprostanes, decreased circulating paraoxonase-1 activity, and increased serum oxidised low-density lipoprotein (LDL) levels and associated systemic inflammation and endothelial dysfunction.

7.2.1.2. Adult and developmental neurotoxicity

The main focus of studies on the effects of methylmercury in experimental animals has been the brain. Both adult and fetal brains are susceptible to methylmercury toxicity. In adult rodents, the major clinical effects include motor disturbances, such as ataxia, tremors and paralysis, as well as signs of sensory dysfunction, such as impaired vision. The predominant neuropathological feature is degenerative changes in the cerebellum, which is likely to be the mechanism involved in many of the motor dysfunctions (US-EPA, 1997). The developing nervous system appears to be more sensitive than that of the adult. Animal studies provide evidence of damage to the nervous system from exposure to methylmercury during development, and these effects remain/continue to develop during aging, even after the exposure stops. Considering the earlier literature (reviewed in NRC, 2000), developmental neurotoxicity has been observed in offspring of monkeys, rats, mice and guinea pigs treated at oral doses of < 1 mg/kg b.w. per day, expressed as methylmercury, during gestation, lactation and/or during the post-weaning period. In monkeys, for example, deficits in social behaviour, and in visual, auditory and somato-sensory function, have been reported. The lowest reported dose of methylmercury causing adverse effects in either rodents or primates was 0.01 mg/kg b.w. per day, expressed as methylmercury.

As with some of the earlier studies, some more recent studies on developmental neurotoxicity of low-dose exposure to methylmercury have indicated adverse effects at or below 0.5 mg/kg b.w. per day, expressed as methylmercury hydroxide, equivalent to 0.47 mg/kg b.w. per day expressed as mercury. Sensory and motor disturbances, cognitive deficits, and depression-like behaviour are among the main alterations observed in rodent offspring following prenatal/perinatal exposure, with males being the most sensitive to the developmental neurotoxic effects of methylmercury (studies reviewed in Onishchenko et al., 2012). For example, the alteration in motivation-driven behaviour (i.e. depression, as measured by inactivity in a forced swim test) has been shown in the offspring of mice exposed to a dose of 0.5 mg/kg b.w. per day, expressed as methylmercury hydroxide, equivalent to 0.47 mg/kg b.w. per day expressed as mercury in the drinking water from gestational day seven until lactational day

seven. The effect is long-lasting and is associated with epigenetic modifications of the brain-derived neurotrophic factor gene in the hippocampus (Onishchenko et al., 2008).

Bourdineaud et al. (2012) have compared the effects of feeding male mice, for one or two months from three weeks of age, a diet containing methylmercury-contaminated fish, with a diet to which methylmercury was directly added, or a control diet. The amount of mercury ingested was equivalent to 0.05 mg/kg b.w. per day, expressed as total mercury, for both treated groups. Those consuming the diet containing methylmercury-contaminated fish showed statistically significant changes in behaviour in a Y-maze (reduction in spontaneous alternations) and in an open field test (decreased grooming and increased time spent in the centre), together with increased dopamine turnover in the hippocampus after 2 months of treatment. There were no statistically significant changes in behaviour after 1 month of treatment. There were no such changes in those given diet to which methylmercury had been directly added.

Paletz et al. (2006) investigated spatial and visual (non-spatial) discrimination reversal in the offspring of rats exposed to methylmercury in the drinking water from 2 weeks before breeding until lactation day 16. The concentrations corresponded to maternal exposures of approximately 0.04 or 0.4 mg/kg b.w. per day, expressed as mercury. Increased errors in both types of discrimination reversal test were observed at both doses in the offspring when adult, aged 15-20 months, particularly in the first reversal trials. There were no effects of treatment when tested later at 24-27 months.

Two of the more recent studies have indicated adverse effects at doses of 0.01 or 0.02 mg/kg b.w. per day. They are described below.

An investigation in 2-month-old mice exposed prenatally to methylmercuric chloride in the diet on gestation days 8 - 18 reported effects on locomotor activity at 0.01 mg/kg b.w. per day, expressed as methylmercury (equivalent to 0.009 mg/kg b.w. per day expressed as mercury), as measured by statistically significantly reduced times on a rotating rod and statistically significantly reduced activity in an open field (Montgomery et al., 2008). However, only one control and one dose group were tested, the number of offspring tested ranged from 4 to 15 per sex, and statistical analyses of the test outcomes did not appear to take account of possible litter effects.

Huang et al. (2011) investigated developmental parameters, locomotor and auditory function in mice following exposure to methylmercury chloride at a dose of 0.02 mg/kg b.w. per day by oral gavage, equivalent to 0.019 mg/kg b.w. per day expressed as mercury (See also Section 7.2.2.3 for more details on this study). Only this one dose was tested. The treatment regime comprised dosing of both male and female parents for four weeks before mating, dosing of the pregnant and lactating dams, and dosing of some of the offspring for a further seven weeks from weaning on postnatal day 21. Some offspring were not exposed prenatally or preweaning but were exposed postnatally for seven weeks from weaning. Motor, behavioural and auditory tests were conducted at the end of the seven-week postweaning dosing period in 12-15 male offspring per treatment group. Statistically significant adverse effects were observed on litter size, male offspring body weight gain to 10 weeks of age, locomotor activity and auditory function. Rats seem to be less sensitive than mice with respect to locomotor activity; in studies in which methylmercuric chloride was given in the drinking water, a no-observed-adverse-effect level (NOAEL) of 0.04 mg/kg b.w. per day, expressed as methylmercury (equivalent to 0.037 mg/kg b.w. per day expressed as mercury), has been reported for effects on locomotor activity following chronic exposure of adult rats, and a NOAEL of 0.4 mg/kg b.w. per day (the highest dose tested), expressed as methylmercury (equivalent to 0.37 mg/kg b.w. per day expressed as mercury), in offspring following prenatal and pre-weaning exposure to methylmercury (Day et al., 2005).

7.2.1.3. Developmental immunotoxicity

The effects of methylmercury on developmental and immune parameters were studied in the offspring of rats given methylmercuric chloride by oral gavage at doses of 0, 0.1, 0.4, 0.7, 1.0, 1.5, or 2.0 mg/kg

b.w. per day, expressed as methylmercuric chloride (equivalent to 0, 0.08, 0.32, 0.56, 0.8, 1.2, or 1.6 mg/kg b.w. per day expressed as mercury) from gestation day 6 to lactation day ten (Tonk et al., 2010). Standard developmental and reproductive parameters were studied together with a wide range of structural and functional immune parameters, covering spleen, thymus and bone marrow development and responses in tests covering the function of the innate, humoral and cellular arms of the immune system. Immune parameters were assessed in male offspring on postnatal day (PND) 21, 42 and 70. Dose-response data were compared using the BMD approach. Methylmercury treatment caused some complete litter losses, reductions in pup growth and increased pup mortality on PND 1-21; the most sensitive developmental parameter was complete litter loss with a BMD of 0.91 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.73 mg/kg b.w. per day expressed as mercury) and a BMDL of 0.18 mg/kg b.w. per day expressed as methylmercuric chloride on a BMR of 10 % loss (equivalent to 0.14 mg/kg b.w. per day expressed as mercury). Effects were observed on a number of immune parameters at one or more of the three postnatal time points and some of these effects were observed at doses lower than those causing effects on litter loss, pup growth and pup mortality. The most sensitive immune parameter was the T-cell dependent antibody response on PND 35, as measured in the primary anti-KLH (Keyhole Limpet Hemocyanin) immunoglobulin (Ig) G response. It showed a dose-related decrease in response for which the BMD was 0.039 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.03 mg/kg b.w. per day expressed as mercury) and the BMDL was 0.010 mg/kg b.w. per day expressed as methylmercuric chloride on a BMR of 5 % (equivalent to 0.008 mg/kg b.w. per day expressed as mercury). Other immune parameters affected at low doses were some red blood cell parameters, and there were dose-dependent decreases in absolute and relative spleen weight, absolute thymus weight, and absolute number and percentage of several splenic lymphocyte subsets. Of the functional parameters, there were dose-dependent decreases in NK cell activity and lymphoproliferative response, and dose-dependent increases in the production of several cytokines. Overall, this study demonstrated that certain immune parameters in developing animals are more sensitive to the effects of methylmercury than are standard developmental parameters, with the lowest BMDL being 0.01 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day expressed as mercury). The Panel noted that the BMD is below the lowest dose tested.

7.2.1.4. Carcinogenicity

Carcinogenicity studies on methylmercury, summarised elsewhere (US-EPA, 1997; NRC, 2000; WHO, 2000, FAO/WHO, 2004, 2007), show some evidence of carcinogenicity in two strains of mice, but studies in rats are negative. In ICR and B6C3F1 mice exposed orally to methylmercuric chloride, only males were observed to have an increased incidence of renal adenomas, adenocarcinomas and carcinomas. Renal epithelial cell hyperplasia and tumours were observed only in the presence of profound nephrotoxicity, suggesting that the tumours may be a consequence of reparative changes to the damaged kidneys. No increase in tumour incidence was observed in studies conducted in rat and cat. In summary, tumours were observed at a single site, in a single animal species and sex. Therefore, they were considered to provide limited evidence of carcinogenicity (US-EPA, 1997; NRC, 2000).

7.2.1.5. Conclusions on methylmercury

Recent studies in experimental animals have indicated effects at low doses. One study has shown adverse effects on litter size and male offspring body weight gain, and changes in locomotor activity and auditory function in mice at a dose of 0.02 mg/kg b.w. per day expressed as mercury (the only dose tested). In a developmental immunotoxicity study the lowest reported BMDL for methylmercury in animal studies was 0.01 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day expressed as mercury). The Panel noted that the BMD is below the lowest dose tested.

7.2.2. Inorganic mercury

The toxicity of inorganic mercury was reviewed by JECFA at its meeting in February 2010 (FAO/WHO, 2011b) and it was concluded that the kidney is the critical target organ. The Panel has

also briefly reviewed the toxicity of inorganic mercury in an earlier opinion on 'Mercury as an undesirable substance in animal feed' (EFSA, 2008). The key information from those reviews is summarised below, updated with information from studies published since the beginning of 2010 that report adverse effects at doses around or below the previously reported lowest-observed-adverse-effect levels (LOAEL) and NOAELs for effects on the kidney. A report of an EFSA contractor (Hassauer et al., 2012) was used as a starting point and details of other animal toxicity studies on inorganic mercury, published since 2002, can be found in that report. These confirm previous findings on inorganic mercury with respect to known targets and modes of action (i.e. kidney, liver, nervous system, immune system, reproductive system, embryo-fetal development and oxidative stress). The critical new studies were evaluated by the Panel from the original publications. Studies with mercuric chloride, also known as mercury(II) chloride, are the most relevant, since studies carried out using mercuric sulphide, also known as cinnabar, have utilised high oral doses.

7.2.2.1. Acute toxicity

The kidney appears to be the critical target organ for the effects of acute ingestion of inorganic mercury compounds, although there are several animal studies in which neurotoxicity induced by inorganic mercury has been reported. Acute oral exposure of rats and mice to inorganic mercury, given as mercuric chloride, at 2 - 5 mg/kg b.w. per day, expressed as mercury, given by oral gavage five days per week over 14 days, resulted in increases in kidney weight; higher doses given using the same dosing regimen or given as single oral gavage doses induced tubular necrosis (ATSDR, 1999). Male rats show higher sensitivity than females, resulting in more severe histological changes (NTP, 1993). At higher doses of inorganic mercury, haematological and hepatic effects were observed and severe gastrointestinal damage was also seen following very high doses, especially with mercuric compounds, which are more corrosive than mercurous compounds (WHO/IPCS, 2003; FAO/WHO, 2011b).

7.2.2.2. Sub-acute and sub-chronic toxicity

The kidney is also the key target organ in repeated-dose, sub-acute and sub-chronic studies in rodents, causing damage to renal tubular epithelium and immunological glomerular disease (US-EPA, 1997; ATSDR, 1999; FAO/WHO, 2011b). Autoimmune glomerular nephritis has been induced by mercuric chloride in genetically susceptible strains of rats and mice and there is evidence that human exposure to inorganic mercury can also trigger an autoimmune response in glomeruli (NRC, 2000).

Prior to the 2011 JECFA review, reviews by other agencies had identified several studies in rodents from the available toxicology databases and used them to derive health-based guidance values, all based on manifestations of kidney damage (WHO/IPCS, 1991, 2003; US-EPA, 1995; ATSDR, 1999). These included proteinuria in the rat (Druet et al., 1978), IgG deposition in the glomeruli and renal arteries in the rat (Bernaudin et al., 1981; Andres, 1984), and changes in kidney weight and cytoplasmic vacuolation of the renal tubular epithelium in mice (NTP, 1993). The JECFA monograph describes the relevant studies in detail (FAO/WHO, 2011b).

The key studies considered by the JECFA (FAO/WHO, 2011b) for derivation of a PTWI for inorganic mercury were the 6-month rat and mouse studies conducted by the NTP (1993). Fischer 344 rats, 10 animals per sex per group, were given mercuric chloride by oral gavage, at 0, 0.312, 0.625, 1.25, 2.5 or 5 mg/kg b.w. per day, 5 days per week, for 6 months (equivalent to 0, 0.23, 0.46, 0.92, 1.9 or 3.7 mg/kg b.w. per day, expressed as mercury). B6C3F1 mice, 10 animals per sex per group, were given mercuric chloride by oral gavage at 0, 1.25, 2.5, 5, 10 or 20 mg/kg b.w. per day, 5 days per week, for 6 months (equivalent to 0, 0.92, 1.9, 3.7, 7.4 or 14.8 mg/kg b.w. per day, expressed as mercury). In the rats, body weight gains were decreased in males at the highest dose and in females at or above 0.46 mg/kg b.w. per day, expressed as mercury. Absolute and relative kidney weights were statistically significantly increased in both sexes at doses of 0.46 mg/kg b.w. per day expressed as mercury or greater, with no effect on kidney weight observed at 0.23 mg/kg b.w., expressed as mercury. Nephropathy was present in the majority of control and test rats; its severity was increased in males given doses of 0.92 mg/kg b.w. per day expressed as mercury or greater and in females at the

highest dose of 3.7 mg/kg b.w. per day, expressed as mercury. In mice, males in the highest dose group showed a decrease in body weight gain. Statistically significant increases in absolute kidney weight were observed at doses of 3.7 mg/kg b.w. per day expressed as mercury, or greater, and statistically significant increases in relative kidney weight at 7.4 and 14.8 mg/kg b.w. per day, expressed as mercury in male mice. The kidney weight changes were accompanied by an increased incidence of cytoplasmic vacuolation of renal tubular epithelium in males exposed to 3.7 mg/kg b.w. per day expressed as mercury or greater. Female mice showed no kidney changes.

7.2.2.3. Adult and developmental neurotoxicity

Compared with the number of studies on methylmercury, there have been relatively few studies on the possible neurotoxicity of mercuric and mercurous salts at low doses in experimental animals.

In a recent, low-dose study (Huang et al., 2011), mice were exposed to mercuric chloride by oral gavage, as part of a larger study (see Section 7.2.1.2. for a description of the rest of study). The treatment regime comprised dosing of both male and female parents for 4 weeks before mating, dosing of the pregnant and lactating dams, and dosing of some of the offspring for a further seven weeks from weaning on postnatal day 21, while others were not dosed postweaning. A further group of offspring were not exposed prenatally or preweaning but were exposed postnatally for seven weeks from weaning. Controls were given vehicle (distilled water) and treated animals were given 0.5 mg/kg b.w. per day expressed as mercuric chloride (equivalent to 0.37 mg/kg b.w. per day, expressed as mercury). Only this one dose was tested. There was a statistically significant reduction in litter size in those exposed pre-mating and during gestation. Male offspring body weight gain by 10 weeks of age was statistically significantly reduced in the groups exposed prenatally and preweaning, but not in those exposed only after weaning. Motor, behavioural and auditory tests were conducted at the end of the seven-week postweaning dosing period in 12 - 15 male offspring per treatment group. In open field tests, treated males, in comparison with controls, showed statistically significant increases in spontaneous locomotor activity, irrespective of the time period(s) at which they had been exposed to mercuric chloride. There was a statistically significant reduction in stereotype-1 activity in those exposed only from weaning and a statistically significant increase in stereotype-1 activity in those exposed continuously during the prenatal, preweaning and postweaning periods. The nature of stereotype-1 behaviour was not further explained by the authors. Males exposed continuously during the prenatal, preweaning and postweaning periods and those exposed only postweaning also showed a statistically significant reduction in retention time on an accelerating rotating rod. Hearing thresholds were measured in anaesthetised animals by auditory brainstem responses (or auditory evoked potentials) in response to clicks of varying sound pressure levels, ranging from 110 dB to -5 dB. Hearing thresholds were statistically significantly raised by 20 to 30 dB compared with controls in all groups exposed to mercuric chloride, irrespective of the time period(s) of treatment. Absolute and interwave latencies of the auditory brainstem response waveform recorded at a fixed sound pressure level of 105 dB were also statistically significantly increased in all treated males. Lipid peroxidation levels in cerebral cortex, cerebellar cortex and brainstem were statistically significantly increased in all treated males. Na^+/K^+-ATPase activity was statistically significantly elevated in the cerebral cortex and brainstem of all treated males and statistically significantly reduced in the cerebellar cortex of male offspring treated only in the postweaning period and statistically significantly increased in those treated in the prenatal and preweaning periods or treated continuously in the prenatal, preweaning and postweaning periods. The concentration of nitric oxide was statistically significantly reduced in whole blood of male offspring treated only in the postweaning period and statistically significantly increased in those treated in the prenatal and preweaning periods or treated continuously in the prenatal, preweaning and postweaning periods. In brain tissue (cerebral cortex, cerebellar cortex and brainstem), nitric oxide was statistically significantly decreased in all treated male offspring, irrespective of the time period(s) of treatment. Measurement of the mercury content of whole blood and brain tissue confirmed that exposure of treated animals was statistically significantly increased by up to 50-fold in whole blood, by up to 20-fold in cerebral cortex and by more than 10-fold in the cerebellar cortex and brainstem, compared with controls. The authors of this study proposed that

mercury-induced ototoxicity may be mediated by oxidative stress, altered Na^+/K^+-ATPase and nitric oxide activities, and the signalling between these three systems.

In an earlier study, exposure to a high dose of mercuric sulphide (1 000 mg/kg b.w. per day, expressed as mercuric sulphide, equivalent to 862 mg/kg b.w. per day, expressed as mercury) by oral gavage also caused adverse effects on the auditory system in mice (Chuu et al., 2001). A lower dose of 100 mg/kg b.w. per day, expressed as mercuric sulphide (equivalent to 86 mg/kg b.w. per day, expressed as mercury) was a NOAEL. The higher dose of mercuric sulphide needed to elicit effects on the auditory system compared with mercuric chloride likely reflects the considerably lower solubility and gastrointestinal absorption of mercuric sulphide compared with mercuric chloride (ATSDR, 1999; Liu et al., 2008).

The study of Huang et al. (2011) indicates ototoxicity in mice after prenatal, perinatal and/or post-weaning exposure to inorganic mercury, at a dose equivalent to 0.37 mg/kg b.w. per day, expressed as mercury (the only dose tested). This effect level is slightly higher than the dose of 0.23 mg/kg b.w. per day expressed as mercury in the NTP (1993) studies, which was without effects on kidney weight and was used by the JECFA to establish a PTWI, but a NOAEL for ototoxicity has not been established, nor have the findings yet been replicated by others. However, it should be noted that the JECFA used the lowest $BMDL_{10}$ of 0.06 mg/kg b.w. per day expressed as mercury for effects on kidney weight as the reference point for deriving the PTWI. The $BMDL_{10}$ is six times lower than the effect level for ototoxicity.

7.2.2.4. Developmental and reproductive toxicity

Oral exposure to inorganic mercury has been reported to cause developmental toxicity, such as increases in resorptions and fetal abnormalities, and reproductive toxicity, such as changes in the oestrous cycle and ovulation (for details see US-EPA, 1997; FAO/WHO, 2011b). These effects occur at doses higher than the lowest $BMDL_{10}$ of 0.06 mg/kg b.w. per day expressed as mercury for kidney weight changes.

In a recent, low-dose, two-generation study on lead, cadmium and mercury (Lukačínová et al., 2011, 2012), Wistar rats were given 1 µM mercuric chloride in the drinking water, starting with the parental generation from 52 days of age and continuing through the F1 and F2 generations, terminating at the 156th week in each generation. Ten males and females per group were used to breed each generation and all animals were allowed to breed repeatedly between 13 and 78 weeks of age. The concentration of mercuric chloride in the drinking water corresponds to 270 µg/L. From the averages given by the authors for body weight and drinking water intake over the entire duration of the experiment, it can be calculated that the average exposure to mercuric chloride across the parental, F1 and F2 generations was 0.03 – 0.04 mg/kg b.w. per day expressed as mercuric chloride, equivalent to 0.022 – 0.029 mg/kg b.w. per day expressed as mercury. At 78 weeks of age, there were statistically significant reductions in body weight of 26 %, 27 % and 40 % in parental, F1 and F2 mercuric chloride-treated generations compared with controls. Exposure to mercuric chloride was reported to cause a statistically significant reduction in percentage survival to three years of age (controls 90 - 100 % versus treated 30 - 35 %), and consequently in lifespan, in all three generations. In those exposed to mercuric chloride, the number of litters from the parental generation was higher than in controls, comparable to controls in the F1 and statistically significantly lower than controls in the F2. The number of pups per litter at birth was reduced in the F2 generation in those exposed to mercuric chloride compared with controls. The proportion of weanlings surviving from birth was also lower in the breedings from all three generations of those exposed to mercuric chloride (56 - 64 % compared with 90 - 91 % in controls). Serum total protein, albumin, transferrin and ferritin levels, considered to be biomarkers for exposure to heavy metals, were statistically significantly increased following mercuric chloride treatment.

The multigeneration study of Lukačínová et al. (2011, 2012) reported adverse effects on survival, lifespan and reproductive parameters at a lower level of mercury exposure than hitherto reported for kidney effects. In the NTP study (NTP, 1993), it is not known to what extent those exposures might

have influenced survival as the study was not a multigeneration study, but rather only six months in duration. It is noted that only one dose and 10 animals per group were used. It is also noted that these findings are unusual in that survival at three years of age in the three generations of untreated control rats was reported to be 90 - 100 %, compared to 30 - 35 % in the corresponding generations of mercury treated animals. Such a high survival rate in control Wistar rats would not be expected at three years of age. For these various reasons, the Panel considers that these results cannot be used for risk assessment. It is, however, noted that adverse effects on fertility/litter size, postnatal survival and offspring body weight in rats and on fertility in mice were also reported by another research group in two earlier multigeneration studies in which mercuric chloride was administered continuously by oral gavage to Sprague-Dawley rats of the parental, F1 and F2 generations and to C57BL/6 mice of the parental and F1 generations (Atkinson et al., 2001; Khan et al., 2004). Doses ranged from 0.5 – 2.5 mg/kg b.w. per day expressed as mercuric chloride (equivalent to 0.37 – 1.85 mg/kg b.w. per day, expressed as mercury) in the rat study and from 0.25 – 1.0 mg/kg b.w. per day expressed as mercuric chloride (equivalent to 0.18 – 0.74 mg/kg b.w. per day, expressed as mercury) in the mouse study. Adverse effects on one or more reproductive parameters were noted in both studies at all dose levels, but it should be noted that in rats the effects were more severe in the parental generation than in the F1 and F2 generations, and in mice the effects on fertility were not dose-related and fertility in controls was low. Although NOAELs were not established in these two studies, the lowest reported levels for reproductive effects are three times higher than the lowest $BMDL_{10}$ for kidney effects of 0.06 mg/kg b.w. per day (expressed as mercury) used as the reference point for establishing the JECFA PTWI.

7.2.2.5. Carcinogenicity

As summarised in a previous opinion (EFSA, 2008), there is equivocal evidence of carcinogenicity of mercuric chloride in animals. In two-year, oral gavage studies conducted by the NTP (1993), groups of 60 B6C3F1 mice were given mercuric chloride at 0, 5 and 10 mg/kg b.w. per day (equivalent to 3.7 and 7.4 mg/kg b.w. per day, expressed as mercury), for five days per week. Groups of 60 Fischer 344 rats were given 0, 2.5 or 5 mg/kg b.w. per day, expressed as mercuric chloride (equivalent to 1.9 and 3.7 mg/kg b.w. per day, expressed as mercury), for five days per week. Focal papillary hyperplasia and squamous cell papillomas of the forestomach, together with thyroid follicular adenomas and carcinomas, were observed in male rats given 3.7 mg/kg b.w., expressed as mercury. An increased incidence of squamous cell forestomach papillomas in female rats at 3.7 mg/kg b.w. (expressed as mercury) and renal adenomas and carcinomas in male mice at 7.4 mg/kg b.w. (expressed as mercury) were also observed. However, as has been noted by the NTP and others, the forestomach tumours did not progress to malignancy (NTP, 1993; US-EPA, 1997). The relevance of the thyroid carcinomas has also been questioned, because these neoplasms are usually seen in conjunction with increased incidences of hyperplasia and adenomas, which were not observed in this study (NTP, 1993; US-EPA, 1997). The kidney tumours observed in mice occurred at doses that were also nephrotoxic, and would be expected to arise by a non-genotoxic mechanism (ATSDR, 1999). In the JECFA review (FAO/WHO, 2011b) the data from the carcinogenicity studies were not considered to be the critical data for dose-response modelling for establishing the PTWI. The CONTAM Panel agrees with this view, particularly in view of the fact that the PTWI is based on kidney effects at a much lower dose than those resulting in tumours.

7.2.2.6. Conclusions on inorganic mercury toxicity

The critical target organ for toxicity of inorganic mercury is the kidney. Other targets include the liver, nervous system, immune system, reproductive system and the developing organism. Having considered the more recent data on experimental animals exposed to inorganic mercury, the CONTAM Panel has not identified any studies in experimental animals exposed to inorganic mercury indicating effects on the kidney at doses lower than the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury, identified for effects on kidney weight from the NTP (1993) study. Table 22 summarises low-dose animal toxicity studies on mercuric chloride. The Panel noted that some recent studies (Huang et al., 2011; Lukačínová et al., 2011, 2012) have reported ototoxicity and reproductive

toxicity at relatively low doses. These studies had limitations, which have been discussed in Sections 7.2.2.3 and 7.2.2.4.

Table 22: Summary of low-dose animal toxicity studies on mercuric chloride.

Species, route, dose, duration	Toxic effects	NOAEL/LOAEL/BMDL expressed as mercury	Comment	Reference
Rat, s.c. 0, 0.05 0.1, 0.25, 0.50, 1.0, 2.0 mg $HgCl_2$/kg b.w., 3 times per week for 8 or 12 weeks	Immune type glomerulonephritis, proteinuria	LOAEL 0.226 mg Hg/kg b.w. per day	Brown Norway rat, regarded as good surrogate for effects of mercury in sensitive humans	Druet et al. (1978)
Rat, oral gavage 3.0 mg $HgCl_2$/kg b.w. once per week for up to 60 days	Immune type glomerulonephritis, proteinuria	LOAEL 0.317 mg Hg/kg b.w. per day	Brown Norway rat	Bernaudin et al. (1981)
Rat, oral gavage 0, 3.0 mg $HgCl_2$/kg b.w., 2 times per week for 60 days	Immune type glomerulonephritis	LOAEL 0.633 mg Hg/kg b.w. per day	Brown Norway rat	Andres (1984)
Rat, oral gavage 0, 0.312, 0.625, 1.25, 2.5, 5 mg $HgCl_2$/kg b.w. per day, 5 days per week, for 6 months	Absolute and relative kidney weights	NOAEL 0.23 mg Hg/kg b.w. per day LOAEL 0.46 mg Hg/kg b.w. per day $BMDL_{10}$ 0.06 mg Hg/kg b.w. per day	Fisher 344 rat $BMDL_{10}$ of 0.06 mg Hg/kg b.w. per day used by JECFA to establish a PTWI of 4 µg/kg b.w.	NTP (1993)
Rat, oral gavage 0, 0.5 – 2.5 mg $HgCl_2$/kg b.w. per day, two-generation study	Dose-related reductions in fertility live pups per litter, postnatal survival and offspring body weight	LOAEL 0.36 mg Hg/kg b.w. per day	NOAEL not established. At lowest dose tested, substantial effects on F_0 fertility and live pups per litter in F_1. In F_2, effects only on live pups per litter and postnatal survival at highest dose tested.	Atkinson et al. (2001)
Mouse, oral gavage 0, 0.25 – 1.0 mg $HgCl_2$/kg b.w. per day, two-generation study	Reduced fertility	LOAEL 0.18 mg Hg/kg b.w. per day	NOAEL not established. At lowest dose tested, substantial effect on fertility, but low in controls (44 %) and no dose-response (16 % in all three dose groups)	Khan et al. (2004)
Mouse, oral gavage 0, 0.5 mg $HgCl_2$/kg b.w. per day, one-generation study	Reduced litter size; offspring had reduced weight gain, changes in motor, behavioural and auditory function	Effects at only dose tested: 0.37 mg Hg/kg b.w. per day	NOAEL not established, only one dose tested	Huang et al. (2011)
Rat, oral in drinking water 0, 0.03 - 0.04 mg $HgCl_2$/kg b.w. per day, two-generation study	Reduced body weight in parents and offspring; reduced litter size, reduced offspring survival to 3 years	Effects at only dose tested: 0.022-0.029 mg Hg/kg b.w. per day	NOAEL not established only one dose tested; very high survival rate to 3 years in controls (see 7.2.2.4.)	Lukačínová et al. (2011, 2012)

b.w.: body weight; BMDL: 95 % benchmark dose lower confidence limit; Hg: mercury; $HgCl_2$: mercuric chloride; LOAEL: lowest-observed-adverse-effect level; NOAEL: no-observed-adverse-effect level; s.c.: subcutaneous.

7.3. Modes of action

Mechanistically cellular toxicity of methylmercury and mercuric mercury is largely dependent upon their electrophilic properties, which allows for their interaction with soft nucleophilic groups, mainly thiols and selenols (especially methylmercury (e.g. Wagner et al., 2010)) from low- and high-molecular-weight biomolecules. These interactions with biomolecules are at the cellular level most likely responsible for oxidative stress, disturbances in calcium homeostasis and, cytoskeletal alterations and contribute to and/or cause toxicity in the target organs.

Based on recent reports of ATSDR (ATSDR 1999), JECFA (FAO/WHO 2007, 2011b), numerous recent reviews and recent original papers, this chapter especially focuses on neurotoxic modes of actions, genotoxic effects and mechanism of vascular/cardiovascular toxicity of mercuric mercury and methylmercury.

Regarding the toxic modes of action of methylmercury it is important to note that the majority of *in vitro* and *in vivo* toxicological studies have used the chloride salt, methylmercuric chloride. However, methylmercury in fish is complexed to cysteine, with cysteine likely to be part of a peptide or protein (Harris et al., 2003), and initial studies indicate that MeHgCys differs from methylmercuric chloride in terms of bioavailability, tissue distribution and toxicity. Therefore, differences between the methylmercury species might depend also on the animal species investigated. Thus, in male Wistar rats fed with fish meal diets containing methylmercury contaminated fish and uncontaminated fish supplemented with methylmercuric chloride at similar levels, Berntssen et al. observed a higher faecal excretion, lower tissue accumulation and metallothionein induction in rats following exposure to methylmercury naturally incorporated in fish compared to methylmercuric chloride supplemented fish (Berntssen et al., 2004). In mice, uptake by liver and brain after intraperitoneal exposure to methylmercuric chloride or MeHgCys was higher in the case of MeHgCys, whereas mercury kidney levels were higher after exposure to methylmercuric chloride (Roos et al., 2010). Glover et al. (2009) determined the impact of methylmercury speciation in the maternal diet on developing offspring of mice and concluded that there are important differences between the mercury species in terms of their toxic impact, although this was not manifested by changes in tissue accumulation. Thus, methylmercuric chloride, but not MeHgCys, disturbed pup behaviour and microarray analyses from pup brains revealed strong differences between the mercury species. There is only one *in vitro* study available that applies shortly before the experiment prepared MeHgCys. This study showed strong differences in cellular toxicity between methylmercuric chloride and the naturally occurring and therefore likely more relevant MeHgCys (Oyama et al., 2000).

7.3.1. Mechanisms of neurotoxicity and neurodevelopmental toxicity

The neurotoxic and neurodevelopmental effects of methylmercury most likely arise from multiple modes of actions, which have been recently summarised in numerous reviews (Castoldi et al., 2008; Aschner et al., 2010; Ceccatelli et al., 2010; Farina et al., 2011a, b; Kaur et al., 2011; Syversen and Kaur, 2012). In the brain methylmercury is converted partly and to unknown extent into mercuric mercury (Clarkson and Magos, 2006). Although there are several studies claiming that mercuric mercury might be the ultimate toxic compound in the brain after methylmercury exposure, many reports provide evidence that mercuric mercury cannot play such a role. Thus, mercuric mercury derived from demethylation of methylmercury in brain cells is most likely not the mercury species responsible for the neurological effects induced by methylmercury intake (summarised in Syversen and Kaur, 2012).

Regarding the search for sensitive brain target cells, Takeuchi et al. (1989) demonstrated a deposition of mercury in the epithelial cells of the choroid plexus of a Minamata disease patient. Additionally, mercury granules have been shown in the choroid plexus of methylmercury-treated rats, and recently high methylmercuric chloride administration to rats has shown to impair blood-cerebrospinal fluid barrier (CSF) function, followed by leakage of albumin-bound methylmercury into CSF (Nakamura et al., 2011). In addition, astrocytes and microglia have been implicated as major targets for methylmercury. By directly comparing effects on primary rat astrocytes and microglia, a recent study

provides evidence that microglia are more sensitive to methylmercuric chloride than astrocytes in terms of the endpoints cell viability and oxidative stress. This finding is consistent with their lower basal glutathione level and higher cellular mercury uptake (Ni et al., 2011). However, although glia cells seem to be the preferential site of methylmercury accumulation in the brain, neurons seem to be more susceptible to methylmercury-induced toxicity, especially in the developing brain.

The mechanisms underlying the high sensitivity of the developing brain to methylmercury exposure can be attributed to the disturbance of the highly regulated processes during brain development, including the very fast and strongly coordinated cell proliferation, differentiation and migration. Very low, sub-cytotoxic methylmercuric chloride concentrations (2.5 - 50 nM, 48 h) have been shown to cause a G1/S cell cycle arrest in primary cultures of progenitor cells from rat embryonic cerebral cortex, most likely via regulating cyclin E expression and perturbing a pathway that involves the extracellular signal regulated kinase, which is one of the key molecules in growth factor signalling (Xu et al., 2010). In rat neuronal stem cells, methylmercuric chloride (2.5 - 5 nM) inhibited neuronal differentiation (Tamm et al., 2006) via activation of Notch signalling (Tamm et al., 2008). In addition, in neural stem cells exposed to nanomolar concentrations of methylmercury long term inherited effects associated with a decrease in global DNA methylation have been recently reported (Bose et al., 2012). The occurrence of gene-specific epigenetic modifications induced by developmental exposure to methylmercury has also been reported in adult mice (Onishchenko et al., 2008). Proliferation of human amniotic fluid stem cells has recently been reported to be inhibited by 300 - 3 000 nM methylmercuric chloride (Gundacker et al., 2012).

In numerous *in vitro* and *in vivo* studies, disruption of cellular redox homeostasis by an increased level of reactive oxygen and nitrogen species (RONS), leading to cumulative oxidative stress, have been shown to play a key role in methylmercury- and mercuric mercury-induced toxicity. The underlying mechanism involved seems to be related to alterations in mitochondrial functions (Garrecht and Austin, 2011), resulting in increased cellular superoxide anion and subsequently hydrogenperoxide and hydroxylradical levels, and a disturbance of the cellular oxidative defence capacity, as shown by decreased glutathione levels and impaired superoxide dismutase, glutathione reductase and glutathione peroxidase activities. Oxidative stress might be accompanied by altered Na^+/K^+-ATPase activities (Huang et al., 2008). Increased RONS levels might result in lipid peroxidation, protein oxidation and oxidative DNA damage (Farina et al., 2011b).

Recent studies in *Caenorhabditis elegans* demonstrate that methylmercuric chloride and mercuric mercury induce oxidative stress, with the organic mercury species inducing oxidative stress at lower concentrations than the inorganic mercury species. Additionally, methylmercuric chloride was more toxic than mercuric chloride regarding endpoints requiring proper neuromuscular activity including feeding, movement and reproduction; effects in terms of *C. elegans* growth were similar (McElwee and Freedman, 2011). In rats, oral administration of methylmercuric chloride 10 mg/kg b.w. per day (equivalent to 8 mg/kg b.w. per day, expressed as mercury) for 5 days caused an inhibition of the electron transport chain activity and induced cytochrome c release in cerebellum mitochondria (Mori et al., 2011). In the brain of developing offspring mice low-dose, oral methylmercuric chloride (0.02 mg/kg b.w. per day, equivalent to 0.016 mg/kg b.w. per day, expressed as mercury) and mercuric chloride (0.5 mg/kg b.w. per day, equivalent to 0.37 mg/kg b.w. per day, expressed as mercury) administration increased lipid peroxidation, nitric oxide levels and changed Na^+/K^+-ATPase activities, which were discussed to contribute to the observed neurobehavioural dysfunction and hearing impairment (Huang et al., 2011).

The impact of mercury species on the cytoskeleton is known since the 1970s. Mechanistically the mercury species target especially microtubules because of the thiol-groups present in tubulin. Depolymerisation of microtubules by mercury species has been shown to disturb numerous cellular processes, including cell survival, proliferation, migration and differentiation (Johansson et al., 2007; Crespo-Lopez et al., 2009).

Methylmercury and mercuric chloride can disrupt glutaminergic, cholinergic and dopaminergic neurotransmitter systems (summarised in Aschner et al. (2010) and intracellular Ca^{2+} homeostasis (Denny and Atchison 1996; Limke et al., 2004). Mercury exposure has been shown in many cell types, including neuronal cells, to increase cellular Ca^{2+} levels, which in turn leads to activation of degradative enzymes, disruption of mitochondrial function and an increase in RONS-induced damage with subsequent cell death. Moreover, cell cycle, cell migration and differentiation might be disturbed (summarised in Aschner et al., 2010; Farina et al., 2011a, b).

7.3.2. Genotoxicity

Several studies have shown that mercuric and methylmercuric chloride induce genotoxicity in various cultured mammalian cells including human lymphocytes (summarised in Crespo-Lopez et al., 2009, 2011; FAO/WHO 2011b). As underlying mechanisms oxidative stress, disruption of microtubules as well as interactions with DNA damage response and DNA repair pathways are discussed (Christie et al., 1986; Cebulska-Wasilewska et al., 2005). Using isolated DNA, mercuric and especially methylmercuric chloride have been shown to bind covalently to endocyclic and exocyclic nitrogen sites of DNA bases (Li et al., 2006). However, to date, formation of such mercury species DNA adducts has not been investigated under physiological conditions.

Data from experimental animals on the genotoxic effects of mercuric chloride are controversial (FAO/WHO, 2011b). Very recently, male rats exposed for 90 days to 50 or 100 mg/L mercuric chloride in drinking water showed a statistically significant increase in the frequency of total chromosomal aberrations and the percentage of aberrant bone marrow metaphases (Boujbiha et al., 2012). Regarding methylmercuric chloride a recent study provide evidence for a genotoxic potential after oral exposure in rats. After 100 days of exposure to 100 µg methylmercuric chloride per day (by gavage), rat white blood cells showed statistically significantly more DNA damage (as measured by the Comet assay) than white blood cells in control animals; co-administration of selenium reduced DNA damage, probably by re-establishment of glutathione peroxidase activity (Grotto et al., 2009a). The same group demonstrated that in direct comparison with rats receiving commercial food or a diet rich in uncontaminated fish, a 12-week diet with methylmercury contaminated fish resulted in an increase of DNA damage in peripheral blood of the respective rats. Oxidative stress biomarkers were not (e.g. reduced glutathione, glutathione peroxidase activity, catalase activity, superoxide dismutase activity, total NO) or only slightly (malondialdehyde) affected (Grotto et al., 2011).

There are no reliable studies investigating genotoxic effects after dietary inorganic mercury intake in humans. Since after inhalation of elemental mercury vapour in the blood elemental mercury is oxidised to mercuric mercury (ATSDR, 1999) the following section summarises genotoxicity in human lymphocytes after exposure towards elemental mercury. In human lymphocytes genetic damage (in terms of chromosome aberrations) has been observed after occupational exposure to elemental and organic mercury (Verschaeve et al., 1976; Popescu et al., 1979; Cebulska-Wasilewska et al., 2005); sister chromatid exchanges (Popescu et al., 1979; Cebulska-Wasilewska et al., 2005) and DNA damage as measured by the alkaline version of the Comet assay (Cebulska-Wasilewska et al., 2005) were not statistically significantly increased in these studies. Repair efficiencies in lymphocytes of 25 workers exposed to elemental mercury vapour were reduced compared with 50 individuals non-occupationally exposed, as measured by the X-rays challenge assay (Cebulska-Wasilewska et al., 2005). In another study increased urinary 8-hydroxy-2-deoxyguanosine levels were observed in occupationally mercury-exposed persons (35 workers, 13 non-occupationally exposed individuals); urinary 8-hydroxy-2-deoxyguanosine levels correlated with both serum and urinary mercury concentration (Chen et al., 2005). On the other hand, studies exist showing no genetic damage after occupational mercury exposure (Verschaeve et al., 1979; Mabille et al., 1984; Barregard et al., 1991; Hansteen et al., 1993).

In a group of 51 fishermen exposed to methylmercury through eating contaminated seafood (6.97 ± 3.49 seafood based meals per week) a statistical correlation was found between micronuclei frequency and total mercury concentration in blood (Franchi et al., 1994); blood mercury levels ranged

from 10.08 to 252.25 µg/L with a mean of 81.97 ± 49.96 µg/L. In lymphocytes of 147 Greenlandic Eskimos, whose main diet consists of seal meat, sister chromatid exchange was found to correlate linearly with blood mercury concentrations (Wulf et al., 1986); thus an increase in the blood mercury concentration of 10 µg/L corresponded to an increase of 0.3 sister chromatid exchanges per cell.

In summary, mercury and methylmercury exert genotoxicity *in vitro* in mammalian cells, whereas data from laboratory animals and humans are inconsistent. The most likely mechanism appears to be via oxidative stress, which would be expected to be thresholded. Inorganic and organic mercury species have been shown to bind covalently to isolated DNA, but the formation of such DNA adducts has not been investigated in cell systems or *in vivo* and therefore the consequences of this interaction for genotoxicity have not been elucidated.

7.3.3. Mechanisms of vascular/cardiovascular toxicity

Mechanisms of mercury-induced vascular/cardiovascular toxicity have recently been summarised and comprise the well known modes of action oxidative stress, inflammation, lipid peroxidation and mitochondrial dysfunction as well as thrombosis, vascular smooth muscle and endothelial dysfunction and dyslipidaemia (Houston, 2011; Roman et al., 2011; Azevedo et al., 2012). Methylmercury exposure-related decreased heart rate variability (HRV) might result from methylmercury toxicity to the neurological system, although specific evidence of this mechanism is still lacking.

In mammalian pulmonary artery endothelial cells, methylmercuric chloride generates oxidative stress and has recently been shown to induce phospholipase D activation and generation of phosphatidic acid, through the upstream activation of phospholipase A2 and formation of cyclooxygenase- and lipoxygenase-catalysed eicosanoids, resulting in pulmonary artery endothelial cell cytotoxicity (Sherwani et al., 2011). Chronic mercuric chloride treatment (intramuscular administration, first dose 4.6 µg/kg b.w., subsequent doses 0.07 µg/kg b.w. per day, 30 days (equivalent to 3.4 µg/kg b.w. and 0.05 µg/kg b.w. per day, expressed as mercury, respectively)) of Wistar rats promoted endothelial dysfunction of coronary arteries, as demonstrated by decreased nitric oxide bioavailability induced by oxidative stress (Furieri et al., 2011a). Moreover, this treatment promoted contractility dysfunction as a result of reduced Na^+/K^+-ATPase activity, decreased sarco/endoplasmic reticulum Ca^{2+}-ATPase and sodium/calcium exchanger and increased phospholamban protein expression in isolated (Langendorff-perfused) hearts of the exposed rats. In the chronically treated animals blood pressure, heart rate and left ventricular systolic pressure were not affected, whereas left ventricular and diastolic pressure was slightly but statistically significantly increased (Furieri et al., 2011b).

7.3.4. Nutrients potentially protective against methylmercury toxicity

Dietary factors that are discussed to reduce or prevent methylmercury toxicity include n-3 LCPUFAs, selenium, iodine, choline and vitamin E. Numerous *in vitro* and *in vivo* studies exist, which have recently been reviewed (e.g. Ralston and Raymond., 2010; Kaur et al., 2011) and are not discussed in detail here.

The most extensively studied substance in food, regarding mechanisms of confounding, seems to be selenium. Mercury binding affinity for selenium is a million times higher than its binding affinity for sulphur in analogous forms and attempts have been made to identify detoxification products, which contain selenium and mercury (e.g. mercury-selenide). Whether those compounds really detoxify the mercury species has never been demonstrated. Besides a sequestration of mercury, potential protective modes of action of selenium against methylmercury toxicity include antioxidant effects, increased glutathione peroxidase activity, glutathione synthesis, high selenoprotein levels and increased demethylation of methylmercury (recently summarised in Syversen and Kaur, 2012).

Mechanistically, DHA seems to protect against methylmercury-induced oxidative stress in neuronal cells. Additionally, in neuronal cell lines and primary cells a pre-treatment with DHA was associated with decreased cellular methylmercury bioavailability (summarised in Kaur et al., 2011).

7.4. Observations in humans

7.4.1. Concentrations in biological samples from the European population

A detailed summary of data on mercury concentrations in biological samples, including blood, cord blood, hair, nails and urine, of the European population since 2000 is given in Appendix F. Only studies that comprise all relevant information, including e.g. the number of samples and the mathematical/statistical indications, are listed. Table 23 summarises the studies given in Appendix F and gives the ranges of the means for total mercury levels measured in cord blood as well as in blood and hair of adults and children. The levels in the Faroe Islands population are presented in Table 24 and were not included in Table 23 because of their particular high exposure from whale meat consumption.

Table 23: Range of mean concentrations of total mercury in biological samples from the European population[(a)] (further details are available in Appendix F).

Matrix (unit)	Adults and elderly	Children
Cord blood (µg/L)		0.86 – 13.9
Blood (µg/L)	0.2 – 4.85	0.12[(b)] – 0.94[(b)]
Hair (mg/kg)	0.17 – 1.45	0.14[(b)] – 1.99

(a): Faroe Islands not included.
(b): Geometric mean.

As indicated from the data presented in these tables, considerable differences exist between European countries. The study by Hrubá et al. (2012) is the only study that directly compared total mercury blood levels in children (7 - 14 years of age) in six European countries.

The respective data indicate that total mercury blood concentrations can differ considerably between European countries and that these differences seem to be related to amalgam fillings and fish intake (Hrubá et al., 2012). The study by Miklavčič et al. (in press) compared total mercury levels in human milk and cord blood in four Mediterranean European countries and observed statistically significant differences between countries. In general children and adolescents have lower urinary and blood mercury levels than adults.

Data on temporal trends based on biomonitoring data from the general population are available from Germany (Karch et al., 2011; Link et al., 2012) and the Czech Republic (Puklová et al., 2010). Whereas in the German studies urinary mercury and blood mercury concentrations decreased over the up to 13 years study period between 1997 - 2010, no clear time trends were observed for adults in the Czech Republic between 1996 - 2008. However, a decrease of both urinary and blood mercury levels were determined in children.

7.4.2. New epidemiological reports on methylmercury

As a starting point for the summary of new developments and epidemiological studies on association between mercury exposure and different endpoints, the report of an EFSA contractor (Hassauer et al., 2012) was used. The JECFA PTWI (FAO/WHO, 2004, 2007) was based on data from cohorts from the Seychelles and Faroe Islands, and a total mercury concentration in maternal hair of 14 mg/kg was used as a point of departure. In order to form a basis for a revision of the health-based guidance value, adverse effects should be associated with an exposure lower than 14 mg total mercury/kg hair. However, different biomarkers of exposure have been used in different epidemiological studies. To have a guidance for evaluating whether new epidemiological studies have high or low exposure relative to the point of departure of the existing PTWI, a blood to hair ratio of 250 was used to calculate a corresponding maternal blood concentration of 56 µg/L. The discussion below builds on the earlier literature, but only discusses in detail studies published since 2004. Publications addressing associations between neurodevelopmental outcomes and mercury exposure from thiomersal-

containing vaccines in combination with methylmercury from fish consumption and/or human milk consumption have not been considered relevant for this opinion since thiomersal releases ethylmercury cation, which is not occurring in food. Publications investigating a mixed exposure from both elemental mercury from mining activities and mercury in food have not been addressed since elemental mercury is not present in food and therefore these studies could not be used for derivation of a health-based guidance value.

7.4.2.1. Neurodevelopmental and neurotoxic endpoints

The scientific discoveries relating to health risks associated with methylmercury exposure began in 1865, with reports describing ataxia, dysarthria, constriction of visual fields, impaired hearing, and sensory disturbance as symptoms of fatal methylmercury poisoning in exposed laboratory workers, see Grandjean et al. (2010a) for an overview. Neurodevelopmental toxicity of methylmercury in a population highly exposed from environmental sources was first recognised in the 1950s in Minamata, Japan, in association with consumption of highly contaminated fish during pregnancy. This resulted in at least 30 cases of cerebral palsy and severe developmental retardation in prenatally exposed children (Harada et al., 1968), as well as in several neurotoxic effects in highly exposed adults. Exposure in affected adults and during pregnancies in Minamata was very high, as reflected in maternal hair mercury concentrations that ranged from above 50 mg/kg up to a maximum of 705 mg/kg (Harada, 1995). In 1972 the consumption of seed treated with methylmercury fungicide in Iraq resulted in the poisoning of several thousand inhabitants, again with newborns and infants seen as the most vulnerable group for neurotoxic effects.

The high incidence of structural brain damage and functional impairment in children in both incidents might be due to (a) the lipophilic characteristics of methylmercury, (b) the ability of methylmercury to cross the placental and blood-brain barriers, (c) the resulting higher concentration in fetal and neonatal blood, and (d) the ability to affect the neurological system and its development directly and irreversibly. The highest vulnerability of the embryo and fetus, as well as the high sensitivity of infants and children was emphasised in the 2006 JECFA evaluation (FAO/WHO, 2007).

7.4.2.1.1. Prenatal exposure

A. Faroe Islands

Five birth cohorts have been established in the Faroe Islands in the period 1986 - 2009, all providing information on mercury exposure.[38] Neurodevelopmental endpoints have been studied in the two first of these cohorts, in Cohort 1 (n = 1022), established in 1986 - 1987 and Cohort 2 (n = 182) established in 1994 - 95. Participants in Cohort 1 performed a variety of neurobehavioural tests at age 7 and 14 years, and the investigation included clinical examinations with a focus on nervous system function. Neurological Optimality Score was examined in Cohort 2 participants at the age of two weeks, 7, 18, 30, 42 months and 4.5 and 5.5 years (an extended medical examination was performed at 42 months) as well as detailed neurobehavioural tests at 7 years and 10 years.

Neurotoxicity in seven year-old children in the Faroese Cohort 1 (together with the data from the Seychelles) was used by the JECFA in establishing the PTWI of 1.6 µg/kg b.w. for methylmercury (FAO/WHO, 2004). The associations between prenatal methylmercury exposure and newborn neurological status in the Faroese Cohort 2 were also taken into consideration. In the later update (FAO/WHO, 2007) two 14-year follow up studies from the Faroese Cohort 1 had become available (Murata et al., 2004b; Debes et al., 2006). Re-analysis and new results of the Faroese cohorts that have become available since the 2004 JECFA evaluation are summarised below and in Table 24.

At the age of 14 years, the children in the Faroese Cohort 1 participated in a clinical investigation assessing brainstem auditory evoked potentials (BAEPs) (Murata et al., 2004b). These are very small electrical voltage potentials, which are recorded in response to an auditory stimulus from electrodes

[38] http://www.chef-project.dk/

placed on the scalp and reflect neuronal activity in the auditory nerve, cochlear nucleus, superior olive and inferior colliculus of the brainstem. The physiological basis of measurement of possible neurological effects is a strength of this approach since the measurement is not influenced by the level of education and social mediated stimulation. Hair samples were collected at age 14 years and the concentration was increased with a factor of about 1.5 compared to the hair measurement data at age seven years (Budtz-Jørgensen et al., 2004), but the geometric mean was less than approximately 25 % of that in maternal hair at the end of pregnancy. The correlation to cord blood mercury concentration (after logarithmic transformations) was moderate ($r_{age=7} = 0.33$ and $r_{age=14} = 0.35$, $p < 0.01$), pointing to a systematic influence of similarity in exposure conditions over time (nutritional habits in the environment and family). The same laboratory technique was applied as at seven years and the same physiological outcomes were measured with blinded examinations. Auditory stimuli click signals with intensity of 65 dB (0.1 ms impulses) were presented to the right ear (20 Hz and 40 Hz) while the other ear was masked with white noise (45 dB HL). Audiometry was performed in a standardised manner to control for possible influence of hearing impairment. The resulting data set was analysed by multiple regression taking age, sex and the exposure indicators as independent variables and the set of variables that was previously included in neuropsychological test analysis as confounders. Additional analyses included polychlorinated biphenyls (PCB) and postnatal methylmercury exposure. The measured BAEP latencies were similar to the results obtained at age seven years. Total mercury in maternal hair and/or cord blood was statistically significantly associated with latencies within the I–III interval ($p < 0.05$). The associations with the full peak III latency was the most robust finding and statistically significant at both frequencies, and in accordance with the findings at age seven. According to the authors, the inclusion of the set of confounders as well as the inclusion of PCB co-exposure for the subset for which this information was available did not affect the regression coefficients. The regression coefficients at age seven were about twice the magnitude observed at age 14 years. This suggests a persistent neurotoxic effect of intrauterine mercury exposure, while the lower values of the resulting regression coefficients at age 14 might indicate some compensation. Prenatal $BMDL_{05}$ results for peak III at the two frequency conditions corresponded at age 14 again to an average of approximately 10 mg/kg hair based on either cord blood or maternal hair. Recent exposure, measured by hair mercury concentration at 14 years, was associated with prolonged III-V interpeak interval ($p < 0.05$ at 40 Hz). Prolonged III-V interpeak interval showed non-significant regression coefficients with prenatal exposure at both frequencies. Adjustment for recent postnatal exposure, did not affect the regression coefficients for the prenatal exposures.

In the re-examination of the Faroese Cohort 1 at age 14 years, 860 of the 1 010 living participants underwent detailed neurobehavioural examination (Debes et al., 2006). The topics of the neuropsychological test battery were selected on the same criteria as applied at the examination at age seven years. The mercury concentrations in maternal hair and cord blood showed, in confounder adjusted regression analysis, statistically significant associations with deficits on finger tapping and measures of reaction time on a continued performance task. Cued naming was statistically significantly negatively associated with mercury in cord blood. The cord tissue mercury concentrations showed no clear association with these outcomes, but were associated with lower test scores for the naming and for the verbal-learning tasks. In contrast to the prenatal exposure variables, markers of postnatal exposure were generally only weakly related to cognitive test scores at 14 years. Co-exposure by PCB showed only weak, non-significant associations with the outcomes. The comparison of the results at age 7 and 14 years suggests that children with a lower performance level at age 7 show a persistent tendency to lower test scores at age 14. An extended analysis of the data by structural equation models found the strongest mercury associations in regard to the group of the motor and attention test results ($p < 0.05$), with associations for the verbal tasks close to statistical significance ($p = 0.051$) after adjustment for fish intake. For a methodological review of the structural equation modelling approach and how to standardise the scores of the selected set of target variables for nervous system functions, see Budtz-Jørgensen et al. (2002). Memory and spatial tasks appeared not to be associated with prenatal methylmercury exposure. Maternal fish consumption during pregnancy appeared to show a weak, but not statistically significant beneficial association.

In another re-evaluation of the 7 and 14 years data from the Faroese Cohort 1 Budtz-Jørgensen et al. (2007b) tried to separate risks and benefits from fish and seafood consumption. The mercury exposure in this cohort is strongly related to the consumption of whale meat (Grandjean et al., 1992), on the other hand the frequency of fish dinners (mainly cod) correlated statistically significantly with mercury concentrations in cord blood ($r = 0.25$) and maternal hair ($r = 0.26$). The extent of confounding bias was analysed by applying structural equation models. The set of confounders included a series of covariates described previously (Budtz-Jørgensen et al., 2007a; Grandjean et al., 1997). Adjustment for fish intake modified the previously reported mercury regression coefficients (Grandjean et al., 1997; Budtz-Jørgensen et al., 2002; Debes et al., 2006) toward a higher explained variance. PCB exposure was not included as a covariate because of limited impact on the mercury association in previous analyses (Grandjean et al., 2001; Debes et al., 2006). In addition, it was not available for more than half of the cohort members. Fish intake, seen as an indicator for a higher intake of beneficial nutrients, influenced test scores on all five neuropsychological outcome variables (motor, attention, spatial, verbal and memory functions). The association was statistically significant for the motor performance (examination at 7 and 14 years of age) and functioning in tasks for spatial orientation and operations (examination at 14 years of age). The authors discussed the role of possible imprecision of the information about fish consumption on the relationship between exposure and neurological outcomes and concluded that using food frequency questionnaire data might have the highest imprecision, followed by methylmercury exposure estimates based on hair analysis. Assuming a reliability ratio up to 43 % (i.e. percentage of the total variation caused by measurement error > 0.57), the authors concluded that the association between prenatal methylmercury exposure and neurodevelopmental outcomes previously reported in the Faroese Cohort 1 might be underestimated by a factor of up to 2 when beneficial effects of fish consumption and imprecision in the measurement of fish consumption were not taken into account.

Analyses of possible consequences of exposure measurement error (mercury measurement in different matrices at different periods/ages as well as dietary questionnaire data) for confounder identification, model misspecification and for the risk of effect underestimation are available in Budtz-Jørgensen et al. (2003), Grandjean et al. (2004a) and Grandjean and Budtz-Jørgensen (2010).

In the literature search, only one study was identified reporting data from Cohort 2 in relation to mercury (Budtz-Jørgensen et al., 2010). The study combined data from the seven-year follow-up in the two first Faroese cohorts, with a focus on the possible PCB confounding of the associations between neurodevelopmental outcomes and mercury. Most of the results are reported for a combined set of data from the two cohorts, but separate results are given for the two cohorts for the associations when not adjusted for PCB. These results provide some information on whether the Cohort 2 results at seven years of age were confirming the observations from Cohort 1 at that age. Among the outcomes reported for Cohort 2 (Neurobehavioral Evaluation System, finger tapping, reaction time in the Continuous Performance Test (CPT), the Boston Naming Test, the Wechsler Intelligence Scale, and the California Verbal Learning Test) only the results for the Boston Naming Test's negative association with mercury were consistently in line with the observations in Cohort 1. In addition, some aspects of the CPT (reaction time and the total number of missed stimuli) and verbal learning (short and long delay) showed results in similar direction as in Cohort 1. The conclusions that can be made from this are very limited due to the smaller size of Cohort 2 (the analysis included ca 900 children from Cohort 1 and 160 from Cohort 2). As to the possible (positive) confounding from PCB, results of statistical analysis were only given for the combined dataset for the two cohorts. PCB was not statistically significant associated with any of the outcomes. However, when mercury and PCB was included in the models simultaneously, the regression coefficients for mercury decreased for the Boston Naming Test from about 2.1 to about 1.5. It is accordingly difficult to exclude confounding from PCB.

A further discussion on confounding from prenatal exposure to PCB on associations between prenatal mercury exposure and neurobehavioural deficits was provided recently (Grandjean et al., 2012), based on new analyses of PCBs in cord blood from almost all the 923 Faroe 1 Cohort members that participated at the examination at seven years age. Prenatal PCB exposure showed statistically

significant negative associations only with the Boston Naming test. The outcomes from the test battery at seven years were analysed by latent variables for motor and verbally mediated functions in a structural equation model. The PCB effects were weak and not statistically significant, and weakened more when adjusting for prenatal mercury exposure. The associations with prenatal mercury exposure remained significant after adjustment for prenatal PCB-exposure, and the regression coefficients increased marginally after adjustment. The authors concluded that PCB exposure does not explain the methylmercury neurotoxicity previously reported in the cohort.

Julvez et al. (2010) reported the results of the examination using the CPT as a measure of the speed and error rates of visual information processing in the examination of 14 year old Faroese Cohort 1 participants. The CPT-Hit Reaction Time latencies (CPT-HRT) test was applied and the test scores were used as indicators for different neuropsychological functions depending on the time of the task using a computer assisted test. This test assesses several visual-cognitive, attention and motor functions. In multivariate regression analysis with confounder adjustment the duration needed for the CPT task depended on prenatal exposure to methylmercury. The scores of the three stages (HRT-outcomes on 1 - 2, 3 - 6 and 7 - 10 minutes) were highly inter-correlated. The learning phase was less associated with methylmercury exposure than the second phase, which was interpreted to include the functions of speed processing and selective focused attention. The scores of this test phase were strongly associated with prenatal methylmercury exposure, even after controlling for motor speed and simple reaction time. The scores of the third test phase, regarded as indicators of sustained attention by the authors, showed the strongest associations with prenatal methylmercury exposure. Current mercury concentrations (mercury in a proximal 2-cm-hair segment) did not show any clear association structure.

In summary, 14 years follow up and re-analysis of data from the Faroe Islands since the JECFA PTWI was established (FAO/WHO, 2004) consistently indicate a detrimental effect of prenatal methylmercury exposure. The association between prenatal exposure and neurological auditory function was still present at 14 years but with a smaller impact, and not related to the estimates of postnatal exposure. Beneficial effects of fish consumption and imprecision in the measurements might confound the neurotoxic associations in the Faroese studies, causing underestimation of the effects of methylmercury, and this has been estimated to be by a factor up to two. Most of the neurodevelopmental outcomes, but not the neurological auditory function, were evaluated in the smaller Cohort 2 at seven years of age. For most of the associations between neurological outcomes and mercury in Cohort 1, the results could not be confirmed. Assessment of Faroese Cohort 1 and 2 together did not identify major confounding from PCB exposure, but it did not exclude the possibility of an overestimation of the mercury effects in Cohort 1 due to such confounding. Reassessment of the neurodevelopmental endpoints at seven years in the Faroese Cohort 1, including new results on cord blood PCBs in almost all participants, did not identify PCB as a strong confounder in the study.

B. Seychelles

Seychellois consume much and frequent ocean fish (deep-sea and reef fish) and more than 80 % of the population consume fish meals at least once a day as the main source of protein. Consumption of marine mammals is rare. The Seychelles have no major local industrial sources of mercury pollution and the PCB exposure is low. Women's alcohol consumption is low (Myers et al., 2007). Association between mercury exposure and child development has been studied in three different cohorts in the Seychelles, and the studies are called the Seychelles Child Developmental Pilot Study, the Main Study (the Seychelles Child Development Study, SCDS) and the Nutrition Study (SCDNS).

The Seychelles epidemiological study programme started in the mid 1980s with a pilot study including approximately 800 infant-mother pairs in 1986. The pilot study was followed by a main study of 779 mother-infant pairs recruited in 1989 - 1990 on the island of Máhe. The main study objective was to determine whether prenatal methylmercury exposure from fish consumption has adverse associations with the children's neurodevelopment. The children were enrolled when they were six

months old. Mothers reported consuming fish on average 12 meals per week. Prenatal methylmercury exposure was measured as total mercury in maternal hair growing during pregnancy (mean 6.9 mg/kg, SD 4.5 mg/kg). The main cohort has been tested for developmental outcomes at 6, 19 and 29 months and at 5.5, 9, 10.5 and 17 years of age. The longest follow-up available at the evaluation by the JECFA in 2004 was at age 9 years (Myers et al., 2003). Conventional linear regression models were used to analyse the outcome of test batteries which covered neurocognitive, language, memory, motor, perceptual-motor, and behavioural functions. The authors concluded that these data did not support the hypothesis that there is a neurodevelopmental risk from prenatal mercury exposure in this population. The results from analysis at 9 years confirmed those from age 5.5 years, which were used (together with the results from the Faroe Islands) as basis for the derivation of the PTWI (FAO/WHO, 2004).

A third nutrition cohort was established to test if nutrients and dietary status during pregnancy could modulate the neurotoxicity of mercury (Myers et al., 2007; Davidson et al., 2008b). A total of 300 women were recruited in 2001 in their first trimester of pregnancy. At enrolment and at delivery, hair and blood from the mothers and cord blood from the infants was obtained. Prenatal mercury exposure was measured as total mercury in maternal hair covering the gestation period. Nutritional factors that might influence child development were measured in the mother's blood taken at 28 weeks (iodine status measured by thyroid stimulating hormone (TSH) and free T4, iron status and different long-chain polyunsaturated fatty acids (LCPUFAs)). Maternal fish consumption was measured by a food use questionnaire covering the preceding 14 days and a four-day diet diary (two week days and two weekend days) at 28 weeks gestation. Dietary choline intake was estimated from the food diaries and used as an indirect measure of choline status. The mothers consumed on average nine fish meals (537 g) weekly. The mean maternal hair mercury concentration covering the gestation period was 5.7 mg/kg (range 0.2 - 18.5). Child development was tested at 5, 9, 25 and 30 months and at five years of age. The main developmental endpoint was Bayley's scale of infant development-II (BSID-II) at 9 and 30 months, giving two primary endpoints, Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI). Additional assessments at 5, 9 and 25 months examined more specific aspects of cognition. These were at 5 and 9 months the Fagan test of infant intelligence (Fagan Infantest, FTII) measuring novelty preference and the Visual Expectations Paradigm measuring visual recognition memory (VRM). The A-not-B and the Delayed Spatial Alteration tests, measuring aspects of planning, inhibition, attention and working memory, were administered at 25 months.

Since the last evaluation (FAO/WHO, 2004), additional follow-ups as well as several approaches of statistical analysis have been reported for the main cohort. Some additional reanalyses were available at the update in 2006 (FAO/WHO, 2007), and these are also included in the summary below and in Table 24. In addition, results from the nutrition cohort have been published. They are summarised below and in Table 24.

The Main Cohort

Davidson et al. (2004) assessed whether the influences of social and environmental factors on the association between prenatal exposure and infant intelligence at 19 months were present also at the 5.5 years evaluations, and whether the 19 months and 5.5 years results were consistent with each other. The authors concluded that evidence of a small influence by social and environmental variables at 5.5 years was not consistent internally or with earlier results, suggesting that any statistically significant results could be due to chance.

Focussing on those endpoints that had been measured repeatedly, a longitudinal analysis of the results from the main cohort at 19, 29, months and 5.5 and 9 years was performed (Davidson et al., 2006a). The analyses involved global cognition with a measure of developmental quotient or intelligence quotient (IQ), and scholastic achievement, social behaviour and memory. Recent postnatal exposure was also taken into consideration. No statistically significant relationship between prenatal mercury exposure and the endpoints were found. As in the previous cross sectional studies from the same cohort, key covariates such as the home observation for measurement of the environment score

(HOME) and socio-economic status (SES) were statistically significantly associated with the endpoints.

The data from the nine years follow up (Myers et al., 2003), were re-analysed by Huang et al. (2005) by using semi-parametric additive models with different degrees of smoothing in order to see if nonlinear associations of prenatal exposure were present. The results showed evidence of a nonlinear significant relationship between prenatal total mercury levels and one test, the Grooved Pegboard dominant hand score (a test of motor speed and coordination). The modelling suggested that no effect occurs up to 12 mg/kg in maternal hair, but indicates a slight adverse effect above this exposure level although the uncertainty was high. The data are also summarised in a review (Davidson et al., 2006b).

BMDL calculations were performed on the results from the nine years follow up based on the endpoints reported by Myers et al. (2003), with the addition of another seven endpoints. The average $BMDL_{10}$ across the 26 endpoints varied from 20.1 mg Hg/kg in maternal hair (logistic model) to 20.4 mg/kg (k-power model) (van Wijngaarden et al., 2006).

In order to address the possibility of non-homogenous susceptibility, Huang et al. (2007) re-analyzed the data from the nine-years follow up by using a regression tree approach. According to the authors, the results supported the previous analyses and outcomes in Myers et al. (2003), confirming that there is no consistent evidence for effects from prenatal methylmercury exposure in the Seychelles main cohort.

Thurston et al. (2009) used a Bayesian approach for a generalised linear mixed model to allow the exposure effects to differ across outcomes within and across broad outcome classes (so-called domains). Using this approach they investigate the relationship between prenatal methylmercury exposure and multiple neurodevelopmental outcomes in four domains (cognition, memory, motor, and social behaviour) measured at nine years of age as previously reported (Myers et al., 2003). The authors reported findings consistent with the earlier results analysed by conventional linear regression. The study focused mainly on methodological questions and is therefore not as informative for this evaluation.

An alternative analysis of the data from the nine years follow up study grouping 18 individual endpoints into one ordinal outcome variable as well as grouping by developmental domains, followed by ordinal logistic regression, showed no association between prenatal methylmercury exposure and developmental outcomes (van Wijngaarden et al., 2009).

Davidson et al. (2008a) investigated in multiple linear regression, the association between prenatal mercury exposure and visuospatial ability at approximately 10.5 years by use of the Bender Visual Motor Gestalt Test, which yields scores for a copying task and a reproduction task. The same testing and scoring methods as previously used in the Faroe Island study at seven years (Grandjean et al., 1997) was applied. In contrast to the Faroese results, no statistically significant association between prenatal methylmercury exposure and copying task scores was observed. A significant negative association between methylmercury and reproduction task scores was observed when all participants were included, but this was no longer significant after removing one outlier with low exposure and high reproduction task score.

Subsequently, Davidson et al. (2010) investigated whether scholastic achievement was associated with prenatal or recent postnatal mercury exposure after adjustment for covariates. Primary endpoints were Seychelles nationally standardised end-of-year examination scores given when the cohort children were 9 and 17 years of age (n = 643). Additional analyses were done in a subgroup (n = 215) from the main Seychelles cohort that participated in a regional test (Southern and Eastern African Consortium for Monitoring Educational Quality, SACMEQ) at age nine years. Multiple linear regression analyses showed no pattern of associations between prenatal or recent postnatal exposure, and either the 9- or 17-year end-of-year examination scores. No associations between prenatal exposure and the SACMEQ test score results were seen. However, recent exposure was associated with lower test scores in boys.

The authors could not explain this finding and concluded that they would need confirmation by further studies.

Only recently, Davidson et al. (2011) investigated associations between prenatal methylmercury exposure and subjects' performance on 27 endpoints at the 17 years follow-up study (n = 371 to 462, depending on outcome measure). The test battery included several cognitive performance tests and some measures of problematic behaviours of the pupils. Besides the wide range of confounders reported before, the statistical analyses for all endpoints were adjusted for recent postnatal methylmercury exposure. For 21 out of the 27 endpoints there was no association with prenatal exposure. Better scores on four endpoints (Woodcock_Johnson-II mathematical calculation scores, reduced number of trials on the Intra-Extradimensional Shift set on the Cambridge Neuropsychological Test Automated Battery, fewer reports of substance use and lower incidents of problematic behaviour in school) were seen with increasing prenatal mercury exposure. Statistically significant association between prenatal exposure and the lowest level (1 - 3) of referrals to a school counsellor was seen, but no associations between prenatal exposure and having more than three referrals. According to the authors, the improved performance might be associated with beneficial nutrients in fish and is in line with what has been found previously at lower age in the cohort. In conclusion, there was no consistent pattern of adverse associations between prenatal mercury exposure and the tested outcome variables at age 17 years.

The Nutrition cohort

Davidson et al. (2008b) used the endpoints resulting from the BSID-II at 9 and 30 months of age (n = 229 children with complete outcome and covariate data for analysis). The primary analysis examined the associations between methylmercury, maternal nutrition measures (fish consumption and choline intake by questionnaire data, TSH, the n-3 LCPUFA DHA, the n-6 long-chain polyunsaturated fatty acid (n-6-LCPUFA) arachidonic acid (AA) and iron (Fe) measured in maternal blood) and children's scores on the BSID-II. The adjusted results showed a negative regression coefficient between prenatal methylmercury and the mean PDI scores at 30 months (regression coefficient = -0.55, p = 0.04). Neither the association with prenatal methylmercury alone (described as 'borderline significant', regression coefficient = -0.44, p = 0.07), nor those with nutrition factors were statistically significant. The additional assessments at 5, 9 and 25 months showed no statistically significant association with prenatal methylmercury exposure. The authors concluded that nutritional status and methylmercury exposure may simultaneously influence developmental outcomes in opposite directions and suggested that beneficial influences of fish nutrients and of overall diet need to be taken into account to evaluate the risk of neurodevelopmental effects from prenatal methylmercury exposure.

Analysing the same cohort data set as above, Strain et al. (2008) reported the results of an analysis of the influence of different sets of n-3 and n-6 LCPUFAs measured in mothers' blood at 28 weeks gestation and 1 day after delivery on test results for psychomotor and mental development (PDI and MDI of BSID-II) at the age of 9 and 30 month. They used five covariate adjusted linear regression models: Model 1 was adjusted for DHA + AA, Model 2 for DHA + eicosapentaenic acid (EPA) (as a measure of marine n-3 LCPUFAs) and AA, Model 3 was adjusted for n-3 LCPUFAs (DHA + EPA + alpha-linolenic acid (ALA)) and n-6 LCPUFAs (AA + linoleic acid (LA)), whereas model 4 adjusted for AA to DHA ratio and Model 5 for n-6 LCPUFA to n-3 LCPUFA ratio. In contrast to the results in Davidson et al., (2008b), the statistical models were not adjusted for other nutrition variables. The results showed that maternal serum n-3 LCPUFA exhibited a statistical significant effect on the PDI at 9 months of age ($p < 0.02$). As maternal values for n-3 LCPUFA increased, the PDI scores improved. Similarly, the PDI score was statistically significant inversely related to the n-6/n-3 LCPUFA ratio ($p < 0.02$) at 9 months. As the n-6/n-3 LCPUFA ratio increased the PDI scores declined. There were no such significant coefficients in the regression analysis with the MDI at 9 or 30 months and the PDI at the 30-month on the LCPUFA indices with or without adjusting for methylmercury exposure. The associations found were strongest when prenatal methylmercury exposure was included in the analyses. The 30-months PDI, but not the 9 months PDI, decreased statistically significantly ($p < 0.04$)

with increasing prenatal mercury exposure when the LCPUFA measures were included in the regression analysis.

Stokes-Riner et al. (2011) used the same data as Strain et al. (2008) and Davidson et al. (2008b), but instead of analysing the data of the two examinations at age 9 and 30 month separately, they combined the outcomes at the two ages in a longitudinal analysis taking the intra-individual association between the first and the second test results into account. This reflects much better the hypothesis that prenatal methylmercury exposure might influence the individual level of psychomotor performance in childhood. Effectively the power of the study is increased. In addition, the longitudinal model allowed exploration of whether methylmercury, LCPUFA, and/or covariate effects on the PDI change from 9 to 30 months. The results show a statistically significant negative (adverse) effect relationship between maternal hair mercury and the children's psychomotor performance (PDI scale) scores. At the same time a significant beneficial relationship between maternal n-3 LCPUFA (measured by DHA + EPA + ALA or only DHA), and cognitive function was shown. Neither association was changed significantly as the children aged. The authors viewed the combination of a significant positive association of n-3 LCPUFAs together with a significant negative association of methylmercury exposure on the children's development as an indication of the need to adjust for maternal nutrition when studying the potential effects of prenatal methylmercury exposure.

Lynch et al. (2011) fitted varying coefficient function models to explore interaction between outcome data from the Nutrition cohort at 9 and 30 months (BSID-II, MDI, PDI), maternal prenatal hair mercury levels and maternal nutritional status by the five fish nutritional components described by Davidson et al. (2008b). The relationship between the five nutrition components and the outcomes was allowed to change as levels of methylmercury change by allowing the regressions coefficients to change as a function of the methylmercury hair levels considered as effect modifiers. A possible effect modification was modelled as a smooth function (using a penalised spline function) of methylmercury in maternal hair. The results of this statistical analysis indicated that increasing levels of methylmercury exposure are associated with a loss of benefit from the nutritional covariate DHA. This finding is observed for all four outcomes (MDI and PDI at 9 and 30 months) at the higher levels of methylmercury exposure. At approximately 11 mg/kg maternal hair mercury, the slope function became negative for the PDI at 30 months, and DHA was no longer positively associated with outcome. The authors stressed that there were few observations above 11 mg/kg with increased variability in function estimates. DHA seemed to be positively associated with the test results from the PDI at the age of 30 months, while the benefits were outweighed by the negative influence of prenatal methylmercury exposure when the mother's methylmercury hair was above about 11 mg/kg. It should be mentioned that this endpoint was also statistically significant in the analysis of Davidson et al. (2008b). The results of data analysis indicate that the beneficial impact of DHA on developmental outcomes may be increasingly attenuated as the prenatal methylmercury exposure increases.

Recently, the five years follow up, which included a battery of developmental tests giving in total ten outcomes, was published (Strain et al., 2012). The developmental tests measured dexterity and finger tapping speed (dominant and non-dominant hand), language by the Preschool Language Scale Revision Edition (yielding a total language score and scores for verbal ability and auditory comprehension), the Woodstock Johnson Scholastic Achievement Test (letter word recognition and applied problems), and behaviour by the Child Behaviour Checklist. Child's IQ was estimated by the Kaufman Brief Intelligence Test, comprising one subtest for verbal knowledge and one for matrices. Associations between test outcomes and different combinations of maternal LCPUFA status were investigated by covariate-adjusted linear regression models, without and with adjustment for prenatal mercury exposure. Analyses to investigate relationships between prenatal mercury exposure and developmental outcomes without adjusting for maternal LCPUFA status were also conducted. Neither were any statistically significant associations found, nor were there any of the point estimates in an adverse direction. Improved test results on preschool language scores were associated with increasing maternal DHA, and diminished with increasing maternal AA. Of note, in contrast to findings at 9 and 30 months in the Nutrition Cohort, prenatal methylmercury was not significantly associated with any outcome in any of the models applied. This observation was not discussed by the authors in relation to

the previous findings of such associations after adjustments for LCPUFAs (Strain et al., 2008; Lynch et al., 2011; Stokes-Riner et al., 2011).

Summary

In summary, reassessments of the 4.5 years results and the 10.5 and 17 years follow up studies from the Main Cohort in the SCDS have not revealed any consistent association between prenatal mercury exposure and neurodevelopmental endpoints. Studies in this cohort did not allow for adjustment for n-3 LCPUFAs. The major new developments are coming from the results from the smaller Nutrition Cohort. The new results indicate a negative association between prenatal mercury exposure and neurodevelopmental endpoints at 9 and 30 months when the n-3 LCPUFA concentration in maternal blood was taken into account. A possible effect modification was modelled as a smooth function of methylmercury in maternal hair. The results indicated that increasing levels of methylmercury exposure are associated with a loss of benefit from the nutritional covariate DHA, and an apparent NOEL at a mercury level of approximately 11 mg/kg maternal hair was observed. No statistically significant associations between prenatal mercury exposure and developmental endpoints were found at the five years follow up of the study and a positive association between maternal prenatal DHA and preschool language scores was reported.

C. Other regions

In addition to the large cohort studies previously mentioned, several smaller cohort and cross-sectional studies have been published. These studies are summarised below and in Table 24.

Prenatal high exposure and observations later in life

Possible effects of relatively high mercury exposure have been studied in a birth cohort with Inuit children born in Nunavik, Canada. These children also had a considerable prenatal exposure to PCB. A follow-up of neuromotor function in 109 children at the age of five years only showed statistically significant associations to prenatal mercury in multivariate linear regression analyses (geometric mean total mercury in cord blood: 15.9 µg/L) for a measure of tremor in pointing movements, but no associations were found with other functions or reaction time (Després et al., 2005). No significant confounder-adjusted regression between cord blood mercury concentration and behavioural outcomes from the BSID-II or observational data related to attention and level of activity was seen (Plusquellec et al., 2010). Visual evoked potentials were studied in a subset of 78 children (Saint-Amour et al., 2006). These potentials are responses (to visual stimuli) that can be electrophysiologically measured and recorded. Three components were observed (N75, P100, N150) at three contrasts (95, 30, and 12 %). Increased latency of the P100 component at 30 % contrast was statistically significantly associated with cord blood mercury concentration in confounder-adjusted linear regression analysis, but not with other measures. In contrast, decreased latencies, i.e. not the direction that a priori was thought to be adverse, were associated with current child mercury for both N75 and P100, at both 95 and 30 % contrast. Further, auditory electrophysiological testing was made in 116 Inuit children at the age of 11 years, revealing associations between cord blood mercury and slower reaction times and greater amplitude and delayed latency of the N1 wave in linear regression analyses, suggesting effects of these relatively high exposures on early processing of sensory information (Boucher et al., 2010). In addition, the authors reported that mercury concentrations were not related to any outcomes in a Go/No-go trial, but that prenatal mercury exposure interacted significantly with prenatal lead exposure on certain outcomes (Boucher et al., 2012).

Chevrier et al. (2009) conducted a cross sectional study of visuospatial performance in 395 Amazonian children aged 7 - 12 years from three villages in Brazil (n = 263) and two villages in French Guyana (n = 172). The subscales of the Stanford–Binet Copying test included the active reproduction of three- and two-dimensional designs with pencil and paper. The authors used a relaxed evaluation scheme (avoiding simple solved/unsolved categorisation) for documentation of performance in order to achieve higher discrimination in the test score distribution as well as

information about the types of errors made by the children. Hair-mercury concentration was available for 95 % of these children from the child's own sample and for 68 % from the mother's sample. The main mercury source was oral exposure via fish consumption. The hair mercury results show a dependency of concentration to the vicinity to gold-mining sites. The correlations between maternal and child hair-mercury concentrations was lower in villages in French Guyana (r = 0.09 - 0.28) than in Brazilian villages (r = 0.50 - 0.57). The confounder-adjusted regression analysis on the joint Brazil and the French Guyana data set indicated that the hair-mercury concentrations of both the child and the mother are associated negatively with both the test performance in both subscales (copying and block score). No interaction between sex and mercury exposure was observed for performance. According to the authors, the deficit on the Stanford-Binet Copying task of children with hair mercury of 10 mg/kg compared to children with a 1 mg/kg level corresponds to a developmental delay equivalent of at least two years. Impacts of prenatal and postnatal exposure could not be distinguished.

Prenatal low and moderate exposure and observations later in life

Oken et al. (2005) studied infant cognition by the percent novelty preference on visual recognition memory testing at 6 months of age in a subset of 135 children of a US cohort. The children whose mothers had consumed much fish performed better in a visual recall test than children of mothers with little fish consumption. This association was stronger when the regression was adjusted for mother's hair mercury level. In the adjusted model, each additional weekly fish serving was associated with a 4.0 points higher score (95 % CI: 1.3 - 6.7). An increase of mother's hair mercury level by one mg/kg was associated with a 7.5 points decrement (95 % CI: -13.7 to -1.2) in test score. The mean maternal hair mercury was 0.55 mg/kg with a range of 0.02 - 2.38 mg/kg. A larger number of children from the same cohort (n = 341, possibly including the 135 from the previous study) was followed up at the age of three years, with developmental aspects tested by the Peabody Picture Vocabulary Test, and the Wide Range Assessment of Visual Motor Abilities (Oken et al., 2008). The pattern from the previous study was repeated, with a positive association to fish consumption and a negative association to prenatal mercury exposure, this time assessed through red blood cell mercury concentration. The overall scores for both tests were decreased in children of women with a mercury concentration in the highest decile (> 9.1 ng/g red blood cells, in this cohort roughly corresponding to a hair mercury concentration of 1.2 mg/kg), after adjustment for fish intake. Though the reports provide data on associations with methylmercury exposure, the main focus was on the apparently beneficial effects of fish consumption.

A study on inhabitants living by Lake Ontario (n = 212) focusing on cognitive development and prenatal PCB exposure found no effect of mercury exposure. A statistically significant interaction between cord blood PCBs and maternal hair mercury concentration was however seen on the outcome at 38 months, but not at 4.5 years (137 children were included in the interaction analysis; Stewart et al., 2003). Cognitive performance was assessed by the McCarthy General Cognitive Index. The median maternal mercury in hair was 0.50 mg/kg. At nine years of age, a test was performed by 183 of the children, of which 145 had both methylmercury and PCB data. The test required that the child managed delays and inhibitions in response. Impaired performance was statistically significantly associated with maternal hair mercury ($p = 0.03$ in a regression model controlled for PCB exposure), as well as with maternal PCB ($p = 0.02$, controlled for maternal hair mercury) (Stewart et al., 2006).

A cohort of 151 New York children born in the period after 11 September 2001 had cord blood and maternal blood mercury data. The children were followed at 12, 24, 36 and 48 months of age. No associations were found between cord blood mercury concentration and the BSID-II results at the first three follow-ups, except for an association observed with a reduction in PDI at 36 months (n = 111, $p = 0.002$) when applying linear regression. Data from 48 months showed reduced cognitive performance (on the Wechsler Preschool and Primary Scale of Intelligence, Revised) with increased cord-blood mercury (n = 107, $p < 0.001$). The model contained possibly an excessive number of variables, considering the limited number of individuals studied (Lederman et al., 2008).

Development (BSID-II) was also studied by a case-control design within a birth cohort with 233 children from Krakow, Poland. Thirty-six of the children were categorised as having delayed performance at one year of age (cases). These children's mothers had higher blood mercury during pregnancy than the mothers of children with normal performance (controls) (geometric mean: 0.75 vs. 0.52 µg/L; p = 0.010). The same difference was close to statistical significance also for cord blood mercury (Jedrychowski et al., 2006). The cohort was then somewhat increased (n = 374) at examination at two and three years of age and the findings did not confirm results from age one year. Further analysis of the PDI and MDI at the two- and three-year follow-ups showed no statistically significant associations (Jedrychowski et al., 2007a).

In addition to the above studies, Daniels et al. (2004) showed statistically significantly lower odds ratio (OR) when associating low developmental assessment scores with higher frequency of maternal fish intake during pregnancy but found no link to prenatal mercury exposure in a subset of 1 054 children from a larger cohort in Bristol, UK. Cord tissue mercury levels (not cord blood) were used for exposure assessment, making comparisons with other studies difficult.

A Japanese cross-sectional study utilised mothers' hair sampled at the time of the investigation when the children were aged approximately seven years, as a possible proxy for maternal mercury levels during pregnancy. Children of mothers who had changed their dietary habits since pregnancy were not included. The study did not reveal any conclusive association for measures of postural sway, tremor, coordination, reaction time, brainstem evoked potentials or HRV with maternal hair-mercury levels at the time of the examination (Murata et al., 2004a). The median maternal hair mercury was 1.63 mg/kg (range: 0.11 - 6.86 mg/kg). Corresponding values for the children at approximately seven years were 1.65 (0.35 - 6.32) mg/kg.

The association between prenatal mercury exposure and fish intake on the one hand, and Attention Deficit Hyperactivity Disorder (ADHD)-related behaviour on the other hand, was investigated in a birth cohort (recruited in 1993 - 1998) in New Bedford, Massachusetts, US (Sagiv et al., 2012) using regression models. Total hair mercury concentrations were analyzed in maternal hair samples collected approximately 10 days postpartum (n = 421) with a median level of 0.45 mg/kg. There were statistically significant associations observed between hair mercury levels and ADHD-related behaviours at age eight years, including inattention and hyperactivity. For outcomes on the Conners Rating Scale-Teachers and CPT reaction time, the authors determined a so-called 'apparent threshold' of approximately 1 mg Hg/kg for ADHD-related behaviour. On the other hand, slightly negative associations of mercury exposure with ADHD-related behaviour were detected at mercury levels below 1 mg/kg. In addition, for some of the outcomes, associations were primarily found in boys. A protective association for fish consumption was found with ADHD-related behaviours, particularly impulsive/hyperactive behaviours.

Observations at birth

A Japanese study of 498 newborn babies found an association ($p < 0.05$ in multiple regression analysis) between neonatal performance at 3 days of age and maternal hair mercury concentrations of 0.29 - 9.35 mg/kg (median 1.96 mg/kg; Suzuki et al., 2010). The relation was adjusted for maternal PCB level. The slope of the regression became steeper after adjustment for seafood intake, while further adjustment for other potential confounders only had a marginal effect.

A study of 384 babies at 3 days of age, born in the Zhejiang Province, China (geometric mean for maternal hair mercury: 1.2 mg/kg), evaluated associations between neonatal behavioural and maternal mercury exposure. For boys, the probability of not getting full score on behaviour, was statistically significant associated with maternal mercury exposure in a logistic regression model. This was not seen for girls, and not for active and passive tones as endpoint (Gao et al., 2007).

Concluding comments on studies from other regions

For cognitive outcomes, a few, but not all, studies found associations with mercury at levels lower than those reported in the Faroe Islands and Seychelles cohorts, but the overall picture at low-level exposure does not provide information to allow conclusions. In addition, there are indications of beneficial effects of fish consumption. In conclusion, these studies did not provide a better basis for dose response assessment than the studies in the Faroe Islands and Seychelles.

Table 24: Overview of epidemiological data on prenatal mercury exposure and neurodevelopmental and neurotoxic endpoints in children.

Author (country)[c]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[e]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Faroe Islands						
Murata et al. (2004b)	Longitudinal cohort study, Faroese Cohort 1	859 children, age: 14 years	THg in cord blood: GM 22.6 (IQR 13.2-40.8) µg/L (highly correlated to maternal hair). THg in maternal hair: GM 4.22 (IQR 2.55-7.68) mg/kg. THg in hair at 7 years: GM 0.60 (IQR 0.34-1.24) mg/kg. THg in hair at 14 years: GM 0.96 (IQR 0.45-2.29) mg/kg	BAEP	Increased latencies III and V by about 0.012 ms by doubling in cord blood Hg concentration. BMDLs similar as those obtained at 7 years. Child's hair Hg at age 14 years associated with prolonged III-V interpeak latencies. The results indicate that some associations between prenatal exposure and neurotoxic endpoints extend into the teenage period	Age, gender, PCB exposure (from cord tissue of 438 cohort members)
Debes et al. (2006)	Longitudinal cohort study, Faroese Cohort 1	860 children, age: 14 years	THg in cord blood: GM 22.5 (IQR 13.1-40.8) µg/L THg in maternal hair: GM 4.21 (IQR 2.53-7.66) mg/kg THg in hair at7 years: GM 2.99 IQR 1.71-6.20) mg/kg[d] THg in whole blood at 7 years: GM 9.00 (IQR 5.00-18.4) µg/L THg in hair at 14 years: GM 0.96 (IQR 0.45-2.29) mg/kg THg in whole blood at 14 years: GM 4.08 (IQR 2.29-7.46) µg/L	motor, attention, working memory/executive function, language, visuospatial and memory functions and mood status	Prenatal Hg exposure associated with decreased finger tapping speed, reaction time in a CPT, and cued naming, but associations were weaker than at 7 years	Age, gender, maternal Raven score, domicile, maternal and paternal employment, time of the day at testing, used language, computer game experience, the participant's grade in school. Prenatal PCB (cord tissue of 438 cohort members) was considered but not statistically significant

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Faroe Islands (continued)						
Budtz-Jørgensen et al. (2007b)	Longitudinal cohort study, Faroese Cohort 1	917 children, age: 7 years 860 children, age: 14 years	7 years (Grandjean et al., 1997): THg in cord blood: GM 22.9 (IQR 13.4-41.3) µg/L THg in maternal hair: GM 4.27 (IQR 2.6-7.7) mg/kg THg in hair at 7 years: GM 2.99 (IQR 1.7-6.1) mg/kg 14 years: see Debes et al. (2006)	motor, attention, working memory/executive function, language, visuospatial and memory functions and mood status	Fish intake improved test scores statistically significant for the motoric performance (7 and 14 years) and for the functioning in tasks for spatial orientation and operations (14 years).	Not specified, refers to Grandjean et al. (1997) and Budtz-Jørgensen et al. (2007a) PCB exposure was not included as a covariate
Budtz-Jørgensen et al. (2010)	Longitudinal cohort studies Faroese Cohort 1 and Faroese Cohort 2	Faroese Cohort 1: about 860 children, age: 7 years Faroese Cohort 2: about 182 children, age: 7 years	Faroe 1: see Murata et al. (2004b), Debes et al. (2006) Faroe 2 (Steuerwald et al., 2000): THg in cord blood: GM 20.4 (range 1.90-120) µg/L THg in cord serum: GM 2.54 (range 0.70-8.74) µg/L THg in maternal hair: GM 4.08 (range 0.36-16.3) mg/kg	motor, attention, working memory/executive function, language, visuospatial and memory functions	The joint analysis using a structural equation model approach showed statistically significant negative coefficients association between prenatal Hg exposure and the verbal function variable while the motor function variable was close to significance. A very close agreement between the cohorts was seen for the Boston Naming Test, whereas the effect estimates for the other outcomes showed less convinced agreement (although test for equality were non-statistically significant except for 'NES2 Finger tapping – preferred hand).	The effect of PCBs were also investigated and a set of variables identified by Grandjean et al. (1997) were included in the models. Finally, the number of maternal pilot whale dinners during pregnancy was included in the models.
Julvez et al. (2010)	Longitudinal cohort study, Faroese Cohort 1	860 children, age: 14 years	See Murata et al. (2004b), Debes et al. (2006)	CPT-HRT latencies	The test phase regarded as indicators of sustained attention by the authors showed the strongest associations with prenatal Hg exposure. Current proximal hair Hg concentrations did not show any clear association structure.	Similar to Debes et al. (2006). In addition in further analyses, Catsys scores, and CPT-HRT during the first 2 min

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: main cohort (SCDS)						
Davidson et al. (2004)	Longitudinal cohort study SCDS	711 children, age: 5.5 years	THg in maternal hair: P50: 5.9 (range 0.5-26.7) mg/kg THg in hair at 5.5 years: P50: 5.8 (range 0.9-26) µg/g	Cognitive ability, language development, drawing and copying, Letter-Word recognition, scholastic achievement, and child behaviour.	No consistent associations between prenatal mercury exposure and the measured outcomes.	Caregiver intelligence, the Hollingshead measure of socioeconomic status, home environment, gender, recent postnatal Hg exposure. Low levels of Pb not considered, 28 PCBs below LOD.
Huang et al. (2005)	Longitudinal cohort study SCDS	643 children, age: 9 years Reassessment of results from Myers et al,, 2003	THg in maternal hair: µ ± SD: 6.9 ± 4.5 mg/kg. THg in hair at 9 years: µ ± SD: 6.1 ± 3.5 mg/kg.	neurocognitive, language, memory, motor, perceptual-motor, behavioural functions as described in Myers et al., 2003	Re-analysis by using semi-parametric additive models with different degrees of smoothing showed little evidence for adverse effects from prenatal mercury exposure in the Seychelles main cohort.	Sex, maternal age, examiner, caregiver's intelligence, the child's medical history, family resource scale, number of biological parents living with the child, Hollingshead measure of socioeconomic status, Henderson's early learning process scale, child's age at testing, Home environment during toddlerhood, the child's hearing score, recent postnatal Hg exposure

Table 24: Continued.

Author (country)[c]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[e]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: main cohort (SCDS) (continued)						
Davidson et al. (2006a)	Longitudinal cohort study SCDS	738 children, age: 19 months 736 children, age 29 months 711 children, age: 5.5 years 643 children, age: 9 years	THg in maternal hair: μ ± SD: 6.8 ± 4.5 (range 0.5-26.7) mg/kg. THg in hair at 5.5 years: μ ± SD: 6.5 ± 3.3 (range 0.9-25.8) mg/kg THg in hair at 9 years: μ ± SD: 6.1 ± 3.5 (range 0.5-24.8) mg/kg[a] THg in hair at 19 and 29 months not reported by Davidson et al. (1995)	global cognition, reading and mathematics scholastic achievement, social behaviour and memory	No statistically significant association between prenatal MeHg exposure and child development.	Sex, maternal age at child's birth, birth weight, the child's medical history, alcohol consumption during pregnancy, the child's hearing status as measured by portable audiometry, the preschool version of the HOME, caregiver intelligence, the Hollingshead measure of socioeconomic status, the Family Resource Scale and the Henderson Environmental Learning Profile Scale
Davidson et al. (2008a)	Longitudinal cohort study SCDS	613 children, age: 10.7 years	THg in maternal hair: μ ± SD: 6.83 ± 4.4 mg/kg THg in hair at 9 years[b]: μ ± SD: 6.07 ± 3.5 mg/kg, see additional information in Davidson et al. 2006a	Visuospatial ability	No statistically significant association between prenatal MeHg exposure and visual motor coordination	Sex, maternal age, the child's medical history, the child's age at testing, the tester who administered the Bender, the preschool version of the HOME, caregiver intelligence, the Hollingshead measure of socioeconomic status, the Family Resource Scale, the Henderson Environmental Learning Profile Scale to measure the quality of stimulation in the current home environment, Child's hair THg at 9 years, and the child's hearing status measured by audiometry at age 9 years.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: main cohort (SCDS) (continued)						
Davidson et al. (2010)	Longitudinal cohort study SCDS	643 children, age: 9 and 17 years	THg in maternal hair: μ±SD: 6.89 ± 4.52 mg/kg THg in hair at 9 years: μ±SD: 6.09 ± 3.47 mg/kg, THg in hair at 17 years: μ±SD: 8.00 ± 4.68 mg/kg The SACMEQ subgroup had higher levels of THg in hair at 9 years (μ±SD: 7.48 ± 3.98 vs 5.39 ± 2.94	Scholastic achievements in nationally standardised end-of-year examinations given at 9 and 17 years of age, and a regional test called SACMEQ at 9 years in a subgroup (n = 215)	No pattern of associations between prenatal or recent postnatal exposure with the 9- or 17-year end-of-year examination scores. No associations between prenatal exposure and the SACMEQ test score results were seen. However, recent postnatal exposure had a negative association with these test scores in boys.	From home and family: Family Resource Scale, the Henderson Environmental Learning Profile Scale to measure home environment, caregiver's intelligence, socioeconomic score. From 9 years study on child: sex, region of school attendance, child's IQ, the long delay free recall score from the California Verbal Learning Test, Visual Memory, and the total T score from the child behaviour. For SACMEQ endpoints: teachers competence
Davidson et al.(2011)	Longitudinal cohort study SCDS	371 to 462 children (n depends on the outcome. measure), age: 17 years	THg in maternal hair: μ±SD: 6.89 ± 4.40 (range 0.54 – 22.74) mg/kg. THg in hair at 17 years: 7.98 ± 4.64 (range 0.33-28.33) mg/kg.	Cognigitive functions including verbal learning, memory, learning and reversal learning and attention and measures of problematic behaviours	No consistent pattern of adverse associations between prenatal mercury exposure and the tested outcome variables at age 17 years was found.	All models adjusted for sex, socioeconomic status, maternal intelligence and recent postnatal Hg exposure. All neurocognitive endpoints adjusted for child' age at testing. The youth risk behaviour an problematic behaviour endpoints were adjusted for IQ measures at 107 months.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: nutrition cohort (SCDNS)						
Davidson et al. (2008b)	Longitudinal cohort study SCDNS	229 children, age 5, 9, 25 and 30 months	THg in maternal hair: μ ± SD: 5.7 ± 3.7 (range: 0.2-18.5) mg/kg	Main outcomes tested were mental and psychomotor development (BSID-II) at 9 and 30 months). In addition, novelty preference and VRM at 5 and 9 months. Aspects of planning, inhibition, attention and working memory at 25 months	The adjusted results showed a negative association between prenatal methylmercury and the mean PDI scores on BSID-II at 30 months (r -0.55, p = 0.04). The association with prenatal methylmercury alone was 'borderline statistically significant', (r -0.44, p = 0.07). The additional assessments at 5, 9 and 25 months showed no association with prenatal methylmercury exposure. The results suggest that maternal fish intake is a possible confounder in studies that investigate the associations between prenatal MeHg exposure and child development.	Maternal blood TSH, DHA, AA, Fe, estimated choline intake, fish consumption, socioeconomic status, home environment, maternal intelligence, the tester for each child (except BSID-II), birth weight, maternal age sex, both parents living with the child at 9 months.
Strain et al. (2008)	Longitudinal cohort study SCDNS	229 children, age: 9 and 30 months	See Davidson et al, 2008b	mental and psychomotor development (BSID-II)	Maternal serum n-3 LCPUFA measured during the last trimester was positively associated with the PDI at 9 months of age. PDI score was inversely related to the n-6/n-3 ratio. Associations between maternal measures of n-3 LCPUFA and positive outcome were strengthened when the confounding factor of prenatal exposure to methylmercury was adjusted for in the regression models.	Same as Davidson et al, 2008b, but not including maternal blood TSH, Fe, estimated choline intake and fish consumption

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Seychelles: nutrition cohort (SCDNS) (continued)						
Lynch et al. (2011)	Longitudinal cohort study SCDNS, longitudinal analysis approach	See Davidson et al., 2008b	See Davidson et al., 2008b	mental and psychomotor development (BSID-II)	The positive effect of DHA on the outcomes (MDI and PDI at 9 and 30 months) was absent or reduced at higher Hg levels (approximately 11 mg/kg). The number of observation with high mercury levels in the study were small.	The same covariates were used as by Davidson et al. (2008b).
Stokes-Riner et al. (2011)	Longitudinal cohort study SCDNS, longitudinal analysis approach	228 children, age 9 and 30 months	See Davidson et al., 2008b	psychomotor development (BSID-II)	Maternal THg was negatively associated with PDI, whereas maternal n-3 LCPUFA was positively associated with PDI. The association was not different at 9 and 30 months of age.	Maternal blood n-3 and n-6 LCPUFAs, socioeconomic status, home environment, maternal intelligence, birth weight, maternal age, sex, both parents living with the child at 9 months
Strain et al. (2012)	Longitudinal cohort study SCDNS	225 children, age: 5 years	THg in maternal hair: μ ± SD: 5.7 ± 3.7 (range: 0.2-18.5) mg/kg	Different outcomes for child development from tests on finger tapping, language, letter word recognition and applied problems, child behaviour, Child's IQ	No statistically significant associations between prenatal mercury exposure and developmental outcomes. Improved test results on preschool language scores were associated with increasing maternal DHA, and diminished with increasing maternal AA.	Sex, number of immediate family members living with the child, maternal age, maternal IQ, socioeconomic status, home environment, child age at testing, birth weight. Different combinations of LCPUFAs in prenatal maternal serum included in different models
South America						
Chevrier et al. (2009) (Brazil and French Guiana)	Cross-sectional study	395 children, age 9.5years,	THg in maternal hair: μ±SE: 10.3 ± 0.5 (range 0.6-41.7) mg/kg THg in hair at 9.5 years: μ±SE: 9.8 ± 0.4 (range 0.5-63.8) mg/kg Correlation child's hair-mother's hair: Higher (r = 0.5-0.57) in Brazil than in French Guiana (r = 0.09-0.28).	Visuospatial ability (Stanford-Binet Copying test)	Mercury exposure negatively associated with scores on the drawing/rotation task: a score reduction of 1.2 (SE 0.3) points was observed in the children with a hair-mercury concentration above 10 mg/kg compared to those with a hair level below 1 mg/kg; the associations appeared to be stronger in the younger children. Components of the test varied according to the study site (e.g. Block organization). Separate impact of pre- and postnatal exposure could not be distinguished	Age, sex, village, maternal marital status, education, alcohol consumption during pregnancy. Maternal Raven Score not determined in the Brazilian study, maternal education used as proxy.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Europe						
Daniels et al. (2004) (United Kingdom)	Longitudinal cohort study	1054 children, age 15 and 18 months	THg in cord tissue: GM ± SD: 0.01±0.4 (IQR of 0.0076-0.0220 mg/kg,	Language and communication development (MCDI) at 15 months, and language, social, fine and gross motor skills (DDST) at 18 months, both assessed by the child's mother and returned by mail.	No association to Hg after adjustments. No crude results given.	Child's age at testing, sex, birth order, fish intake, breastfeeding status, and maternal fish intake, age, education, dental treatment, smoking and alcohol use during pregnancy, and HOME score.
Jedrychowski et al. (2006) (Poland)	Longitudinal cohort study	233 children, age: 1 year	THg in cord blood: P50: 0.85 µg/L, GM: 0.88 (range: 0.10-5.00) µg/L THg in maternal blood: P50: 0.60 µg/L, GM: 0.55 (range: 0.10-3.40) µg/L µg/L	mental and psychomotor development (BSID-II), dichotomised into normal and delayed performance.	36 children with delayed performance had higher maternal blood Hg than those with normal performance (GM: 0.75 vs. 0.52 µg/L; p = 0.010). The same association was close to statistical significance also for cord blood Hg. In a logistic regression model, the RR for delayed performance at maternal blood Hg > 0.50 µg/L was 2.82, 95 % CI 1.17-6.79 (3.58; 1.40-9.14 for cord blood Hg > 0.80 µg/L).	Sex, gestational age, maternal age, and maternal education was used as covariates in the logistic regression model.
Jedrychowski et al.(2007a) (Poland)	Longitudinal cohort study	374 children, age: 1, 2 and 3 years	THg in cord blood and maternal blood. Concentrations not given, but can be assumed to be similar to those in Jedrychowski et al., 2006.	mental and psychomotor development (BSID-II)	Mental and Psychomotor Development Indices showed negative association with cord blood Hg (dichotomised with cut-off at 0.90 µg/L) at 1 year (p = 0.01 and 0.04, respectively), but not at 2 or 3 years (p-values between 0.20 and 0.42)	Sex, environmental tobacco smoke, parity, and maternal education.
North America						
Després et al. (2005) (Canada)	Longitudinal cohort study	109 Inuit children, age: 5.4 years (mean).	THg in cord blood: µ ± SD: 22.2 ± 18.4 µg/L, GM15.9 (range: 1.8-104.0) µg/L	Different measures of neuromotor function	No association to Hg for reaction time, measures related to sway or alternating movements. Both prenatal Hg and current Pb was associated with tremor in pointing movements.	Pb. A range of other covariates considered, including PCB and socioeconomic factors.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
North America (continued)						
Saint-Amour et al. (2006) (Canada)	Longitudinal cohort study	78 Inuit children, age: 5.4 years (mean) (Same cohort as Després et al., 2005)	THg in cord blood: μ ± SD: 24 ± 20 μg/L, GM: 17 (range: 1.8-104) μg/L THg in blood at 5.4 years: μ ± SD: 10 ± 9 μg/L GM: 5.9 (range: 0.2-38) μg/L	Latency (ms) and amplitude (μV) of visual evoked potentials as measured in electrophysiological recordings at three different contrasts, three components each (N75, P100, N150)	Increased latency of the P100 component at 30 % contrast was associated with cord Hg after confounding adjustment. Decreased latencies were associated with current child Hg for both N75 and P100, at both 95 and 30 % contrast.	Considered confounders included socioeconomic variables, caretakers education, n-3 LCPUFA, and PCB.
Boucher et al. (2010) (Canada)	Longitudinal cohort study	116 Inuit children, age: 11 years	THg in cord blood: μ ± SD: 21.5± 18.8 μg/L, P50: 14.2 (range: 1.8-99.3) μg/L μg/L THg in blood at 11 years: μ ± SD: 4.69 ± 4.9 μg/L, P50: 2.8 (range: 0.2-28.1) μg/L	ERPs in EEG recording	MeHg in cord blood was associated with slower reaction times and greater amplitude and delayed latency of the N1 wave. Current blood Hg was not associated with outcome.	DHA, Se, Pb, PCB, breast-feeding. Other factors were considered, e.g. mother's smoking and alcohol consumption.
Plusquellec et al. (2010) (Canada)	Longitudinal cohort study	110 Inuit children, age: 5.4 years, (Same cohort as Després et al., 2005 and Saint-Amour et al., 2006)	THg in cord blood: μ±SD: 22.2 ± 18.4 (range: 1.8-104.0) μg/L THg in blood at 5.4 years: μ ± SD: 9.6 ± 8.9 (range: 0.2-38.2) μg/L	behaviour, attention and emotional expression, (including the Infant Behaviour Rating Scale from BSID-II and observational data).	No associations between outcomes and Hg	Considered confounders included socioeconomic variables, caretakers education, cord and child's Se and LCPUFA, PCB and lead.
Boucher et al. (2012) (Canada)	Longitudinal cohort study (same cohort as Boucher et al., 2010	193 Inuit children, age: 11 years	THg in cord blood: μ ± SD: 21.2 ± 17.6 μg/L, P50: 16.6 (range: 1.0-99.3) μg/L THg in blood at 11 years: μ ± SD: 4.69 ± 4.9 μg/L, P50: 2.8 (range: 0.2-28.1) μg/L	ERPs in EEG recording, but the N1 wave, for which Hg associations have been observed, was not included.	No associations with Hg in adjusted model, but interaction with effects of other contaminants was suggested.	PCB and Pb, which were the pollutants in focus

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
North America (continued)						
Stewart et al. (2003) (USA)	Longitudinal cohort study follow up at 38 months and 4.5 years of age	212 children, age: 38 months and 4.5 years	THg in maternal hair, first half of pregnancy: P50: 0.50 (IQR 0.40-0.60) mg/kg THg in maternal hair, second half of pregnancy: P50: 0.50 (IQR 0.40-0.70) mg/kg	Cognitive performance, as assessed by the McCarthy General Cognitive Index.	No direct association between cognitive performance and Hg was observed, but an interaction between cord blood PCBs and maternal hair Hg was found at 38 months, but not at 4.5 years	A large range of covariates was considered, including maternal and paternal factors, nutrition, drugs, etc, but not variables related to fish consumption or n-3 LCPUFAs.
Oken et al. (2005) (USA)	Prospective cohort study	135 children, age: 6 months.	THg in maternal hair: µ: 0.55 (range: 0.02-2.38) mg/kg	VRM (assessing the magnitude of preference for the child to look at a picture of new face, as compared to a picture of a face the child has seen before).	For each additional weekly fish serving, the VRM score was 4.0 points higher (95 % CI: 1.3-6.7) after adjusting for Hg, for which each mg/kg was associated with a 7.5 points decrement (95 % CI: -13.7 to -1.2).	Participant characteristics, such as maternal age, education, marital status, birth weight, etc.
Stewart et al. (2006) (USA)	Longitudinal cohort study	183 children, age: 9.5 years (from the same cohort as Stewart et al., 2003)	THg in maternal hair at first or second half of pregnancy: µ: 0.56 mg/kg	Performance on a task that requires the child to manage delays in response, a so called differential reinforcement of low rates schedule.	Impaired performance was associated with maternal hair Hg ($p = 0.029$ in a model controlled for PCB exposure).	A large range of covariates was considered, including maternal and paternal factors, nutrition, drugs, etc, and also PCB, but not variables related to fish consumption or n-3 LCPUFAs.
Lederman et al. (2008) (USA)	Longitudinal cohort study	151 children with at least one follow-up (at 1, 2, 3, or 4 years of age) .	THg in cord blood: µ ± SD: 7.82 ± 9.71µg/L, P50: 4.3 (range: <0.2-63) µg/L THg in maternal blood: µ±SD: 2.32 ± 2.3µg/L, P50: 1.7 (range: <0.14-16.4) µg/L	Mental and psychomotor development at 1, 2, and 3years (BSID-II), and performance, verbal and full IQ scores at 4 years (Wechsler Preschool and Primary Scale of Intelligence, Revised).	In an adjusted model of outcome vs. Log Hg no associations with cognitive functions was observed at 1 or 2 years. At 3 years an association was observed with PDI ($p = 0.007$) and at 4 years with Performance ($p = 0.023$), Verbal ($p = 0.023$), and Full IQ scores ($p = 0.002$).	Race, maternal IQ, per capita family income, and child's sex and gestational age at birth. Another model controlled for additional potential confounders.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
North America (continued)						
Oken et al. (2008) (USA)	Prospective cohort study	341 children, age: 3 years (in part same children as in Oken et al., 2005)	THg in maternal red blood cells sampled during the second trimester: μ ± SD: 3.8 ± 3.8 (range: <0.5-21.9) ng/g	Cognitive performance, as assessed by the Peabody Picture Vocabulary Test, and Wide Range Assessment of Visual Motor Abilities	The overall score for both tests were decreased in children of women with Hg in the highest decile (> 9.1 ng/g, in this cohort roughly corresponding to hair Hg 1.2 mg/kg), after adjustment for fish intake, which was associated with increased scoring.	Fish intake and other potential confounders, such as gestational length, primary language, maternal vocabular test score and education.
Sagiv et al. (2012) (USA)	Longitudinal cohort study	421 children, age: 8 years	THg in maternal hair collected about 10 days postpartum: P50: 0.45 (range: 0.03-5.14) mg/kg	Inattentive and impulsive/hyperactive behaviour (teacher rating scale and neuropsychological testing)	Statistically significant associations between maternal THg in hair and ADHD-related behaviours at age 8 years. Threshold associations were detected at approximately 1 mg/kg.	Fish intake and other potential confounders. There was a protective association for fish consumption and ADHD-related behaviours.
Asia and other regions						
Murata et al. (2004a) (Japan)	Cross-sectional	210 Japanese children, age: 6.3-7.5 years (mothers have not reported changes of dietary habits since pregnancy)	THg in current maternal hair: P50: 1.63 (range: 0.11-6.86) mg/kg	Postural sway, tremor, ear-hand coordination, eye-hand coordination, reaction time, brainstem evoked potentials, HRV	Two out of 39 tested correlations were statistically significant (one of 16 sway tests and one of four ear-hand coordination tests).	Age, gender, height
Suzuki et al. (2010) (Japan)	Cross-sectional	498 babies at 3 days of age	THg in maternal hair: μ ± SD: 2.22 ± 1.16 mg/kg, P50: 1.96 (range: 0.29-9.35) mg/kg	behaviour and reflexes according to the NBAS	Impairment related to maternal hair mercury ($p < 0.05$) after adjustment for PCB. Further adjustment for seafood intake increased the magnitude of the association, while further adjustment for potential confounders only marginally affected the association.	Seafood intake, maternal PCB level, as well as a range of other potential confounders, such as maternal age, birth weight, and thyroid related hormones.

Table 24: Continued.

Author (country)[(c)]	Study design	Study participants	Ascertainment of mercury concentration	Outcome	Results[(e)]	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Asia and other regions (continued)						
Gao et al. (2007) (China)	Cross-sectional	384 babies at 3 days of age	THg in cord blood: GM: 5.6 (IQR: 4.0-7.8) µg/L THg in maternal hair: GM: 1.2 (0.9-1.7) mg/kg	according to the NBNA scale	In logistic regression analysis, the probability of getting full mark for behaviour score was negatively associated with maternal Hg (both cord blood and hair) for boys but not girls. For cord blood Hg an OR of 1.235 (95 % CI 1.078-1.414) was calculated, presumably for each increment of 1 µg/L. There were no associations for active and passive tones.	Several potential confounders were considered, but only paternal smoking and maternal Hg exposure qualified for the logistic regression model for behaviour score.

µ: mean; AA: arachidonic acid; ADHD: Attention Deficit Hyperactivity Disorder; BAEP: Brainstem Auditory Evoked potentials; BMDL: 95 % benchmark dose lower confidence limit; BSID-II: Bayley Scales of Infant Development-II; CI: confidence interval; CPT: Continuous performance test; CPT-HRT: Continuous Performance Test-Hit Reaction Time latencies; DDST: Denver Development Screening Test; DHA: docosahexaenoic acid; ERP: event-related potential; Fe: iron; GM: geometric mean; Hg: mercury; HOME: Home Observation for Measurement of the Environment; HRV: heart-rate variability; IQ: intelligence quotient; IQR: interquartile range; LCPUFA: long-chain polyunsaturated fatty acids; LOD: limit of detection; MCDI: MacArthur Communicative Development Inventory; MeHg: methylmercury; n.r.: not reported; n-3 LCPUFA: n-3 long-chain polyunsaturated fatty acids; NBAS: Neonatal behaviour assessment scale; NBNA: Neonatal behavioural neurological assessment; OR: odds ratio; P50: 50th percentile; Pb: lead; PCB: polychlorinated biphenyls; PDI: Psychomotor Developmental Index; RR: relative risk; SACMEQ: Southern and Eastern African Consortium for Monitoring Educational Quality; SCDNS: Seychelles Child Development Nutrition Study; SCDS: Seychelles Child Development Study; SD: standard deviation; SE: standard error; SES: socio-economic status; THg: total mercury; TSH: thyroid stimulating hormone; VRM: Visual recognition memory.

(a): values in 143 males with shaved heads were missing at nine years and were substituted by previous measurements;

(b): no concentrations of THg in hair are reported by the authors at 10.7 years of age;

(c): country specified except for the cohorts from the Seychelles and Faroe Islands;

(d): the levels of THg in hair at seven years are reported by both Debes et al. (2006) and Murata et al. (2004b). The CONTAM Panel noted that the levels in both papers are substantially different.

(e): associations were assessed in some cases by correlation, but mostly by (multiple) linear regression of the outcome on the respectively used mercury measures available. However, only the more advances statistical regression methods are mentioned in the table.

7.4.2.1.2. Postnatal exposure and observations in childhood

A cross-sectional study of 72 four-year old boys in Spain (geometric mean mercury level in hair 1.81 mg/kg) found decrements in cognitive abilities (general cognitive, memory and verbal scores) for boys with hair mercury levels above 1 mg/kg – about half of the studied children – compared with those with lower levels (Freire et al., 2010). The authors adjusted for fish consumption and a number of potential confounders.

A study of a cohort of 780 US children enrolled in a clinical trial on treatment of lead-exposed children study did not reveal any cognitive effects of methylmercury at low levels (median blood level 0.5, interquartile range (IQR) 0.4 - 0.8 µg/L). In contrast, the authors noted tendencies for increased IQ and decreased behavioural problems as methylmercury increased. They suggested the possibility that this could be due to nutritional contribution with e.g. n-3 LCPUFAs from fish consumption that was not accounted for in the analyses (Cao et al., 2010).

A cross-sectional study on 355 US children found no statistically significant associations with a range of cognitive outcomes (Surkan et al., 2009). The mercury concentrations in hair were low with a mean of ca. 0.32 mg/kg. Two of the outcomes deviated from linearity in their relation to hair mercury. Modelling these outcomes with smoothed curves suggested positive slopes for hair mercury concentrations below 0.5 mg/kg and negative slopes between 0.5 and 1.5 mg/kg. The number of observations above 0.5 mg/kg was however small and none of the suggested associations in the higher range was statistically significant.

An analysis of the possible influence of postnatal methylmercury exposure from fish consumption (mean ± SD hair level: 6.5 ± 3.3 mg/kg at 5.5 years (n = 694) and 6.1 ± 3.6 mg/kg at 9 years (n = 537)) on multiple outcomes at 5.5 and 9 years of age and association with children's intelligence coefficients at 9 years was reported by Myers et al. (2009). The correlation between maternal and child's hair mercury decreased with the child's age. It ranged from moderate (r = 0.3) at 6 months to low correlation (r = 0.16) at 5.5 years, down to fairly low correlation (r = 0.07) at 9 years. The authors used three different metrics of postnatal exposure in linear regression analyses and included a broad set of confounders. Postnatal mercury exposure metrics did not predict the nine-years intelligence coefficients and the authors concluded that the regression analysis showed no consistent influence of postnatal exposure. Furthermore, the authors acknowledged that the SCDS study might not provide sufficient information on postnatal exposure.

One study of 100 children (Torrente et al., 2005) was not further reviewed because of its limitations in size and lack of confounding adjustment. Two studies of children living in different communities with different exposures (Tavares et al. 2005; de Fonseca et al., 2008) were also not further reviewed because of the limitations in the study designs.

A few studies have specifically focused on ADHD in children. A case-control study from Hong Kong showed higher blood mercury levels among 52 children with ADHD, compared to 59 controls: geometric mean: 3.6 vs. 2.3 µg/L; $p < 0.001$ (Cheuk and Wong, 2006). The analyses were adjusted for age, gender and parental occupational status, but not for variables related to fish consumption.

A cross-sectional study of 1 778 Korean children found no association between ADHD and blood mercury (mean ± SD ca 2.9 ± 1.5 µg/L; Ha et al., 2009). A tendency towards a decreased risk of ADHD with increasing blood mercury appeared ($p = 0.10$).

A cross-sectional study of 83 Romanian children, aged 8 - 12 years, did not find any association between features related to ADHD and blood mercury concentrations ranging between 0.5 and 5 µg/L (Nicolescu et al., 2010).

In addition, Myers et al. (2009) used the Connor's Teacher Ratings Scale ADHD Index in the Seychelles nine year follow-up (n = 537) and observed a highly statistically significant association ($p < 0.0001$) with recent postnatal hair mercury in a regression model.

A number of studies have investigated the relation between mercury levels and autism in children (Holmes et al., 2003; Ip et al., 2004; Adams et al., 2007; Kern et al., 2007; Geier et al., 2010; Hertz-Picciotto et al., 2010; Majewska et al., 2010; Woods et al., 2010; Kaluzna-Czaplinska et al., 2011; Lakshmi Priya and Geetha, 2011; De Palma et al., 2012; Wright et al., 2012). The results of these studies do not give a coherent picture of an association between biomarkers of mercury and autism in children. Associations have been observed in both positive and negative directions, but the studies are generally small. Only two studies attempted to study markers of mercury exposure prior to diagnosis: Adams et al. (2007) measured mercury in baby teeth in 16 children with autism and 11 controls, and Holmes et al. (2003) found lower mercury concentrations in first baby haircut (mean: 0.47 mg/kg) from 94 children with autism than in 45 controls (3.63 mg/kg). The concentration in the control hair samples must however be considered high for USA. The other studies compared children with autism with controls from a cross-sectional study, giving the possibility of bias through an influence of the disorder or its diagnosis on fish consumption or dental amalgam status. Such bias is one of several possible reasons of the differing results. Some studies have focused on porphyrins that may be affected by mercury (Geier and Geier, 2007; Geier et al., 2009a,b; Kern et al., 2010; Woods et al., 2010), but these could not be interpreted in terms of dietary mercury intake. It has been suggested that porphyrins may be associated with autism, but without an association to mercury (Woods et al., 2010). An ecological study of autism and environmental mercury release (Palmer et al., 2006) was not considered relevant for risk assessment of dietary intake.

In conclusion, as regards children's postnatal mercury exposure, the inconsistent observations from the studies above do not give reasons for any increased concern for neurotoxic effects. The studies on autism do not indicate any increased risk from dietary mercury exposure, but for ADHD some studies have found associations with mercury. Taken together, however, the results do not provide information to allow conclusions.

7.4.2.1.3. Neurotoxicity in adults

A range of follow-up studies and reassessment of outcomes from the Minamata area, which also includes control groups from Japan with lower exposure, have been published since the assessment by JECFA (Futatsuka et al., 2005; Ninomiya et al., 2005; Uchino et al., 2005; Ekino et al., 2007; Yorifuji et al., 2008, 2009a, 2009b, 2011; Gilbertson, 2009; Sakamoto et al., 2010). However, the previous methylmercury exposure has been higher than in the Faroese and Seychelles cohorts on which the JECFA PTWI is based. Consequently, the CONTAM Panel does not consider these studies suitable when evaluating if the existing PTWI is sufficiently protective.

In a cross sectional study, Carta et al. (2003) performed neurobehavioural and tremor tests on adult Italian consumers of fresh tuna (n = 22) and non-consumers (n = 22). Colour word reaction time, digit symbol reaction time and finger tapping speed was statistically significantly lower in the tuna fish eaters, and was associated with organic mercury in blood in multiple stepwise regression analysis. However, mercury in blood and urine (total mercury and organic mercury) was available for only 10 consumers and 6 non-consumers (total mercury in blood (µg/L); consumers 44.0 (range 15 - 93); non-consumers 3.9 (range 1.2 - 5.4)). Due to the small sample size the study is regarded as preliminary by the authors, and the CONTAM Panel noted that the exposure in the tuna fish consumers was high.

Neurotoxicity in 240 adults (99 women) living near a chloralkali plant in Taiwan that was closed in 1982 was investigated by Chang et al. (2008). The mean duration of residence was 49.3 years and the majority had age 40 - 70 years. Their current mercury exposure was mainly through fish consumption. Total mercury and methylmercury in blood was measured, and the participants were divided into high exposure (n = 46, mean blood methylmercury 27.0 ± 10.4 µg/L) and low exposure groups (n = 92, 11.6 ± 4.7 µg/L) and matched for age, gender and education. The Cognitive Abilities Screening

Instrument and Mini-Mental State Examination were used to assess the participants' cognitive functions. When comparing the high and low methylmercury groups, lower scores were seen for tests covering remote memory (OR 10.0, 95 % CI 1.7 - 216.1), mental manipulation (OR 5.3, 95 % CI 1.7 - 29.7), orientation (OR 3.3, 95 % CI 1.7 - 9.6) and verbal fluency (OR 5.0, 95 % CI 1.1 - 39.4) in the high exposure group. No differences were seen for tests covering recent memory, attention, abstract thinking, language and drawing.

Choi et al. (2009) studied a group of 41 whaling men (for more details, see Section 7.4.2.2 and Table 25) and found no associations between mercury exposure and BAEPs.

Levels of n-3 LCPUFA or total mercury in whole blood in relation to the risk of dementia or Alzheimer's disease among 149 dementia patients and 514 unaffected participants in the Canadian Study of Health and Aging were investigated (Kröger et al., 2009). No association was found between dementia and n-3 LCPUFA. Mercury in blood in the highest quartile (mean ± SD: 2.48 ± 1.64 µg/L) was associated with a statistically significant lower risk of dementia (0.53, 95 % CI 0.33 - 0.88) in participants with n-3 LCPUFA levels above the median compared to those with lower levels. The authors considered that the results regarding mercury may indicate a spurious association.

In a cross-sectional study on 243 fresh water fish eaters from two regions of Québec, Canada, Philibert et al. (2008) did not observe any association between neuropsychiatric symptoms measured with Brief Symptom Inventory and n-3 LCPUFA in blood, and no interaction of n-3 LCPUFA with mercury. The participants had low n-3 LCPUFA values (median EPA + DHA was 0.11 g/L) and low mercury exposure (median in blood 2.22 µg/L and in hair 0.54 mg/kg).

Twenty scores from 12 neurobehaviour tests were measured in a cross-sectional study on 474 adults (185 women) in the Baltimore Memory Study (50 - 70 years, mean age 59 years and median blood mercury 2.1 µg/L (range 0 - 16 µg/L)) (Weil et al., 2005). In linear regressions, increasing blood mercury was associated with worse performance on a test of visual memory, and with better performance on a test of manual dexterity (finger tapping). The authors concluded that overall, the data did not provide strong evidence for an association between mercury in blood and lower scores on neurobehavioural performance tests in this population.

Benefice et al. (2010) examined neurological abnormalities and blood pressure among two ethnic groups of Amerindian women living along the banks of the Beni River (n = 170). Total mercury in hair (mean 5.5, SD 4.2 mg/kg) and frequency of fish consumption was recorded by a 24-h food recall questionnaire. The authors reported statistically significant associations between the fishing practices or the frequency of fish consumption and hair mercury levels. Women with hair mercury concentration above 5 mg/kg were more likely to have neurological abnormalities (paresthesia, static and dynamic imbalance, poor motor coordination) than women with hair mercury below 5 mg/kg. No relationship was found between blood pressure and mercury levels. Women with higher mercury concentration in hair reported higher rates of infant deaths than did women with lower levels. The women with high mercury concentration and who reported higher infant deaths tended to belong to a population groups practicing traditional fishing and were younger and with poorer health than those with lower mercury levels.

In summary, the studies referred to above do not show relevant associations between mercury exposure, at low levels, and adverse neurological outcomes in the adult population.

7.4.2.2. Cardiovascular effects

When JECFA evaluated methylmercury in 2006, in addition to neurodevelopmental endpoints they also considered cardiovascular outcomes in adults. Five epidemiological studies of mercury concentrations in adults in relation to cardiovascular disease were considered and tabulated (the first five studies in Table 25; FAO/WHO, 2007). It was noted that two of these (Guallar et al., 2002; Virtanen et al., 2005) found an increased risk of acute coronary event or myocardial infarction with higher mercury concentrations; one study (Hallgren et al., 2001) found a decreased risk of myocardial

infarction with higher concentrations of mercury (considered by the authors as a biomarker for fish consumption); and the other two studies (Ahlqwist et al., 1999; Yoshizawa et al., 2002) did not show a statistically significant association between myocardial infarction and mercury concentrations. One study (Salonen et al., 1995) was not included among these five, because it concerned the same cohort as that described by Virtanen et al. (2005).

The JECFA evaluation (FAO/WHO 2007) considered cardiovascular function also in young children with prenatal methylmercury exposure. Two studies of HRV (Grandjean et al., 2004b; Murata et al., 2006), reflecting cardiac autonomy, were reviewed by JECFA. Results suggested that prenatal exposure to methylmercury is associated with impaired cardiac autonomy. The study by Murata et al. (2006) suggested an association already at a median of estimated maternal hair mercury concentration at parturition of 2.24 mg/kg. This value is lower than that for neurodevelopmental endpoints. The value was noted by the JECFA, but did not influence the PTWI.

Cardiovascular disease in adults

Six major epidemiological studies of cardiovascular disease and mercury have been published since 2005 and are summarised in Table 25 (Wennberg et al., 2007; Engström et al., 2011; Mozaffarian et al., 2011; Wennberg et al., 2011; Bergdahl et al., 2012; Virtanen et al., 2012). Of these, one (Engström et al., 2011) evaluated gene-environment interactions in the same individuals as had been studied in other studies (Hallgren et al., 2001; Wennberg et al., 2011). Therefore, these data are not further considered here and the study is not included in Table 25. In addition, a risk-benefit model has been published (Wennberg et al., 2012) for mercury and n-3 LCPUFA based on pooled, previously published, data from Finland and Sweden. One ecological study of Minamata with cardiovascular outcomes during the period 1953 to 1970 (Inoue et al., 2012) was not included in the current review, due to the difficulties of interpreting results in terms of dose-response that follows from the lack of individual exposure information.

Wennberg et al. (2007) studied the risk of a first stroke in relation to mercury, fish consumption and n-3 LCPUFA. The study was a case-control study nested within a cohort study with blood samples stored in a biobank. Hence, 369 cases who had experienced a stroke after their enrolment in the study were identified, and 738 controls were matched by age, sex, time of sampling and place of residence. Total mercury was measured in erythrocytes and n-3 LCPUFA in erythrocyte membranes. Information on fish consumption was obtained from a food frequency questionnaire. The median erythrocyte mercury concentration for the study population (cases and control) was reported as 3.63 ng/g. No association was observed between stroke risk and either mercury (OR: 0.99 per ng Hg/g erythrocytes; 95 % CI: 0.93 - 1.06), or n-3 LCPUFA (OR: 1.08 per % EPA + DHA; 95 % CI 0.92 - 1.28).

Wennberg et al. (2011) studied the risk also of a first acute myocardial infarction in relation to fish consumption. Just like in the stroke study and the study by Hallgren et al. (2001), this was a case-control study nested in a cohort with prospectively collected blood samples. The study comprised 150 female and 350 male cases and 275 female and 350 male controls, matched for sex, age, time of blood sampling, and place of residence. Mercury was measured in erythrocytes and n-3 LCPUFA in plasma phospholipids. The median mercury concentration was reported as 3.54 µg/L. Mercury and n-3 LCPUFA were correlated. Mercury was associated with a decreased risk for acute myocardial infarction. This was interpreted by the authors as a protective effect of fish consumption.

Data from Wennberg et al. (2011) was later combined with data from Hallgren et al. (2001) and Virtanen et al. (2005). When combined, these data provided wider exposure ranges for both mercury and n-3 LCPUFA, which facilitated modelling of acute myocardial risk as a function of both mercury and n-3 LCPUFA (Wennberg et al., 2012). Though this study did not include any new participant, the resulting model illustrates how the risk can be related to both mercury, with an increase in risk, and n-3 LCPUFA, with a decrease in risk. At low serum concentrations of LCPUFAs, a statistically significant association between myocardial risk and hair mercury was seen at hair mercury concentrations above ca 3 mg/kg. Based on readings from a figure, the model indicates a relative risk

(RR) of ca 1.2 at hair-mercury concentrations of 4 - 5 mg/kg, when comparing individuals with the same serum concentrations of LCPUFAs.

Mozaffarian et al. (2011) studied 3 427 cases with cardiovascular disease and 3 427 controls. The study was nested in two cohorts with prospectively collected toenails, in part the same cohort as previously studied by Yoshizawa et al. (2002). The interdecile range for toenail mercury concentration was 0.06 - 0.94 mg/kg in cases and 0.07 - 0.97 mg/kg in controls. Mercury was correlated with fish consumption ($r = 0.39$, $p < 0.001$), but not with any increased risk for coronary heart disease or stroke. Adjustments were made for a number of factors, including intake of n-3 LCPUFA from fish. The latter was not chemically measured but estimated based on data from a dietary questionnaire. Validation studies have shown correlation coefficients of 0.43 - 0.49 between marine n-3 LCPUFA, as assessed from questionnaire data, and on measurements in subcutaneous fat samples (Hunter et al., 1992). No association with cardiovascular outcome was indicated for the estimated n-3 LCPUFA, or for other dietary risk factors, such as trans fatty acids. The study thus found no association between mercury exposure and cardiovascular disease. The highest decile of 0.97 mg/kg in toenails was specifically studied, but revealed no increased cardiovascular risk. The authors indicated that this toenail concentration corresponded to about 2.7 mg/kg in hair.

Bergdahl et al. (2012) followed up the same cohort as was studied earlier by Ahlqwist et al. (1999). The median serum mercury concentration was 1.4 (range: 0.1 - 13) µg/L, reflecting a combination of inorganic and organic mercury at low exposure levels. In accordance with the first study, higher mercury concentration in serum was associated with decreased risk of acute myocardial infarction, i.e. no adverse effect was indicated. When adjustments were made for socioeconomic factors and fish intake (based on 24 hours recall, which is insufficient for a proper adjustment), the association with a reduction in fatal acute myocardial infarction remained statistically significant and an increased risk for stroke appeared, while the association to total acute myocardial infarction incidence did not remain statistically significant. While the study was conducted at low mercury exposure levels and indicated reduced myocardial infarction risks, its main conclusions relate to the relevance for cardiovascular disease, in protective terms, of dental health and/or fish consumption. The results also suggested that effects related to fish consumption and mercury exposure may differ between stroke and acute myocardial infarction, as well as between fatal and non-fatal acute myocardial infarction.

A new follow up (20 years) of the Finnish cohort (described by Salonen et al., 1995 and Virtanen et al., 2005) found 91 new cases of sudden cardiac death (Virtanen et al., 2012). An association with hair mercury was found when treating mercury in hair as a continuous variable, with a 7 % (95 % CI: 3 - 11) increased risk of sudden cardiac death per 0.5 mg/kg increase in mercury. An interaction with n-3 LCPUFA was observed: Among those with hair mercury below the median (1.28 mg/kg), each 0.5 percentage unit increase in the serum n-3 LCPUFA was associated with a hazard ratio of 0.77 (95 % CI: 0.64 - 0.93), whereas no association with n-3 LCPUFA was seen among those with higher hair mercury (p for interaction: 0.01). The authors suggested that an effect of mercury on HRV or oxidative stress may play a role.

Recent literature has suggested an association between persistent organic pollutants present in fish and cardiovascular risks (Goncharov et al., 2011; Lee et al., 2012), none of the studies above control for that.

To summarise the main new results on stroke and cardiac disease, neither the study by Wennberg et al. (2007), at low exposures, nor the one by Mozaffarian et al. (2011), at somewhat higher exposures, indicate any association between stroke and mercury exposure. For acute myocardial infarction, two Swedish studies at low mercury levels (Wennberg et al., 2011 and Bergdahl et al., 2012) showed associations between mercury and decreased risk, suggested by the authors to be caused by beneficial effects of fish consumption. One study (Mozaffarian et al., 2011) showed no association between mercury and the risk of cardiac disease. A study of sudden cardiac disease showed an association with hair mercury (Virtanen et al., 2012). The latter also showed an interaction effect between mercury and n-3 LCPUFA. All these studies are, wholly or in part, based on longer follow-ups of previously

studied cohorts. A model for the acute myocardial infarction risk related to mercury and benefit related to n-3 LCPUFA was described, combining data from Finland and Sweden (Wennberg et al., 2012).

Blood pressure and heart rate variability/cardiac autonomy in adolescents and adults

As mentioned above in this section, results have suggested that fetal exposure to methylmercury is associated with impaired cardiac autonomy. Recently, studies have also been made on adults with relatively high methylmercury exposure in order to find out if there is an effect of current mercury exposure on cardiac autonomy. These studies are summarised below and in Table 25.

A well-functioning cardiac system maintains homeostasis by continuously adjusting heart rate, blood pressure, etc. While doing that, small variations in heart rate can be observed. If the variation in heart rate is too small, this is a sign of poor regulation of the heart. HRV can be used to describe autonomic balance (Akselrod, 1988) and can reflect adaptive mechanisms of the autonomic nervous system (Aubert and Ramaekers, 1999). Activity of the nerves of the autonomic nervous system influence heart rate by means of two pathways: the sympathetic pathway, which causes cardio-acceleration, and the vagal pathway, causing a deceleration in heart rate. Feedback is provided from baroreceptors located in the most important arteries. A shift in the sympatho-vagal balance may become a major risk for cardiac events (Malliani, 2000).

The cardiovascular rhythmicity is usually studied within different frequency domains. Three major spectral components are usually detected, in humans centered at ca 0.00 Hz (very low frequency, VLF), at 0.11 Hz (low frequency, LF), and 0.25 Hz (high frequency, HF), respectively. LF and HF components are evaluated in terms of frequency and amplitude, the latter commonly assessed by the area (i.e. power) of each component. In addition, normalised units are often used, obtained by dividing the power of a given component by the total power (from which VLF has been subtracted) and multiplying by 100, thus giving a percentage. Different frequency bands correspond to modulation of the different branches of the autonomic nervous system. LF oscillations (LF: 0.04 - 0.15 Hz) correspond predominantly to sympathetic modulation, but also vagal influences and the baroreflex, while HF fluctuations (0.16 - 0.4 Hz) are related to vagal or parasympathetic modulation of heart rate.

Valera et al. (2008, 2011a) studied adults with high (total blood mercury up to more than 100 µg/L) and moderate methylmercury exposure. The results showed associations between mercury and decreased HRV, though not completely consistent through crude and adjusted regression models and between the two studies. Another study, comparing an urban and a rural area, the latter with high fish consumption, indicated mercury-related differences in some HRV parameters in teenagers but not in adults (Valera et al., 2011b). However, these results are to a large degree reflecting differences between individuals of two different populations, making conclusions difficult to draw. Choi et al. (2009) studied a group of 41 whaling men and found associations with increased HRV for both high and LF components. However, decreased variability was the hypothesised negative effect of mercury exposure. In a Korean population with moderate exposure levels (mean mercury concentration in hair: 1.02 mg/kg), a large cross-sectional study showed a mercury-associated decrease of the variability in the HF parameter (Lim et al., 2010).

An intervention study in which 27 subjects consumed fish containing 1.08 mg THg/kg (corresponding to 1.0 mg methylmercury/kg) for 14 weeks, showed an increased variability of the LF component, as compared to both baseline observations and a control group (Yaginuma-Sakurai et al., 2010). The individuals in the experimental group were supplied with around 200 g per week bigeye tuna and swordfish meat. The amount of fish supplied to each person was depending on b.w., so that all the 27 exposed individuals would receive a weekly dose of 3.4 µg methylmercury/kg b.w. This consumption resulted after 14 weeks in a mean hair mercury concentration of 8.76 mg/kg. Consumption of fish containing high levels of methylmercury, other than the supplied tuna and swordfish, was restricted. The 27 individuals of the control group were instructed to continue their usual diet. HRV, along with DHA and EPA in plasma, was examined at baseline, week 15, and week 29. The HRV for the LF component for the experimental group was increased at week 15 but had in

week 29, i.e. after a washout time, returned to the baseline level. No such change appeared in the control group. The increase in the LF component was not accompanied by a change in the HF component, thus resulting in an alteration in the ratio between the two components. The plasma concentrations of DHA + EPA showed a small variation between the three observation times, but did not show the same changes in pattern as the HRV. Instead the concentrations in the experimental group were slightly lower in week 29, as compared to baseline, and were at week 15 in-between those. The result for HRV, with an increased variability in the LF component, is in part similar to the results of Choi et al. (2009). However in the intervention study, the LF component increased without a change of the HF component, suggesting a shift in the sympatho-vagal balance towards sympathetic activity. Therefore, this alteration in HRV cannot be considered beneficial, but it is difficult to conclude about its degree of adversity.

Taken together, the studies of cardiac autonomy suggest an influence of mercury on HRV, but the results are not consistent between studies and the implications for health are currently unclear. The well-designed intervention study showed a change in HRV after 14 weeks of a weekly intake of 3.4 µg methylmercury/kg b.w. The variability returned to baseline values after a 15 weeks washout period.

In a study of men and women originating from Greenland (n = 145) and Denmark (n = 41), representing largely varying food consumption patterns, mercury was not associated with systolic blood pressure, but diastolic blood pressure decreased with increased blood mercury. In accord with this, pulse pressure was associated with blood mercury (Pedersen et al., 2005). The mean blood mercury concentration in the Greenlanders was 16.2 µg/L and in the Danes 2.2 µg/L. A study of 545 Amazon Indians with mean hair mercury 4.2 mg/kg (ranging up to ca 40 mg/kg) did not show any consistent association between hair mercury and blood pressure. The statistical analyses did not include adjustments for age, gender, etc (Dórea et al., 2005).

In a study of a non-indigenous fish-eating population in the Brazilian Amazon, Fillion et al. (2006) found an OR of 2.91 (1.26 - 7.28, supposedly denoting 95 % CI) for elevated systolic blood pressure for individuals with hair mercury above 10 mg/kg. In addition, the risk for elevated diastolic blood pressure was increased. A study of Inuit adults showed an association between systolic blood pressure and mercury (ranging up to very high blood concentrations, over 100 µg/L; Valera et al., 2008). A later report on a larger study (Valera et al., 2009), incorporating the individuals from the previous one in addition to others, also showed an association with systolic blood pressure, but with smaller slope (adjusted regression coefficient 2.14, 95 % CI 0.94 - 3.33, $p < 0.001$), suggesting the possibility that the association in the latter study may to some extent be driven by the individuals from the first study. Studies in Canada (Valera et al., 2011a, 2012) and French Polynesia (Valera et al., 2011b) did not show any association between blood pressure and mercury levels after adjustments for potential confounders. A small study (n = 101) of members of a US cohort established to study sleep related factors, found a 4.19 (95 % CI: 1.28 - 13.76) times higher risk for hypertension for individuals with hair mercury exceeding 0.496 mg/kg vs. the other cohort members (Bautista et al., 2009).

A study of 495 older US men did not find any association between systolic or diastolic blood pressure, or pulse pressure, and toenail mercury (Mordukhovich et al., 2012). The point estimates were slightly negative (higher mercury levels related to lower blood pressure), but they were far from statistical significance. The median toenail mercury concentration was 0.22 mg/kg.

A cross-sectional study among adult Inuit in Greenland with high mercury exposure from consumption of marine food showed a relation between lower diastolic blood pressure and higher mercury concentration in blood, but only for men, not for women (Nielsen et al., 2012). The study comprised 1 861 individuals, of which 615 men and 787 women without anti-hypertensive drug therapy were included in linear and logistic regressions of blood pressure and blood mercury. Systolic blood pressure in men gave results in the same direction as for diastolic blood pressure, but not statistically significant. In addition, the risk of hypertension (defined as blood pressure ≥ 140/90 mmHg or usage of anti-hypertensive drugs according to guidelines) was decreased in men with high blood mercury, but not in women, and not with consistency throughout the different

statistical models used. Pulse pressure did not show any associations with mercury. The median blood mercury concentration was 18 µg/L, with an inter-quartile range of 8.8 - 34.1 µg/L.

A study of 507 men and 509 women in Sweden with low blood mercury concentrations (median for men: 1.9 µg/L with an IQR of 1.6 µg/L; for women: 1.7 and 1.5 µg/L, respectively) showed no association to systolic blood pressure (Olsén et al., 2012), but increased LDL-cholesterol and decreased high-density lipoprotein (HDL)-cholesterol. Smoking was however associated with blood mercury but was not adjusted for. It is unknown to what extent the mercury stemmed from methylmercury contaminated food or inorganic mercury from dental amalgams. The study of 41 whaling men from the Faroe Islands (Choi et al., 2009) also found statistically significant associations between blood pressure and biomarkers of mercury exposure. The latter study also found an association with carotid intima-media thickness, in line with previous findings by Salonen et al. (2000).

Blood pressure in relation to mercury was studied in US women (Vupputuri et al., 2005), showing no associations among fish consumers, but non-fish consumers of the highest mercury quintile (blood mercury from 2.1 µg/L) had ca 5 mmHg higher systolic blood pressure, as compared to the lower quintiles. As this occurred in non-fish consumers it must be assumed that the major source of mercury was not the diet but rather dental amalgam.

In addition, blood pressure in adolescents was studied in relation to prenatal exposure in the Seychelles cohort (Thurston et al., 2007). An association was found for diastolic blood pressure in boys at 15 years of age (slope: 0.36; SE 0.12 mmHg) but no associations were found at the age of 12 years or in girls.

Some studies report on resting heart rate in relation to mercury. This outcome has not been considered in this review. An increase was reported in a recent study (Valera et al., 2012), but is not in accordance with previous studies in adults with environmental mercury exposure.

In all, the observations on blood pressure give a somewhat inconsistent picture, e.g. as regards whether diastolic or systolic blood pressure may be affected. There is no firm basis for assessment of a dose-response relationship.

Concluding comments

At the time of the evaluation by the JECFA in 2006, there were only two major epidemiological studies that indicate an association between methylmercury and increased the risk of cardiovascular disease (Guallar et al., 2002; Virtanen et al., 2005). Both these concern acute coronary events or myocardial infarction. Reported mercury levels ranged from 0.14 to 0.57 mg/kg in toenails (Guallar et al., 2002) and from 0 to 15.7 mg/kg in hair (mean: 1.9 mg/kg) (Virtanen et al., 2005). Results in the same direction were found in a recent study on sudden cardiac death (Virtanen et al., 2012) from a longer follow up of the cohort previously studied by Virtanen et al. (2005). The negative results of Yoshizawa et al. (2002) have been further strengthened by the recent study by Mozaffarian et al. (2011), in which no increased cardiovascular risk was observed even in the group with hair mercury > 2.7 mg/kg. Some other studies have dealt with lower exposure levels and provided negative findings.

The importance of taking the beneficial effects of fish consumption into account when studying cardiovascular outcomes of methylmercury has become evident. The studies by Yoshizawa et al. (2002) and Mozaffarian et al. (2011) have based the correction for n-3 LCPUFA confounding on dietary questionnaires, while the studies by Guallar et al. (2002) and Virtanen et al. (2005) have used biochemical measurements, and this may explain part of the discrepancy.

Thus, the observations related to myocardial infarction, HRV and possibly blood pressure are of potential importance, but still not conclusive.

Table 25: Overview of epidemiological data on cardiovascular effects.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
CVD considered by JECFA (adapted from FAO/WHO, 2007)						
Guallar et al. (2002) Eight European countries and Israel	Case-control	Cases: 684 men Controls: 724 men	THg in toenail: range 0.14-0.57 mg/kg (authors presented averages in control patients across study centers) (toenails collected after occurrence of MI, analysed in 1991-1992)	First acute MI	Adjusted OR for MI: highest quintile of Hg compared with lowest quintile: 2.16 (95 % CI 1.09-4.29)	
Yoshizawa et al. (2002) USA	Case-control within prospective cohort study	Cases: 470 men Controls: 464 men matched on age and smoking status	THg in toenail : controls: range: 0.03-14.6 mg/kg dentists: μ±SD: 0.91±1.47 mg/kg others: μ±SD: 0.45±0.40 mg/kg (toenails collected before the onset of CHD, analysed in 1987)	CHD	Adjusted OR for CHD: Highest quintile of Hg compared with lowest quintile in dentists: 0.97 (95 % CI, 0.63-1.50) Adjusted OR for CHD: Highest quintile of Hg compared with lowest quintile, excluding dentists: 1.27 (95 % CI, 0.62 to 2.59)	
Hallgren et al. (2001) Sweden	Case-control within a prospective cohort study	Cases: 78 men and women	THg in erythrocytes: range: 0.6-67 ng/g (blood samples stored in 1985 for future research purposes, analysed 1998) N.B. Slightly incorrect: stored after 1984 would be correct.	First MI	Adjusted OR for MI: Intermediate Hg (3-6 ng/g) compared with lowest Hg (< 3 ng/g): 0.9. Highest Hg (< 6 ng/g) compared with lowest Hg (< 3 ng/g): 0.4 (95 % CI, 0.19-0.95)	
Ahlqwist et al. (1999) Sweden	Prospective cohort study of women	1462 women, enrolled in 1968-1969	Serum THg (blood samples collected in 1968-69, then 1980-81 for future research; mostly used earlier samples)	MI (n = 87, 39 died); all-cause death (n = 253)	An inverse, but not statistically significant correlation between serum Hg and MI was found. A statistically significant negative correlation between serum Hg and death from all causes was found after adjusting for age and education.	

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
CVD considered by JECFA (adapted from FAO/WHO, 2007) (continued)						
Virtanen et al. (2005) Eastern Finland	Prospective cohort study of men, 14 year follow-up	1871 men who were free of CVD at baseline (1984-1989)	THg in hair: μ: 1.9 (range: 0-15.7) mg/kg (hair collected before onset of disease or death, analysed in 1992-1993)	Acute CE (n = 282); Death from CVD (n = 132), Death from CHD (n = 91), All-cause death (n = 525)	Adjusted RR for acute CE: Middle third of Hg compared with lowest third: 1.1. Highest third of Hg compared with lowest third: 1.7*. Adjusted RR for CVD death: Middle third of Hg compared with lowest third: 0.7. Highest third of Hg compared with lowest third: 1.3. Adjusted RR for CHD death: Middle third of Hg compared with lowest third: 0.6. Highest third of Hg compared with lowest third: 1.2. Adjusted RR for any death: Middle third of Hg compared with lowest third: 0.9. Highest third of Hg compared with lowest third: 1.3* *range of 95 % CI above 1.0.	
Recent CVD studies, not considered by JECFA						
Wennberg et al. (2007) Sweden	Case-control within prospective cohort study	Cases: 369 men and women. Controls: 738 men and women	THg in erythrocyte: P50: 3.63 (range up to 24) ng/g. Hg in erythrocytes sampled after 1984 and before any diagnosed stroke	First stroke	No association to Hg or EPA+DHA.	

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Recent CVD studies, not considered by JECFA (continued)						
Mozaffarian et al. (2011) USA	Case-control within two prospective cohort studies (nurses and male health professionals)	Cases: 1211 men, 2216 women. Controls 1211+2216	THg in toenail: IDR: 0.06-0.94 mg/kg in cases and 0.07-0.97 mg/kg in controls. Prospectively collected	CHD, stroke	RRs for fifth quintile of Hg vs. the first: CHD: 0.85 (95 % CI 0.69-1.06); stroke: 0.83 (95 % CI 0.30-1.15)	Matched for age, sex, race, smoking, time of toenail sampling. Adjusted for BMI, physical activity, alcohol, diabetes, hypertension, cholesterol, estimated intake of EPA and DHA.
Wennberg et al. (2011) Sweden	Case-control within prospective cohort study	Cases: 150 women and 350 men. Controls: 275 women and 350 men.	THg in erythrocyte: P50: 3.54 (range 0.01-87) µg/L. (sampled after 1984 and before any diagnosed MI)	First MI	OR for > 4.98 µg/L (adjusted model): 0.55, after adjustment for EPA+DHA: 0.61 (the latter not statistically significant).	
Bergdahl et al. (2012) Sweden (Gothenburg)	Prospective cohort study of women. New follow up of Ahlqwist et al. (1999)	1397 adult women with serum Hg, total 1462 in cohort	THg in serum: P50: 1.4 (range: 0.1-13) µg/L. Serum Hg	Mortality, AMI, stroke	HR for highest quartile (from 1.8 µg/L) adjusted only for age: Total mortality: 0.76; 95 % CI: 0.59–0.97; incident AMI: 0.56; 95 % CI: 0.34–0.93, fatal AMI: 0.31; 95 % CI: 0.15–0.66; stroke: 1.26; 95 % CI: 0.81–1.97. After adjustments only fatal AMI 0.43 (0.19–0.98) and stroke (1.80; 1.11–2.92) was statistically significant. Confirms indications from Ahlqwist et al. (1999). Lower risk of AMI associated with S-Hg.	Age, number of teeth, social class, education, serum triglycerides, wine consumption. (Considered but not related to exposure and therefore not potential confounders: smoking, waist/hip ratio, serum cholesterol, hypertension, and diabetes.)

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Recent CVD studies, not considered by JECFA (continued)						
Virtanen et al., (2012) Finland	Prospective cohort study of men, 20 year follow-up	1857 men who were free of CVD at baseline (1984-1989)	THg in hair: μ: 1.91 (range: 0-15.67) mg/kg. (hair collected before onset of disease or death, analysed in 1992-1993)	Sudden cardiac death (n = 91)	HR in highest tertile (2-15.67 mg/kg) vs. the lowest: 1.48 (95 % CI: 0.87-2.54). In continuous model: HR changed 1.07 (95 % CI: 1.03-1.11) for each 0.5 μg/g. Both results come from adjusted models. EPA+DPA+DHA was associated with decreased risk in individuals below the median hair Hg concentration (1.28 μg/g): HR: 0.77 (95 % CI: 0.64-0.93) for each 0.5 percentage unit increase in n-3 LCPUFA, while not so in individuals with hair Hg concentration at or above the median: HR: 1.02 (95 % CI: 0.95-1.09).	Association between sudden cardiac death and Hg was adjusted for age, examination year, body mass index, pack-years of smoking, alcohol intake, EPA+DPA+DHA content in serum.
Effect indicators that are not disease outcome, e.g. blood pressure (BP), heart-rate variability (HRV), carotid intima-media thickness						
Dórea et al. (2005), Brazil	Cross-sectional	621 (545 with Hg data) Amazon Indians, men, women and children, age ca 14-80 years	THg in hair: μ: 4.2 (range ca 0-40) mg/kg. Hair Hg	BP	Hair Hg was not associated with BP, except when the village with highest exposure was excluded.	None

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Effect indicators that are not disease outcome, e.g. blood pressure (BP), heart-rate variability (HRV), carotid intima-media thickness (continued)						
Pedersen et al. (2005) Greenland and Denmark	Cross-sectional	Men and women originating from Greenland (n = 145) and Denmark (n = 41)	THg in blood: Greenlanders: μ: 16.2 μg/l Danes: μ: 2.2 μg/L, Range up to ca 150 μg/L.	BP, Pulse pressure	Diastolic, but not SBP, was decreased with increasing log blood Hg (p = 0.014). Pulse pressure increased with increasing log blood Hg (p = 0.001).	Age, BMI, gender, residence.
Vupputuri et al. (2005) US (NHANES)	Cross-sectional	1240 women, 16-49 years	THg in blood: μ: 1.8μg/L; P50: 0.9 (range: 0.1-21.4) μg/L.	BP	No association among fish consumers, but in non-fish consumers, the highest Hg quintile (from 2.1 μg/L) had ca 5 mmHg higher SBP vs. other groups (95 % CI available only for model estimates).	Age, race, income, BMI, pregnancy status, and dietary sodium, potassium, and total calories.
Fillion et al. (2006) Brazilian Amazon	Cross-sectional	118 women, 133 men, adults >=15 years	THg in hair: μ: 17.8 (range 0.21-77.2) mg/kg	Blood pressure	OR 2.91 [1.26-7.28, supposedly 95 % CI] for elevated SBP (>=130 mmHg) with hair Hg >=10 mg/kg. OR 2.29 [0.95-6.06] for DBP (>=90 mmHg)	Age, sex, BMI, smoking, community
Thurston et al. (2007) Seychelles	Prospective	343 girls 336 boys BP at age 12 and 15. Hg exposure *in utero*.	THg in maternal hair: μ: 7.0 (girls), 6.5-6.6 (boys); range 0.5-26.7 mg/kg.	BP	DBP at 15 years increased in boys only (slope: 0.36 mmHg; SE: 0.12). No associations at 12 years or in girls.	Birth weight, BMI, height, maternal hypertension
Valera et al. (2008) Canada, Nunavik	Cross-sectional	120 women 85 men Inuit adults > 40 years	Range of blood Hg: 0.5-152 μg/L.	BP, HRV	BP: SBP (also pulse pressure) positively associated with Hg. DBP close to statistical significance. SDANN negatively associated with Hg. Both after adjustments. Other HRV variables negatively associated with Hg in crude model.	Potential confounders considered: gender, age, waist circumference, insulin sensitivity, LDL- and HDL-cholesterol, triglycerides, smoking, alcohol, physical leisure-time activity, income, n-3 LCPUFA in erythrocyte membranes. For BP also blood Se.

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Effect indicators that are not disease outcome, e.g. blood pressure (BP), heart-rate variability (HRV), carotid intima-media thickness (continued)						
Bautista et al. (2009) US (sleep cohort study)	Cross-sectional	48 women 53 men adults	THg in hair: GM: 270 mg/kg; P75: 496 mg/kg THg in blood: GM: 1.16 µg/L, P75: 2.01 µg/L.	Hypertension, vasodilating function	4.19 (95 % CI: 1.28-13.76) higher risk for hypertension for those in the highest hair Hg quartile vs. others. Corresponding for blood Hg: 1.93 (0.66-5.65).	Sex, age, BMI, fish intake.
Choi et al. (2009) Faroe Islands	Cross-sectional	41 whaling men	THg in blood: GM: 29.5 (range: 5.19-128.4) µg/L THg in hair: GM: 7.31 (range: 4.52 -13.4) mg/kg; THg in toenail: GM: 2.04 (range: 1.35-3.29) mg/kg.	HRV, BP, carotid intima-media thickness, BAEP	Structural equation models showed statistically significant associations between some, but not all, Hg biomarkers and blood pressure and carotid intima-media thickness. An association with slight delays of BAEP latencies was also observed. Associations with measures of HRV were partly in the opposite direction vs. expected (i.e. increased variability).	Age, smoking, BMI, consumption of alcohol and fish, cholesterol, triglycerides and PCB were considered, though not all included in the model.
Valera et al. (2009) Canada, Nunavik	Cross-sectional	413 women 319 men > 18 years Includes the 205 of Valera et al. (2008)	THg in blood: range: 0-240 µg/L	BP	SBP associated with Hg, but with smaller regression and correlation coefficients, as compared to the 2008 article, suggesting that the association is mainly driven by the same individuals as in the previous article.	Potential confounders considered, as in Valera et al. (2008) with minor additions.
Lim et al. (2010)	Cross-sectional	Mainly adults, but 10-20 % children. 852 females 737 males	THg in hair: µ: 1.02 (range 0.01-13.36) mg/kg	HRV	The HF parameter decreased by 8.4 % (95 % CI: 2.2-15.1 %) with an 1 mg/kg increase in hair Hg.	Age, heart rate, history of diabetes, smoking. Other variables, e.g. cholesterol and triglycerides were considered.
Yaginuma-Sakuri et al. (2010)	Intervention	Adult volunteers 26 women 28 men	Controlled MeHg intake. THg in hair: µ at week 15: 8.76 mg/kg µ in control group: 2.14 mg/kg	HRV	14 weeks intake at Japan's PTWI 3.4 µg/kg b.w. LF component CV increased at 15 weeks, compared to both baseline and control group.	

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Effect indicators that are not disease outcome, e.g. blood pressure (BP), heart-rate variability (HRV), carotid intima-media thickness (continued)						
Valera et al. (2011a) Canada, James Bay	Cross-sectional	724 adults (663 with HRV data) (> 18 years) from Cree communities	THg in blood: IQR: 1-9 µg/L THg in hair: IQR: 0.2-1.6 mg/kg.	BP, HRV	BP associated with Hg only in crude data, not after adjustments. HRV: SDANN and other parameters negatively associated in unadjusted analysis, but not in adjusted models. In contrast, LF, HF and LF/HF associated with Hg in adjusted models.	Potential confounders considered: sex, age, waist circumference, fasting glucose, triglycerides, smoking, physical activity, PCB 153, lead, selenium, n-3 LCPUFAs.
Valera et al. (2011b) French Polynesia	Cross-sectional	157 adults 82 teenagers Recruited from an urban area and a rural area, representing different Hg exposure and different life-styles	THg in blood: IQR: 8.5-22 µg/L	BP, HRV	No effects observed in adults on BP or any HRV variable. In teenagers: Tertile 3 vs 2 showed lower square root of the mean squared differences of successive R-R intervals (rMSSD), lower HF, though not in normalised units, higher LF/HF ratio.	Age, gender, triglycerides, fasting glucose, obesity, selenium, n-3 LCPUFAs. Smoking and alcohol consumption was considered but not adjusted for, due to lack of statistically significant associations.
Mordukhovich et al., 2012 USA	Cross-sectional	495 older men with mean age 72 years	THg in toenail: P50: 0.22 (range: 2.40; IQR: 0.31) mg/kg	BP	The point estimates for Hg in relation to SBP and DBP, as well as pulse pressure, were all negative, but far from statistical significance.	Age, smoking, season and year of clinical visit, BMI, education, race/ethnicity, alcohol and fish intake.
Nielsen et al., 2012 Greenland	Cross-sectional	805 men and 1040 women with Hg data. All were Inuit aged 30-69.	THg in blood: P50: 18 (IQR: 8.8-34.1) µg/L.	BP	Lower DBP, was associated with higher Hg in men but not in women. Weaker and non-statistically significant results in the same direction was found for SBP, but no associations were shown for pulse pressure. The risk for hypertension decreased with blood Hg in men only, but not with statistical significance in all chosen models.	Age, smoking, selenium, ratio of n-3/n-6 LCPUFA, waist circumference.
Olsén et al., 2012 Sweden	Cross-sectional	507 men and 509 women at age 70.	THg in blood: P50 for men: 1.9 (IQR: 1.6) µg/L; for women 1.7 (1.5) µg/L.	BP	No association was found to SBP (but with increased LDL-cholesterol and decreased HDL-cholesterol.	Gender and kidney function (glomerular filtration rate)

Table 25: Continued.

Author/ Country	Study design	Study participants	Ascertainment of mercury concentration	Disease or death	Results	Adjustments for confounding (or case matching), fish, LCPUFA, SES, etc.
Valera et al. (2012) Canada, Nunavik	Cross-sectional	313 adults with complete data on potential confounders	THg in blood: P50: 17 (IQR: 9.0-28.4; range: 0.8-112.0) µg/L.	BP, resting heart rate	No statistically significant associations between Hg and SBP, DBP, or pulse pressure. Resting heart rate increased (p for trend: 0.02), with 6.9 beats per minute more in the fourth vs. the first quartile.	Age, sex, fasting glucose, LDL-cholesterol, HDL-cholesterol, triacylglycerol, alcohol, smoking, physical activity, anti-hypertensive treatment, lead, PCB, and n-3 LCPUFAs were all considered, but only those that changed the regression coefficient more than 10 % were retained in the model.

µ: mean; AMI: acute myocardial infarction; BAEP: Brainstem Auditory Evoked potentials; BMI: body mass index; BP: blood pressure; CE: coronary event; CHD: coronary heart disease; CI: confidence interval; CVD: cardiovascular disease; DBP: diastolic blood pressure; DHA: docosahexaenoic acid; DPA: docosapentaenoic acid; EPA: eicosapentaenoic acid; GM: geometric mean; HDL: high-density lipoprotein; HF: high frequency; Hg: mercury; HR: hazard ratio; HRV: heart-rate variability; IQR: interquartile range; LCPUFA: long-chain polyunsaturated fatty acids; LDL: low-density lipoprotein; LF: low frequency; MeHg: methylmercury; MI: myocardial infarction; n-3 LCPUFA: n-3 long-chain polyunsaturated fatty acids; n-6 LCPUFA: n-6 long-chain polyunsaturated fatty acids; NHANES: National Health and Nutrition Examinations Survey; OR: odds ratio; P50: 50th percentile; PCB: polychlorinated biphenyls; PTWI: provisional tolerable weekly intake; RR: relative risk; SBP: systolic blood pressure; SD: standard deviation; SDANN: standard deviation of the average R-R intervals calculated over 5-minute periods; SE: standard error; SES: socio-economic status; THg: total mercury.

7.4.2.3. Other endpoints

Immunotoxicity

A Canadian study compared immunological status between newborns in a maritime population (n = 48) with a reference group which comprised newborns from a coastal urban centre (n = 60) (Belles-Isles et al., 2002). The maritime population had three times higher levels of PCBs and two times higher levels of mercury in cord blood (mean levels of mercury were 1.8 µg/L and 0.9 µg/L, respectively). Compared to the reference group, in the maritime population the proportion of a subset of naive helper T-cells was negatively correlated to mercury and PCBs, T-cell proliferation following an *in vitro* mitogenic stimulation was negatively associated with PCBs, and plasma IgM levels were negatively correlated to mercury, while IgG levels showed a positive correlation with PCBs.

For evaluation of the hypothesised association between exposure to methylmercury and titers of total Igs and specific antibodies in mothers and fetuses, maternal as well as cord serum samples were analysed in a cross-sectional study including 61 mother-infant pairs from the Brazilian Amazon region (Nyland et al., 2011). The total mercury level was higher in the cord blood as compared to the maternal blood (geometric means 9.63 µg/L and 6.90 µg/L, respectively). Total IgG levels were statistically significantly correlated with both maternal (r = 0.60) and cord blood mercury levels (r = 0.61), but IgG isotypes were not.

Antinuclear antibodies (ANA) were compared between two Amazon populations; high fish eaters (n = 105) and an urban control group with a low intake of fish (n = 105) (Alves et al., 2006). The mean mercury levels in hair were significantly higher among the fish eaters (35.4 mg/kg) as compared to the control group (1.0 mg/kg). Although positive serum ANA was more frequently observed in fish eaters (12.4 %) than controls (2.9 %), there was no statistically significant association between hair mercury and ANA. The authors concluded that an autoimmune dysfunction is unlikely to occur as a result of mercury exposure due to fish consumption.

A population-based study in Korea investigated the hypothesised association between mercury exposure and prevalence of atopic dermatitis in an adult population (Park and Kim, 2011). The investigated population consisted of 1990 adults, of which 10.9 % had a history of atopic dermatitis. Blood mercury concentrations were positively associated with lifetime prevalence of atopic dermatitis (OR for highest [> 6.04 µg/L] vs lowest [3.56 µg/L] tertile was 1.50, 95 % CI 1.02 - 2.21; p for trend = 0.057). The association was stronger for one-year atopic dermatitis prevalence (OR 1.82, 95 % CI 1.17 - 2.83; p for trend = 0.026).

The association between mercury levels in maternal and children's hair and the risk of wheeze and eczema were investigated among 582 Japanese children at 29 - 39 months of age (Miyake et al., 2011). The range of mercury levels was 0.26 - 6.05 mg/kg in mothers and 0.13 - 9.51 mg/kg in children. The adjusted ORs of wheeze and eczema were not statistically significantly different between exposure groups whether maternal or children's hair mercury levels were used.

In a birth cohort from the Faroe Islands that was recruited in 1999 - 2001 (the Faroese Cohort 3) sensitization and development of allergic disease was studied in relation to exposure to PCBs and methylmercury, and duration of breast feeding (Grandjean et al., 2010b). The study included 464 children who were clinical examined at five and seven years of age regarding asthma and atopic dermatitis. PCB and mercury concentrations were determined in blood samples obtained at parturition and at follow-up. The geometric mean mercury concentrations were: maternal hair 2.21 mg/kg; cord blood 11.3 µg/L; child's blood at five years of age 2.65 µg/L; child's blood at seven years of age 2.01 µg/L. Whereas positive associations were observed between duration of breast feeding and PCB concentrations on the one hand and some of the outcomes on the other hand, there was a positive association (protective) between prenatal methylmercury concentrations and grass-specific serum IgE concentrations.

Heilmann et al. (2010) studied serum concentrations of antibodies against vaccine toxoids at age five and seven years in the same cohort (the Faroese Cohort 3) as Grandjean et al. (2010b). Associations were seen between increased PCB exposure and reduction in antibody titres after diphtheria and to a less extent tetanus vaccination, but prenatal or recent postnatal mercury exposure did not seem to affect the outcomes.

Reproductive toxicity

A study from the Michigan communities, US, found an association between mercury levels and the prevalence of preterm births (Xue et al., 2007). The study comprised 1 024 women from the Pregnancy Outcomes and Community Health study and the mean level of total mercury in hair was 0.29 mg/kg (range 0.01 to 2.50). Women who delivered before 35 weeks´ gestation were more likely to have hair mercury levels at or above the 90th percentile (≥ 0.55 mg/kg) compared with women delivering at 37 weeks or later (OR 3.0, 95 % CI 1.3 - 6.7).

A study among 1 425 women from the National Health and Nutrition Examinations Survey (NHANES), 1999 - 2002, investigated the hypothesised associations between metals and endometriosis and uterine myomas (Jackson et al., 2008). The women included in the study were between 20 and 49 years of age, premenopausal and neither pregnant nor breastfeeding. Regarding blood mercury after taking potential confounders into account, there were no statistically significant associations with the outcomes. The mean blood level of mercury was 1.00 µg/L (95 % CI 0.94 - 1.05).

Within the BioCycle Study in Buffalo, New York, US, the associations between metals and reproductive hormones and anovulation in 252 premenopausal women were investigated (Pollack et al., 2011). The geometric mean for mercury in blood was 1.03 µg/L (IQR 0.58 - 2.10). There were no statistically significant associations between mercury and the outcomes investigated.

The association between methylmercury and semen parameters was investigated among 195 fishermen from Sweden (Rignell-Hydbom et al., 2007). The group of men was selected according to relatively high intake of locally caught fish. Blood levels of methylmercury were calculated as the difference between the concentrations of total mercury and inorganic mercury in blood and ranged from 0.11 to 16.59 µg/L (median 2.25 µg/L). Methylmercury in blood was not associated with the outcomes investigated (sperm motility, total sperm count, sperm chromatin integrity, and the proportion of Y-chromosome bearing sperms). Within the project it was also investigated whether an interaction between methylmercury exposure and PCB-153 (2,2',4,4',5,5'-hexachlorobiphenyl) was present, but no interaction was observed.

A study in Hong Kong included 111 males of infertile couples undergoing *in vitro* fertilization treatment (Choy et al., 2002). The mean blood mercury concentration was 8.3 µg/L and the mean seminal fluid mercury concentration was 4.4 µg/L. Neither the overall percentage of motile sperm nor sperm concentrations were correlated with mercury concentrations. On the other hand, seminal fluid mercury concentrations were statistically significantly ($p < 0.05$) correlated with abnormal sperm morphology ($r_s = 0.26$), particularly head ($r_s = 0.49$) and midpiece defects ($r_s = 0.30$). Also some sperm motion characteristics were statistically significantly correlated with seminal fluid mercury concentrations.

Developmental toxicity other than neurotoxicity and immunotoxicity

In the EDEN mother-child-cohort, fish intake was estimated through a questionnaire and hair mercury levels were analysed among 691 French women (Drouillet-Pinard et al., 2010). The relation between these two parameters and fetal growth was estimated. The median mercury level for the mothers was 0.52 mg/kg and no association was found between mercury and fetal growth in the whole sample of women.

In a Canadian study, the associations between n-3 LCPUFA and environmental contaminants (such as mercury, lead and PCBs) and gestational age and birth weight were investigated (Lucas et al., 2004). n-3 LCPUFA and contaminant concentrations were measured in cord plasma in a seafood eating population (Nunavik, n = 454) and in a comparison group from southern Québec (n = 29). There were positive associations between n-3 LCPUFA and the birth outcomes (statistically significant for gestational age but not for birth weight), whereas there was no evidence that contaminants had negative effects on the birth outcomes. The geometric mean of cord blood mercury concentrations was about 18 times higher in the Nunavik population as compared to the population from the Southern Québec (14.1 vs 0.8 µg/L).

A study among women from Korea suggested that the interactions of mercury with GSTM1 and GSTT1 play a role in reducing birth weight (Lee et al., 2010). The study included 417 Korean women and newborns in the Mothers and Children´s Environmental Health study and the geometric means of total mercury concentrations (µg/L) were 3.67 in early pregnancy maternal blood, 3.30 in late pregnancy maternal blood, and 5.53 in cord blood, respectively. For mothers with the GSTT1 null genotype, elevated mercury levels in maternal blood during late pregnancy were associated with an increased risk of lower birth weight. For mothers with both GSTM1 and GSTT1 null genotype, both maternal and cord blood mercury levels were associated with lower birth weight.

A study which investigated the relation between cord mercury levels and early child development in a World Trade Centre Cohort (New York), found no significant associations between exposure and birth outcomes (birth weight, length, head circumference, and gestational duration) (Lederman et al., 2008).

Cace et al. (2011) measured cerebellum length and width in 30 newborn babies of mothers with hair mercury levels above 1 mg/kg (mean: 2.37 mg/kg) and compared to 107 controls (mean: 0.46 mg/kg). The children of mothers with high mercury levels had shorter cerebellum, compared to the controls (18.4 vs. 20 mm, $p = 0.019$). No difference was observed for cerebellum width.

A study within the INMA Valencia cohort, Spain, investigated the association between total cord blood mercury concentrations and birth outcomes among 554 infants born 2004 to 2006 (Ramón et al., 2009). The geometric mean concentration of total mercury was 9.4 µg/L. Newborns in the highest quartile of total mercury weighed statistically significantly less (143.7 g) and had higher odds of being small for gestational age (OR 5.3, 95 % CI 1.2 - 23.9, $p = 0.03$) compared to those in the lowest quartile. In the statistical analyses consumption of fish was included as covariate together with others.

Miscellaneous

A cross-sectional study included 135 adult volunteers recruited from 12 fish-eating communities in the Brazilian Amazon had the objective to examine possible relations between different biomarkers of mercury exposure and oxidative stress using linear regression (Grotto et al., 2010). Medians of mercury were in blood 40.5 µg/L (range 1.70 to 179.3), in plasma 4.7 µg/L (0.2 to 30.9), and in hair 10.1 mg/kg (1.0 to 57.8). The study showed statistically significant inverse relations between glutathione peroxidase, glutathione, catalase, δ-aminolevulinate dehydratase (ALA-D) activity and blood mercury or hair mercury ($p < 0.05$), ALA-D reactivation index was significantly positively related to blood mercury ($p < 0.0001$). Plasma mercury was directly related to ALA-D reactivation index and inversely associated with glutathione peroxidase, glutathione, and ALA-D activity ($p < 0.05$). There were, however, some gender differences.

An earlier study in the Amazonas region in Brazil evaluated the association between hair mercury levels and the strengths of antioxidant defences (evaluated by glutathione levels and catalase activity) (Pinheiro et al., 2008). The study comprised women from three populations, two ‘exposed’ and one ‘non-exposed’. In total, 87 women participated and the levels in the exposed populations were much higher. The geometric means for hair mercury varied between 9.81 mg/kg and 17.32 mg/kg for different age groups in the ‘exposed’ populations and between 2.72 mg/kg and 3.89 mg/kg for the

different age groups among the 'non-exposed' populations. A statistically significant correlation was found between higher mercury content, higher glutathione level, and lower catalase activity.

Age-related cataract is a cause of impaired vision among elderly populations. Within the Amazonas region in Brazil, 211 participants from 12 regions were investigated in a cross-sectional study regarding the hypothesised association between exposure to mercury and selenium (Se) on the one hand and the prevalence of age-related cataract on the other hand (Lemire et al., 2010). For the individuals with plasma Se below the 25th percentile (110 µg/L) and blood mercury above the 25th percentile (25 µg/L), the prevalence of age-related cataract was statistically significantly increased for individuals younger than 65 years compared to individuals with plasma Se above 110 µg/L and blood mercury below 25 µg/L. However, the increase was not statistically significant for individuals of 65 years or older. Due to the limited number of participants and the relative low number of cases (n = 69), the results must be interpreted with caution.

One study which included 81 mother-newborn pairs from Paris, France, reported a relationship between calcium pump activity in pregnant women and their newborns on the one hand and mercury exposure on the other hand (Huel et al., 2008). Mercury explained about 7 % of total variance of calcium pump activity in mothers and newborns using stepwise linear regression. The median mother hair mercury level was 1.20 mg/kg.

The relationship between minerals and metabolic syndrome by analysis of hair tissue minerals was investigated among 343 subjects from Korea (Park et al., 2009). The mean concentration of hair mercury was 1.7 mg/kg in the normal group (n = 270) and 2.9 mg/kg in the metabolic syndrome group (n = 73). When subjects in the highest mercury quartile were compared with the subjects in the lowest mercury quartile group an OR of 7.35 (95 % CI 1.73 - 31.1) was obtained.

Cho and colleagues (2012) investigated the association between heavy metals and bone mineral density and osteoporosis in 481 postmenopausal Korean women. The women with highest blood mercury concentrations (upper quartile ≥ 5.23 µg/L) had a decreased prevalence of osteoporosis as compared to the women in the lowest concentrations (lowest quartile < 2.67 µg/L). An OR of 0.36 (95 % CI 0.19 - 0.68) was obtained.

Among 59 non-occupationally exposed women from northern Japan (mean age 20 years), total mercury levels in hair, toenail, and urine were investigated in relation to renal tubular function (Ohno et al., 2007). Mean mercury levels in the women were 1.51 mg/kg in hair, 0.59 mg/kg in toenail, and 0.86 mg/kg creatinine in urine. Among the women, the N-acetyl-β-D-glucosaminidase activity and the α1-microglobulin were positively correlated (although weakly) with both the daily mercury intake (estimated using a food frequency questionnaire) and mercury levels in hair, toenail, and urine ($p < 0.001$).

Within the NHANES in the US the hypothesised association between mercury and homocysteine in 1 005 children aged three to five years was examined, differentiated by higher and lower methylmalonic acid (an indicator of vitamin B-12 deficiency) and folate status (Gallagher and Meliker, 2011). An inverse association was observed in the subgroup of boys with higher methylmalonic acid and lower folate (n = 135), but not in other children. Children with mercury > 700 µg/L showed 189 µg/L lower homocysteine ($p < 0.001$) relative to the lowest quartile (≤ 140 µg/L).

Summary

There are a number of outcomes that have been investigated in single or few studies and the importance of the findings from these studies is accordingly difficult to evaluate. In addition, some of the studies are relatively small and other studies have investigated a number of outcomes, which raise the question about chance findings.

7.4.2.4. Summary of new developments since the last EFSA opinion of 2004

The new epidemiological observations in relation to methylmercury are as follows:

- The results of the new nutrition cohort suggest an effect of methylmercury at age 9 and 30 months, but not at five years, after adjustment for the beneficial effects related to n-3 LCPUFA. The previous interpretation from the main Seychelles cohort that there were no effects on children's cognitive performance following prenatal methylmercury exposure needs to be reconsidered. The results from the main cohort were not adjusted for n-3 LCPUFA.

- New results from the Faroese Cohort 1 show that the association between prenatal methylmercury exposure and neurodevelopmental outcomes was still present, although weaker, at the age of 14 years. In addition, results from a smaller Cohort 2 have become available. Most of the associations between neurological outcomes and mercury in Cohort 1 at seven years of age could not be confirmed in Cohort 2.

- Adjustment for the beneficial effects related to maternal fish consumption in the statistical analyses of the Faroese Cohort 1 indicated that the effects of prenatal methylmercury exposure may have previously been underestimated. Assessment of the Faroese Cohorts 1 and 2 together and further analyses in the Faroese Cohort 1 did not identify major confounding from PCB exposure.

- New studies of cardiac autonomy suggest an influence of mercury on HRV. In addition to a number of epidemiological studies, a well-designed intervention study found a change in HRV after a weekly intake of 3.4 µg methylmercury/kg b.w. However, the results are not consistent between studies and the implications for health are currently unclear.

- A recent study from Finland showed an association between mercury and sudden cardiac death. No other new epidemiological studies of cardiovascular disease have been identified that indicate an association between methylmercury and increased risk of cardiovascular disease.

- The importance of taking the beneficial effects of fish consumption into account when studying cardiovascular outcomes of methylmercury has become evident. The previous studies indicating an association between methylmercury and myocardial infarction risk, based the correction for n-3 LCPUFA confounding on biochemical measurements. One recent large study indicated no increased risk of cardiovascular disease associated with methylmercury, but adjustment for dietary n-3 LCPUFA was based on dietary questionnaires, and this may explain part of the discrepancy.

- Thus, the observations related to myocardial infarction, HRV and possibly blood pressure are of potential importance, but still not conclusive.

7.4.3. Epidemiological data on inorganic mercury

Human data on the adverse health effects of oral exposure to inorganic mercury mainly consist of case reports that cannot be used to identify a dose-response relationship, as summarised in (FAO/WHO, 2011b). Case reports and epidemiological studies addressing the toxicity after oral exposure to inorganic mercury, and that were not included in (FAO/WHO, 2011b) were summarised in a report of an EFSA contractor and this was used as a starting point (Hassauer et al., 2012). The epidemiological studies report on effects on the immune system, liver, kidney, endocrine systems and cyto-genotoxicity. The CONTAM Panel finds that these epidemiological studies suffer from several limitations, such as small study group, insufficient control for confounders, inadequate exposure assessment and insufficient differentiation between mercury compounds and routes of exposure. Therefore, the existing human data could not form the basis for a risk assessment of inorganic mercury.

7.5. Derivation of Health-based Guidance Value

7.5.1. Methylmercury

In the present opinion the CONTAM Panel has evaluated new developments in methylmercury toxicity since the last EFSA opinion from 2004, which referred to the PTWI of 1.6 µg/kg b.w. set by JECFA (FAO/WHO, 2004). This PTWI was based on neurodevelopmental endpoints from epidemiological studies. The point of departure behind this PTWI was based on the mean of the highest NOEL for prenatal exposure in the Seychelles main cohort (15.3 mg/kg in maternal hair) and the $BMDL_{05}$ for neurodevelopmental effects at age seven years in the Faroese Cohort 1 (12 mg/kg in maternal hair), giving a point of departure of 14 mg/kg in maternal hair.

A recent study in rats on developmental immunotoxicity indicated effects at low doses and the $BMDL_{05}$ for reduction in antibody response was 0.01 mg/kg b.w. per day expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day expressed as mercury) (Tonk et al., 2010). The Panel noted that the BMD is below the lowest dose tested. These data need to be confirmed, and the Panel has therefore not identified any new experimental animal studies that could provide a better primary basis than the human epidemiological data for a health-based guidance value. The reported associations between methylmercury exposure and cardiovascular disease were addressed by JECFA in their update in 2006 (FAO/WHO, 2007), and additional studies have become available. Although the observations related to myocardial infarction, HRV and possibly blood pressure are of potential importance, they are still not conclusive. Consequently, after carefully considering endpoints other than neurodevelopmental outcomes, and in particular cardiovascular disease, the CONTAM Panel concludes that associations between methylmercury exposure and neurodevelopmental outcomes after prenatal exposure still form the best basis for derivation of a health-based guidance value for methylmercury.

A major development since the previous EFSA opinion from 2004 is the understanding of confounding by beneficial factors in fish on associations between prenatal methylmercury exposure and neurodevelopmental endpoints. In the results from a new cohort from the Seychelles and in re-analysis of previous results from the Faroe Islands, confounding from fish consumption has been investigated. The new information partly modifies the interpretation of the previous results.

The previously derived NOEL of 15.3 mg/kg in maternal hair from the Seychelles main cohort did not take the concomitant intake of n-3 LCPUFAs into consideration. Results from the newer nutrition cohort at 9 and 30 months examinations indicated that at a mercury concentration in maternal hair of above approximately 11 mg/kg, the positive effects from n-3 LCPUFA intake can no longer outweigh detrimental effects from methylmercury exposure. However, the number of observations above this exposure level was low, increasing the uncertainty. Of note, at the follow up examination when the children's age was five years, positive associations between prenatal n-3 LCPUFA exposure and improved neurodevelopmental scores were seen, and inclusion of mercury in the regression did not affect the results. Based on the observations in the Seychelles nutrition cohort at 9 and 30 months, the CONTAM Panel finds that a methylmercury concentration of 11 mg/kg hair is an apparent NOEL which has been adjusted for maternal blood concentration of n-3 LCPUFA, and therefore forms a better point of departure than the unadjusted NOEL (15.3 mg/kg) derived from the Seychelles main cohort.

The new results presented from the Faroese cohorts are limited, and of note, the results at seven years in the Faroese Cohort 2 did not confirm the results of the Faroese Cohort 1, and this can not be only explained by a lower statistical power in the smaller Cohort 2. The question concerning confounding by PCB exposure in the Faroese cohorts was addressed by analysing the Faroese Cohorts 1 and 2 together, and the evidence for confounding by PCB exposure is considered as weak. Although some evidence for confounding by the beneficial effects of maternal fish consumption has been presented from the Faroese Cohort 1, the evidence for confounding from maternal blood n-3 LCPUFA is stronger in the nutrition cohort from the Seychelles. Even though the CONTAM Panel noted these

additions to the previous results from the Faroese Cohorts, it could not identify a better point of departure from the Faroese studies than the $BMDL_{05}$ of 12 mg/kg in maternal hair that has been selected previously by JECFA.

Based on what is summarised above, the CONTAM Panel decided to use the mean of the apparent NOEL from the Seychelles nutrition cohort at 9 and 30 months (11 mg/kg maternal hair) and the $BMDL_{05}$ from the Faroese Cohort 1 at age seven years (12 mg/kg in maternal hair), giving 11.5 mg/kg maternal hair as the basis for derivation of a health-based guidance value.

By use of a one-compartment toxicokinetic model as described in formula (i) (WHO, 1990), the JECFA calculated the steady state concentration in blood related to an average daily intake of mercury (FAO/WHO, 2004).

$$\text{(i)} \qquad C = (d*A*f*b.w.)/(b*V)$$

JECFA incorporated some refinements in the parameters used by the WHO in order to better reflect the situation in pregnant women. The following parameters were used by the JECFA:

C = concentration of mercury in blood (µg/L)
d = daily dietary mercury intake (µg/kg b.w. per day)
A = absorption factor (0.95)
f = the absorbed fraction distributed to the blood (0.05)
b.w. = body weight (65 kg for a pregnant woman)
b = elimination rate constant (ln 2 / half-life in blood = 0.014 per day)
V = blood volume (9 % of the body weight in a pregnant female).

By application of a maternal hair to maternal blood ratio of 250, the maternal hair concentration associated with no appreciable adverse effect (11.5 mg/kg) was converted into a maternal blood concentration of 46 µg/L. Using a one-compartment toxicokinetic model the value of 46 µg/L in maternal blood was converted to a daily dietary mercury intake of 1.2 µg/kg b.w.

A data-derived factor of 2 for variation in hair to blood ratio was applied by JECFA (FAO/WHO, 2004). Interindividual variation in toxicokinetics when converting the steady state concentration of mercury in blood to an estimated daily intake was taken into account by a standard factor of 3.2 ($10^{0.5}$).

The CONTAM Panel did not identify studies providing a sufficient basis to change the parameters in the one-compartment model and the uncertainty factors used by JECFA (FAO/WHO, 2004).

Therefore, the CONTAM Panel established a tolerable weekly intake (TWI) for methylmercury of 1.3 µg/kg b.w., expressed as mercury. The Panel noted that this TWI provides a margin of about 40 compared to the $BMDL_{05}$ for the reduction in antibody response reported by Tonk et al. in rats (Tonk et al., 2010).

7.5.2. Inorganic mercury

As summarised in Section 7.4.3 and by FAO/WHO (2011b) the human data on toxicity after oral exposure to inorganic mercury were not suitable for dose-response assessment, but they clearly indicated that kidney effects observed in experimental animals are relevant for humans. The JECFA review (FAO/WHO, 2011b) noted that kidney effects are consistently observed in various experimental animal species (weight changes, proximal tubule damage and progressive nephropathy) and that relative kidney weight increases observed in rats following exposure to mercuric chloride are also associated with a dose-dependent increase in renal mercury accumulation and with significant changes in the renal cortex, including increases in both proximal tubule and glomerular volumes. The JECFA therefore considered it appropriate to model kidney weight changes, which generally occurred at doses similar to or lower than other renal effects. The 6-month exposure was deemed sufficient to establish a health-based guidance value because the half-life of mercuric chloride in rats is estimated

at less than 30 days, steady-state renal mercury concentrations were reached by 4 - 6 months, and exposures in the same dose range for longer durations produced early mortality (FAO/WHO, 2011b).

The JECFA calculated BMD and BMDL values for a BMR of a 10 % increase in relative kidney weight. The EFSA Scientific Committee has recommended that a default BMR value of 5 % should be used for continuous data from animal studies, and that this could be modified based on statistical or toxicological considerations (EFSA, 2009). The CONTAM Panel noted that in the NTP study, statistically significant increases in relative kidney weight, all of approximately 120 % of control, were reported in male rats at 0.625, 1.25. 2.5 and 5.0 mg/kg b.w. per day expressed as mercuric chloride (equivalent to 0.46, 0.92, 1.9 and 3.7 mg/kg b.w. per day, expressed as mercury) (Table 26). At 0.312 mg/kg b.w. per day, expressed as mercuric chloride (equivalent to 0.23 mg/kg b.w. per day, expressed as mercury) the relative kidney weight was 110 % of control, which was not statistically significantly different. The lowest dose at which there was an increase in nephropathy was 0.625 mg mercuric chloride/kg b.w. per day (equivalent to 0.46 mg/kg b.w. per day). The CONTAM Panel concluded that, in this study, a 10 % increase in relative kidney weight was not accompanied by nephropathological changes and therefore represented an appropriate BMR.

The JECFA based its PTWI on the changes in relative kidney weights in male rats, because rats were more sensitive than mice and the data for male rats gave lower BMD and BMDL values than the data for female rats. The lowest BMD_{10} was 0.220 mg/kg b.w. per day, expressed as mercuric chloride with a corresponding $BMDL_{10}$ of 0.112 mg/kg b.w. per day, expressed as mercuric chloride (see Figure 9[39]). After correction of these values for the amount of mercury in mercuric chloride (73.9 %) and an adjustment to account for 5 days per week dosing, rather than 7 days per week dosing, these values result in a BMD_{10} of 0.12 mg/kg b.w. per day, expressed as mercury and a $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury. After application of a 100-fold uncertainty factor to this $BMDL_{10}$ and converting to a weekly basis with rounding to one significant figure, the JECFA established a PTWI for inorganic mercury of 4 µg kg b.w., expressed as mercury (FAO/WHO, 2011b). The Panel confirmed these BMD calculations.

[39] Reprinted from FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2011. Safety evaluation of certain food additives and contaminants. Methylmercury. WHO Food Additives Series, 63, 605-684, with permission from WHO.

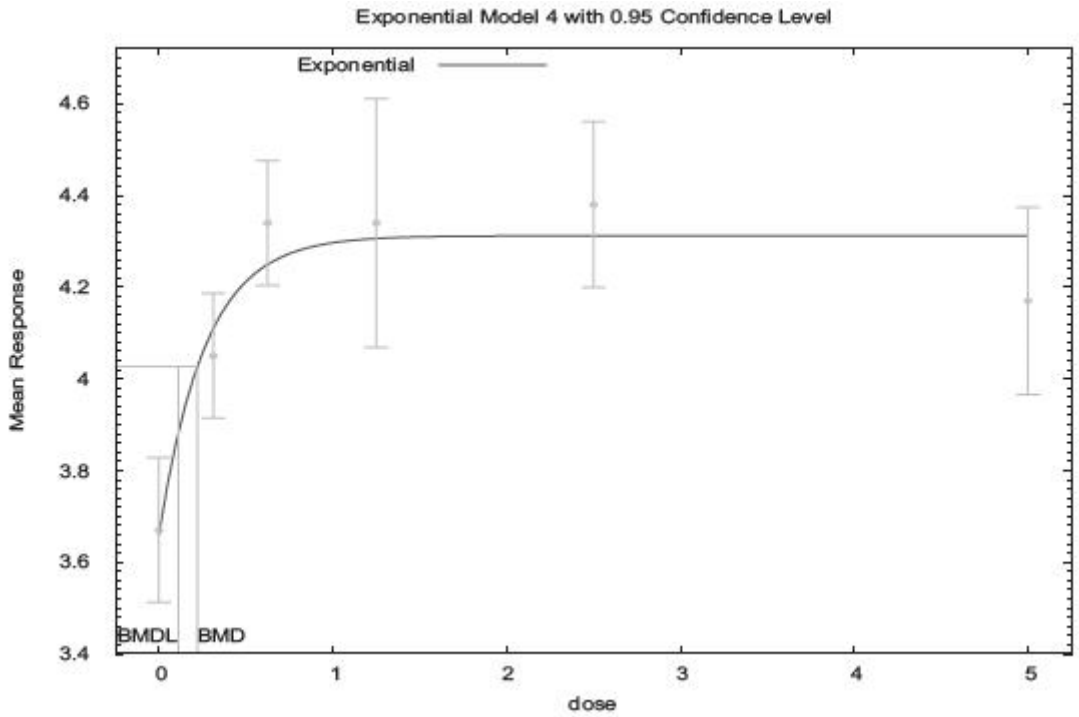


Figure 9: Exponential four-parameter model of relative kidney weight data in male F344 rats from 6-month NTP (1993) study (reprinted from FAO/WHO, 2011b[39]). Notes: Mean response = relative kidney weight (g); BMD(L)s are expressed as mercuric chloride and have not been corrected for dosing schedule.

Table 26: Results from US NTP study for rats gavaged with mercuric chloride for 6 months (modified from FAO/WHO, 2011b): Relative kidney weights in males and females and kidney pathology in males.

Dose (mg $HgCl_2$/kg b.w. per day)	Dose (mg Hg/kg b.w. per day)	n	Relative (to body weight) kidney weights (g)					Male nephropathy	
			Males			Females			
			mean	SE	SD	mean	SE	minimal	mild
0	0	10	3.67	0.07	0.22	3.80	0.07	8/10	0/10
0.312	0.23	10	4.05	0.06	0.19	4.09	0.10	10/10	0/10
0.625	0.46	10	4.34(b)	0.06	0.19	4.29(a)	0.05	9/10	1/10
1.25	0.92	10	4.34(b)	0.12	0.38	4.46(a)	0.09	6/10	4/10(a)
2.5	1.9	10	4.38(b)	0.08	0.25	4.57(a)	0.11	7/10	3/10
5.0	3.7	10	4.17(b)	0.09	0.28	4.62(a)	0.11	6/10	4/10(a)

$HgCl_2$: mercuric chloride; n: number of animals; SD: standard deviation; SE: standard error.
(a) : $p \leq 0.05$
(b) : $p < 0.01$
Source: NTP (1993)

Having considered the more recent data on experimental animals exposed to inorganic mercury, the Panel has not identified any studies in experimental animals exposed to inorganic mercury indicating effects on the kidney at doses lower than the $BMDL_{10}$ of 0.112 mg mercuric chloride/kg b.w. per day identified for effects on kidney weight in the NTP (1993) study, and from which the $BMDL_{10}$ of 0.06 mg/kg b.w. per day expressed as mercury was derived (FAO/WHO, 2011b).

The Panel noted that some recent studies (Huang et al., 2011; Lukačínová et al., 2011, 2012) have reported ototoxicity and reproductive toxicity at relatively low doses. These studies had some limitations, which have been discussed in Sections 7.2.2.3. and 7.2.2.4, and were not taken into further consideration. The Panel therefore agreed with the rationale of JECFA in setting a health-based guidance value of 4 µg/kg b.w. per week (FAO/WHO, 2011b), based on the $BMDL_{10}$ of 0.06 mg/kg b.w. per day for kidney weight changes in male rats as the pivotal effect and application of a total uncertainty factor of 100 to account for intra- and interspecies differences. The CONTAM Panel therefore established a TWI for inorganic mercury of 4 µg/kg b.w., expressed as mercury.

8. RISK CHARACTERISATION

8.1. Risk characterisation of methylmercury

Dietary exposure to methylmercury was calculated from fish and other seafood only, and since the data available for methylmercury were too limited, total mercury was regarded as methylmercury in fish, and 80 % in other seafood. Less than 10 % of the total mercury occurrence data were LC and since there were practically no differences between the UB and the LB dietary exposure estimates, the MB dietary exposure to methylmercury has been used in the risk characterisation.

The medians of mean methylmercury dietary exposures across surveys showed low variation between the age groups and were between 0.24 (adults) and 0.32 µg Hg/kg b.w. per week (other children), which is well below the TWI of 1.3 µg/kg b.w. The mean dietary exposure for adults ranged from 0.07 to 1.08 µg Hg/kg b.w. per week across European surveys and was highest for toddlers and other children, ranging from 0.09 to 1.57 µg Hg/kg b.w. per week. This indicates that a proportion of children with mean exposure can exceed the TWI. Also the medians of 95th percentile dietary exposures across surveys showed low variation between age groups, and were between 1.13 µg Hg/kg b.w. per week and 1.6 µg Hg/kg b.w. per week, which is close to or slightly exceeding the TWI for all age groups. The 95th percentile dietary exposure for adults ranged from 0.51 to 3.04 µg Hg/kg b.w. per week across European surveys and the dietary exposure was highest for other children and adolescents, ranging from 0.42 to 5.05 µg Hg/kg b.w. per week. For the 95th percentile dietary exposure, the maximum across surveys exceeded the TWI in all age groups.

The food category 'Fish meat' contributed most to methylmercury dietary exposure, and people with high and frequent fish consumption are at higher risk of exceeding the TWI. When only fish meat consumers were included in the exposure assessment, the intake estimates were generally two-fold higher compared to those for the total population. The highest dietary exposure of high consumers of fish meat across surveys and European countries was for other children at 7.48 µg Hg/kg b.w. per week, which is approximately six-fold the TWI.

Since the TWI is based on neurodevelopmental effects after prenatal dietary exposure, it is of importance that pregnant women have dietary exposure below the TWI in order to protect the unborn child. The women aged 18 - 45 years participating in the consumption surveys appeared to have similar dietary exposure as the general adult population. In the adult population, the median dietary exposure among high consumers of fish meat was 2.08 µg Hg/kg b.w. per week, but ranged up to 6.17 µg Hg/kg b.w. per week (4.7-fold the TWI).

Dietary exposure to methylmercury from human milk was calculated based on few observations. The mean weekly dietary exposure to methylmercury for infants with an average milk consumption ranged from 0.09 to 0.62 µg Hg/kg b.w. per week, and for infants with a high milk consumption the range was from 0.14 to 0.94 µg Hg/kg b.w. per week. This is below the TWI. However, since both the contribution of methylmercury to total mercury in human milk and the concentrations of total mercury in human milk shows high variation, the possibility of higher dietary exposure to methylmercury from human milk in Europe cannot be excluded.

In order to validate the exposure assessment to methylmercury, the CONTAM Panel calculated the level of mercury in blood that would correspond with the calculated dietary exposure for adults and

compared it with the observed concentration of total mercury in blood and hair in Europe. Using a similar one-compartment kinetic model as described in Section 7.5.1., but with blood volume as in non-pregnant adults, and the MB mean and 95th percentile exposure values for adults (Table 11), the corresponding levels in blood were calculated (Table 27).

Table 27: Predicted concentration of mercury in blood (µg/L) based on calculated chronic dietary middle bound mean and 95th percentile exposure to methylmercury across European dietary studies among adults as described in Table 11.

	Mean[(a)]	P95[(a)]
Minimum	0.48	3.5
Median	1.7	7.8
Maximum	7.5	21

P95: 95th percentile.

(a): Calculations are based on the following assumptions: C = d*A*f*b.w./(b*V), where C = mercury concentration in blood (µg/L), d = daily mercury intake (µg/kg b.w. per day), b = elimination constant (0.014 days-1), V = blood volume in the body (5 L in adults of 70 kg b.w), A = absorption factor (0.95), f = fraction of daily intake distributed to the blood (0.05), b.w. = body weight (70 kg).

As described in Section 7.4.1., the mean concentration of total mercury in blood among adults and elderly is in the range 0.2 - 4.85 µg/L (Table 23). The mean concentrations reported among adults in Europe are therefore in the same range and possibly a little lower than the means that can be predicted from the dietary exposure (Table 27). The high percentile concentrations were approximately 10 - 15 µg/L, although up to 40 µg/L was reported (see Appendix F, Tables F1 and F2). This is also in accordance with the predicted values from the 95th percentile exposures (Table 27).

The mean mercury levels in blood are supported by the mean hair concentrations in Europe, which ranged from 0.17 to 1.45 in the adult population (Table 23). With few exceptions, hair mercury concentrations in the higher percentiles in different studies were below 10 mg/kg. The reported hair concentrations of mercury in the European population are therefore, with a few exceptions, lower than the highest concentrations (point of departure) associated with low risk.

Exposure to methylmercury above the TWI is of concern, but if measures to reduce methylmercury exposure are considered then the potential beneficial effects of fish consumption should also be taken into account.

8.2. Risk characterisation of inorganic mercury

The dietary exposure assessment was based on occurrence of total mercury. The CONTAM Panel allocated 20 % of total mercury in fish and 50 % in crustaceans and molluscs. In all other foods 100 % was regarded as inorganic mercury. This was done in order to not underestimate dietary exposure. For human milk, the concentration of inorganic mercury was calculated as the difference between total and methylmercury, since the mean contribution of inorganic mercury to total mercury was not evaluated as sufficiently robust to form basis for exposure assessment. More than 60 % of the occurrence data on total mercury in food were reported as below LOD or LOQ (LC), and the CONTAM Panel decided to use the LB and UB to represent a possible range within which the real dietary exposure would fall for its risk characterisation.

Dietary mean LB to UB estimates of exposure to inorganic mercury across European surveys and countries varied widely. The mean dietary exposure for adults ranged from 0.14 to 0.70 µg Hg/kg b.w. per week (minimum LB – maximum UB) across European surveys and was the highest for toddlers, ranging from 0.27 to 2.16 µg Hg/kg b.w. per week. The 95th percentile dietary exposure for adults ranged from 0.36 to 1.83 µg Hg/kg b.w. per week (minimum LB – maximum UB) across European surveys and was the highest for toddlers and other children, ranging from 0.50 to 4.06 µg Hg/kg b.w. per week. Mean and 95th percentile UB dietary exposures are well below the TWI of 4 µg/kg b.w in most of the studies. Although the highest UB 95th percentile dietary exposure for toddlers is similar to

the TWI, this value represents an overestimate and is associated with high uncertainty, as indicated by the wide LB to UB ranges.

Based on limited data on the occurrence of inorganic mercury in human milk in Europe, the dietary exposure for a 3 month old exclusively breast-fed infant is approximately 0.17 to 1.29 µg/kg b.w. per week with mean human milk consumption and at mean occurrence. For high consuming breast-fed infants, the intake ranged from 0.25 to 1.94 µg/kg b.w. per week. This is below the TWI. However, since both the contribution of inorganic mercury to total mercury in human milk and the concentrations of total mercury in human milk shows high variation, the possibility of higher dietary exposure to inorganic mercury from human milk in Europe cannot be excluded.

The estimated dietary exposure to inorganic mercury in Europe does not indicate a concern. Outgassing from amalgam fillings will increase total mercury exposure. Since elemental mercury is oxidised in the human body to mercuric mercury, a high number of amalgam fillings is likely to increase the internal inorganic mercury exposure; thus the TWI might be exceeded. Exposure from ambient air can be considered negligible. Mercury-containing skin care products are not permitted in the EU but would be an additional source and might be a concern if used.

9. UNCERTAINTY ANALYSIS

The evaluation of the inherent uncertainties in the assessment of exposure to methylmercury and inorganic mercury has been performed following the guidance of the Opinion of the Scientific Committee related to Uncertainties in Dietary Exposure Assessment (EFSA, 2006). In addition, the report on 'Characterizing and Communicating Uncertainty in Exposure Assessment' has been considered (WHO/IPCS, 2008). According to the guidance provided by the EFSA opinion (2006) the following sources of uncertainties have been considered: Assessment objectives, exposure scenario, exposure model, and model input (parameters).

9.1. Assessment objectives

The objectives of the assessment were defined in the terms of reference. The CONTAM Panel considered the new developments regarding the toxicity of inorganic mercury and methylmercury to evaluate whether the PTWIs established by JECFA of 1.6 µg/kg b.w. for methylmercury and of 4 µg/kg b.w. for inorganic mercury are still considered appropriate. The CONTAM Panel also assessed human dietary exposure, taking into account specific sensitive groups and considered the non-dietary sources of exposure to mercury. There was no uncertainty in addressing the objectives as outlined in the terms of reference.

9.2. Exposure scenario/Exposure model

In response to the EFSA call for data on mercury, 59 650 data points from the period 2002 to 2011 from 20 European countries were included in the analyses. The major contributors of the data were Slovakia (35 %), followed by Germany (26 %) and Norway (11 %), while several other countries contributed a very low number of results. There is an uncertainty in possible regional differences in mercury contamination of food commodities and it is evident that the dataset is not fully representative of food on the EU market.

There are considerable differences in the number of analytical results reported across the food groups with the most samples belonging to the fish and seafood category, followed by meat and meat products category and only few samples on other food categories (e.g. composite food, snacks, herbs etc.), which created uncertainty for the inorganic mercury dietary exposure estimate.

Only when results were ten times higher than the second highest value and significantly influenced the mean concentration, they were excluded. However, there was uncertainty whether some included high values were really measured or erroneously reported and they might lead to an overestimation of the dietary exposure.

The occurrence data come from monitoring programmes, and also from routine measurements within the frame of official food controls, so they originated from both random and targeted sampling and this might lead to overestimation.

The majority of the data were reported as total mercury and only a limited number of results were available for methylmercury (n = 1 083) and inorganic mercury (n = 3). For this reason the conversion factors based on contributions of methylmercury and inorganic mercury to total mercury derived from the literature data were applied in order to achieve the contribution of methylmercury and inorganic mercury to total mercury. The CONTAM Panel used a conservative approach and assumed that 100 % of mercury in fish is in the form of methylmercury and 20 % inorganic mercury. In seafood it was assumed that 80 % of total mercury is methylmercury and 50 % inorganic mercury. And in all other food categories it was assumed that 0 % is methylmercury and 100 % inorganic mercury. These assumptions resulted in an overestimation of dietary exposure.

For human milk, the exposure assessment was based on a low number of studies reporting concentrations of total and methylmercury. The limited available data on the contribution of methylmercury to total mercury in human milk showed a wide variation, and the mean contribution was not considered sufficiently robust to form a basis for exposure assessment. Therefore, concentrations of methylmercury in human milk were used and the difference between total mercury and methylmercury concentrations in human milk was used for inorganic mercury exposure assessment. However, a study reporting only total mercury in human milk has shown higher concentrations than the studies that provided speciation analyses (about 5 to 11 fold higher). Therefore, the possibility of higher dietary exposure to methylmercury from human milk in Europe cannot be excluded.

Some types of food processing have been shown to have an influence on the concentration of methylmercury in fish due to weight (moisture and fat) change but the change will depend on the method of cooking and processing.

The significant proportion of samples with values below LOD/LOQ introduced considerable uncertainties to the overall dietary exposure estimate, particularly for inorganic mercury. The use of the LB in this opinion tends to underestimate, while UB tends to overestimate the dietary exposure.

Two specific population subgroups (women in childbearing age and high and frequent fish consumers) were considered separately in the assessment. Since the number of women of childbearing age participating in the surveys was low (less than 500 participants in 10 out of 15 surveys), there will be uncertainty in extrapolation to the wider European population. Similar uncertainty exists in the age group of infants where only two surveys with low number of participants were available.

When the survey duration covers a low number of days and the dietary exposure is assessed for ‘consumers only’, this can lead to some overestimation of dietary exposure in high and frequent consumers of fish meat. This is especially true for countries where these food commodities are consumed rarely or seasonally. As the duration of surveys increase, the observed percentage of subjects reporting consumption of commonly and rarely eaten foods becomes larger, whereas the observed mean and high percentiles consumption, in consumers only, decreases (Merten et al., 2011).

9.3. Other uncertainties

Methylmercury

The TWI is based on neurodevelopmental endpoints associated with mercury exposure in the cohort studies from the Seychelles and the Faroe Islands. Whereas the Seychelles population are exposed to methylmercury via fish consumption, the main source is whale meat in the Faroe Islands, with a minor contribution coming from fish consumption. Since confounding from the beneficial effects of fish consumption is addressed, and the mercury source is fish in only one of the cohorts, such confounding

might affect the outcomes differently in these cohorts, which might increase the uncertainty in the assessment.

The point of departure from the nutrition cohort in the SCDS was at a level with few observations, this also increases the uncertainty in the risk assessment.

A developmental immunotoxicity study in rats indicated that immunosuppressive effects might be the most sensitive endpoint (see Section 7.2.1.3.). Immunotoxicity is not well characterised in epidemiological studies, increasing the uncertainty in whether the TWI has been based on the most sensitive endpoint.

Observations in humans on myocardial infarction and HRV are of potential importance, which contributes to the uncertainty regarding whether the TWI has been based on the most sensitive endpoint, and whether only pregnant women and fetuses belong to the groups at risk.

There is high inter-study and inter-individual variation in the ratio between total mercury in hair and blood, and a mean ratio of 250:1 was used for converting the concentration of total mercury in hair into its concentration in blood. A data-derived factor of 2 for variation in hair to blood ratio was applied and the new data available for hair to blood ratio from adults, including the critical group of women in child bearing age, indicated that the factor covers the variance. There are, however, some indications that the total mercury hair to blood ratio is higher in children, and this might lead to an underestimation of the risk if postnatal effects of exposure were of higher significance. There is uncertainty connected to the half-life of methylmercury in blood and the absorbed fraction distributed to the blood, which are parameters used for the conversion of blood levels to dietary intake in the one-compartment toxicokinetic model.

Inorganic mercury

The TWI established by the Panel is based on the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury, for effects on kidney weight in male rats dosed with mercuric chloride for 6 months (see Section 7.2.2.2.). Selection of this value as the point of departure is supported by results from other studies that have investigated effects on the kidney, for which effect levels were all higher, including those for the immune-type kidney reaction in the Brown Norway rat, which is considered a sensitive animal model.

Some more recent laboratory animal studies have reported other effects at low levels of exposure to mercuric chloride, for which NOAELs or BMDLs could not be identified. The lowest effect level in these studies was 0.022 – 0.029 mg/kg b.w. per day, expressed as mercury for reproductive parameters (see Section 7.2.2.4.). These studies had limitations, discussed earlier, and therefore were not used to derive the TWI.

9.4. Summary of uncertainties

In Tables 28 and 29, a summary of the uncertainty evaluation is presented for methylmercury and inorganic mercury respectively, highlighting the main sources of uncertainty and indicating an estimate of whether the respective source of uncertainty might have led to an over- or underestimation of the exposure or the resulting risk.

Table 28: Summary of qualitative evaluation of the impact of uncertainties on the risk assessment of the dietary exposure of methylmercury.

Sources of uncertainty	Direction
Measurement uncertainty of analytical results	+/-[(a)]
Extrapolation of occurrence data to whole Europe	+/-
Use of analytical data from both targeted and random sampling	+
Applying conversion factors to convert total mercury to methylmercury	+
Not including exposure from food groups other than fish and other seafood	-
Exposure estimation from rarely consumed food and/or in high consumers	+/-
Exposure from human milk based on limited data	+/-
Value of point of departure from the Seychelles and the Faroe Islands cohorts	+/-
Possibility that other endpoints are more sensitive (e.g. developmental immunotoxicity and cardiovascular effects)	-

(a): + = uncertainty with potential to cause over-estimation of exposure/risk; - = uncertainty with potential to cause under-estimation of exposure/risk.

Table 29: Summary of qualitative evaluation of the impact of uncertainties on the risk assessment of the dietary exposure of inorganic mercury.

Sources of uncertainty	Direction
Measurement uncertainty of analytical results	+/-[(a)]
Extrapolation of occurrence data to whole Europe	+/-
Use of analytical data from both targeted and random sampling	+
Applying conversion factors to convert total mercury to inorganic mercury	+
Use of LB and UB occurrence data in the dietary exposure estimations	+/-
Limited occurrence data from several food groups	+/-
Exposure from human milk based on limited data	+/-

LB: lower bound; UB: upper bound.
(a): + = uncertainty with potential to cause over-estimation of exposure/risk; - = uncertainty with potential to cause under-estimation of exposure/risk.

The CONTAM Panel concluded that the impact of the uncertainties on the risk assessment of exposure to methylmercury and inorganic mercury is considerable and that the assessment is likely to be conservative.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

Background

- Mercury is a metal that is released into the environment from both natural and anthropogenic sources. Once released into the environment, mercury undergoes a series of complex transformations and cycles between atmosphere, ocean and land.
- The three chemical forms of mercury are (i) elemental mercury (Hg^0), (ii) inorganic mercury (mercurous (Hg_2^{2+}) and mercuric (Hg^{2+}) cations) and (iii) organic mercury (e.g. methylmercury).
- In 2003, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) reviewed the provisional tolerable weekly intake (PTWI) for methylmercury and established a revised PTWI of 1.6 µg/kg body weight (b.w.).

- In 2010, the JECFA reviewed the PTWI for total mercury and established a PTWI of 4 µg/kg b.w. for inorganic mercury.

Sampling and methods of analysis

- For total mercury, cold vapour - atomic absorption spectrometry (CV-AAS) or cold vapour - atomic fluorescence spectrometry and increasingly inductively coupled plasma mass spectrometry (ICP-MS) are the most widely used techniques. Two European standardised methods with CV-AAS and ICP-MS detection are available.

- For speciation analysis, gas chromatography coupled to mass spectrometry or ICP-MS is the most widely used technique. High-performance liquid chromatography techniques are increasingly being used but usually, gas chromatography methods have higher sensitivity than liquid chromatography. No fully validated or standardised methods are available for the separation and detection of mercury species.

- Several standard or certified reference materials are available for both total mercury and methylmercury. Regular proficiency testing schemes are organised by a number of providers for both total mercury and methylmercury in foodstuffs to demonstrate and maintain analytical quality assurance.

Occurrence

- Following a call for data, 20 European countries submitted approximately 60 000 analytical results of mercury concentrations, covering the period from 2002 to 2011; 98 % of the data were on total mercury.

- The food group 'Fish and other seafood' (12 % left-censored (LC) data) dominated the total number of samples. This food category was followed by 'Meat and meat products' (56 % LC data) and 'Grains and grain products' (60 % LC data). The percentage of samples below the limit of detection or limit of quantification in the individual food groups at FoodEx Level 1 ranged between 12 % to 90 %.

- The highest mean total mercury concentrations were detected in the following food commodities: fish and other seafood, particularly in fish meat (especially swordfish and sharks), wild mushrooms and dietary supplements.

- Mercury can be transferred into human milk. In the literature, mean concentrations of total mercury between 0.3 and 3.53 µg/L in Europe are reported.

- The contribution of methylmercury to total mercury is typically 80 - 100 % in fish and 50 - 80 % in seafood other than fish. In other foods, mercury is presumed to be present as inorganic mercury.

- Three European studies were identified in which both methylmercury and total mercury were analysed in human milk and the mean contribution of methylmercury to total mercury ranged from 26 to 63 %.

- There is little impact on the content of mercury in foods resulting from cooking or processing. Therefore data for mercury in raw foods are suitable to use for dietary exposure estimates.

Human dietary exposure

- For dietary exposure to methylmercury, the EFSA Scientific Panel on Contaminants in the Food Chain (CONTAM Panel) used a conservative approach by assuming that 100 % of total mercury in fish and 80 % in seafood other than fish is in the form of methylmercury.

- For dietary exposure to inorganic mercury, the CONTAM Panel used a conservative approach by assuming that 20 % of total mercury in fish and 50 % in seafood other than fish and 100 % in other foods is in the form of inorganic mercury.

- In order to estimate dietary exposure, the consumption data of each individual within the surveys were multiplied by the mean occurrence data for the relevant food categories, resulting in a distribution of exposure, from which the mean and 95th percentile were identified for each survey and age class.

- For human milk, the limited available data on the contribution of methylmercury to total mercury showed a wide variation, and the mean contribution was not evaluated as sufficiently robust to form a basis for dietary exposure assessment. Therefore, concentrations of methylmercury in human milk were used for methylmercury dietary exposure assessment and the difference between total mercury and methylmercury concentrations in human milk was used for inorganic mercury dietary exposure assessment.

Methylmercury

- Only the consumption of fish and other seafood was considered relevant and therefore was used for assessment of dietary exposure to methylmercury from food (other than human milk).

- The estimation of dietary exposure to methylmercury was based on middle bound (MB) data since there was virtually no difference between lower bound (LB) and upper bound (UB).

- The mean MB methylmercury dietary exposure varied from the lowest minimum of 0.06 µg/kg b.w. per week seen in elderly and very elderly to the highest maximum of 1.57 µg/kg b.w. per week in toddlers.

- The 95th percentile MB dietary exposure ranged from the lowest minimum of 0.14 µg/kg b.w. per week in very elderly to the highest maximum of 5.05 µg/kg b.w. per week in adolescents. For consumers that report consumption of fish meat during the course of the surveys, the 95th percentile MB dietary exposure ranged from the lowest minimum of 0.54 µg/kg b.w. per week in elderly to the highest maximum of 7.48 µg/kg b.w. per week in other children.

- Dietary exposure for the child age groups (toddlers and other children) was higher compared to the adult age groups, and this is explained by the higher food consumption in relation to their body weight.

- Based on the reported mean concentrations of methylmercury in human milk, the mean weekly dietary exposure to methylmercury for infants with an average milk consumption ranges from 0.09 to 0.62 µg/kg b.w. per week and from 0.14 to 0.94 µg/kg b.w. per week for infants with a high milk consumption. However, the possibility of higher dietary exposure to methylmercury from human milk in Europe cannot be excluded.

- Dietary exposure of women of child-bearing age did not differ appreciably from dietary exposure of the general adult population.

- Fish meat, particularly tuna, swordfish, cod and whiting, and pike were identified as the most important contributors for all age groups with hake also being important for children because of high consumption in some population groups.

Inorganic mercury

- All main food categories were considered for the dietary exposure to inorganic mercury.
- The estimation of dietary exposure to inorganic mercury was based on minimum LB and maximum UB data due to the high proportion of LC data and the large difference between LB and UB concentrations.
- The mean dietary exposure to inorganic mercury ranged from the lowest minimum LB of 0.13 µg/kg b.w. per week in elderly to the highest maximum UB of 2.16 µg/kg b.w. per week in toddlers.
- The 95th percentile dietary exposure ranged from the lowest minimum LB of 0.25 µg/kg b.w. per week in elderly and very elderly to the highest maximum UB of 4.06 µg/kg b.w. per week in toddlers.
- The 95th percentile dietary exposure, to inorganic mercury from dietary supplements (consumers only) was up to 0.24 µg/kg b.w. per week (UB), and dietary supplements were not considered a major source.
- Dietary exposure for the child age groups (toddlers and other children) was higher compared to the adult age groups, and this is explained by the higher food consumption in relation to their body weight.
- At FoodEx Level 1, 'Fish and other seafood', 'Non-alcoholic beverages' and 'Composite food' were the most important contributors to inorganic mercury dietary exposure in the European population. Dietary exposure to inorganic mercury was driven by high concentrations in the case of fish and other seafood and composite food (where a high proportion of the data were LC), but was more likely driven by high consumption in the case of non-alcoholic beverages.
- At FoodEx Level 2, different groups of food commodities were estimated as the major contributors to inorganic mercury dietary exposure: (i) tea (infusion), driven by high consumption; (ii) fish meat, cereal-based dishes, prepared salads, wild mushrooms, when the contribution was based on high mercury concentration; (iii) ready to eat soups, driven by high percentage of LC data; and (iv) fruit juices and bread and rolls, driven by both high consumption and high percentage of LC data.
- Based on mean concentrations of inorganic mercury in human milk, the mean weekly dietary exposure for infants with an average milk consumption ranges from 0.17 to 1.29 µg/kg b.w. per week and from 0.25 to 1.94 µg/kg b.w. per week for infants with a high milk consumption. However, the possibility of higher dietary exposure to inorganic mercury from human milk in Europe cannot be excluded.

Human non-dietary exposure

- Non-dietary exposure to methylmercury is likely to be of minor importance for the general population in the European Union.

- In the case of a high number of amalgam fillings, exposure to elemental mercury via the outgassing of dental amalgam is believed to strongly contribute to the internal inorganic mercury exposure.

Hazard identification and characterisation

Toxicokinetics

- After oral intake, methylmercury is much more extensively and rapidly absorbed than mercuric and mercurous mercury.

- In human blood mercuric mercury is divided between plasma and erythrocytes, with more being present in plasma, whereas methylmercury is accumulated to a large extent (> 90 %) in the erythrocytes.

- Due to its low lipophilicity, mercuric mercury does not readily cross the placental, the blood-brain or the blood-cerebrospinal fluid (CSF) barrier, whereas organic mercury species are able to enter the hair follicle, and to cross the placenta as well as the blood-brain and blood-CSF barriers, allowing accumulation in hair, the fetus and the brain.

- Mercuric mercury in the brain is generally the result of either in situ demethylation of organic mercury species or oxidation of elemental mercury.

- Excretion of absorbed mercuric mercury occurs mainly via urine, whereas the main pathway of excretion of absorbed methylmercury is via faeces (in the form of mercuric mercury).

- Urinary total mercury might be a suitable biomarker of inorganic (and elemental) mercury, but not for methylmercury exposure. Total mercury in hair and blood are routinely used as biomarkers to assess long term methylmercury exposure. A frequently cited total mercury blood to hair ratio is 1:250, however large variations exist, especially in people with infrequent fish consumption.

Toxicity

Methylmercury

- A recent developmental study applying only one low dose in mice indicated effects on body weight gain, locomotor function and auditory function. A large study in rats showed developmental immunotoxic effects at low doses, and the lower 95 % confidence limit for a benchmark response of 5 % ($BMDL_{05}$) of 0.01 mg/kg b.w. per day, expressed as methylmercuric chloride (equivalent to 0.008 mg/kg b.w. per day, expressed as mercury) for the specific antibody response in rats was the lowest BMDL.

- Methylmercury exerts genotoxicity *in vitro* in mammalian cells, whereas data from laboratory animals and humans are inconsistent.

Inorganic mercury

- The critical target for toxicity of inorganic mercury is the kidney.

- Other targets include the liver, nervous system, immune system, reproductive and developmental systems.

- Effects on reproduction have been reported at a low dose ($BMDL_{10}$ for kidney weight) but the study had limitations and the CONTAM Panel did not consider the data sufficiently robust to be used as a basis for establishing a health-based guidance value.

- From repeated-dose studies, no effects were observed on the kidney at 0.23 mg/kg b.w. per day, expressed as mercury or below. The CONTAM Panel confirmed the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury, for effects on kidney weight calculated by JECFA.

- Mercuric mercury exerts genotoxicity *in vitro* in mammalian cells, whereas data from laboratory animals and humans are inconsistent.

Mode of action

- Most of the *in vitro* and *in vivo* studies used methylmercuric chloride, which differs in bioavailability, tissue distribution and toxicity from methylmercury species present in fish.

- Molecular mechanisms of methylmercury toxicity include protein binding, disturbances in calcium homeostasis and oxidative stress including lipid peroxidation. The modes of action described are mitochondrial dysfunction, disruption of the neurotransmitter systems, neuronal and vascular/cardiovascular cell damage possibly leading to adverse effects such as inflammation, thrombosis, dyslipidemia, vascular smooth muscle and endothelial damage, neurotoxicity and neurodevelopmental toxicity.

- The most likely mechanism of genotoxicity appears to be via oxidative stress, which would be expected to be thresholded. Inorganic and organic mercury species have been shown to bind covalently to isolated DNA but the formation of such DNA adducts has not been investigated in cell systems or *in vivo* and therefore the consequences of this interaction for genotoxicity have not been elucidated.

Observations in humans

Methylmercury

- In the European population, mean concentrations of total mercury ranged from 0.86 to 13.9 µg/L in cord blood, from 0.2 to 4.85 µg/L in blood from adults and elderly, from 0.17 to 1.45 mg/kg in hair from adults and elderly and from 0.14 (geometric mean) to 1.99 mg/kg in hair from children.

- New data from the Faroe Islands Cohort 1 at children's age 14 years indicated that the association between prenatal exposure and neurological auditory function was still present at 14 years, but with a smaller impact than at seven years, and not related to the estimates of recent postnatal exposure. Reassessment of the data from the Faroese Cohort 1 participants at age seven years indicated that beneficial effects of fish consumption together with imprecision in the measurements of fish consumption and determination of mercury in hair might underestimate the effects of methylmercury by a factor up to two.

- Most of the assessments of the neurobehavioural outcomes in the smaller Faroe Islands Cohort 2 at age seven years could not confirm the associations between neurological outcomes and mercury found in the Faroese Cohort 1. Assessment of the Faroese Cohorts 1 and 2 together and further analyses in the Faroese Cohort 1 did not identify major confounding from polychlorinated biphenyls exposure.

- Reassessments of the 4.5 years results and the 10.5 and 17 years follow up studies from the Main Cohort in the Seychelles Child Developmental Study have not revealed any consistent association between prenatal mercury exposure and neurodevelopmental endpoints.

- Results from the smaller Nutrition Cohort in the Seychelles Child Developmental Study indicated an association between prenatal mercury exposure and decreased scores on neurodevelopmental indices at 9 and 30 months after adjustment for prenatal blood maternal n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFA). An apparent no-observed-effect level (NOEL) at a mercury level of approximately 11 mg/kg maternal hair was observed. No statistically significant associations between prenatal mercury exposure and developmental endpoints were found at the five years follow up of the study. However, a positive association between maternal prenatal docosahexaenoic acid and preschool language scores was reported from the five years follow up.

- A few, but not all, studies from other regions found associations between prenatal mercury exposure and cognitive outcomes at lower mercury levels than those reported in the Faroe Islands and Seychelles cohorts, but the overall picture at low-level exposure does not provide information to allow conclusions.

- As regards children's postnatal mercury exposure, the inconsistent observations from the identified studies do not give reasons for increased concern for neurological effects. The studies on autism do not indicate increased risk from dietary mercury exposure, but for attention deficit hyperactivity disorder some studies have found associations with mercury. Taken together, the results do not provide information to allow conclusions.

- In the adult population, no association is observed between low levels of mercury exposure and adverse neurological outcomes.

- The importance of taking the beneficial effects of fish consumption into account when studying cardiovascular outcomes of methylmercury has become evident.

- Studies on stroke in relation to mercury exposure do not suggest an association.

- Some studies indicate an association between methylmercury and increased risk for acute myocardial infarction and acute cardiac death. Other studies do not show increased cardiac disease risk. The studies that showed association had used biochemical measurements as basis for adjustment for n-3 LCPUFA, while the ones that found no association had based adjustments on dietary questionnaire data. Some additional studies have dealt with lower exposure levels and provided no associations.

- The observations related to myocardial infarction, heart rate variability and possibly blood pressure are of potential importance, but still not conclusive.

- Endpoints other than neurodevelopmental toxicity, neurotoxicity and cardiovascular toxicity have been investigated only in single or few studies and the importance of the findings from these studies are accordingly difficult to evaluate.

Inorganic mercury

- Human data on the adverse health effects from oral exposure to inorganic mercury mainly consist of case reports that are not suitable to identify a dose-response relationship and they could not form the basis for a risk assessment of inorganic mercury.

Derivation of Health-based Guidance Values

Methylmercury

- The CONTAM Panel has not identified any new, experimental animal studies that could provide a better primary basis than the human epidemiological data for a health-based guidance value.
- Associations between methylmercury exposure and neurodevelopmental outcomes after prenatal exposure still form the best basis for derivation of a health-based guidance value.
- The mean of the apparent NOEL from the Seychelles nutrition cohort at 9 and 30 months (11 mg/kg maternal hair) and the $BMDL_{05}$ from the Faroese cohort 1 at age seven years (12 mg/kg in maternal hair), resulting in 11.5 mg/kg maternal hair, was used as basis for derivation of a health-based guidance value.
- By application of a maternal hair to maternal blood ratio of 250, the maternal hair mercury concentration with no appreciable adverse effect was converted into a maternal blood mercury concentration of 46 µg/L.
- Using a one-compartment toxicokinetic model the value of 46 µg/L in maternal blood was converted to a daily dietary mercury intake of 1.2 µg/kg b.w.
- A data-derived uncertainty factor of 2 was applied to account for variation in the hair to blood ratio. In addition a standard factor of 3.2 was applied to account for interindividual variation in toxicokinetics, resulting in a total uncertainty factor of 6.4.
- The CONTAM Panel established a tolerable weekly intake (TWI) for methylmercury of 1.3 µg/kg b.w. expressed as mercury.
- The Panel noted that this TWI provides a margin of about 40 compared to the $BMDL_{05}$ for the reduction in antibody response in rats.

Inorganic mercury

- Having considered the data on inorganic mercury, including some recent studies not reviewed by JECFA in its evaluation of 2010, the Panel agrees with the rationale of JECFA in setting a health-based guidance value, based on kidney weight changes in male rats as the pivotal effect.
- Based on the $BMDL_{10}$ of 0.06 mg/kg b.w. per day, expressed as mercury and an uncertainty factor of 100 to account for inter and intra species differences with conversion to a weekly basis and rounding to one significant figure, the Panel established a TWI for inorganic mercury of 4 µg/kg b.w., expressed as mercury.

Risk characterisation

Methylmercury

- The mean dietary exposure across age groups does not exceed the TWI for methylmercury, with the exception of toddlers and other children in some surveys. The medians of 95th percentile dietary exposures across surveys are close to or above the TWI for all age groups.
- High consumers of fish meat may exceed the TWI by up to approximately six-fold.

- Unborn children constitute the most vulnerable group for developmental effects of methylmercury exposure, and pregnant women can be present in the group of high and frequent fish consumers.

- Biomonitoring data on blood and hair concentrations indicate that in the general European population, methylmercury exposure is generally below the TWI. However, higher levels in blood and hair are also observed, confirming higher dietary exposure in some population groups.

- Exposure to methylmercury above the TWI is of concern, but if measures to reduce methylmercury exposure are considered then the potential beneficial effects of fish consumption should also be taken into account.

Inorganic mercury

- The estimated exposure to inorganic mercury in Europe from the diet alone does not exceed the TWI. Inhaled elemental mercury vapour from dental amalgam, which after absorption is converted to inorganic mercury, is an additional source that is likely to increase the internal inorganic mercury exposure; thus the TWI might be exceeded.

RECOMMENDATIONS

- There is a need to develop certified reference materials and proficiency testing schemes for inorganic mercury in foodstuffs other than fish and seafood.

- Further effort should be made to increase the number of methylmercury and inorganic mercury data in all food groups that contribute significantly to overall exposure.

- In order to decrease the uncertainty in the point of departure derived from the epidemiological studies, more reliable definition of the dose response taking confounding factors into account is needed.

- Future studies should elucidate the relevance of additional endpoints, such as immunological and cardiovascular endpoints.

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APPENDICES

A. OCCURRENCE

Table A1: Statistical description of the total mercury occurrence data by food group (µg/kg).

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Grains and grain-based products	4 545	60	0	1.0	1.6	0.9	2.0	3.1	4.0	5.3	10	5.5	9.6	12	9.0	12	20	254
Vegetables and vegetable products	4 299	62	0	0.8	1.2	6.0	7.0	7.8	8.3	10	11	19	20	20	96	96	100	2 080
Starchy roots and tubers	1 234	75	0	0.5	1.0	0.2	0.8	1.4	0.8	2.5	5.0	1.5	5.0	10	3.0	5.7	10	20
Legumes, nuts and oilseeds	1 311	51	0	1.0	2.0	2.3	2.8	3.3	9.6	10	10	12	13	14	18	19	20	257
Fruit and fruit products	1 368	74	0	0.6	1.0	0.3	1.2	2.1	1.0	5.0	9.6	1.9	5.1	10	9.7	10	20	37
Meat and meat products	10 304	56	0	1.1	2.0	1.9	2.7	3.5	9.0	10	11	14	15	17	28	28	30	233
Fish and other seafood	21 539	12	40	43	48	131	133	136	540	540	540	852	852	852	1 400	1 400	1 400	6 890
Milk and dairy products	3 345	64	0	0.3	0.4	0.9	1.5	2.1	4.3	8.0	11	12	12	16	17	17	20	50
Eggs and egg products	798	58	0	0.6	1.0	0.6	1.2	1.8	3.2	4.6	6.3	4.4	5.0	10	7.0	7.0	10	13
Sugar and confectionery	1 617	73	0	1.0	1.7	0.6	2.6	4.7	2.9	10	20	4.9	10	20	10	30	60	60
Animal and vegetable fats and oils	835	61	0	0.6	0.9	1.1	1.6	2.0	6.0	6.0	6.0	8.0	10	10	12	22	23	100
Fruit and vegetable juices	651	89	0	0.5	1.0	0.1	3.2	6.2	0.4	10	20	0.7	10	20	2.1	10	20	20
Non-alcoholic beverages	699	46	0.1	1.0	2.0	3.4	4.0	4.5	16	16	20	21	21	21	31	31	31	87
Alcoholic beverages	652	79	0	0.2	0.3	0.1	0.4	0.7	0.3	1.0	2.0	0.7	1.5	2.1	1.7	1.7	3.0	6.0
Drinking water	1 637	90	0	0.1	0.1	0.0	0.1	0.2	0.1	0.3	0.5	0.5	0.5	0.6	0.5	0.5	0.6	5.0
Herbs, spices and condiments	529	47	0.4	2.0	2.0	3.1	4.3	5.5	10	13	20	17	20	23	41	41	50	160
Food for infants and small children	834	63	0	1.0	1.0	0.6	1.6	2.5	3.0	5.0	6.0	6.0	6.0	11	9.0	9.0	11	50
Products for special nutritional use	1 608	68	0	2.9	5.0	96	99	102	35	38	43	64	64	76	300	300	300	64 000
Composite food	304	41	3.0	6.6	10	16	18	19	59	59	59	101	101	101	274	274	274	486
Snacks, desserts, and other foods	451	54	0	0.5	0.5	1.2	1.5	1.9	3.0	4.7	5.0	5.0	5.0	10	16	16	20	110

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

Table A2: Statistical description of concentrations of total mercury for the food group 'Grains and grain-based products' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Grains for human consumption	2 680	52	0	1.0	2.0	1.0	2.1	3.2	4.0	5.5	10	6.3	8.0	12	12	15	20	63
Grain milling products	671	65	0	1.0	1.2	0.6	1.6	2.6	3.6	4.5	9.0	5.0	5.5	9.0	6.0	10	10	20
Bread and rolls	596	75	0	0.5	1.0	0.7	1.7	2.7	1.6	4.5	9.0	2.6	4.5	9.0	5.0	5.0	9.0	254
Pasta (raw)	81	77	0	1.5	3.0	0.5	2.2	4.0	3.0	4.9	9.0	4.0	5.0	10	5.0	5.0	10	10
Breakfast cereals	230	82	0	2.1	3.0	0.5	3.1	5.6	3.0	12	23	5.5	12	23	10	12	23	23
Fine bakery wares	287	73	0	0.5	1.0	0.5	1.7	2.9	3.0	10	20	4.0	10	20	6.0	10	20	20

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

Table A3: Statistical description of concentrations of total mercury for the food group 'Vegetables and vegetable products (including fungi)' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Vegetable and vegetable products	103	47	0.1	0.4	0.4	0.5	1.0	1.4	1.6	3.0	3.0	3.0	10	10	4.8	10	20	20
Root vegetables	724	71	0	0.7	1.2	0.4	1.5	2.6	1.3	5.0	10	3.5	5.0	10	10	10	10	23
Bulb vegetables	325	76	0	0.5	1.0	0.1	1.2	2.3	0.6	5.0	10	1.1	5.0	10	2.0	5.0	10	10
Fruiting vegetables	669	70	0	0.5	1.0	0.2	0.9	1.6	0.8	2.5	5.0	1.0	5.0	10	2.0	5.0	10	100
Brassica vegetables	481	61	0	0.4	0.4	0.4	0.8	1.3	1.6	2.5	5.0	4.5	5.0	5.0	8.0	8.0	9.5	14
Leaf vegetables	339	83	0	1.5	2.0	0.5	2.1	3.8	2.1	5.0	10	3.9	5.0	10	8.9	17	17	100
Legume vegetables	13	46	0.1	0.2	0.3	0.3	0.6	0.9	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	5.0
Stem vegetables (fresh)	246	91	0	0.5	1.0	0.1	1.5	2.9	0.2	5.0	10	0.3	5.0	10	2.0	5.0	10	100
Sugar plants	65	22	0.2	0.2	0.3	0.7	0.7	0.8	2.1	2.1	2.1	3.3	3.3	3.3	16	16	16	16
Sea weeds	1	100	0	2.5	5.0	0	2.5	5.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	5.0
Tea and herbs for infusions (solid)	85	68	0	5.0	9.7	6.0	7.7	9.5	20	20	20	43	43	43	110	110	110	110
Cocoa beans and cocoa products	126	56	0	2.5	3.2	1.7	3.7	5.7	7.0	10	20	12	12	20	24	24	24	30
Coffee beans and coffee products (solid)	298	49	0.4	0.9	1.0	1.4	1.7	1.9	6.4	6.4	6.4	11	11	11	15	15	15	20
Coffee imitates (solid)	13	46	0.5	0.7	0.9	0.7	0.9	1.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2.1
Vegetable products	139	55	0	0.3	0.3	13	13	13	6.8	6.8	6.8	22	22	22	395	395	395	973
Fungi, cultivated	508	32	3.0	4.0	5.0	9.1	10	11	26	26	26	54	54	54	102	102	102	620
Fungi, wild, edible	165	19	5.0	8.0	8.3	105	106	107	575	575	575	1 083	1 083	1 083	1 640	1 640	1 640	2 080

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A4: Statistical description of concentrations of total mercury for the food group 'Starchy root and tubers' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Potatoes and potatoes products	421	92	0	0.6	1.1	0.1	1.1	2.1	0.3	5.0	10	0.8	5.0	10	1.5	5.0	10	16
Other starchy roots and tubers	813	67	0	0.3	0.3	0.3	0.6	1.0	0.9	1.0	2.0	2.0	2.6	2.6	5.2	10	10	20

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

Table A5: Statistical description of concentrations of total mercury for the food group 'Legumes, nuts and oilseeds' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Legumes, beans, green, without pods	102	75	0	0.6	1.2	0.4	1.0	1.5	3.0	3.0	5.0	3.0	3.0	5.0	4.0	4.0	5.0	9.0
Legumes, beans, dried	483	53	0	0.5	1.0	1.4	1.8	2.2	7.0	7.0	7.7	9.0	9.0	10	11	11	14	45
Tree nuts	170	65	0	1.0	2.0	2.6	3.8	4.9	5.3	7.0	8.6	7.0	18	20	21	21	38	257
Oilseeds	556	39	0.9	1.9	2.0	3.2	3.7	4.2	12	12	13	16	16	18	23	23	23	42

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

Table A6: Statistical description of concentrations of total mercury for the food group 'Fruit and fruit products' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Fruit and fruit products	3	33	0.1	0.2	0.3	0.1	0.2	0.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.3
Citrus fruits	150	69	0	0.2	0.3	0.1	0.6	1.1	0.6	2.5	5.0	0.9	3.0	6.0	1.6	3.0	6.0	6.0
Pome fruits	349	63	0	0.3	0.3	0.2	0.6	0.9	0.6	1.0	2.0	1.2	2.0	3.0	2.4	2.5	5.0	37
Stone fruits	143	72	0	0.5	1.0	0.1	1.0	1.9	0.7	2.5	5.0	1.0	5.0	5.0	2.2	5.0	10	10
Berries and small fruits	358	87	0	1.0	1.8	0.1	1.5	2.9	1.0	5.0	10	1.0	5.0	10	4.0	5.0	10	10
Miscellaneous fruits	149	89	0	0.5	1.0	0.1	1.0	1.9	0.5	2.5	5.0	1.0	2.7	5.0	2.0	5.0	10	10
Dried fruits	33	73	0	2.7	5.3	0.2	1.7	3.2	1.0	2.7	5.3	1.1	2.7	5.3	1.1	2.7	5.3	5.3
Jam, marmalade and other fruit spreads	57	44	1.0	4.6	8.9	3.3	5.6	7.8	13	13	20	14	14	20	18	18	20	20
Other fruit products	126	75	0	0.6	1.0	0.2	1.3	2.5	1.1	3.6	5.0	1.8	10	20	1.9	10	20	21

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A7: Statistical description of concentrations of total mercury for the food group 'Meat and meat products (including edible offal)' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Meat and meat products	23	61	0	0.5	1.0	0.7	1.3	1.9	1.7	6.1	6.1	6.1	10	20	6.1	10	20	20
Livestock meat	3 078	66	0	0.7	1.0	0.8	1.7	2.5	3.0	5.0	9.7	6.1	8.0	12	13	17	18	100
Poultry	1 450	66	0	1.3	2.0	1.2	2.3	3.5	5.1	6.5	10	10	10	16	32	33	33	100
Game mammals	1 613	54	0	1.4	2.0	2.4	3.3	4.3	11	11	15	17	17	20	30	30	30	123
Game birds	376	81	0	1.9	3.6	0.6	2.0	3.4	2.7	3.0	4.3	4.5	5.1	5.1	12	12	13	40
Mixed meat	382	46	0.3	0.5	1.0	0.9	1.1	1.3	4.3	4.3	4.4	6.5	6.5	6.5	8.9	8.9	8.9	12
Edible offal, farmed animals	2 453	38	1.0	2.0	2.6	3.1	3.6	4.1	11	11	11	17	17	17	30	30	30	124
Edible offal, game animals	259	30	4.0	4.4	5.0	11	11	12	35	35	35	40	40	40	190	190	190	233
Preserved meat	174	65	0	1.0	2.0	1.0	2.9	4.9	7.0	13	25	12	13	25	16	16	25	25
Sausages	364	63	0	0.5	0.5	0.8	1.4	1.9	3.2	3.2	5.0	8.0	8.0	8.0	20	20	20	40
Meat specialities	27	33	0.2	0.2	0.2	0.9	0.9	1.0	5.0	5.0	5.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
Pastes, pâtés and terrines	96	33	0.4	0.5	0.5	1.3	1.4	1.5	4.1	4.1	4.1	15	15	15	30	30	30	30
Meat imitates	9	56	0	1.0	1.4	1.2	1.4	1.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	5.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A8: Statistical description of concentrations of total mercury for the food group 'Fish and other seafood' in µg/kg (FoodEx Level 2).

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Fish and other seafood, unspecified[(b)]	1 968	3	64	64	65	100	100	101	273	273	273	423	423	423	672	672	672	2 143
Fish meat	13 737	7	53	53	60	177	178	180	710	710	710	1 043	1 043	1 043	1 775	1 775	1 775	6 890
Fish products	241	8	22	22	22	37	38	38	109	109	109	233	233	233	310	310	310	622
Fish offal	158	58	0	15	28	12	19	26	67	67	70	88	88	88	92	92	92	121
Crustaceans	1 478	21	17	20	20	43	47	50	189	189	189	282	282	282	374	374	374	1 040
Molluscs	3 926	26	16	21	25	31	36	41	100	100	100	160	160	160	300	300	300	955
Amphibians, reptiles, snails, insects	31	48	0.8	2.5	3.7	19	20	21	140	140	140	280	280	280	280	280	280	280

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.

(a): The 95th, P97.5th and P99th percentile obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

(b): Data available only on FoodEx Level 1.

Table A9: Statistical description of concentrations of total mercury for the food group 'Fish meat' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(c)]			P97.5[(c)]			P99[(c)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Anchovy	110	33	50	50	60	73	83	92	200	200	200	291	291	291	891	891	891	1 249
Angler fish	61	30	78	78	100	186	195	204	551	551	551	920	920	920	2 900	2 900	2 900	2 900
Babel	10	0	205	205	205	211	211	211	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	430
Barracuda	1	0	340	340	340	340	340	340	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	340
Bass	78	10	89	89	97	199	203	206	698	698	698	1 000	1 000	1 000	4 169	4 169	4 169	4 169
Bonito	25	8	400	400	400	580	583	586	1 920	1 920	1 920	2 080	2 080	2 080	2 080	2 080	2 080	2 080
Bream	253	11	135	135	135	224	225	226	883	833	883	1 124	1 124	1 124	1 400	1 400	1 400	2 909
Capelin	11	82	0	4.4	8.3	2.0	5.0	8.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10
Carp	338	5	28	28	29	55	55	55	194	194	194	244	244	244	403	403	403	985
Char	8	0	37	37	37	32	32	32	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	40
Cod, whiting	1 308	18	54	54	56	91	94	96	340	340	340	460	460	460	590	590	590	1 000
Dentex	3	0	832	832	832	2 019	2 019	2 019	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	4 450
Eel	487	2	130	130	130	177	178	178	461	461	461	719	719	719	1 100	1 100	1 100	1 880
Flounder	23	17	40	50	70	85	91	97	185	185	185	205	205	205	578	578	578	578
Garfish	3	0	590	590	590	590	590	590	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 000
Grenadier	3	0	98	98	98	104	104	104	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	137
Grey mullet	52	23	85	85	100	152	159	167	566	566	566	784	784	784	1 000	1 000	1 000	1 000
Grouper	2	0	195	195	195	195	195	195	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	320
Gurnard	4	25	75	75	75	103	109	116	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	262
Hake	131	16	90	90	100	130	136	142	420	420	420	510	510	510	620	620	620	660
Halibut	1 713	0	170	170	170	209	209	209	610	610	610	710	710	710	860	860	860	2 280
Herring	1 272	0	30	30	30	36	36	36	78	78	78	94	94	94	120	120	120	400
Jack mackerel	3	0	110	110	110	127	127	127	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	170
John Dory	6	0	212	212	212	302	302	302	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	620
Lizardfish	2	0	611	611	611	611	611	611	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	650
Luvarus	1	0	590	590	590	590	590	590	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	590
Mackerel	1 348	5	40	40	40	106	108	109	520	520	520	735	735	735	976	976	976	1 560
Meagre	2	50	145	170	195	145	170	195	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	290
Perch	423	0	130	130	130	165	165	165	370	370	370	490	490	490	560	560	560	780
Pike	267	0	290	290	290	394	394	394	979	979	979	1 200	1 200	1 200	3 276	3 276	3 276	5 139
Plaice	194	2	46	46	46	64	64	65	160	160	160	200	200	200	240	240	240	400
Ray	32	3	108	108	108	229	229	230	1 170	1 170	1 170	1 350	1 350	1 350	1 350	1 350	1 350	1 350

Table A9: Continued.

Food category	N	% LC	Median			Mean			P95[c]			P97.5[c]			P99[c]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Redfish	221	0	100	100	100	189	189	189	676	676	676	847	847	847	940	940	940	1 574
Roach	17	0	113	113	113	122	122	122	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	240
Salmon, trout	1 741	7	30	30	30	31	33	35	57	57	70	67	67	67	100	100	100	950
Sardine and pilchard	399	18	16	27	30	32	38	44	116	116	116	127	127	127	153	153	153	244
Scorpion fish	1	0	422	422	422	422	422	422	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	422
Sea bass	10	0	288	288	288	300	300	300	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	610
Sea catfish, wolf-fish	67	54	0	10	13	103	109	114	770	770	770	850	850	850	950	950	950	950
Shad	1	0	173	173	173	173	173	173	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	173
Shark	272	11	495	495	495	688	691	695	1 900	1 900	1 900	2 720	2 720	2 720	3 518	3 518	3 518	5 560
Smelt	2	0	325	325	325	325	325	325	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	370
Sole	49	24	48	50	64	69	77	84	180	180	180	325	325	325	500	500	500	500
Sprat	107	1	19	19	19	21	21	21	50	50	50	84	84	84	100	100	100	117
Sturgeon	4	50	36	61	79	40	52	65	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	86
Swordfish	264	5	1 010	1 010	1 010	1 210	1 212	1 214	3 300	3 300	3 300	4 500	4 500	4 500	5 300	5 300	5 300	6 760
Tuna	849	5	189	189	189	286	290	291	850	850	850	1 182	1 182	1 182	1 620	1 620	1 620	3 370
Turbot	4	0	56	56	56	62	62	62	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	89
Weever	11	0	741	741	741	763	763	763	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 927
Whitefish	37	16	70	70	80	77	85	93	250	250	250	260	260	260	260	260	260	260
Wrasse	12	0	427	427	427	511	511	511	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 730
Fish meat, unspecified, as reported[a]	1 502	10	57	57	57	279	280	280	1 194	1 194	1 194	1 900	1 900	1 900	3 270	3 270	3 270	6 890
Fish meat, overall results[b]	12 235	10	117	117	118	164	166	168	499	500	501	661	661	665	922	922	922	6 760

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): Data described as reported.

(b): Data calculated on overall concentrations of individual specified fish species excluding fish meat unspecified and such used for exposure calculation.

(c): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A10: Statistical description of concentrations of methylmercury for the food group 'Fish and other seafood' in µg/kg (FoodEx Level 2).

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Fish meat	969	6	39	50	54	131	135	139	598	598	598	810	810	810	1 213	1 213	1 213	5 740
Fish products	33	12	23	23	23	39	39	40	95	95	95	538	538	538	538	538	538	538
Fish offal	4	100	26	26	26	23	23	23	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	26
Crustaceans	42	48	0	50	100	70	102	134	280	280	280	309	309	309	970	970	970	970
Molluscs	35	57	0	50	100	15	61	107	151	151	151	390	390	390	390	390	390	390

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A11: Statistical description of concentrations of methylmercury for the food group 'Fish meat' in µg/kg **(FoodEx Level 3).**

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Anchovy	5	80	0	50	100	22	62	102	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	112
Angler fish	3	33	148	148	148	173	190	206	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	370
Bass	5	60	0	50	100	31	61	91	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	104
Bream	4	50	51	76	101	61	86	111	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	141
Carp	33	21	10	10	10	13	13	13	39	39	39	51	51	51	51	51	51	51
Cod and whiting	183	4	10	10	10	19	19	20	51	51	54	74	74	74	106	106	106	400
Eel	8	0	93	93	93	172	172	172	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	455
Flounder	45	0	50	50	50	66	66	66	167	167	167	202	202	202	205	205	205	205
Grey mullet	8	88	0	50	100	18	62	106	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	144
Hake	11	64	0	50	100	32	64	96	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	200
Halibut	61	0	79	79	79	127	127	127	400	400	400	624	624	624	1 213	1 213	1 213	1 213
Herring	39	0	26	26	26	30	30	30	63	63	63	63	63	63	63	63	63	63
Mackerel	122	9	29	34	34	123	127	132	547	547	547	598	598	598	905	905	905	1 114
Perch	2	0	56	56	56	56	56	56	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	77
Salmon and trout	28	50	3.5	50	100	13	38	63	39	50	100	106	106	106	106	106	106	106
Sardine and pilchard	16	88	0	50	100	14	58	102	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	121
Sea catfish, wolf-fish	1	0	121	121	121	121	121	121	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	121
Shark	4	0	1 510	1 510	1 510	1 520	1 520	1 520	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 730
Smelt	1	0	73	73	73	73	73	73	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	73
Sole	4	0	0	50	100	0	50	100	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	100
Sprat	25	0	8	8	8	8	8	8	16	16	16	18	18	18	18	18	18	18
Swordfish	10	0	795	795	795	819	819	819	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1 079
Tuna	125	2	133	133	133	220	221	221	784	784	784	880	880	880	1 162	1 162	1 162	1 728
Fish meat, unspecified	226	1	113	113	113	225	225	225	700	700	700	1 079	1 079	1 079	1 414	1 414	1 414	5 740

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A12: Statistical description of concentrations of total mercury for the food group 'Milk and dairy products' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Milk and dairy products	32	97	0	8.0	16	0.0	6.7	13	0	8.0	16	1.0	10	20	1.0	10	20	20
Liquid milk	1 624	74	0	0.2	0.3	0.2	0.7	1.1	2.0	2.5	4.3	2.0	5.0	10	3.1	8.0	16	16
Milk based beverages	3	33	0.2	0.2	0.2	2.9	3.0	3.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	8.7
Concentrated milk	96	55	0	0.3	0.3	0.8	1.1	1.3	4.6	4.6	4.6	5.0	6.7	6.7	13	13	20	20
Whey and whey products	2	100	0	0.2	0.3	0	0.2	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.3
Cream and cream products	140	60	0	0.2	0.3	0.5	0.7	0.9	3.0	3.0	4.9	4.0	4.0	5.0	4.8	4.8	5.0	8.1
Fermented milk products	323	67	0	0.5	0.8	0.4	2.1	3.8	2.5	10	20	3.5	10	20	4.3	10	20	20
Cheese	1 095	49	0.1	0.5	0.5	2.0	2.4	2.8	14	14	14	17	17	17	20	20	20	23
Milk and milk product imitates	30	90	0	2.0	4.0	2.0	3.6	5.3	8.3	8.3	10	50	50	50	50	50	50	50

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A13: Statistical description of concentrations of total mercury for the food group 'Eggs and egg products' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Eggs, fresh	790	58	0	0.5	1.0	0.6	1.2	1.8	3.2	4.5	6.0	4.4	5.0	10	7.0	7.0	10	13
Eggs, powder	8	88	0	1.0	2.0	0.4	1.8	3.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A14: Statistical description of concentrations of total mercury for the food group 'Sugar and confectionery' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Sugar and confectionery	15	93	0	0.5	1.0	0.1	1.0	1.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1.2
Sugars	51	82	0	0.2	0.3	0.1	0.3	0.4	0.8	0.8	0.8	0.8	0.8	0.8	3.0	3.0	3.0	3.0
Sugar substitutes	2	50	0.2	0.2	0.3	0.2	0.2	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.3
Chocolate (Cocoa) products	314	60	0	1.5	2.0	1.4	2.1	3.2	7.2	9.5	10	7.4	10	20	9.5	10	20	20
Confectionery (non-chocolate)	280	73	0	1.5	2.2	0.5	4.3	8.1	2.4	30	60	3.7	30	60	4.8	30	60	60
Dessert sauces	11	45	0.5	0.9	0.9	1.1	1.4	1.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	4.0
Molasses and other syrups	52	60	0	0.2	0.3	0.2	0.3	0.5	1.1	1.1	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3
Honey	892	64	0	1.0	2.0	0.5	2.7	4.8	1.4	10	20	3.9	10	20	14	14	20	32

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A15: Statistical description of concentrations of total mercury for the food group 'Animal and vegetable fats and oils' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Animal and vegetable fats and oils	3	0	3.0	3.0	3.0	3.6	3.6	3.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	6.2
Animal fat	396	52	0	0.5	0.5	1.1	1.3	1.5	5.0	5.0	5.0	7.0	7.0	7.0	23	23	23	44
Fish oil	103	99	0	0.7	1.4	0.2	1.5	2.9	0	1.8	3.6	0	13	16	0	16	25	100
Vegetable fat	36	75	0	0.2	0.3	0.9	1.1	1.3	6.8	6.8	6.8	12	12	12	12	12	12	12
Vegetable oil	268	56	0	0.5	0.6	1.5	2.1	2.6	6.3	8.0	9.0	10	12	12	18	25	25	100
Margarine and similar products	29	72	0	0.2	0.3	0.6	0.7	0.8	3.3	3.3	3.3	5.3	5.3	5.3	5.3	5.3	5.3	5.3

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A16: Statistical description of concentrations of total mercury for the food group 'Fruit and vegetable juices' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Fruit and vegetable juices	44	89	0	0.2	0.3	0.1	0.3	0.5	0.5	1.0	2.0	0.6	1.0	2.0	1.0	1.0	2.0	2.0
Fruit juice	416	63	0	0.5	1.0	0.1	2.9	5.7	0.4	10	20	0.5	10	20	1.8	10	20	20
Concentrated juice fruit	27	26	0	10	20	0	7.6	15	0	10	20	0	10	20	0	10	20	20
Fruit nectar	44	64	0	0.2	0.3	0.4	3.5	6.7	0.6	10	20	6.0	10	20	9.5	10	20	20
Mixed fruit juice	35	23	0	10	20	0	7.8	16	0	10	20	0	10	20	0	10	20	20
Dehydrated/powdered fruit juice	23	70	0	0.2	0.3	0.2	0.4	0.6	0.3	1.5	2.9	2.9	2.9	3.0	2.9	2.9	3.0	3.0
Vegetable juice	49	88	0	2.0	2.0	0.2	2.2	4.2	2.0	5.0	10	2.0	5.0	10	2.1	10	20	20
Mixed vegetable juice	4	50	0	5.3	11	0	5.3	11	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20
Mixed fruit and vegetable juice	9	0	0	10	20	1.1	10	19	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A17: Statistical description of concentrations of total mercury for the food group 'Non-alcoholic beverages (excepting milk based beverages)' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Non-alcoholic beverages	17	47	0	0.5	0.5	0.1	3.7	7.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20
Soft drinks	301	71	0	0.2	0.3	0.0	0.8	1.6	0.4	10	20	0.7	10	20	1.2	10	20	20
Tea (Infusion)	369	20	4.0	4.0	4.0	6.4	6.6	6.8	20	21	21	24	25	29	35	35	38	87
Coffee (Beverage)	12	33	0.8	0.8	1.0	1.9	2.0	2.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A18: Statistical description of concentrations of total mercury for the food group 'Alcoholic beverages' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Beer and beer-like beverage	256	79	0	0.2	0.3	0.1	0.4	0.8	0.3	1.5	3.0	0.9	1.5	3.0	2.0	2.0	3.0	6.0
Wine	359	77	0	0.2	0.3	0.1	0.4	0.7	0.3	1.0	2.0	0.6	1.0	2.0	1.2	1.2	2.0	5.5
Fortified and liqueur wines	2	50	0.1	0.1	0.1	0.1	0.1	0.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.1
Wine-like drinks	16	88	0	0.2	0.3	0.1	0.4	0.7	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	3.0
Spirits	19	95	0	0.5	1.0	0.0	0.6	1.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A19: Statistical description of concentrations of total mercury for the food group 'Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Drinking water	73	99	0	0.1	0.2	0.0	0.1	0.2	0.0	0.1	0.2	0	0.1	0.2	0.5	0.5	0.5	0.5
Tap water	22	77	0	0.1	0.2	0.1	0.2	0.2	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Well water	422	76	0	0.1	0.1	0.0	0.1	0.2	0.2	0.3	0.5	0.5	0.5	0.5	0.5	0.5	0.6	2.0
Bottled water	1 120	95	0	0.1	0.1	0.0	0.1	0.2	0	0.3	0.5	0.5	0.5	0.6	0.5	0.5	0.6	5.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A20: Statistical description of concentrations of total mercury for the food group 'Herbs, spices and condiments' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Herbs, spices and condiments	3	67	0	8.0	16	27	32	37	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	80
Herbs	34	62	0	2.0	4.0	13	15	17	94	94	94	160	160	160	160	160	160	160
Spices	174	37	2.0	3.9	5.0	3.7	5.3	6.8	13	13	20	18	18	20	31	31	31	41
Herb and spice mixtures	38	66	0	4.8	7.4	2.3	7.3	12	12	25	50	20	25	50	20	25	50	50
Seasoning or extracts	69	61	0	0.5	1.0	1.4	1.9	2.3	5.0	5.0	8.0	8.0	8.0	10	17	17	17	17
Condiment	54	61	0	0.2	0.3	0.8	0.9	1.0	4.0	4.0	4.0	8.0	8.0	8.0	10	10	10	10
Dressing	22	45	0.8	0.8	1.0	2.1	2.2	2.2	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0
Chutney and pickles	3	0	1.3	1.3	1.3	0.9	0.9	0.9	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	1.5
Savoury sauces	5	60	0	0.2	0.3	0.1	0.2	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.4
Flavourings or essences	8	50	0.1	1.2	1.2	0.7	4.0	7.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	40
Baking ingredients	119	33	1.0	1.1	1.3	1.8	1.9	2.1	6.7	6.7	6.7	7.5	7.5	7.5	8.0	8.0	8.0	13

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A21: Statistical description of concentrations of total mercury for the food group 'Food for infants and small children' in µg/kg.

Food category	N	% LC	Median			Mean			P95			P97.5			P99			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Food for infants and small children	222	11	1.0	1.0	1.0	1.1	1.2	1.3	3.9	3.9	4.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Infant formulae, powder	144	79	0	2.5	3.4	1.0	2.2	3.5	8.0	8.0	11	10	10	11	12	12	12	13
Infant formulae, liquid	1	100	0	0.2	0.4	0	0.2	0.4	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.4
Follow-on formulae, powder	128	86	0	2.5	5.0	0.7	2.7	4.7	8.0	8.0	8.0	8.0	9.0	9.0	11	12	12	50
Cereal-based food for infants and young children	102	90	0	0.5	1.0	0.2	1.3	2.4	1.3	2.7	5.3	3.0	4.0	5.3	4.0	5.0	10	11
Ready-to-eat meal for infants and young children	228	77	0	0.3	0.4	0.1	1.0	1.9	0.4	3.0	5.3	0.7	5.5	11	2.0	5.5	11	11
Yoghurt, cheese and milk-based dessert for infants and young children	8	100	0	0.1	0.1	0	0.1	0.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.1
Fruit juice and herbal tea for infants and young children	1	0	6.0	6.0	6.0	6.0	6.0	6.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	6.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.

Table A22: Statistical description of concentrations of total mercury for the food group 'Products for special nutritional use' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Products for special nutritional use	82	52	0	0.1	1.0	1.0	2.6	4.2	2.0	10	20	2.5	10	20	17	17	20	20
Food for weight reduction	15	80	0	1.5	3.0	0.6	2.0	3.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20
Dietary supplements[(b)]	1 233	66	0	3.0	5.7	123	126	129	38	40	45	75	75	80	410	410	410	64 000
Food for sports people	168	57	0	2.5	4.0	19	22	25	57	57	60	116	116	116	600	600	600	1 236
Dietetic food for diabetics	51	96	0	0.5	1.0	0.3	0.8	1.3	0	1.5	3.0	0.1	1.5	3.0	17	17	17	17
Medical food	59	95	0	0.5	3.0	0.2	1.7	3.3	1.7	2.5	5.0	4.0	4.0	5.0	8.0	8.0	8.0	8.0

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; UB: upper bound; MB: middle bound; n/a: not available.

(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

(b): Correct values: mean values are higher than P95 values because of right-skewed distribution.

Table A23: Statistical description of concentrations of total mercury for the food group 'Composite food (including frozen products)' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Composite food	83	66	0	0.5	1.0	2.8	4.6	6.4	13	13	20	21	25	33	33	33	50	50
Cereal-based dishes	15	13	0.2	10	13	6.9	9.7	12	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	25
Potato based dishes	2	0	1.3	1.3	1.3	1.3	1.3	1.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	2.0
Beans-based meals	5	100	0	0.2	0.3	0	0.2	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.3
Meat-based meals	37	35	0	2.8	2.8	4.6	6.6	8.6	13	13	20	61	61	61	61	61	61	61
Fish and seafood based meals	84	4	21	23	23	42	42	43	126	126	126	274	274	274	486	486	486	486
Vegetable-based meals	3	67	0	5.0	5.6	1.9	3.7	5.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10
Ready to eat soups	33	73	0	0.5	1.0	11	11	12	13	13	20	321	321	321	321	321	321	321
Prepared salads	42	7	11	11	11	15	15	15	41	41	41	41	41	41	74	74	74	74

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
(a): The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

Table A24: Statistical description of concentrations of total mercury for the food group 'Snacks, desserts, and other foods' in µg/kg.

Food category	N	% LC	Median			Mean			P95[(a)]			P97.5[(a)]			P99[(a)]			Max
			LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	LB	MB	UB	UB
Snacks, desserts, and other foods	1	100	0	0.1	0.1	0	0.1	0.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0.1
Snack food	248	58	0	0.5	0.6	0.7	0.9	1.2	3.1	3.1	3.1	5.0	5.0	5.0	7.5	7.5	7.5	15
Ices and desserts	135	43	0.2	0.2	0.3	0.8	0.8	0.9	2.5	2.5	2.5	2.8	2.8	2.8	9.0	9.0	9.0	30
Other foods	31	68	0	2.5	5.0	8.3	10	12	86	86	86	110	110	110	110	110	110	110

N: number of samples; % LC: percentage of left-censored data; P95: 95th percentile; P97.5: 97.5th percentile; P99: 99th percentile; Max: maximum concentration; LB: lower bound; MB: middle bound; UB: upper bound; n/a: not available.
The P95, P97.5 and P99 obtained on occurrence data with less than 60 analytical results may not be statistically robust (EFSA, 2011b) and therefore are considered only indicative.

B. RELATIONSHIP BETWEEN CONCENTRATIONS OF TOTAL MERCURY AND METHYLMERCURY

Table B1: Overview of previously reported literature data on relationship between concentrations of total mercury and methylmercury in fish.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Largetooth flounder (*Pseudorhombus arsicus*)	The Persian Gulf	Sea	4	28	23-34	27	18-39	96.4[f]	64-100	1
Spotfin flathead (*Gramnopolites suppositus*)	The Persian Gulf	Sea	8	39	14-73	34	11-60	87.2[f]	83-100	1
Spotfin flathead (*Gramnopolites suppositus*)	The Persian Gulf	Sea	7	27	22-32	17	14-21	63.0[f]	63-67	1
Japanese threadfin bream (*Nemipterus japonicus*)	The Persian Gulf	Sea	8	49	30-87	48	25-97	98.0[f]	84-100	1
Greater Lizardfish (*Saurida tumbil*)	The Persian Gulf	Sea	9	43	12-86	47	11-100	109.3[f]	92-100	1
Greater Lizardfish (*Saurida tumbil*)	The Persian Gulf	Sea	12	17	15-20	18	15-17	105.9[f]	100	1
Giant Seacatfish (*Arius thalassinus*)	The Persian Gulf	Sea	10	45	30-78	45	30-74	100.0[f]	95-100	1
Elongate Sole (*Solea elongata*)	The Persian Gulf	Sea	5	28	18-42	23	17-32	82.1[f]	75-99	1
Sharpnose mullet (*Liza saliens*)	The Caspian Sea	Fresh [a]	3	20	n.r.	20	n.r.	100.0[f]	100	1
Sharpnose mullet (*Liza saliens*)	The Caspian Sea	Fresh [a]	3	108	n.r.	107	n.r.	99.1[f]	99	1
Sharpnose mullet (*Liza saliens*)	The Caspian Sea	Fresh [a]	3	10.2	n.r.	10	n.r.	98.0[f]	99	1
Sharpnose mullet (*Liza saliens*)	The Caspian Sea	Fresh [a]	3	20	n.r.	19.5	n.r.	97.5[f]	97	1
Roach (*Rutilus rutilus*)	Swarzedzkie lake, Poland	Fresh	n.r.	2.95	n.r.	2.63	n.r.	89.2[f]	n.r.	2
Roach (*Rutilus rutilus*)	Swarzedzkie lake, Poland	Fresh	n.r.	0.38	n.r.	0.34	n.r.	89.5[f]	n.r.	2
Roach (*Rutilus rutilus*)	Swarzedzkie lake, Poland	Fresh	n.r.	0.6	n.r.	0.59	n.r.	98.3[f]	n.r.	2
Roach (*Rutilus rutilus*)	Swarzedzkie lake, Poland	Fresh	n.r.	0.25	n.r.	0.18	n.r.	72[f]	n.r.	2
Chub (*Leuciscus cephalus*)	Czech rivers, Dyje - Pohansko	Fresh	7	97[c]	n.r.	76	n.r.	78.4[f]	n.r.	3
Chub (*Leuciscus cephalus*)	Czech rivers, Labe - Obristvi	Fresh	10	263[d]	n.r.	256	n.r.	97.3[f]	n.r.	3
Shad (*Hilsa ilisha*)	Padma river and Moheshkhali, Cox Bazar, Bangladesh	Fresh/ Sea	64	19[e]	2-60	6[e]	1-13	31.6[f]	n.r.	4
Shad (*Hilsa kelee*)	Padma river, Bangladesh	Fresh	30	21[e]	7-52	4[e]	3-13	19.0[f]	n.r.	4
Jewelled shad (*Ilisha indica*)	Padma river, Bangladesh	Fresh	15	15[e]	4-43	4[e]	3-7	26.7[f]	n.r.	4
Jewelled shad (*Ilisha filigera*)	Moheshkhali, Bangladesh	Sea	15	16[e]	7-40	4[e]	2-7	25.0[f]	n.r.	4
Major carp (*Catla catla*)	Aurial Beel, Bangladesh	Fresh	30	29[e]	10-70	21[e]	7-58	72.4[f]	n.r.	4
Major carp (*Labeo rohita*)	Buriganga river, Bangladesh	Fresh	18	42[e]	28-70	29[e]	16-59	69.0[f]	n.r.	4
Feather back (*Notopterus notopterus*)	Aurial Beel, Bangladesh	Fresh	20	64[e]	33-154	48[e]	20-138	75.0[f]	n.r.	4
Minor carp (*Puntius sarana*)	Aurial Beel, Bangladesh	Fresh	19	21[e]	9-50	14[e]	6-34	66.7[f]	n.r.	4
Catfish (*Heteropneustes fossilis*)	Aurial Beel, Bangladesh	Fresh	28	34[e]	18-83	27[e]	13-79	79.4[f]	n.r.	4
Perch (*Pama pama*)	Meghna river, Bangladesh	Fresh	15	55[e]	35-97	30[e]	13-54	54.5[f]	n.r.	4

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Perch (*Pama pama*)	Meghna river, Bangladesh	Fresh	15	67[e]	27-108	28[e]	13-73	41.8[f]	n.r.	4
Perch (*Tilapia nilotica*)	Dhanmondi lake, Bangladesh	Fresh	26	26[e]	20-42	19[e]	6-35	73.1[f]	n.r.	4
Catfish (*Mystus seenghala*)	Meghna river, Bangladesh	Fresh	42	104[e]	29-427	82[e]	67-402	78.8[f]	n.r.	4
Catfish (*Silonia silondia*)	Meghna river, Bangladesh	Fresh	30	145[e]	51-302	124[e]	32-295	85.5[f]	n.r.	4
Catfish (*Wallago attu*)	Padma river, Bangladesh	Fresh	8	145[e]	60-320	126[e]	42-305	86.9[f]	n.r.	4
Murrel (*Channa punctatus*)	Aurial Beel, Bangladesh	Fresh	21	88[e]	49-148	73[e]	27-142	83.0[f]	n.r.	4
Spiny eel (*Mastacembalus armatus*)	Buriganga river, Bangladesh	Fresh	21	134[e]	83-240	121[e]	67-238	90.3[f]	n.r.	4
Southest European nase (*Chondrostoma miegii*)	Tagus river, Spain	Fresh	10	270[g]	116-532[g]	227[g]	97-440[g]	84.1[f]	n.r.	5
Carp (*Cyprinus carpio*)	Tagus river, Spain	Fresh	3	630[g]	200-1240[g]	530[g]	120-1090[g]	84.1[f]	n.r.	5
Carp (*Cyprinus carpio*)	Tagus river, Spain	Fresh	5	1057[g]	451-1335[g]	917[g]	381-1158[g]	86.8[f]	n.r.	5
Catfish (*Ameiurus melas*)	Tagus river, Spain	Fresh	4	460[g]	150-850[g]	340[g]	110-590[g]	73.9[f]	n.r.	5
Catfish (*Ameiurus melas*)	Tagus river, Spain	Fresh	12	159[g]	38-321[g]	122[g]	31-268[g]	76.7[f]	n.r.	5
Hardhead catfish (*Arius felis*)	Biscayne Bay, Florida	Sea	1[h]	1580[g]	n/a	1960[g]	n/a	124.1[f]	n/a	6
Hardhead catfish (*Arius felis*)	Tampa Bay, Florida	Sea	3[h]	2090[g]	720-4640[g]	1700[g]	250-4420[g]	81.3[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Charlotte Harbour, Florida	Sea	2[h]	1310[g]	1120-1500[g]	1000[g]	n.r.	76.3[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Florida Bay, Florida	Sea	7[h]	2640[g]	1790-3900[g]	1680[g]	1460-1800[g]	63.6[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Pine Island Sound, Florida	Sea	2[h]	400[g]	340-450[g]	300[g]	180-410[g]	75.0[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Whitewater Bay, Florida	Sea	1[h]	3390[g]	n/a	3540[g]	n/a	104.4[f]	n/a	6
Hardhead catfish (*Arius felis*)	Boca Ciega Bay, Florida	Sea	2[h]	860[g]	440-1280[g]	840[g]	360-1320[g]	97.7[f]	n.r.	6
Hardhead catfish (*Arius felis*)	Card Sound, Florida	Sea	1[h]	2120[g]	n/a	2000[g]	n/a	94.3[f]	n/a.	6
White grunt (*Haemulon plumieri*)	Biscayne Bay, Florida	Sea	2[h]	870[g]	710-1030[g]	900[g]	800-990[g]	103.4[f]	n.r.	6
White grunt (*Haemulon plumieri*)	Florida Bay, Florida	Sea	7[h]	390[g]	280-470[g]	390[g]	320-530[g]	100.0[f]	n.r.	6
White grunt (*Haemulon plumieri*)	Cudjoe Basin, Florida	Sea	1[h]	440[g]	n/a	310[g]	n/a	70.5[f]	n/a	6
Sand perch (*Diplectrum formosum*)	Tampa Bay, Florida	Sea	2[h]	470[g]	400-540[g]	390[g]	380-400[g]	83.0[f]	n.r.	6
Sand perch (*Diplectrum formosum*)	Florida Bay, Florida	Sea	1[h]	490[g]	n/a	490[g]	n/a	100.0[f]	n.r.	6
Lane snapper (*Lutjanus synagris*)	Florida Bay, Florida	Sea	4[h]	830[g]	300-1200[g]	860[g]	330-1270[g]	103.6[f]	n.r.	6
Lane snapper (*Lutjanus synagris*)	Pine Island Sound, Florida	Sea	2[h]	360[g]	350-360[g]	340[g]	290-380[g]	94.4[f]	n.r.	6
Lane snapper (*Lutjanus synagris*)	Sarasota Bay, Florida	Sea	2[h]	280[g]	220-340[g]	260[g]	190-320[g]	92.9[f]	n.r.	6
Gafftopsail catfish (*Bagre marinus*)	Tampa Bay, Florida	Sea	2[h]	4000[g]	2620-5400[g]	2240[g]	2060-2420[g]	56.0[f]	n.r.	6
Gafftopsail catfish (*Bagre marinus*)	Charlotte Harbour, Florida	Sea	3[h]	1700[g]	860-2160[g]	1490[g]	720-2270[g]	87.6[f]	n.r.	6
Gafftopsail catfish (*Bagre marinus*)	Florida Bay, Florida	Sea	1[h]	3130[g]	n/a	1640[g]	n/a	52.4[f]	n/a	6
Gafftopsail catfish (*Bagre marinus*)	Pine Island Sound, Florida	Sea	2[h]	960[g]	760-1160[g]	920[g]	n.r.	95.8[f]	n.r.	6
Gafftopsail catfish (*Bagre marinus*)	Hillsborough Channels, Florida	Sea	1[h]	4980[g]	n/a	4500[g]	n/a	90.4[f]	n/a	6
Gafftopsail catfish (B*agre marinus*)	Boca Ciega Bay, Florida	Sea	1[h]	1650[g]	n/a	1300[g]	n/a	78.8[f]	n/a	6
Gafftopsail catfish (*Bagre marinus*)	Caloosahatchee river, Florida	Sea	1[h]	1320[g]	n/a	1140[g]	n/a	86.4[f]	n/a	6
Gafftopsail catfish (*Bagre marinus*)	Gordon river, Florida	Sea	1[h]	10100[g]	n/a	2000[g]	n/a	19.8[f]	n/a	6

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Pinfish (*Lagodon rhomboides*)	Charlotte harbour, Florida	Sea	1[(h)]	320[(g)]	n/a	200[(g)]	n/a	62.5[(f)]	n/a	6
Pinfish (*Lagodon rhomboides*)	Florida bay, Florida	Sea	1[(h)]	1 060[(g)]	n/a	900[(g)]	n/a	84.9[(f)]	n/a	6
Pinfish (*Lagodon rhomboides*)	Pine Island Sound, Florida	Sea	3[(h)]	430[(g)]	410-460[(g)]	370[(g)]	270-430[(g)]	86.0[(f)]	n.r.	6
Pinfish (*Lagodon rhomboides*)	Sarasota Bay, Florida	Sea	2[(h)]	550[(g)]	460-630[(g)]	430[(g)]	320-530[(g)]	78.2[(f)]	n.r.	6
Spot (*Leiostomus xanthurus*)	Pine Island Sound, Florida	Sea	1[(h)]	330[(g)]	n/a	260[(g)]	n/a	78.8[(f)]	n/a	6
Spot (*Leiostomus xanthurus*)	Boca Ciega Bay, Florida	Sea	1[(h)]	110[(g)]	n/a	60[(g)]	n/a	54.5[(f)]	n/a	6
Spot (*Leiostomus xanthurus*)	Gordon river, Florida	Sea	1[(h)]	430[(g)]	n/a	40[(g)]	n/a	9.3[(f)]	n/a	6
Pigfish (*Orthopristis chrysoptera*)	Pine Island Sound, Florida	Sea	1[(h)]	380[(g)]	n/a	310[(g)]	n/a	81.6[(f)]	n/a	6
Sand seatrout (*Cynoscion arenarius*)	Tampa Bay, Florida	Sea	2[(h)]	2410[(g)]	2210-2610[(g)]	2040[(g)]	1600-2470[(g)]	84.6[(f)]	n.r.	6
Brown shrimp (*Penaeus aztecus*)	Charlotte Harbour, Florida	Sea	2[(h)]	180[(g)]	160-190[(g)]	130[(g)]	120-140[(g)]	72.2[(f)]	n.r.	6
Fresh trout (*Onchorchynchus mykiss*)	unknown		1	45		42		93	n.r.	7
Fresh tuna (*Thunnus thynnus*)	Indonesia		3	596	162-1110	559	n.r.	93	81-101	7
Fresh salmon (*Salmo salar*)	Norway, Holland		3	36	33- 40	27	15- 39	74	45-98	7
Fresh Euoropean flounder (*Platichthys flesus*)	Holland, Denmark		1	14	n/a	10	n/a	71	n/a	7
Fresh euoropean flounder (*Platichthys flesus*)	Holland, Denmark		1	5	n/a	2	n/a	40	n/a	7
Fresh Cod (*Gadus morhua*)	Holland, Denmark, Croatia		4	69	31 – 139	66	20–149	87	54-107	7
Fresh squid (*Lolligu vulgaris*)	France		1	47	n/a	31	n/a	66	n/a	7
Fresh Conger (*Conger conger*)	Croatia		1	864	n/a	731	n/a	85	n/a	7
Fresh octopus (*Octopus vulgaris*)	Phillipines		1	12	n/a	11	n/a	92	n/a	7
Fresh turbot (*Psetta maxima*)	Spain		1	42	n/a	36	n/a	86	n/a	7
Fresh angler (*Lophius piscatorius*)	Croatia		3	291	71–678)	287	45-702	86.00	63-104	7
Feresh Scorpaena (*Scorpaena scrofa*)	Morocco		1	134	n/a	134	n/a	100	n/a	7
Feresh Scorpaena (*Scorpaena scrofa*)	Morocco		1	371	n/a	265	n/a	71	n/a	7
Fresh goatfish (*Mullus barbatus*)	Croatia		1	210	n/a	221	n/a	105	n/a	7
Fresh goatfish (*Mullus barbatus*)	Croatia		1	108	n/a	80	n/a	74	n/a	7
Fresh common pandora (*Pagellus eruthinus*)	Croatia		1	70	n/a	76	n/a	109	n/a	7
Fresh common pandora (*Pagellus eruthinus*)	Croatia		1	936	n/a	719	n/a	77	n/a	7
Fresh grey mullet (*Mugil chepalus*)	Croatia		1	69	n/a	76	n/a	110	n/a	7
Fresh grey mullet (*Mugil chepalus*)	Croatia		2	31	n.r.	23	n.r.	74	n.r.	7
Fresh atlantic herring (*Clupea harengus*)	Denmark		1	40	n/a	40	n/a	100	n/a	7
Fresh Atlantic herring (*Clupea harengus*)	Denmark		2	38	n.r.	26	n.r.	68	n.r.	7

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Fresh trout (*Salmo trutta*)	Slovenia		1	25	n/a	25	n/a	100	n/a	7
Fresh trout (*Salmo trutta*)	Slovenia		1	37	n/a	25	n/a	68	n/a	7
Fresh Nile perch (*Lates niloticus*)	Tanzania		1	134	n/a	118	n/a	88	n/a	7
Fresh Nile perch (*Lates niloticus*)	Tanzania		1	45	n/a	46	n/a	102	n/a	7
Fresh Atlantic chub mackerel (*Scomber scomber*)	Slovenia		1	56	n/a	54	n/a	96	n/a	7
Fresh Atlantic chub mackerel (*Scomber scomber*)	Slovenia		1	35	n/a	19	n/a	54	n/a	7
Fresh sea bass (*Dicentrachus labrax*)	Croatia		1	137	n/a	92	n/a	67	n/a	7
Fresh sea bass (*Dicentrachus labrax*)	Croatia		1	66	n/a	45	n/a	68	n/a	7
Fresh dover sole (*Solea vulgaris*)	Denmark		1	24	n/a	25	n/a	104	n/a	7
Fresh common dentex (*Dentex dentex*)	Morocco		1	77	n/a	64	n/a	83	n/a	7
Fresh common dentex (*Dentex dentex*)	Morocco		1	53	n/a	32	n/a	60	n/a	7
Fresh gilt head bream (*Sparus aurata*)	Turkey, Croatia, unknown		4	138	103-159	109	79-134	82.00	50-102	7
Fresh sparidae (*Lithognathus mormyrus*)	Croatia		1	238	n/a	246	n/a	103	n/a	7
Fresh sparidae (*Lithognathus mormyrus*)	Croatia		1	78	n/a	40	n/a	51	n/a	7
Fresh John Dory (*Zeus faber*)	Morocco		1	66	n/a	68	n/a	103	n/a	7
Fresh pilchard (*Clupea pilchardus*)	Slovenia		1	70	n/a	77	n/a	110	n/a	7
Fresh pilchard (*Clupea pilchardus*)	Slovenia		1	143	n/a	66	n/a	46	n/a	7
Fresh swordfish (*Xiphias gladius*)	Croatia		1	1 160	n/a	1 080	n/a	93	n/a	7
Fresh European hake (*Merluccius merluccius*)	Croatia		1	52	n/a	56	n/a	108	n/a	7
Canned tuna in vegetable oil	Spain, Thailand, Croatia(i), Thailand(i)		9	125	17-384	93	7-323	68	41-88	7
Canned sardine in vegetable oil	France(i), Croatia(i), Thailand(i)		8	94	4-144	70	2-109	71	42-109	7
Canned anchovy in vegetable oil	Spain(i)		1	22	n/a	16	n/a	73	n/a	7
Canned tuna in olive oil	Italy(i), Spain(i), Thailand		15	243	22-800	212	14-654	85	64-105	7
Canned mackerel in olive oil	Portugal(i)		1	44	n/a	18	n/a	41	n/a	7
Canned mackerel in seed oil	Croatia(i)		1	63	n/a	59	n/a	94	n/a	7
Canned tuna in sunflower oil	Cote d'Ivoire		3	129	103-180	112	92-151	87	84-89	7
Canned mackerel	Slovenia(i)		1	46	n/a	27	n/a	59	n/a	7
Canned tuna in own juice	France(i), Italy(i), Thailand, Thailand(i), Cote d'Ivoire		8	118	24-238	93	16-259	74	57-109	7
Canned mackerel with white wine aroma	France(i)		1	49	n/a	24	n/a	49	n/a	7

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Canned tuna with vegetables	France[(i)], Italy[(i)], Spain[(i)], Thailand[(i)], Slovenia[(i)], Spain[(i)] Cote d'Ivoire, Thailand		17	132	21-858	122	10-862	90	45 -109	7
Canned sardine with vegetables	Croatia[(i)], Thailand		3	62	3-93	35	30-55	71	53-100	7
Canned cod	Croatia[(i)]		1	111	n/a	46	n/a	41	n/a	7
Canned salmon with vegetables	Thailand		1	27	n/a	22	n/a	81	n/a	7
Canned sardines in seed oil	Croatia[(i)]		1	75	n/a	48	n/a	64	n/a	7
Canned salmon in own juice	USA		1	29	n/a	20	n/a	69	n/a	7
Canned herring in tomato sauce	Austria[(i)]		1	51	n/a	26	n/a	51	n/a	7
Canned mackerel with vegetables	Slovenia[(i)]		3	29	18-39	20	10-31	70	51-103	7
Grass carp (*Ctenopharyngodon idella Valenciennes)*	Wanshan, China	fresh	12[(b)]	292	61-680	60	24-98	28.4	7.4-93	8
Blackmouth dogfish (*Galeus melastomus*)	Adriatic Sea, Italy	sea	164	2 660	680-5 030	2 110	470-3 700	79.8	57-100	9
Blackmouth dogfish (*Galeus melastomus*)	Adriatic Sea, Albania	sea	164	1 010	250-2 060	1 010	230-1 990	92.3	72-100	9
Blackmouth dogfish (*Galeus melastomus*)	Ionian Sea	sea	273	820	250-2 840	740	250-2 200	91.5	72-100	9
Blackmouth dogfish (*Galeus melastomus*)	Aegean Sea	sea	218	2 140	850-5 470	1 550	580-4 320	70.3	43-100	9
Small spotted shark (*Scyliorhinus canicula*)	Adriatic Sea, Italy	sea	70	1 490	790-2 560	1 230	680-2 000	82.6	77-89.5	9
Kitefin shark (*Dalatias licha*)	Ionian Sea	sea	3	4 380	3 580-6 000	3 810	3 240-5 000	88	78-95	9
Gulper shark (*Centrophorus granulosus*)	Adriatic Sea, Albania	sea	25	9 660	8 750-10 510	9 090	7 900-10 000	92.9	89.4-96.9	9
Longnose spurdog (*Squalus blainvillei*)	Adriatic Sea, Albania	sea	20	4 530	3 900-7 440	4 050	3 220-7 240	91.8	81-98	9
Velvet belly (*Etmopterus spinax*)	Ionian Sea	sea	120	630	170-1 070	580	170-970	90.8	86.3-100	9
Sharpnose sevengill (*Heptranchias perlo*)	Adriatic Sea, Italy	sea	15	1 270	1 130-1 410	1 200	1 000-1 410	91.3	86.3-100	9
Smoothhound (*Mustelus mustelus*)	Ionian Sea	sea	8	310	230-370	230	180-280	75	69-80	9
Hammerhead (*Sphyrna zygaena*)	Ionian Sea	Sea	1	18 290	n/a	16 060	n/a	87.7	n/a	9
Bokkem (*Trachurus trachurus*)	central and southern Adriatic Sea	sea	100	230	ND-1 870	180	ND-1 210	94	65-100	10
Gilt sardine (*Sardinella aurita*)	central and southern Adriatic Sea	sea	150	90	ND-300	80	ND-300	93	56-100	10
Pilchard (*Sardina pilchardus*)	central and southern Adriatic Sea	sea	300	130	ND-400	90	ND-300	87	80-100	10
Sprat (*Sprattus sprattus*)	central and southern Adriatic Sea	sea	70	60	ND-140	60	ND-140	100	100	10

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Pandora (*Pagellus erythrinus*)	central and southern Adriatic Sea	sea	170	220	ND-700	200	ND-540	93	73-100	10
Megrim (*Lepidorhombus whiffiagonis*)	central and southern Adriatic Sea	sea	150	390	90-1 170	300	90-870	70	54-100	10
Four spotted megrim (*Lepidorhombus bosci*)	central and southern Adriatic Sea	sea	180	350	140-690	350	14-690	100	100	10
Red fish (*Helicolenus dactylopterus*)	central and southern Adriatic Sea	sea	220	420	110-840	400	110-610	98	70-100	10
Striped mullet (*Mullus barbatus*)	central and southern Adriatic Sea	sea	270	390	ND-1 740	370	ND-1 740	89	65-100	10
Skate (*Starry ray*)	central and southern Adriatic Sea	sea	120	730	90-1 780	710	50–1460	80	68-100	10
Forkbeard (*Phycis blennoides*)	central and southern Adriatic Sea	sea	330	360	160-570	260	140-390	71	52-82	10
Goldline (*Sarpa salpa*)	central and southern Adriatic Sea	sea	140	80	60-160	80	60-160	100	100	10
Frost fish (*Lepidopus caudatus*)	central and southern Adriatic Sea	sea	300	610	90-1 610	600	50-1 510	99	78-100	10
Angler fish (*Lophius budegassa*)	central and southern Adriatic Sea	sea	200	760	190-1 770	640	130-1 660	83	67-100	10
Picarel (*Spicara flexuosa*)	central and southern Adriatic Sea	sea	180	200	90-600	120	50–330	77	63-100	10
Hake (*Merluccius merluccius*)	Ionian Sea	sea	n.r.	90	ND-300	90	ND-300	98.3	73-100	11
Hake (*Merluccius merluccius*)	Aegean Sea	sea	n.r.	180	40-480	160	40-480	90.8	60-100	11
Striped mullet (*Mullus barbatus*)	Ionian Sea	sea	n.r.	400	ND-1 500	400	ND-1 500	98.9	92-100	11
Striped mullet (*Mullus barbatus*)	Aegean Sea	sea	n.r.	490	80-1 740	440	80-1 740	79.8	68-100	11
Long rough dab (*Hippoglossoides platessoides*)	Barents Sea, Arctic water	sea	4	160[e, g]	n.r.	47[e, g]	10-130	29.4[e]	9-67	12
Long rough dab (*Hippoglossoides platessoides*)	Barents Sea, Atlantic water	sea	14	290[e, g]	n.r.	47[e, g]	10-400	16.2[e]	3- >100	12
Long rough dab (*Hippoglossoides platessoides*)	Greenland Sea	sea	9	900[e, g]	n.r.	440[e,g]	10-930	48.9[e]	16-49	12
Greenland halibut (*Reinhardtius hippoglossoides*)	Barents Sea, Arctic water	sea	1	70[e, g]	n.r.	13[e, g]	n/a	18.6[e]	n/a	12
Greenland halibut (*Reinhardtius hippoglossoides*)	Barents Sea, Atlantic water	sea	2	310[e, g]	n.r.	40[e, g]	40-40	12.9[e]	1-17	12
Greenland halibut (*Reinhardtius hippoglossoides*)	Greenland Sea	sea	8	1 360[e, g]	n.r.	53[e, g]	260-1 630	3.9[e]	24-53	12
Halibut (*Hippoglossus hippoglossus*)	Barents Sea, Arctic water	sea	8	210[e, g]	n.r.	80[e, g]	70-200	38.1[e]	24->100	12
Halibut (*Hippoglossus hippoglossus*)	Barents Sea, Atlantic water	sea	1	200[e, g]	n.r.	760[e,g]	n/a	68[e]	n/a	12
Starry ray (*Raja radiata*)	Barents Sea, Atlantic water	sea	1	200[e, g]	n.r.	8[e, g]	n/a	4[e]	n/a	12
Atlantic cod (*Gadus morhua*)	Barents Sea, Atlantic water	sea	6	110[e, g]	n.r.	21[e, g]	10-50	19.1[e]	11-57	12
Atlantic cod (*Gadus morhua*)	Barents Sea, Atlantic water	sea	6	150[e, g]	n.r.	15[e, g]	10-40	10.0[e]	6-30	12
Plaice (*Pleuronectes platessa*)	Southern North Sea	sea	5	300[e, g]	n.r.	150[e, g]	120-440	50.0[e]	43-100	12
Angler	greater North Sea	sea	20	87	n.r.	80	n.r.	92.5	n.r.	13

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Lesser spotted dogfish	greater North Sea	sea	20	613	n.r.	598	n.r.	97	n.r.	13
Thornback ray	greater North Sea	sea	19	39	n.r.	37	n.r.	97.8	n.r.	13
Lemon sole	greater North Sea	sea	20	52	n.r.	49	n.r.	95.7	n.r.	13
Pouting	greater North Sea	sea	5	172	n.r.	160	n.r.	92.4	n.r.	13
Whiting	greater North Sea	sea	5	101	n.r.	91	n.r.	90.9	n.r.	13
Atlantic cod (*Gadus morhua*)	greater North Sea	sea	5	53	n.r.	49	n.r.	93.2	n.r.	13
Brill	greater North Sea	sea	5	64	n.r.	59	n.r.	91.8	n.r.	13
Ling	greater North Sea	sea	5	117	n.r.	106	n.r.	91	n.r.	13
Saithe	greater North Sea	sea	5	91	n.r.	88	n.r.	97.4	n.r.	13
Dab	greater North Sea	sea	13	101	n.r.	98	n.r.	97.2	n.r.	13
Sand sole	greater North Sea	sea	9	327	n.r.	308	n.r.	94.4	n.r.	13
Plaice (*Pleuronectes platessa*)	greater North Sea	sea	17	45	n.r.	43	n.r.	97	n.r.	13
Common sole	greater North Sea	sea	16	88	n.r.	86	n.r.	96.2	n.r.	13
Megrim (*Lepidorhombus whiffjagonis*)	greater North Sea	sea	6	83	n.r.	80	n.r.	96.7	n.r.	13
Ghostshark (*Chimaera monstruosa*)	South Adriatic Sea	sea	10(h)	3 140	1 300-5 160	2 670	1 140-4 560	83.6	74-97	14
Electric ray (*Torpedo nobiliana*)	South Adriatic Sea	sea	3(h)	2 420	1 650-3 590	1 900	1 150-2 760	81	51-97	14
Eagle ray (*Myliobatis aquila*)	South Adriatic Sea	sea	2(h)	830	670-1 010	630	400-840	71.6	61-83	14
Herring (*Nematalosa flyensis*)	Lake Murray, Papua New Guinea	fresh	11	49	n.r.	26	n.r.	54	n.r.	15
Herring (*Nematalosa papuensis*)	Lake Murray, Papua New Guinea	fresh	14	48	n.r.	26	n.r.	56	n.r.	15
Groove snouted catfish (*Arius berneyi*)	Lake Murray, Papua New Guinea	fresh	15	230	n.r.	181	n.r.	75	n.r.	15
Seven spotted archerfish (*Toxotes chatareus*)	Lake Murray, Papua New Guinea	fresh	8	360	n.r.	289	n.r.	80	n.r.	15
Sepic garpike (*Strongylura kreffti*)	Lake Murray, Papua New Guinea	fresh	9	380	n.r.	382	n.r.	94	n.r.	15
Giant freshwater anchovy (*Thryssa scratchleyi*)	Lake Murray, Papua New Guinea	fresh	5	380	n.r.	337	n.r.	79	n.r.	15
Barramundi (*Lates calcarifer*)	Lake Murray, Papua New Guinea	fresh	33	500	n.r.	458	n.r.	88	n.r.	15
Silver carp (*Hypophtalmichthys molitrtix*)	Ya-Er lake, China	fresh	13	429	205-928	195	57-360	48	27-72	16
Common carp (*Cyprinus carpio*)	Ya-Er lake, China	fresh	10	79	24-210	39	5-126	44	18-85	16
Crucian carp (*Carassius carassius*)	Ya-Er lake, China	fresh	11	423	131-1 360	185	52 -644	43	29-55	16
Snakehead fish (*Ophiocephalus argus cantor*)	Ya-Er lake, China	fresh	6	827	429-1 199	371	164-499	46	38-54	16
Golden grey mullet (*Liza aurata*)	Rio de Aveiro, Portugal, reference	estuarine	15	63(g)	n.r.	70(g)	n.r.	94	n.r.	17
Golden grey mullet (*Liza aurata*)	Rio de Aveiro, Portugal, moderately contaminated	estuarine	15	120(g)	n.r.	110(g)	n.r.	97	n.r.	17

Table B1: Continued.

Species (*latin name*)	Sample collected at location/origin	Sea or fresh water	n	THg (µg/kg w.w.)		MeHg (µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Golden grey mullet (*Liza aurata*)	Rio de Aveiro, Portugal, heavily contaminated	estuarine	15	240[(g)]	n.r.	200[(g)]	n.r.	85	n.r.	17

n: number of samples; w.w.: wet weight; THg: total mercury; MeHg: methylmercury; Ref.: reference; n.r.: not reported; n/a: not applicable; ND: not detected.
(a): semi saline;
(b): samples from mercury mining area;
(c): result from the sampling site with the lowest concentration;
(d): result from the sampling site with the highest concentration;
(e): median;
(f): calculated from the mean (or median) THg and MeHg concentrations;
(g): reported as dry weight;
(h): each sample represents a pooled sample;
(i): country or producer, unknown origin.

References: 1: Agah et al. (2007); 2: Baralkiewicz et al. (2006); 3: Kružiková et al. (2008); 4 Holsbeek et al. (1997); 5: Berzas Nevado et al. (2011); 6: Kannan et al. (1998); 7: Miklavčič et al. (2011a); 8: Qiu et al. (2009); 9: Storelli et al. (2002a); 10: Storelli et al. (2003); 11: Storelli et al. (2005); 12: Joiris et al. (1997); 13: Baeyens et al. (2003); 14: Storelli et al. (2002b); 15: Bowles et al. (2001); 16: Jin et al. (2006); 17: Mieiro et al. (2009).

Table B2: Overview of previously reported literature data on relationship between concentrations of total mercury and methylmercury in seafood.

Species (*latin name*)	Sample collected at location / origin	F, S, E	n	THg(µg/kg w.w.)		MeHg(µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Factory (small)	F	20	750.3	695.4-805.2	n.r.	n.r.	78.5	n.r.	1
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Factory (medium)	F	50	442.7	410.3-475.1	308[(a)]	220-589	59.4	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Factory (large)	F	40	381.3	353.4-409.2	n.r.	n.r.	49.6	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Wildlife reserve (small)	F	9	127.9	118.5 -137.2	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Wildlife reserve (medium)	F	27	38.4	35.6-41.2	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Wildlife reserve (large)	F	50	31.7	29.4-34.0	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Upstream (small)	F	7	45.7	42.4-49.1	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Upstream (medium)	F	40	21.1	19.4-22.4	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Upstream (large)	F	30	16	14.8-17.1	n.r.	n.r.	n.r.	n.r.	
Zebra mussel (*Dreissena polymorpha*)	Ebro river, Spain. Meander (large)	F	12	106.8	84.6-141.4	n.r.	n.r.	n.r.	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 1	S	n.r.	559[(b)]	n.r.	150[(b)]	n.r.	26[(b)]	n.r.	2
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 2	S	n.r.	320[(b)]	n.r.	90[(b)]	n.r.	28[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 3	S	n.r.	410[(b)]	n.r.	93[(b)]	n.r.	23[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 4	S	n.r.	236[(b)]	n.r.	75[(b)]	n.r.	32[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 5	S	n.r.	360[(b)]	n.r.	141[(b)]	n.r.	39[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 6	S	n.r.	383[(b)]	n.r.	66[(b)]	n.r.	17[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 7	S	n.r.	434[(b)]	n.r.	155[(b)]	n.r.	36[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 8	S	n.r.	370[(b)]	n.r.	105[(b)]	n.r.	28[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 9	S	n.r.	262[(b)]	n.r.	75[(b)]	n.r.	29[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Mar Piccolo, Taranto, Italy Site 10	S	n.r.	280[(b)]	n.r.	137[(b)]	n.r.	49[(b)]	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	10 locations on Sardinian coast, campaign 1	S	n.r.	n.r.	35 – 115[(b,c)]	39[(b)]	15-51[(b,c)]	n.r.	33-91[(b,c)]	3
Mediterranean mussel (*Mytilus galloprovincialis*)	10 locations on Sardinian coast, campaign 2	S	n.r.	n.r.	40-830[(b,c)]	65[(b)]	17 – 116[(b,c)]	n.r.	14-98[(b,c)]	
Dall's porpoise (*Phocoenoides dalli*)	Japan	S	9	1 230	830-2 390	1 020	680-1 950	84	n.r.	4
Short-finned pilot whale (*Globicephala macrorhynchus*),northern form	Japan	S	8	1 500	790-2 240	1 250	500-1 880	81	n.r.	
Baird's beaked whale (*Berardius bairdii*),	Japan	S	22	1 770	750-6 460	1 250	560-3 470	78	n.r.	
pantropical spotted dolphin (*Stenella attenuata*)	Japan	S	4	4 870	4 280-5 320	2 620	2 010-3 160	54	n.r.	
Risso's dolphin (*Grampus griseus*)	Japan	S	17	4 460	1 710-9 210	3 150	1 330-8 780	74	n.r.	
Rough-toothed dolphin (*Steno bredanensis*)	Japan	S	5	5 020	1 220-9 980	3 510	1 110-6 060	74	n.r.	

Table B2: Continued.

Species (*latin name*)	Sample collected at location / origin	F, S, E	n	THg(µg/kg w.w.)		MeHg(µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Striped dolphin (*Stenella coeruleoalba*)	Japan	S	20	8 550	1 040-63 400	3 740	970-26 200	63	n.r.	
Short-finned pilot whale (*Globicephala macrorhynchus*), southern form	Japan	S	34	11 600	1 210-37 600	6 450	930-17 200	64	n.r.	
Bottlenose dolphin (*Tursiops truncatus*),	Japan	S	37	17 800	590-98 900	6 830	580-15 400	54	n.r.	
False killer whale (*Pseudorca crassidens*)	Japan	S	4	39 500	17 400-81 000	11 200	9 020-13300	36	n.r.	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-2 Sampling 1	E	1[(d)]	18.6	n/a	6.2	n/a	33	n/a	5
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-2 Sampling 2	E	1[(d)]	16.3	n/a	7.2	n/a	44	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-2 Sampling 3	E	1[(d)]	14.5	n/a	8.5	n/a	59	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-2 Sampling 4	E	1[(d)]	30.2	n/a	n.r.	n/a	n.r.	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-4 Sampling 1	E	1[(d)]	21.1	n/a	5.3	n/a	25	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-4 Sampling 2	E	1[(d)]	17.4	n/a	6.1	n/a	35	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-4 Sampling 3	E	1[(d)]	15.6	n/a	6.5	n/a	42	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-4 Sampling 4	E	1[(d)]	27.7	n/a	n.r.	n/a	n.r.	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-5 Sampling 1	E	1[(d)]	22.3	n/a	5.1	n/a	23	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-5 Sampling 2	E	1[(d)]	20.1	n/a	5.3	n/a	26	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-5 Sampling 3	E	1[(d)]	15.9	n/a	6.7	n/a	42	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station E-5 Sampling 4	E	1[(d)]	28.3	n/a	n.r.	n/a	n.r.	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station C-1 Sampling 1	S	1[(d)]	23.7	n/a	4.1	n/a	17	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station C-1 Sampling 2	S	1[(d)]	22.9	n/a	4.8	n/a	21	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station C-1 Sampling 3	S	1[(d)]	20.2	n/a	5.1	n/a	25	n/a	
Mediterranean mussel (*Mytilus galloprovincialis*)	Krka river estuary, Croatia Station C-1 Sampling 4	S	1[(d)]	22.6	n/a	n.r.	n/a	n.r.	n/a	

Table B2: Continued.

Species (*latin name*)	Sample collected at location / origin	F, S, E	n	THg(µg/kg w.w.)		MeHg(µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Dunkirk and Calais	S	12[(d)]	84[(b)]	n.r.	56[(b)]	n.r.	66[(b)]	n.r.	6
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Boulogne and Canche	S	4[(d)]	97[(b)]	n.r.	65[(b)]	n.r.	65[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Authie and Somme	S	7[(d)]	65[(b)]	n.r.	34[(b)]	n.r.	54[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Caux region	S	12[(d)]	287[(b)]	n.r.	98[(b)]	n.r.	45[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Seine estuary	S	16[(d)]	176[(b)]	n.r.	73[(b)]	n.r.	44[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Calvados	S	15[(d)]	152[(b)]	n.r.	75[(b)]	n.r.	53[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Veys bay, St Vaast	S	10[(d)]	131[(b)]	n.r.	67[(b)]	n.r.	54[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Cherbourg	S	4[(d)]	127[(b)]	n.r.	53[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	West Cotentin	S	6[(d)]	78[(b)]	n.r.	38[(b)]	n.r.	51[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Cancale	S	8[(d)]	125[(b)]	n.r.	40[(b)]	n.r.	33[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Arguenon-Fresnaye	S	4[(d)]	58[(b)]	n.r.	20[(b)]	n.r.	35[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Saint Brieuc	S	11[(d)]	75[(b)]	n.r.	34[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Paimpol-Perros-Guirec	S	4[(d)]	92[(b)]	n.r.	48[(b)]	n.r.	52[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Lannion	S	4[(d)]	102[(b)]	n.r.	62[(b)]	n.r.	61[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Morlaix	S	8[(d)]	128[(b)]	n.r.	70[(b)]	n.r.	55[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Benoit Aber	S	4[(d)]	78[(b)]	n.r.	26[(b)]	n.r.	34[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Brest	S	16[(d)]	145[(b)]	n.r.	64[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Concarneau	S	4[(d)]	107[(b)]	n.r.	76[(b)]	n.r.	68[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Aven-Belon-Laita	S	4[(d)]	131[(b)]	n.r.	86[(b)]	n.r.	65[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Lorient	S	4[(d)]	153[(b)]	n.r.	11[(b)]	n.r.	74[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Etel	S	3[(d)]	138[(b)]	n.r.	77[(b)]	n.r.	57[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Gulf of Morbihan	S	12[(d)]	134[(b)]	n.r.	63[(b)]	n.r.	49[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Vilaine	S	16[(d)]	121[(b)]	n.r.	48[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	loire and Bourgneuf	S	19[(d)]	129[(b)]	n.r.	52[(b)]	n.r.	41[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Vendee	S	4[(d)]	329[(b)]	n.r.	99[(b)]	n.r.	33[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Pertuis Breton	S	8[(d)]	232[(b)]	n.r.	76[(b)]	n.r.	35[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Pertuis de Antioche	S	4[(d)]	253[(b)]	n.r.	51[(b)]	n.r.	21[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Marennes-Oleron	S	24[(d)]	207[(b)]	n.r.	54[(b)]	n.r.	28[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Gironde	S	11[(d)]	211[(b)]	n.r.	61[(b)]	n.r.	33[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Arcachon	S	16[(d)]	222[(b)]	n.r.	71[(b)]	n.r.	32[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Basque region	S	16[(d)]	199[(b)]	n.r.	94[(b)]	n.r.	52[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Roussillon	S	14[(d)]	103[(b)]	n.r.	43[(b)]	n.r.	41[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Languedoc	S	13[(d)]	132[(b)]	n.r.	88[(b)]	n.r.	64[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Rhone delta and Fos	S	16[(d)]	155[(b)]	n.r.	86[(b)]	n.r.	57[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Marseille	S	4[(d)]	169[(b)]	n.r.	70[(b)]	n.r.	43[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Toulon-St Raphael	S	6[(d)]	220[(b)]	n.r.	73[(b)]	n.r.	37[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	Cannes-Menton	S	6[(d)]	124[(b)]	n.r.	49[(b)]	n.r.	42[(b)]	n.r.	

Table B2: Continued.

Species (*latin name*)	Sample collected at location / origin	F, S, E	n	THg(µg/kg w.w.)		MeHg(µg/kg w.w.)		Proportion % (MeHg/THg)		Ref.
				Mean	Range	Mean	Range	Mean	Range	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	West Corsica-Ajaccio	S	4[(d)]	173[(b)]	n.r.	83[(b)]	n.r.	53[(b)]	n.r.	
Mussels (*Mytilus* spp.), Oysters (*Crassostrea gigas*)	East Corsica	S	7[(d)]	99[(b)]	n.r.	45[(b)]	n.r.	45[(b)]	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Rio-Niteroy Bridge	E	20	41.1	n.r.	12.2	n.r.	29.6	n.r.	7
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Rio-Niteroy Bridge	E	10	29.2	n.r.	8.9	n.r.	30.5	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Rio-Niteroy Bridge	E	20	25.3	n.r.	8.5	n.r.	32.9	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Boa Viagem	E	10	32.7	n.r.	11.5	n.r.	35.2	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Boa Viagem	E	10	18.6	n.r.	5.9	n.r.	31.9	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Boa Viagem	E	10	11.6	n.r.	4.5	n.r.	38.4	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Marina da Gloria	E	25	48.3	n.r.	13.8	n.r.	28.7	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Marina da Gloria	E	29	51.3	n.r.	18.0	n.r.	35.1	n.r.	
Common mussel (*Perna perna*)	Brazil, Guanbara Bay, Marina da Gloria	E	10	45.4	n.r.	21.0	n.r.	46.2	n.r.	
Oyster (*Crassostrea tulipa*)	Ghana, Benya lagoon, dry season	S	54	210[(b,e, f)]	100-470[(b,f)]	130[(b,e)]	30-390[(b)]	54[(e)]	19->100	8
Oyster (*Crassostrea tulipa*)	Ghana, Benya lagoon, wet season	S	15	140[(b,e,g)]	100-310[(b,g)]	90[(b,e)]	30-240[(b)]	36[(e)]	17->100	
Oyster (*Crassostrea tulipa*)	Ghana, Sakumo lagoon, dry season	S	25	130[(b,e)]	80-180[(b)]	100[(b,e)]	60-230[(b)]	80[(e)]	39->100	
Oyster (*Crassostrea tulipa*)	Ghana, Sakumo lagoon, wet season	S	45	120[(b,e,h)]	60-230[(b,h)]	50[(b,e,i)]	30-130[(b,i)]	39[(e)]	17-68	
Oyster (*Crassostrea tulipa*)	Ghana, Ningo lagoon, dry season	S	19	160[(b,e,j)]	30-230[(b,j)]	80[(b,e,j)]	40-190[(b,j)]	50[(e)]	17->100	
Oyster (*Crassostrea tulipa*)	Ghana, Ningo lagoon, wet season	S	5	130[(b,e,k)]	100-160[(b,k)]	50[(b,e)]	40-90[(b)]	47[(e)]	40-58	
Common mussel (*Perna perna*)	Ghana, Benya lagoon, dry season	S	30	370[(b,e)]	190-660[(b)]	160[(b,e,l)]	70-550[(b,l)]	43[(e)]	12->100	
Common mussel (*Perna perna*)	Ghana, Benya lagoon, wet season	S	14	200[(b,e,m)]	110-300[(b,m)]	90[(b,e,n)]	40-190[(b,n)]	38[(e)]	14-79	
Common mussel (*Perna perna*)	Ghana, Sakumo lagoon, dry season	S	15	330[(b,e,o)]	200-530[(b,o)]	100[(b,e,o)]	40-180[(b,o)]	29[(e)]	9-50	
Common mussel (*Perna perna*)	Ghana, Sakumo lagoon, wet season	S	10	260[(b,e,p)]	170-760[(b,p)]	70[(b,e)]	30-180[(b)]	33[(e)]	28-100	

n: number of samples or sampling sites; ww: wet weight; THg: total mercury; MeHg: methylmercury; Ref.: reference; n.r.: not reported; n/a: not applicable; F: freshwater; S: seawater; E: estuarine.

(a): MeHg only analysed in samples from the sampling site that showed the highest concentrations of THg;
(b): reported as dry weight;
(c): results are mean values from 2 measurements on the same station at different times;
(d): each sample represents a pooled sample;
(e): median;
(f): n = 59;
(g): n = 24;
(h): n = 55;

(i): n = 71;
(j): n = 31;
(k): n = 12;
(l): n = 35;
(m): n = 30;
(n): n = 25;
(o): n = 19;
(p): n = 18.

References: 1: Carrasco et al. (2008); 2: Di Leo et al. (2010); 3: Ipolyi et al. (2004); 4: Endo et al. (2005); 5: Mikac et al. (1996); 6: Claisse et al. (2001); 7: Kehrig et al. (2002); 8: Joiris et al. (2000).

C. CONSUMPTION

Table C1: Overview on 'Fish and other seafood' consumption (g/day) in the total population by age class. Minimum, median and maximum of the mean and 95th percentile values across European countries and dietary surveys are shown.

	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Mean consumption in the total population (g/day)							
Minimum	0.5	3.2	5.2	5.6	8.8	5.5	5.2
Median	1.3	5.2	10.3	17.3	25.9	27.7	25.8
Maximum	2.2	32.6	40.2	48.9	75.3	46.1	33.8
P95 consumption in the total population (g/day)[(a)]							
Minimum	-	20.5	35.0	42.0	54.7	50.0	45.8
Median	-	26.1	44.0	72.8	100.0	120.5	99.7
Maximum		33.3	132.0	169.5	194.3	137.5	117.4

P95: 95th percentile.
(a): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b) and therefore they were not included in this table.

Table C2: Overview on 'Fish and other seafood' consumption (g/day) in the consumers only by age class. Minimum, median and maximum of the mean, 95th percentile values and percentage of consumers across European countries and dietary surveys are shown.

	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Percentage of consumers (%)[(a)]							
	7.1	31.6	44.2	50.2	55.2	54.0	52.3
Mean consumption in the consumers only (g/day)							
Minimum	17.2	13.9	14.6	14.5	20.3	25.9	30.2
Median	21.8	18.6	28.8	51.7	62.7	67.4	55.1
Maximum	26.5	74.5	58.8	74.5	83.4	74.9	68.9
P95 consumption in the consumers only (g/day)[(b)]							
Minimum	-	35.7	40.5	43.2	54.4	57.5	87.1
Median	-	63.3	62.5	138.7	150.0	158.8	134.8
Maximum	-	90.9	154.7	181.8	201.1	180.1	150.0

P95: 95th percentile.
(a): Based on average of percentages from all included surveys.
(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b) and therefore they were not included in this table.

Table C3: Overview on 'Fish meat' consumption (g/day) in the total population by age class. Minimum, median and maximum of the mean and 95th percentile values across European countries and dietary surveys are shown.

	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Mean consumption in the total population (g/day)							
Minimum	0.5	1.2	2.2	4.4	4.8	5.5	5.2
Median	1.3	4.1	7.9	12.6	16.9	21.8	21.0
Maximum	2.2	29.0	30.8	36.4	57.3	35.5	26.3
P95 consumption in the total population (g/day)[(a)]							
Minimum	-	9.4	15.0	34.3	36.1	50.0	45.8
Median	-	18.3	37.5	60.3	96.0	100.0	76.4
Maximum	-	33.3	101.5	142.5	159.1	137.5	100.0

P95: 95th percentile.
(a): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b) and therefore they were not included in this table.

Table C4: Overview on 'Fish meat' consumption (g/day) in the consumers only by age class. Minimum, median and maximum values of the mean, 95th percentile values and percentage of consumers across European countries and dietary surveys are shown.

	Infants	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Percentage of consumers (%)[(a)]							
	7.1	24.3	34.6	39.7	48.0	50.3	49.1
Mean consumption in the consumers only (g/day)							
Minimum	17.2	12.6	13.0	12.6	18.1	23.5	27.1
Median	21.8	17.1	28.0	47.1	55.9	56.6	51.3
Maximum	26.5	95.0	53.5	69.6	79.1	74.7	69.0
P95 consumption in the consumers only (g/day)[(b)]							
Minimum	-	35.7	39.8	38.3	51.0	53.9	76.4
Median	-	63.3	76.7	107.0	139.6	134.4	123.2
Maximum	-	90.9	115.0	175.0	179.0	180.5	149.5

P95: 95th percentile.
(a): Based on average of percentages from all included surveys.
(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b) and therefore they were not included in this table.

D. EXPOSURE

Table D1: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in toddlers in µg/kg body weight per week. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	Regional Flanders	36	0.20	0.21	0.21	-(a)	-(a)	-(a)
Bulgaria	NUTRICHILD	428	0.25	0.27	0.28	1.51	1.53	1.58
Germany	DONALD 2006	92	0.31	0.31	0.31	2.11	2.13	2.15
Germany	DONALD 2007	85	0.18	0.19	0.19	0.85	0.86	0.87
Germany	DONALD_2008	84	0.26	0.27	0.27	1.63	1.65	1.66
Spain	enKid	17	1.32	1.42	1.51	-(a)	-(a)	-(a)
Finland	DIPP	497	0.58	0.59	0.60	2.70	2.72	2.74
Italy	INRAN SCAI 2005/06	36	1.49	1.57	1.65	-(a)	-(a)	-(a)
the Netherlands	VCP kids	322	0.09	0.09	0.09	0.66	0.68	0.70
Minimum			**0.09**	**0.09**	**0.09**	**0.66**	**0.68**	**0.70**
Median			**0.26**	**0.27**	**0.28**	**1.57**	**1.59**	**1.62**
Maximum			**1.49**	**1.57**	**1.65**	**2.70**	**2.72**	**2.74**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
Calculation of P95 not possible due to low number of participants.

Table D2: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in other children in µg/kg body weight per week. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	Regional Flanders	625	0.28	0.29	0.29	1.59	1.60	1.62
Bulgaria	NUTRICHILD	433	0.21	0.22	0.23	1.40	1.43	1.49
Czech Republic	SISP04	389	0.50	0.50	0.51	3.32	3.35	3.38
Germany	DONALD 2006	211	0.22	0.23	0.23	1.15	1.16	1.17
Germany	DONALD 2007	226	0.20	0.20	0.20	1.11	1.12	1.13
Germany	DONALD_2008	223	0.24	0.24	0.24	1.52	1.53	1.55
Denmark	Danish Dietary Survey	490	0.37	0.38	0.39	1.20	1.21	1.24
Spain	enKid	156	1.05	1.09	1.14	4.47	4.69	4.90
Spain	NUT INK05	399	1.19	1.23	1.28	4.08	4.14	4.24
Finland	DIPP	933	0.49	0.49	0.50	2.33	2.36	2.38
Finland	STRIP	250	0.27	0.27	0.28	1.36	1.38	1.38
France	INCA2	482	0.61	0.63	0.64	1.88	1.97	1.99
Greece	Regional Crete	839	0.59	0.61	0.63	2.75	2.79	2.96
Italy	INRAN SCAI 2005/06	193	1.45	1.49	1.54	4.60	4.96	5.04
Latvia	EFSA TEST	189	0.20	0.20	0.21	1.61	1.63	1.64
the Netherlands	VCP kids	957	0.13	0.14	0.14	0.73	0.75	0.76
Sweden	NFA	1 473	0.31	0.32	0.32	1.28	1.31	1.33
Minimum			**0.13**	**0.14**	**0.14**	**0.73**	**0.75**	**0.76**
Median			**0.31**	**0.32**	**0.32**	**1.59**	**1.60**	**1.62**
Maximum			**1.45**	**1.49**	**1.54**	**4.60**	**4.96**	**5.04**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D3: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in adolescents in µg/kg body weight per week. The minimum, median and maximum of mean and 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	584	0.19	0.20	0.20	1.15	1.16	1.19
Cyprus	Childhealth	303	0.40	0.41	0.43	1.77	1.83	1.85
Czech Republic	SISP04	298	0.33	0.33	0.34	2.46	2.49	2.51
Germany	National Nutrition Survey II	1 011	0.08	0.08	0.09	0.41	0.42	0.42
Denmark	Danish Dietary Survey	479	0.23	0.23	0.24	0.78	0.79	0.80
Spain	AESAN FIAB	86	0.51	0.54	0.58	1.49	1.60	1.78
Spain	enKid	209	0.93	0.96	0.99	3.35	3.45	3.56
Spain	NUT INK05	651	0.74	0.77	0.80	2.70	2.80	2.85
France	INCA2	973	0.29	0.29	0.30	0.99	1.01	1.02
Italy	INRAN SCAI 2005/06	247	1.06	1.09	1.12	5.04	5.05	5.06
Latvia	EFSA TEST	470	0.07	0.08	0.08	0.62	0.64	0.65
Sweden	NFA	1 018	0.21	0.22	0.22	0.98	0.99	1.00
Minimum			**0.07**	**0.08**	**0.08**	**0.41**	**0.42**	**0.42**
Median			**0.31**	**0.31**	**0.32**	**1.32**	**1.38**	**1.48**
Maximum			**1.06**	**1.09**	**1.12**	**5.04**	**5.05**	**5.06**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D4: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in adults in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	1 304	0.24	0.24	0.25	1.34	1.35	1.38
Czech Republic	SISP04	1 666	0.20	0.20	0.20	1.50	1.52	1.53
Germany	National Nutrition Survey II	10 419	0.16	0.16	0.17	1.11	1.12	1.13
Denmark	Danish Dietary Survey	2 822	0.17	0.17	0.18	0.53	0.53	0.55
Spain	AESAN	410	0.89	0.92	0.95	2.91	2.98	3.08
Spain	AESAN FIAB	981	1.04	1.08	1.12	2.76	2.86	2.97
Finland	FINDIET 2007	1 575	0.36	0.36	0.37	2.01	2.03	2.05
France	INCA2	2 276	0.34	0.34	0.35	1.11	1.13	1.17
Great Britain	NDNS	1 724	0.30	0.30	0.31	1.01	1.02	1.03
Hungary	National Representative Survey	1 074	0.12	0.12	0.12	0.81	0.82	0.82
Ireland	NSIFCS	958	0.20	0.20	0.20	0.74	0.76	0.78
Italy	INRAN SCAI 2005/06	2 313	0.82	0.84	0.86	3.00	3.04	3.08
Latvia	EFSA TEST	1 306	0.20	0.20	0.20	1.26	1.28	1.29
the Netherlands	DNFCS 2003	750	0.07	0.07	0.07	0.50	0.51	0.53
Sweden	Riksmaten 1997/98	1 210	0.28	0.29	0.29	0.94	0.96	0.97
Minimum			**0.07**	**0.07**	**0.07**	**0.50**	**0.51**	**0.53**
Median			**0.24**	**0.24**	**0.25**	**1.11**	**1.13**	**1.14**
Maximum			**1.04**	**1.08**	**1.12**	**3.00**	**3.04**	**3.08**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D5: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in elderly in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	518	0.25	0.26	0.26	1.24	1.27	1.30
Germany	National Nutrition Survey II	2 006	0.19	0.19	0.19	1.23	1.24	1.26
Denmark	Danish Dietary Survey	309	0.18	0.18	0.19	0.50	0.51	0.52
Finland	FINDIET 2007	463	0.47	0.47	0.48	2.49	2.49	2.49
France	INCA2	264	0.41	0.42	0.43	1.11	1.13	1.14
Hungary	National Representative Survey	206	0.06	0.06	0.07	0.34	0.34	0.35
Italy	INRAN SCAI 2005/06	290	0.61	0.63	0.65	1.71	1.73	1.74
Minimum			**0.06**	**0.06**	**0.07**	**0.34**	**0.34**	**0.35**
Median			**0.25**	**0.26**	**0.26**	**1.23**	**1.24**	**1.26**
Maximum			**0.61**	**0.63**	**0.65**	**2.49**	**2.49**	**2.49**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D6: Lower, middle and upper bound mean and 95th percentile methylmercury exposure in very elderly in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	712	0.25	0.25	0.26	1.40	1.41	1.42
Germany	National Nutrition Survey II	490	0.21	0.21	0.21	1.38	1.42	1.42
Denmark	Danish Dietary Survey	20	0.23	0.24	0.24	-(a)	-(a)	-(a)
France	INCA2	84	0.37	0.38	0.39	1.08	1.11	1.13
Hungary	National Representative Survey	80	0.05	0.06	0.06	0.13	0.14	0.16
Italy	INRAN SCAI 2005/06	228	0.33	0.35	0.36	1.15	1.17	1.19
Minimum			**0.05**	**0.06**	**0.06**	**0.13**	**0.14**	**0.16**
Median			**0.24**	**0.25**	**0.25**	**1.15**	**1.17**	**1.19**
Maximum			**0.37**	**0.38**	**0.39**	**1.40**	**1.42**	**1.42**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a): Calculation of P95 not possible due to low number of participants.

Table D8: Lower, middle and upper bound 95th percentile methylmercury exposure among fish meat consumers only by survey and age class in µg Hg/kg body weight per week.

Country	Survey	Age class	N	P95		
				LB	MB	UB
Spain	AESAN	Adults	279	3.03	3.08	3.20
Spain	AESAN FIAB	Adults	796	2.88	2.95	3.09
Cyprus	Childhealth	Adolescents	88	2.53	2.56	2.58
Denmark	Danish Dietary Survey	Other children	379	1.39	1.41	1.43
		Adolescents	394	0.80	0.80	0.81
		Adults	2.392	0.56	0.57	0.58
		Elderly	279	0.54	0.54	0.55
Belgium	National Diet 2004	Adolescents	128	2.38	2.40	2.42
		Adults	399	2.05	2.08	2.10
		Elderly	162	2.12	2.14	2.16
		Very elderly	201	2.29	2.31	2.33
Finland	DIPP	Toddlers	221	4.60	4.66	4.72
		Other children	443	2.89	2.90	2.92
the Netherlands	DNFCS 2003	Adults	87	1.65	1.66	1.67
Latvia	EFSA TEST	Adults	351	2.41	2.44	2.46
Spain	enKid	Other children	67	4.71	4.82	5.03
		Adolescents	101	4.86	5.09	5.22
Finland	FINDIET 2007	Adults	620	3.25	3.26	3.27
		Elderly	220	4.52	4.52	4.52
France	INCA2	Other children	336	1.96	2.00	2.02
		Adolescents	617	1.19	1.21	1.23
		Adults	1.716	1.21	1.22	1.23
		Elderly	224	1.08	1.11	1.15
		Very elderly	69	1.07	1.10	1.12
Italy	INRAN SCAI 2005/06	Other children	103	7.47	7.48	7.49
		Adolescents	140	7.22	7.25	7.29
		Adults	1.432	6.15	6.16	6.17
		Elderly	180	2.42	2.45	2.47
		Very elderly	118	1.30	1.31	1.32
Germany	National Nutrition Survey II	Adolescents	87	3.05	3.05	3.05
		Adults	2.304	2.02	2.04	2.07
		Elderly	565	1.95	1.95	1.95
		Very elderly	150	1.95	1.96	1.98
Hungary	National Represent. Survey	Adults	136	3.36	3.39	3.42
Great Britain	NDNS	Adults	1.136	1.22	1.24	1.25
Sweden	NFA	Other children	489	1.88	1.89	1.95
		Adolescents	290	1.30	1.32	1.33
Ireland	NSIFCS	Adults	609	0.84	0.85	0.86
Spain	NUT INK05	Other children	236	4.71	4.85	4.99
		Adolescents	370	3.11	3.14	3.25
Bulgaria	NUTRICHILD	Toddlers	62	4.87	5.10	5.32
		Other children	69	3.51	3.88	4.09
Greece	Regional Crete	Other children	252	5.86	5.86	5.86
Belgium	Regional Flanders	Other children	133	3.33	3.36	3.40
	Riksmaten 1997/98	Adults	725	1.04	1.05	1.06
Czech Republic	SISP04	Other children	95	5.13	5.18	5.23
		Adults	333	2.54	2.56	2.59
Finland	STRIP	Other children	94	2.30	2.32	2.34
the Netherlands	VCP kids	Other children	69	4.73	4.78	4.83

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D9: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in toddlers in µg Hg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	Regional Flanders	36	0.56	1.36	2.16	-(a)	-(a)	-(a)
Bulgaria	NUTRICHILD	428	0.41	1.13	1.84	0.86	1.99	3.26
Germany	DONALD 2006	92	0.31	0.82	1.33	0.88	1.52	2.36
Germany	DONALD 2007	85	0.27	0.79	1.31	0.67	1.35	2.18
Germany	DONALD_2008	84	0.28	0.83	1.38	0.72	1.55	2.39
Spain	enKid	17	0.51	1.16	1.80	-(a)	-(a)	-(a)
Finland	DIPP	497	0.37	0.94	1.51	1.07	2.30	3.54
Italy	INRAN SCAI 2005/06	36	0.59	1.15	1.71	-(a)	-(a)	-(a)
the Netherlands	VCP kids	322	0.35	1.16	1.98	0.82	2.24	4.06
Minimum			**0.27**	**0.79**	**1.31**	**0.67**	**1.35**	**2.18**
Median			**0.37**	**1.13**	**1.71**	**0.86**	**1.62**	**2.20**
Maximum			**0.59**	**1.36**	**2.16**	**1.07**	**2.30**	**4.06**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a): Calculation of P95 not possible due to low number of participants.

Table D10: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in other children in µg Hg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	Regional Flanders	625	0.39	0.99	1.60	0.82	1.69	2.66
Bulgaria	NUTRICHILD	433	0.35	0.92	1.50	0.74	1.62	2.56
Czech Republic	SISP04	389	0.29	0.59	0.89	0.87	1.27	1.66
Germany	DONALD 2006	211	0.25	0.70	1.14	0.59	1.22	2.06
Germany	DONALD 2007	226	0.24	0.67	1.10	0.51	1.23	2.05
Germany	DONALD_2008	223	0.25	0.66	1.08	0.67	1.23	1.93
Denmark	Danish Dietary Survey	490	0.26	0.71	1.17	0.50	1.12	1.81
Spain	enKid	156	0.43	0.84	1.26	1.14	1.73	2.35
Spain	NUT INK05	399	0.47	0.85	1.24	1.12	1.67	2.20
Finland	DIPP	933	0.38	1.06	1.75	0.86	1.99	3.37
Finland	STRIP	250	0.47	0.95	1.43	1.17	1.77	2.37
France	INCA2	482	0.35	0.78	1.21	0.74	1.38	2.16
Greece	Regional Crete	839	0.55	0.94	1.33	1.27	1.79	2.38
Italy	INRAN SCAI 2005/06	193	0.76	1.13	1.50	1.85	2.27	2.82
Latvia	EFSA TEST	189	0.44	0.69	0.94	0.98	1.36	1.78
the Netherlands	VCP kids	957	0.29	0.97	1.65	0.65	1.83	3.19
Sweden	NFA	1 473	0.42	0.81	1.21	0.88	1.41	2.01
Minimum			**0.24**	**0.59**	**0.89**	**0.50**	**1.12**	**1.66**
Median			**0.38**	**0.84**	**1.24**	**0.86**	**1.62**	**2.20**
Maximum			**0.76**	**1.13**	**1.75**	**1.85**	**2.27**	**3.37**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D11: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in adolescents in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	584	0.19	0.39	0.60	0.53	0.83	1.17
Cyprus	Childhealth	303	0.27	0.46	0.65	0.62	0.85	1.16
Czech Republic	SISP04	298	0.20	0.41	0.61	0.65	0.85	1.22
Germany	National Nutrition Survey II	1 011	0.17	0.42	0.67	0.48	0.91	1.42
Denmark	Danish Dietary Survey	479	0.16	0.42	0.68	0.31	0.71	1.16
Spain	AESAN FIAB	86	0.23	0.41	0.59	0.57	0.79	1.00
Spain	enKid	209	0.33	0.54	0.75	1.04	1.35	1.53
Spain	NUT INK05	651	0.29	0.51	0.74	0.70	0.99	1.33
France	INCA2	973	0.17	0.41	0.64	0.38	0.78	1.20
Italy	INRAN SCAI 2005/06	247	0.51	0.73	0.94	1.70	1.85	2.33
Latvia	EFSA TEST	470	0.34	0.52	0.70	0.76	1.02	1.30
Sweden	NFA	1 018	0.29	0.53	0.78	0.63	0.95	1.32
Minimum			**0.16**	**0.39**	**0.59**	**0.31**	**0.71**	**1.00**
Median			**0.25**	**0.44**	**0.68**	**0.62**	**0.88**	**1.26**
Maximum			**0.51**	**0.73**	**0.94**	**1.70**	**1.85**	**2.33**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D12: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in adults in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	1 304	0.19	0.35	0.51	0.52	0.72	1.01
Czech Republic	SISP04	1 666	0.14	0.26	0.38	0.42	0.55	0.72
Germany	National Nutrition Survey II	10 419	0.22	0.40	0.59	0.59	0.86	1.23
Denmark	Danish Dietary Survey	2 822	0.16	0.32	0.49	0.37	0.59	0.84
Spain	AESAN	410	0.30	0.46	0.61	0.79	1.03	1.25
Spain	AESAN FIAB	981	0.33	0.49	0.65	0.87	1.10	1.30
Finland	FINDIET 2007	1 575	0.20	0.36	0.52	0.63	0.81	1.02
France	INCA2	2 276	0.21	0.36	0.51	0.50	0.71	0.96
Great Britain	NDNS	1 724	0.27	0.41	0.55	0.59	0.77	0.97
Hungary	National Representative Survey	1 074	0.15	0.27	0.39	0.36	0.53	0.72
Ireland	NSIFCS	958	0.29	0.44	0.59	0.53	0.72	0.93
Italy	INRAN SCAI 2005/06	2 313	0.40	0.53	0.67	1.52	1.66	1.83
Latvia	EFSA TEST	1 306	0.30	0.41	0.53	0.70	0.86	1.07
the Netherlands	DNFCS 2003	750	0.23	0.42	0.61	0.56	0.78	1.06
Sweden	Riksmaten 1997/98	1 210	0.34	0.52	0.70	0.66	0.88	1.16
Minimum			**0.14**	**0.26**	**0.38**	**0.36**	**0.53**	**0.72**
Median			**0.23**	**0.41**	**0.55**	**0.59**	**0.78**	**1.02**
Maximum			**0.40**	**0.53**	**0.70**	**1.52**	**1.66**	**1.83**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D13: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in elderly in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	518	0.18	0.30	0.43	0.46	0.63	0.84
Germany	National Nutrition Survey II	2 006	0.22	0.37	0.52	0.56	0.75	1.01
Denmark	Danish Dietary Survey	309	0.17	0.32	0.47	0.39	0.58	0.86
Finland	FINDIET 2007	463	0.22	0.35	0.48	0.69	0.84	1.09
France	INCA2	264	0.23	0.37	0.50	0.54	0.72	0.92
Hungary	National Representative Survey	206	0.13	0.23	0.33	0.25	0.40	0.55
Italy	INRAN SCAI 2005/06	290	0.30	0.42	0.55	0.77	0.94	1.12
Minimum			**0.13**	**0.23**	**0.33**	**0.25**	**0.40**	**0.55**
Median			**0.22**	**0.35**	**0.48**	**0.54**	**0.72**	**0.92**
Maximum			**0.30**	**0.42**	**0.55**	**0.77**	**0.94**	**1.12**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.

Table D14: Lower, middle and upper bound mean and 95th percentile inorganic mercury exposure in very elderly in µg/kg body weight per week. The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.

Country	Survey	N	Mean			P95		
			LB	MB	UB	LB	MB	UB
Belgium	National Diet 2004	712	0.17	0.29	0.42	0.47	0.62	0.83
Germany	National Nutrition Survey II	490	0.24	0.38	0.52	0.61	0.78	1.01
Denmark	Danish Dietary Survey	20	0.19	0.34	0.49	-(a)	-(a)	-(a)
France	INCA2	84	0.19	0.31	0.44	0.34	0.54	0.78
Hungary	National Representative Survey	80	0.14	0.25	0.35	0.25	0.40	0.54
Italy	INRAN SCAI 2005/06	228	0.24	0.37	0.49	0.64	0.81	0.98
Minimum			**0.14**	**0.25**	**0.35**	**0.25**	**0.40**	**0.54**
Median			**0.19**	**0.33**	**0.47**	**0.47**	**0.62**	**0.82**
Maximum			**0.24**	**0.38**	**0.52**	**0.64**	**0.81**	**1.01**

N: number of participants; P95: 95th percentile; LB: lower bound; MB: middle bound; UB: upper bound.
(a) Calculation of P95 not possible due to low number of surveys.

Table D15: Contribution (%) of the all food groups, FoodEx Level 1 to chronic dietary exposure to inorganic mercury using middle bound concentrations. Range of the average contribution is shown.

Food category	Lowest average contribution (%) – Highest average contribution (%)					
	Toddlers	Other children	Adolescents	Adults	Elderly	Very elderly
Fish and other seafood	1.6-29	2.9-32	3.0-38	3.7-53	5.6-35	4.5-26
Composite food	0.3-12	0-40	0-35	0-40	0-8.3	0-9.9
Non-alcoholic beverages	0-7.2	0.7-21	2.1-22	1.6-43	3.8-31	5.4-32
Vegetables and vegetable products	3.7-13	1.6-23	1.4-21	1.4-26	5.0-24	4.5-22
Fruit and vegetable juices	8.9-34	1.1-34	0.6-31	0.3-19	1.5-12	2.0-10
Grains and grain-based products	6.8-11	6.2-17	9.3-18	6.9-17	7.3-17	9.8-17
Milk and dairy products	16-29	6.5-22	5.4-16	4.8-14	5.4-13	6.6-12
Meat and meat products	2.3-6.8	2.6-9.4	4.1-11	2.6-13	4.2 - 12	3.7-12
Starchy roots and tubers	1.2-6.0	1.3-4.0	1.2- 4.3	1.1-5.9	1.4-4.9	1.7-5.3
Alcoholic beverages	0 – 0.0	0.0-0.1	0.0-0.7	0.6-5.8	0.5-3.8	0.7-3.7
Fruit and fruit products	2.4-8.2	2.0-8.2	2.3-6.8	2.1-5.5	4.6-7.3	5.1-7.6
Drinking water	0.6-3.8	0.0-3.1	0.0-3.3	0.3-5.0	0.5-2.5	0.3-3.0
Products for special nutritional use	0-0.1	0-1.6	0-6.9	0-3.8	0-1.1	0-5.7
Animal and vegetable fats and oils	0.2-1.7	0.3-2.2	0.2-2.5	0.2-2.6	0.7-2.6	0.8-3.0
Legumes, nuts and oilseeds	0.1-1.5	0.1-2.1	0.2-2.4	0.2-1.4	0.3-1.5	0.3-1.6
Herbs, spices and condiments	0.1-1.6	0.1-1.9	0.1-1.6	0.3-1.4	0.5-1.7	0.5-1.9
Sugar and confectionery	0.4-3.1	0.5-3.6	0.4-2.3	0.2-1.3	0.2-0.8	0.3-0.7
Eggs and egg products	0-0.7	0-0.9	0-0.9	0.1-1.1	0.2-1.1	0.2-1.0
Snacks, desserts, and other foods	0.1-6.0	0.4-6.0	0.4-1.1	0.1-0.9	0.1-0.5	0-0.6
Food for infants and small children	0.6-18	0-0.7	0-0.1	0	0	0

E. OVERVIEW OF REPORTED RATIOS OF BIOMARKERS

Table E1: Reported blood to hair ratios.

	Ratio	Additional information	Reference
THg blood / THg hair	1:250 (1:140 – 1:370)		FAO/WHO (2004)
THg blood / THg hair	median ratio 1:190; 5-95 % 1: 74 – 1:442 median ratio 1:370; 5-95 % 1:137 – 1:932 median ratio 1:264; 5-95 % 1: 67 – 1:632	Faroese children at birth (n = 993) 7 years of age (n = 665) 14 years of age (n = 780)	Budtz-Jorgensen et al. (2004)
THg blood / THg hair	mean ratio about 1:350	Japanese pregnant women (n = 115)	Sakamoto et al. (2007)
THg blood / THg hair	median ratio 1:254 (linear regression) THg blood/THg hair (calculated from mean values) 1:345 IHg blood/THg hair (calculated from mean values) 1:2 174 (OHg blood/THg hair (calculated from mean values) 1:416)* *OHg = THg-IHg	Swedish men (n = 5) and women (n = 23)	Berglund et al. (2005)
THg blood / THg hair	unadjusted medians 1:194 – 1:433 adjusted (for the lag from blood to hair on the scalp) medians 1:315 – 1:370 adjusted mean 1:344 (SD 54)	Healthy Japanese adults (n = 27), 29 weeks, 3.4 µg/kg b.w. per week methylmercury from the consumption of tuna/swordfish	Yaginuma-Sakurai et al. (2012)
THg blood / THg hair	1:250	42 male members of Faroese whaling society	Choi et al. (2009)

b.w.: body weight; THg: total mercury; IHg: inorganic mercury; OHg: organic mercury, SD: standard deviation.

Table E2: Reported ratios for cord blood to maternal biomarkers.

	Ratio	Additional information	Reference
THg cord blood / THg maternal blood	calculated unweighted ratio 1.48	review, 19 study populations	Murata et al. (2007)
THg cord blood / THg maternal blood	number-weighted ratio 1.51	review, meta analysis from 10 selected studies	Stern and Smith (2003)
MeHg cord blood / MeHg maternal blood	calculated unweighted ratio 1.72	Review, 9 study populations	Murata et al. (2007)
MeHg cord blood / MeHg maternal blood	number-weighted ratio 1.89	review, meta analysis from 10 selected studies	Stern and Smith (2003)
cord RBC / maternal RBC THg	1.6	Healthy pregnant Japanese women (n = 40) without any particular exposure to Hg	Sakamoto et al. (2008)
THg cord blood / THg maternal hair	1:190 (1:80 – 1:330)	585 pregnant women	Miklavčič et al. (2011b)
MeHg cord blood / THg hair	1:220 (1:110 – 1:390)	585 pregnant women	Miklavčič et al. (2011b)

THg: total mercury; MeHg: methylmercury.

Table E3: Reported blood to toenail ratios.

	Ratio	Additional information	Reference
THg blood / THg toenail	1:70 (calculated from mean values)	42 male members of Faroese whaling society	Choi et al. (2009)
THg blood / THg toenail	1:56 (calculated from mean values)	30 deceased individuals (not occupationally exposed)	Björkman et al. (2007)
MeHg blood / THg toenail	1:104	30 deceased individuals (not occupationally exposed)	Björkman et al. (2007)
IHg blood / THg toenail	1:122	30 deceased individuals (not occupationally exposed)	Björkman et al. (2007)

THg: total mercury; MeHg: methylmercury.

Table E4: Reported hair to toenail ratios.

	Ratio	Additional information	Reference
THg hair / THg toenail	3	42 male members of Faroese whaling society	Choi et al. (2009)
THg hair / THg toenail	2.56 (in the paper calculated from the mean values)	59 women (not occupationally exposed to Hg)	Ohno et al. (2007)
THg hair / THg toenail	2.38 (calculated from mean values) 1.41 (calculated from mean values)	161 non occupationally exposed individuals 155 dentists	Ritchie et al. (2002)
THg hair / THg toenail	2.39 (calculated from mean values) 1.65 (calculated from mean values)	155 non occupationally exposed individuals 161 dental workers (dentists, dental nurses)	Morton et al. (2004)

THg: total mercury.

F. OVERVIEW OF CONCENTRATIONS IN THE EUROPEAN POPULATION

Table F1: Overview of mercury concentrations in blood and hair samples from mother-child pairs.

Country	Additional information	Blood Hg (µg/L)[k]					Cord blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
FR												81	T:1.37 T:1.19[a]	T:0.94	T:1.2	T:0.54-2.90[d]	1
FR												144	0.67	0.5		0.33-0.81[c]	2
SE	Mothers	112 112			I:0.32 M:0.73	I:0.03-1.2[d] M:0.19-2.1[d]	98 98			I:0.34 M:1.4	I:0.09-0.79[d] M:0.26-3.8[d]						3
AT	Mothers	52			T:0.7	T:0.3-1.2[e]	43			T:1.1	T:0.4-1.9[e]	30			T:0.184	T:0.109-0.417[e]	4
FR	Mothers Children											691 87			0.52 0.38	0.30-0.82[e] 0.30-0.43[e]	5
SI	All mothers Mothers of which the THg in hair ≥ 1 mg/kg Mothers of which the THg in hair < 1 mg/kg						446 13 44	T:2.0[h] M:6.4[h] M:1.7[h]	M:2.3[h] M:1.5[h]	T:1.5[h] M:6.2[h] M:1.3[h]	T:0.5-4.2[c,h] M:3.3-9.9[c,h] M:0.3-4.0[c,h]	574 15	T:0.377 M:1.270	M:0.359	T:0.297 M:1.350	T:0.073-0.781[c] M:0.624-1.63[c]	6
SK	Mothers	99	0.79 0.67[a]		0.63	0.14-2.9[b]	99	0.86 0.74[a]		0.80	0.15-2.54[b]						7
IT	Mothers Children											242 208 203 116	T:1.33 M:0.96 T:1.22 M:0.86	T:1.22 M:0.84 T:1.22 M:0.76	T:0.93 M0.74 T:0.79 M0.56	T:1.56[f] M:1.13[f] T:1.53[f] M:1.11[f]	8
HR	Mothers											137	0.88	1.24		0.02-8.71[b]	9
PL	Mothers	231	0.55[a]		0.600		220	0.88[a]		0.850							10
PL		313	0.833	0.681	0.600		313	1.093	0.675	0.900							11
ES	• Valencia						554	T:13.1 T:9.5[a]		T:9.5	T:5.3-18.0[e] T:26.5[g]						12
	• Sabadell						460	T:8.2 T:6.3[a]		T:6.4	T:4.1-10.0[e] T:16.0[g]						
	• Asturias						340	T:13.9 T:10.8[a]		T:12.0	T:6.6-18.8[e] T:25.9[g]						
	• Gipuzkoa						529	T:9.3 T:7.5[a]		T:8.1	T:5.1-12.0[e] T:17.0[g]						
	• Total						1883	T:11.0 T:8.2[a]		T:8.5	T:5.0-14.0[e] T:22.0[g]						

Table F1: Continued.

Country	Additional information	Blood Hg (µg/L)[k]					Cord blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
SW	Mothers	20					20			M:0.99	M:0.52-3.8[b]						13
	• delivery				M:0.45 I:0.09	M:0.24-1.5[b] I:0.03-0.75[b]											
	• 13 weeks postpartum				M:0.60 I[i]	M:0.20-1.6[b] I[i]											
	Children	20															
	• 4 days				M:1.1 I:0.09	M:0.62-4.4[b] I:0.02-0.34[b]											
	• 13 weeks after birth				M:0.38 I:0.05	M:0.10-1.1[b] I:0-0.13[b]											
ES							1683	T:8.4[a]									14
GR	Mothers						391			T:5.8[h]	T:1.2-20[d,h] T:0.2-33[b,h]	454			T:1.12	T:0.242-3.84[d]	15
IT	Mothers	871			T:2.4[h]	T:0.05-40[b,h]	614			T:3.9[h]	T:0.1-33[b,h]	891			T:0.77	T:0.235-2.57[d]	
HR	Mothers	255			T:2.0[h]	T:0.6-21[b,h]	210			T:2.9[h]	T:0.3-32[b,h]	234			T:0.604	T:0.076-2.48[d]	

n: number of samples; µ: mean; SD: standard deviation; PX: X^{th} percentile; Ref.: reference; M: methylmercury; T: total mercury; I: inorganic mercury; FR: France; SE: Sweden; HR: Croatia; ES: Spain; AT: Austria; SI: Slovenia; SK: Slovakia; PL: Poland; GR: Greece.

1: Huel et al. (2008); 2: Abdelouahab et al. (2010); 3: Ask et al. (2002); 4: Gundacker et al. (2010a); 5: Drouillet-Pinard et al. (2010); 6: Miklavčič et al. (2011b); 7: Palkovicova et al. (2008); 8: Valent et al. (2011); 9: Cace et al. (2011); 10: Jedrychowski et al. (2006); 11: Jedrychowski et al. (2007b); 12: Ramon et al. (2011); 13: Björnberg et al. (2005); 14: Llop et al. (2012); 15: Miklavčič et al. (in press).

(a): geometric mean;
(b): minimum-maximum;
(c): P10-P90;
(d): P5-P95;
(e): P25-P75;
(f): P75;
(g): P90;
(h): µg/kg;
(i): about the same level as at delivery;
(j): maternal blood samples were collected at gestational week 36;
(k): maternal blood unless specified differently in the population.

Table F2: Overview of mercury concentrations in the European population in blood and hair.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Sweden	Fishermen[(o)]	189	M:2.9	M:2.4	M:2.3	M:0.5-6.9[(d)]						1
Finland	Fishermen and family members	299	M:3.6		M:2.7	M:<0.15-22[(b)] M:8.0[(h)]						2
Norway	Pregnant women	119	1.88	1.21	1.67	0.32-4.30[(d)]						3
France	Women of childbearing age (18-44 years old)	133	M:2.68	M:1.99		M:5.58 [(f)]						4
France	Pregnant women at 12 weeks of pregnancy Pregnant women at 32 weeks of pregnancy						161 137	0.82 0.79		0.67 0.65	1.89[(f)] 1.95[(f)]	5
Croatia	Women 25-45 years old						12				T:0.03-3.4[(b)]	6
Greece	Pregnant women and mothers of children of under 5 years						246 238	T:1.36[(a)] M:1.07[(a)]			T:0.046-17.5[(b)] M:0.031-16.2[(b)]	7
Norway	Women • 2nd trimester of pregnancy • 3 days postpartum • 6 weeks postpartum	 211 211 211	 1.5 1.2[(a)] 1.2 1.0[(a)] 1.8 1.5[(a)]	 1.1 0.7 1.0		 0.1-6.6[(b)] 0.2-3.7[(b)] 0.2-6.4[(b)]						8
Italy	Pregnant women • Syracusan industrial area • Augusta						 100 100	 1.45 1.14	 0.96 0.77	 1.15 0.87	 0.09-4.98[(b)] 0.18-4.18[(b)]	9
Czech Republic	Schoolchildren (13-14 years) from Kasperské Hory (a non-polluted control area) Schoolchildren (13-14 years) from Stary Plzenec (located close to the heavily industrialised zone of city Plzen) Schoolchildren (13-14 years) from Benesov (a predominantly agricultural area)									T:0.28 M:0.13 I: 0.17 T:0.38 M:0.17 I:0.22 T:0.46 M:0.12 I:0.36	T:0.14-0.42[(c)] M:0.07-0.19[(c)] I:0.08-0.34[(c)] T:0.25-0.53[(c)] M:0.11-0.23[(c)] I:0.14-0.32[(c)] T:0.25-0.85[(c)] M:0.07-0.21[(c)] I:0.19-0.72[(c)]	10
Spain	Preschool children Menorca Preschool children Ribera d'Ebre Newborns Madrid Newborns Sabadell Total						65 71 57 25 218	T:0.706 M:0.490 T:1.093 M:0.914 T:1.417 T:1.999 T:1.416 M:0.973	T:0.665 M:0.638 T:1.016 M:1.107 T:0.901 T:1.925 T:1.387 M:1.104		T:0.225-3.826[(b)] M:0.110-3.644[(b)] T:0.189-5.627[(b)] M:0.081-6.992[(b)] T:0.126-5.095[(b)] T:0.132-8.426[(b)] T:0.126-8.426[(b)] M:0.081-6.992[(b)]	11
Germany	Children	1240	0.24[(a)]		0.3	1.0[(f)]						12

Table F2: Continued.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Poland	Children 3-4 years of age						38	0.23[a]				13
	Children 7-9 years of age						37	0.14[a]				
Denmark	Children (3-14 years)	1552	0.33 0.23[g]		0.2	<0.2-0.7						14
Croatia	Children (7-14 years)	52	0.44[a]			0.14-1.9[b]						15
Czech Republic		21	0.21[a]			<0.07-0.75[b]						
Poland		30	0.12[a]			<0.07-1.4[b]						
Slovakia		57	0.52[a]			0.12-2.3[b]						
Slovenia		45	0.94[a]			0.36-3.0[b]						
Sweden		41	0.43[a]			0.10-1.4[b]						
Czech Republic	Children											16
	• 1996	380			0.57	1.98[f]	412			0.23	0.54[f]	
	• 1997						372			0.20	0.54[f]	
	• 1998	384			0.39	1.25[f]	359			0.16	0.30[f]	
	• 1999	362			0.38	1.38[f]	360			0.16	0.37[f]	
	• 2000						343			0.26	0.84[f]	
	• 2001	354			0.42	1.48[f]	325			0.20	0.72[f]	
	• 2002						319			0.20	0.50[f]	
	• 2003						292			0.14	0.50[f]	
	• 2006	382			0.45	1.39[f]	372			0.13	0.28[f]	
	• 2008	198			0.35	1.32[f]	316			0.18	0.61[f]	
Spain	Boys (48-57 months)						72	T:0.96[a]		T:1.04		17
							23	M:1.81[a]				
France	Adult males (18-64 years old)	93	M:3.41	M:2.25		M:7.17[f]						4
	Adult females (18-64 years old)	254	M:3.67	M:4.26		M:8.63[f]						
	Elderly (65 years old and over)	38	M:4.85	M:3.15		M:10.7[f]						
Ukraine	Residents of Horlivka (geological and industrial sources of environmental mercury)	29	1.31		1.01	0.17-7.72[b]	31	0.22		0.14	0.00-1.15[b]	18
	Residents of Artemivsk (city outside the mercury-enriched area)	29	0.96		0.92	0.25-1.93[b]	30	0.64		0.42	0.08-5.82[b]	
	Total	58	1.13		0.95	0.17-7.72[b]	61	0.42		0.24	0.00-5.82[b]	
Norway	Deceased adults, elderly and very elderly (47-91 years of age)	30	T:5	T:5.3	T:3.3	T:1.4-12.5[c]						19
		30	I:2.3	I:4.2	I:1.0	I:0.2-5.2[c]						
		30	M:2.7	M:2.3	M:2.2	M:0.9-6.2[c]						
Austria	Men, women and children						104			M:0.017	M:0.340[e]	20

Table F2: Continued.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Italy	General population of Umbria	288	0.78[(m)] 0.79[(a,m)]	0.02[(m,n)]	0.75 [(m)]	0.29-1.43[(m,d)]						21
	General population of Calabria	215	0.65[(m)] 0.57[(a,m)]	0.02[(m,n)]	0.58 [(m)]	0.24-1.37[(m,d)]						
Austria	Adults (18 to 65 years)	152	T:2.38	T:1.55		T:0.34-9.97[(b)]						22
United Kingdom	Staff of the University of Glasgow						161	0.43[(a)]			0.04-3.86[(b)]	23
Czech Republic	Men											16
	• 1996	284			0.79	2.01[(f)]						
	• 1997	291			0.84	3.86[(f)]						
	• 1998	314			0.53	2.22[(f)]						
	• 1999	297			0.78	2.29[(f)]						
	• 2000	300			1.31	3.34[(f)]						
	• 2001	286			0.81	2.84[(f)]						
	• 2002	290			0.80	3.1[(f)]						
	• 2003	290			0.95	2.87[(f)]						
	• 2005	233			0.91	2.66[(f)]						
	• 2007	248			0.85	2.56[(f)]						
	Women											
	• 1996	134			0.83	2.04[(f)]						
	• 1997	103			0.93	3.35[(f)]						
	• 1998	81			0.81	3.50[(f)]						
	• 1999	101			0.94	2.66[(f)]						
	• 2000	98			1.33	4.37[(f)]						
	• 2001	114			0.93	3.60[(f)]						
	• 2002	107			0.92	4.15[(f)]						
	• 2003	105			0.99	3.51[(f)]						
	• 2005	172			1.16	3.46[(f)]						
	• 2007	163			0.89	2.94[(f)]						
Portugal	Adults – <5 km from an incineration facility (Lisbon)											24
	• T0	138	1.0	0.7	0.8	0.2-4.6[(b)]						
	• T1	75	0.5	0.4	0.4	0.1-1.8[(b)]						
	• T2	75	0.3	0.2	0.2	0.1-1.1[(b)]						
	Adults – > 5 km from the incineration facility (Lisbon)											
	• T0	29	1.5	0.6	1.4	0.7-4.2[(b)]						
	• T1	75	0.6	0.5	0.4	0.1-2.1[(b)]						
	• T2	75	0.3	0.3	0.3	0.1-1.2[(b)]						

Table F2: Continued.

Country	Additional information	Blood Hg (µg/L) n	µ	SD	P50	Variation (specified by footnotes)	Hair Hg (mg/kg) n	µ	SD	P50	Variation (specified by footnotes)	Ref.
Portugal (continued)	Adults –total (Lisbon)											
	• T0	167	1.1	0.7	0.9	0.2-4.6[b]						
	• T1	150	0.5	0.4	0.4	0.1-2.1[b]						
	• T2	150	0.3	0.3	0.3	0.1-1.2[b]						
	Adults – <5 km from the incineration facility (Madeira)											
	• T0	55	0.9	1.0	0.5	0.1-4.4[b]						
	• T1	55	0.2	0.2	0.1	0.1-0.8[b]						
	Adults – >5 km from the incineration facility (Madeira)											
	• T0	55	0.7	0.5	0.7	0.1-1.8[b]						
	• T1	55	0.3	0.3	0.3	0.1-1.3[b]						
	Adults –total (Madeira)											
	• T0	110	0.8	0.8	0.5	0.1-4.4[b]						
	• T1	110	0.3	0.2	0.2	0.1-1.3[b]						
United Kingdom	Staff of the University of Glasgow						161	0.57	0.48	0.47	0.04-3.86[b]	25
Poland	Men[p] drinking water from steel pipelines						22	0.224	0.192			26
	Men[p] drinking water from copper pipelines						7	0.167	0.114			
	Men[p] drinking water from plastic pipelines						12	0.230	0.203			
	Women[p] drinking water from steel pipelines						35	0.176	0.122			
	Women[p] drinking water from copper pipelines						18	0.195	0.159			
	Women[p] drinking water from plastic pipelines						23	0.252	0.168			
	Total population										0.03-0.8[b]	
Germany	Office workers in a harbour (administrative work)	84			2.2	0.3-9.4[b]						27
Italy	Habitual consumers of fresh tuna	10			T:44.0 O:41.5	T:15-93[b] O:13-85[b]	8			9.6	1.4-34.5[b]	28
	Controls	6			T:3.9 O:2.6	T:1.2-5.4[b] O:0.8-4.0[b]						
Germany	Patients with health complaints and amalgam fillings	27			T:1.28[k] I:0.37[k] O:0.91[k] T:0.49[j] I:0.38[j] O:0.11[j]	T:0.82-2.18[g,k] I:0.17-0.50[g,k] O:0.53-1.43[g,k] T:0.30-0.81[g,j] I:0.19-0.59[g,j] O:0.08-0.16[g,j]						29

Table F2: Continued.

Country	Additional information	Blood Hg (µg/L)					Hair Hg (mg/kg)					Ref.
		n	µ	SD	P50	Variation (specified by footnotes)	n	µ	SD	P50	Variation (specified by footnotes)	
Germany (continued)	Healthy amalgam bearers	27			T:1.19 [k] I:0.35 [k] O:0.81 [k] T:0.51 [j] I:0.36 [j] O:0.12 [j]	T:0.69-2.07 [g,k] I:0.19-0.49 [g,k] O:0.28-1.43 [g,k] T:0.36-0.78 [g,j] I:0.26-0.47 [g,j] O:0.05-0.20 [g,j]						
	Healthy amalgam-free patients	27			T:0.96 [k] I:0.08 [k] O:0.88 [k] T:0.16 [j] I:0.08 [j] O:0.10 [j]	T:0.58-1.87 [g,k] I:0.06-0.13 [g,k] O:0.53-1.71 [g,k] T:0.10-0.31 [g,j] I:0.04-0.11 [g,j] O:0.06-0.21 [g,j]						
Greenland Denmark	Adults				16.2 2.2							30
Germany	Adults (20-29 years)											31
	2010	457	0.9 0.8 [a]	0.7	0.8	0.2-2.1 [d]						
	2001-1010	4353	1.24 0.96 [a]	0.94	1.01	0.25-2.98 [d]						
United Kingdom	Adults (16-64 years)	1216	1.13 [a]			0.26-4.45 [b]						32
Sweden	Adults (28-60 years)	28	T:2.2 I:0.35 O:1.8 T:0.65 [j] I:0.39 [j] O:0.26 [j] T:4.1 [k] I:0.29 [k] O:3.8 [k]	T:1.4 I:0.23 O:1.3 T:0.30 [j] I:0.26 [j] O:0.16 [j] T:2.6 [k] I:0.18 [k] O:2.5 [k]	T:2.0 I:0.35 O:1.6 T:0.63 [j] I:0.37 [j] O:0.22 [j] T:4.0 [k] I:0.26 [k] O:3.6 [k]	T:0.34-7.3 [b] I:0-0.94 [b] O:0.26-6. 9 [b] T:0.07-1.3 [b,j] I:0-1.1 [b,j] O:0.05-0.70 [b,j] T:0.40-14 [b,k] I:0-0.70 [b,k] O:0.25-13 [b,k]	28	T:0.76 I:0.062 O:0.69	T:0.40 I:0.030 O:0.37	T:0.71 I:0.060 O:0.66	T:0.08-2.0 [b] I:0.010-0.12 [b] O:0.072-1.9 [b]	33

n: number of samples; µ: mean; SD: standard deviation; PX: X^{th} percentile; Ref.: reference; M: methylmercury; T: total mercury; I: inorganic mercury; O: organic mercury; T0: baseline; T1: observation 1; T2: observation 2.

1: Rignell-Hydbom et al. (2007); 2: Airaksinen et al. (2010); 3: Brantsæter et al. (2010); 4: Sirot et al. (2008); 5: Pouzaud et al. (2010); 6: Holcer and Vitale (2009); 7: Gibičar et al. (2006); 8:Hansen et al. (2011); 9: Madeddu and Sciacca (2008); 10: Čejchanova et al. (2008); 11: Diéz et al. (2009); 12: Schulz et al. (2007); 13: Majewska et al. (2010); 14: Becker et al. (2008); 15: Hrubá et al. (2012); 16: Puklová et al. (2010); 17: Freire et al. (2010); 18: Gibb et al. (2011); 19: Björkman et al. (2007); 20: Hohenblum et al. (2012); 21: Bocca et al. (2010); 22: Gundacker et al. (2006); 23: Morton et al. (2004); 24: Reis et al. (2007); 25: Ritchie et al. (2004); 26: Chojnacka et al. (2011); 27: Wegner et al. (2004); 28: Carta et al. (2003); 29: Melchart et al. (2008); 30: Pedersen et al. (2005); 31: Karch et al. (2011); 32: Bates et al. (2007); 33: Berglund et al. (2005).

(a): geometric mean;

(b): minimum-maximum;

(c): P10-P90;
(d): P5-P95;
(e): maximum;
(f): P95;
(g): P25-P75;
(h): P90;
(i): P33-P67;
(j): concentration in plasma (µg/L);
(k): concentration in erythrocytes (µg/L);
(l): concentration in erythrocytes (ng/g);
(m): concentration in serum (µg/L);
(n): standard error;
(o): concentrations calculated as the difference between total Hg and inorganic Hg;
(p): students.

Table F3: Overview of mercury concentrations in the European population in nails.

Country	Additional information	Fingernails Hg (mg/kg)					Toenails Hg (mg/kg)					Reference
		n	μ	SD	P50	Variation (specified by footnotes)	n	μ	SD	P50	Variation (specified by footnotes)	
Ukraine	Residents of Horlivka (geological and industrial sources of environmental mercury)	31	0.41		0.31	0.01-2.63[(b)]	31	0.35		0.31	0.00-1.14[(b)]	Gibb et al. (2011)
Ukraine	Residents of Artemivsk (city outside the mercury-enriched area)	28	0.18		0.09	0.00-1.18[(b)]	26	0.12		0.11	0.00-0.58[(b)]	
Ukraine	Total	59	0.3		0.2	0.00-2.63[(b)]	57	0.25		0.18	0.00-1.14[(b)]	
Norway	Deceased adults, elderly and very elderly (47-91 years of age)						29	0.28	0.214	0.236	0.067-0.624[(c)]	Björkman et al. (2007)
United Kingdom	Staff of the University of Glasgow	155	0.24[(a)]			0.02-2.49[(b)]	155	0.18[(a)]			0.02-1.22[(b)]	Morton et al. (2004)
United Kingdom	Staff of the University of Glasgow	155	0.32	0.30	0.23	0.02-2.49[(b)]	155	0.24	0.19	0.18	0.02-1.22[(b)]	Ritchie et al. (2004)
France	Healthy volunteers	130			0.29	0.06-0.83[(d)]						Goullé et al. (2009)
		50			0.20	0.09-0.56[(d)]	50			0.16	0.07-0.38[(d)]	

n: number of samples; μ: mean; SD: standard deviation; PX: X^{th} percentile.
(a): geometric mean;
(b): minimum-maximum;
(c): P10-P90;
(d): P5-P95.

Table F4: Overview of mercury concentrations in the European population in urine.

Country	Population	Urine Hg (µg/L)					Reference
		n	µ	SD	P50	Variation (specified by footnotes)	
Poland	Healthy children	20	2.1	1.0	2.0	0.25-4.8[(b)]	Kałuzna-Czaplińska et al. (2011)
Spain	Male adults	35	0.96[(a,g)]				Castaño et al. (2012)
	Female adults	130	1.31[(a,g)]				
	Total	165	1.23[(a,g)]		1.19[(g)]	0.45-3.30[(g,d)] 0.56-2.72[(g,c)]	
Czech Republic	Children						Puklová et al. (2010)
	• 1996	435			0.25[(g)]	2.54[(g,f)]	
	• 1997	397			0.38[(g)]	2.56[(g,f)]	
	• 1998	399			0.27[(g)]	4.22[(g,f)]	
	• 1999	393			0.28[(g)]	2.40[(g,f)]	
	• 2000	384			0.35[(g)]	3.15[(g,f)]	
	• 2002	349			0.43[(g)]	3.94[(g,f)]	
	• 2003	270			0.28[(g)]	4.46[(g,f)]	
	• 2006	364			0.26[(g)]	2.19[(g,f)]	
	• 2008	312			0.16[(g)]	1.01[(g,f)]	
Germany	Children	1354	0.10[(a)]		<0.1	0.52[(f)]	Schulz et al. (2007)
Germany	Children (age 9-11 years)	510			<0.2	1.2[(f)]	Wilhelm et al. (2006)
Germany	Children (3-14 years)	1734	0.19 <0.1[(a)]		<0.1	<0.1-0.3	Becker et al. (2008)
Germany	Children (9-11 years)						Link et al. (2012)
	• 1996/1997	1324	0.78	1.98	0.25	<0.2-3.1[(d)]	
	• 1998/1999	1255	0.59	1.43	0.20	<0.2-2.3[(d)]	
	• 2000/2001	1276	0.57	4.01	<0.2	<0.2-1.6[(d)]	
	• 2002/2003	510	0.31	0.62	<0.2	<0.2-1.2[(d)]	
	• 2004/2005	448	0.24	0.47	<0.2	<0.2-0.8[(d)]	
	• 2008/2009	1294	0.13	0.24	<0.2	<0.2-<0.2[(d)]	
Ukraine	Residents of Horlivka (geological and industrial sources of environmental Hg)	31	0.18[(g)]		0.15[(g)]	0-0.51[(g,b)]	Gibb et al. (2011)
	Residents of Artemivsk (city outside the mercury-enriched area)	30	0.37[(g)]		0.26[(g)]	0.09-1.28[(g,b)]	
	Total	61	0.27[(g)]		0.21[(g)]	0-1.28[(g,b)]	
United Kingdom[(a)]	Adults	78	1.12[(g)]		0.55[(g)]	<LOD-13.47[(g,b)]	Levy et al. (2007)
United Kingdom	Staff of the University of Glasgow	163	0.67[(a,g)]			0.05-7.45[(b,g)]	Morton et al. (2004)
Czech Republic	Men						Puklová et al. (2010)
	• 1996	247			0.61[(g)]	2.79[(g,f)]	
	• 1998	294			0.51[(g)]	2.70[(g,f)]	
	• 2000	275			0.63[(g)]	5.23[(g,f)]	
	• 2002	251			0.44[(g)]	5.39[(g,f)]	
	• 2003	246			0.63[(g)]	4.93[(g,f)]	

Table F4: Continued.

Country	Population	Urine Hg (µg/L) n	µ	SD	P50	Variation (specified by footnotes)	Reference
Czech Republic (continued)	• 2005	165			0.84[g]	5.13[g,f]	Puklová et al. (2010)
	• 2007	170			0.90[g]	4.72[g,f]	
	Women						
	• 1996	114			1.29[g]	4.66[g,f]	
	• 1998	73			0.99[g]	13.27[g,f]	
	• 2000	84			0.90[g]	7.07[g,f]	
	• 2002	84			1.05[g]	11.81[g,f]	
	• 2003	76			1.09[g]	10.52[g,f]	
	• 2005	113			2.18[g]	10.37[g,f]	
	• 2007	109			1.57[g]	8.55[g,f]	
United Kingdom	Staff of the University of Glasgow	163	1.19[g]	1.21[g]	0.89[g]	<0.02-7.45[b,g]	Ritchie et al. (2004)
Germany	Office workers in a harbour (administrative work)	84			0.7[g]	0.1-4.2[b,g]	Wegner et al. (2004)
Italy	Habitual consumers of fresh tuna	22			6.5[g]	1.8-21.5[b,g]	Carta et al. (2003)
	Controls	22			1.5[g]	0.5-5.3[b,g]	
Italy	General population[n]	203	1.2[g]			<LOD-16.2[b,g]	Jarosińska et al. (2008)
Poland		160	0.22[g]			<LOD-19.3[b,g]	
Sweden		215	0.21[g]			<LOD-9.6[b,g]	
Germany	Residents living on a highly contaminated grounds	28	0.08[a]		<0.05	<0.05-0.4[b]	Ewers et al. (2004)
	Controls	22	0.2[a]		0.2	<0.05-1.4[b]	
Germany	Patients with health complaints and amalgam fillings	27			0.40	0.25-0.85[d]	Melchart et al. (2008)
	Healthy amalgam bearers	27			0.73	0.20-0.94 [d]	
	Healthy amalgam-free patients	27			0.16	0.11-0.25 [d]	
Germany	Adults (20-29 years)						Karch et al. (2011)
	2010	461	0.2 0.1[a]	0.42	0.1	0.1-1.0[d]	
	1997-2010	5810	0.4 0.2[a]	0.65	0.18	0.03-1.49[d]	
Sweden	Adults (28-60 years)	28	T:1.9[g] I:1.9[g] O:0.013[g]	T:2.0[g] I:2.1[g] O:0.12[g]	T:1.3[g] I:1.2[g] O:0.018[g]	T:0.12-10[b,g] I:0.12-11[b,g] O:0-0.23[b,g]	Berglund et al. (2005)

n: number of samples; µ: mean; SD: standard deviation; PX: X^{th} percentile.
(a): geometric mean
(b): minimum-maximum
(c): P10-P90
(d): P5-P95
(e): maximum
(f): P95

GLOSSARY AND ABBREVIATIONS

GLOSSARY OF FISH SPECIES

English name	Latin name
Anchovy	*Engraulis* Cuvier spp.
Barbel	*Barbus* Cuvier spp.
Barracuda	*Sphyraenidae*
Bass	*Morone* Mitchill spp.
Bonito	*Sarda sarda* Bloch
Bream	*Diplodus* Rafinesque spp. (old name *Charax* Scopoli spp.)
Capelin	*Mallotus villosus* Müller
Carp	*Cyprinus* L. spp.
Char	*Salvelinus* L. spp.
Cod and whiting	*Gadus* L. spp.
Dentex	*Dentex* Cuvier spp.
Dories, John Dory	*Zeiformes* (order), *Zeomorphi*
Eels	*Anguillidae*
Flounder	*Platichthys flesus* L.
Garfish	*Belone belone* L. and *Belone acus* Risso
Grey mullet	*Mugil* L. spp.
Grenadiers	*Coryphaenoides* spp.
Grouper	*Acanthistius* Gill. spp., *Ephinephelus* Bloch spp., *Mycteroperca* Gill spp., *Myctoperca* Gill spp. and *Serranus* Cuvier spp.
Gurnard	*Triglidae*
Hake	*Merluccius* Rafinesque spp.
Halibut	*Hippoglossus* Cuvier spp.
Herring	*Clupea* L. spp.
Lizardfish	*Saurida* Valenciennes spp. and *Synodus* L. spp.
Lophiiformes (syn. Anglerfish)	*Lophiiformes* Garman (order)
Luvarus	*Luvarus imperialis* Rafinesque
Mackerel	*Scomber* spp.
Mackerel and Jack Mackerel (except Scomber)	*Carangidae*
Meagre	*Sciaena* L. spp.
Perch	*Perca* spp.
Pike	*Esox* L. spp
Plaice	*Pleuronectes* L. spp.
Rays	*Rajiformes* (syn. *Hypotremata)* (order)
Redfish	*Centroberyx* Gill spp. and *Centroberyx affinis* Günther
Roach	*Rutilus* Rafinesque spp.
Salmon and trout	*Salmo* L. spp.
Sardine and pilchard	*Sardina* Antipa spp.
Scorpion fish	*Scorpaenidae*
Sea bass	*Morone labrax* L.; *Dicentrarchus labrax* L. and *Morone saxatilus* Walbaum
Sea catfish and wolf-fish	*Anarhichas* L. spp.
Selachoidei or sharks	*Pleurotremata* (syn. *Euselachii) (superorder)*
Shad	*Alosa* Linck spp., *Hilsa* Regan spp. and *Ethmalosa fimbriata* Bowdich
Smelt	*Osmerus* L. spp.
Sole	*Limanda* Gottsc spp., *Solea* Quensel spp.

English name	Latin name
Sprat	*Sprattus sprattus* L.
Sturgeons	*Acipenseriformes* Berg (order)
Swordfish	*Xiphiidae*
Tuna	*Thunnus* South spp.
Turbot	*Scophthalmidae*
Weever	*Trachinidae*
Whitefish	*Coregonus* spp.
Wrasse	*Labridae* Cuvier

ABBREVIATIONS

μ	Mean
AA	Arachidonic acid
AAS	Atomic absorption spectrometry
ADHD	Attention Deficit Hyperactivity Disorder
AFS	Atomic fluorescence spectrometry
ALA	alpha-linolenic acid
ALA-D	δ-aminolevulinate dehydratase
AMI	Acute myocardial infarction
ANA	Antinuclear antibodies
AT	Austria
ATSDR	Agency for Toxic Substances and Disease Registry
BAEPs	Brainstem auditory evoked potentials
BMD	Benchmark dose
BMDL	The 95 % benchmark dose lower confidence limit
BMI	Body mass index
BMR	Benchmark response
BP	Blood pressure
BSID-II	Bayley's scale of infant development-II
b.w.	Body weight
CE	Coronary event
CEN	European Committee for Standardization
CHD	Coronary heart disease
CI	Confidence interval
CONTAM Panel	EFSA Scientific Panel on Contaminants in the Food Chain
CPT	Continuous Performance Test
CPT-HRT	Continuous Performance Test-Hit Reaction Time latencies
CRM	Certified reference material
CSF	Cerebrospinal fluid
CV	Cold vapour
CV-AAS	Cold vapour atomic absorption spectrometry
CV-AFS	Cold vapour atomic fluorescence spectrometry
CVD	Cardiovascular disease
CY	Cyprus
CZ	Czech Republic
DBP	Diastolic blood pressure
DCM Unit	EFSA Dietary and Chemical Monitoring Unit (former DATEX)
DDST	Denver Development Screening Test
DE	Germany
DHA	Docosahexaenoic acid
DK	Denmark
DPA	Docosapentaenoic acid
d.w.	Dry weight
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic acid
ERP	Event-related potential
ES	Spain
ET-AAS	Electrothermal atomic absorption spectrometry
EU	European Union
FAPAS	Food Analysis Performance Assessment Scheme
Fe	Iron
FI	Finland
FR	France

FTII	Fagan infantest
GC	Gas chromatography
GC-ICP-MS	Gas chromatography inductively coupled plasma mass spectrometry
GC-MS	Gas chromatography coupled with mass spectrometry
GC-pyro-AFS	Gas chromatography - pyrolysis atomic fluorescence
GM	Geometric mean
GR	Greece
GST	Glutathione S-transferase
HDL	High-density lipoprotein
HF	High frequency
Hg	Mercury
Hg^0	Elemental or metallic mercury
Hg_2^{2+}	Mercurous cation
Hg^{2+}	Mercuric cation
$HgCl_2$	Mercuric chloride
HgO	Mercuric oxide
HgS	mercuric sulphide
HOME	Home Observation for Measurement of the Environment
HPLC	High-performance liquid chromatography
HR	Hazard ratio
HRT	Hit Reaction Time latencies
HRV	Heart-rate variability
IAEA	International Atomic Energy Agency
ICP-AES	Inductively coupled plasma atomic emission spectroscopy
ICP-MS	Inductively coupled plasma mass spectrometry
I/IHg	Inorganic mercury
Ig	Immunoglobulin
IGGE	Institute of Geophysical Exploration
IQ	Intelligence quotient
IQR	Interquartile range
IRMM	Institute for Reference Materials and Measurements
IT	Italy
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LA	Linoleic acid
LB	Lower bound
LC	Left-censored
LCD	Liquid crystal displays
LCPUFA	Long-chain polyunsaturated fatty acids
LDL	Low-density lipoprotein
LF	Low frequency
LOAEL	Lowest-observed-adverse-effect level
LOD	Limit of detection
LOQ	Limit of quantification
LU	Luxembourg
LV	Latvia
M/MeHg	Methylmercury
MB	Middle bound
MCDI	MacArthur Communicative Development Inventory
MDI	Mental Developmental Index
MeHgCys	Methylmercury L-cysteine complex
MI	Myocardial infarction
ML	Maximum level
MRL	Maximum residue level
MS	Mass spectrometry
MT	Malta

N	Number of samples/results/participants/surveys
n/a	Not available/not applicable
n.r.	not reported
n-3 LCPUFA	n-3 long-chain polyunsaturated fatty acids
n-6 LCPUFA	n-6 long-chain polyunsaturated fatty acids
$NaBEt_4$	Sodium tetraethylborate
$NaBPr_4$	Sodium tetrapropylborate
NAS	National Academy of Sciences
NADPH	Nicotinamide adenine dinucleotide phosphate
NBAS	Neonatal behaviour assessment scale
NBNA	Neonatal behavioural neurological assessment
ND	Not detected
NHANES	National Health and Nutrition Examinations Survey
NIST	National Institute of Standards and Technology (USA)
NL	the Netherlands
NO	Norway
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect-level
NRC	National Research Council
NRCC	National Research Council of Canada
NRL	National Reference Laboratory
O/OHg	Organic mercury
OR	Odds ratio
Pb	Lead
PCB	Polychlorinated biphenyls
PDI	Psychomotor Developmental Index
PND	postnatal day
PT	Portugal
PTFE	Polytetrafluoroethylene
PTWI	Provisional tolerable weekly intake
PX	X^{th} percentile
RfD	Reference dose
RO	Romania
RONS	Reactive oxygen and nitrogen species
RR	Relative risk
r_s	Spearman correlation coefficient
SACMEQ	Southern and Eastern Africa Consortium for Monitoring Educational Quality
SBP	Systolic blood pressure
s.c.	subcutaneous
SCDNS	Seychelles Child Development Nutrition Study
SCDS	Seychelles Child Development Study
SD	Standard deviation
SDANN	Standard deviation of the average R-R intervals calculated over 5-minute periods
Se	Selenium
SE	Sweden/Standard error
SES	Socio-economic status
SI	Slovenia
SK	Slovakia
SRM	Standard reference material
TDS	Total diet study
T/THg	Total mercury
TSH	Thyroid stimulating hormone
TWI	Tolerable weekly intake
UB	Upper bound

UBA	Umweltbundesamt
UK	United Kingdom
US-EPA	United States Environmental Protection Agency
USA	United States of America
VLF	Very low frequency
VRM	Visual recognition memory
w.w.	Wet weight

EUROPEAN COMMISSION

Health & Consumer Protection
Directorate-General

Scientific Committee on Emerging and Newly Identified Health Risks

SCENIHR

The safety of dental amalgam and alternative dental restoration materials for patients and users

Scientific Committees
on consumer products
on emerging and newly identified health risks
on health and environmental risks

The SCENIHR adopted this opinion via written procedure on 6 May 2008, after public consultation.

About the Scientific Committees

Three independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.

They are: the Scientific Committee on Consumer Products (SCCP), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and are made up of external experts.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Evaluation Agency (EMEA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCENIHR

Questions concerning emerging or newly-identified risks and on broad, complex or multi-disciplinary issues requiring a comprehensive assessment of risks to consumer safety or public health and related issues not covered by other Community risk- assessment bodies.

In particular, the Committee addresses questions related to potential risks associated with interaction of risk factors, synergic effects, cumulative effects, antimicrobial resistance, new technologies such as nanotechnologies, medical devices, tissue engineering, blood products, fertility reduction, cancer of endocrine organs, physical hazards such as noise and electromagnetic fields and methodologies for assessing new risks.

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ABSTRACT

In order to reconcile oral health and the aim of the Community Strategy concerning mercury, it has become necessary to review the safety and performance of both dental amalgam and their alternatives, such as composite resins, glass ionomer cements, ceramics and gold alloys. This Opinion concerns the scientific evidence about any links that may exist between either amalgam or these alternatives and allergies, neurological disorders or other health disorders.

SCENIHR recognises that dental amalgam is an effective restorative material and may be considered the material of choice for some restorations, but because it is neither tooth-coloured nor adhesive to remaining tooth tissues, its use has been decreasing in recent years and the alternative tooth-coloured filling materials have become increasingly more popular. Independent of risk management decisions, a sustained reduction in the use of dental amalgam in oral health care provision is expected across the European Union, the rate of which is dependant on trends in dental education towards the increasing use of alternative materials in place of amalgam and the possible reduced availability of mercury products in general.

Mercury is the major metallic element used in dental amalgam. In general it does constitute a toxicological hazard, with reasonably well defined characteristics for the major forms of exposure. Some local adverse effects are seen with amalgam fillings but the incidence is low and normally readily managed. There have been claims of causation with respect to a variety of systemic conditions, particularly neurological and psychological/psychiatric effects. It is concluded however, that there is no scientific evidence for risks of adverse systemic effects exist and the current use of dental amalgam does not pose a risk of systemic disease. The main exposure to mercury in individuals with amalgam restorations occurs during placement or removal of the fillings. The removal of amalgam restorations will transiently increase the exposure of individual patients to relatively high levels of mercury and there is no clinical justification for removing clinically satisfactory amalgam restorations, except in patients suspected of having allergic reactions to amalgam constituents. The mercury release during placement and removal also results in exposure to the dental personnel. However, this may be minimized by the use of appropriate clinical techniques. No studies have shown that dental personnel suffer classical signs of mercury intoxication.

The alternative materials are not without clinical limitations and toxicological hazards. They frequently contain a variety of organic substances and undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement, and some of the monomers used are cytotoxic to pulp and gingival cells in vitro. There is evidence that some of these are also mutagenic in vitro although it is far from clear whether this has any clinical significance. Allergies to some of these substances have been reported, both in patients and in dental personnel. There are very limited scientific data available concerning exposure to these substances and, although the pervasiveness of some of the low molecular weight species throughout dental clinics is apparent, their use has revealed little evidence of clinically significant adverse events.

We conclude that dental health can be adequately ensured by both types of material. All the materials are considered safe to use and they are all associated with very low rates of local adverse effects with no evidence of systemic disease. There is, obviously, a greater level of aesthetic appeal with those alternatives that are tooth coloured compared to the metallic amalgam. Furthermore, these alternatives allow the use of minimally interventional adhesive techniques. These clinical trends themselves ensure that there will continue to be a sustained reduction in the use of dental amalgams in clinical practice across the European Union.

Keywords : Dental amalgam, mercury, toxicology, exposure, composite resins, glass ionomer cements, allergy, systemic health effects, SCENIHR.

Opinion to be cited as: SCENIHR (Scientific Committee on Emerging and Newly-Identified Health Risks), Scientific opinion on the Safety of Dental Amalgam and Alternative Dental Restoration Materials for Patients and Users, 6 May 2008.

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EXECUTIVE SUMMARY

This Opinion concerns one of the oldest controversies in medicine, that is whether there is a causal relationship between mercury-containing amalgams for the restoration of teeth and the aetiology of a variety of diseases in individuals with amalgam restorations.

In order to reconcile oral health and the aim of the Community Strategy concerning mercury, it has become necessary to review the safety and performance of both dental amalgam and their alternatives, such as composite resins, glass ionomer cements, ceramics and gold alloys. SCENIHR has therefore been asked to provide an Opinion on whether there is scientific evidence that supports a link between either amalgam or these alternative materials and allergies, neurological disorders or other health disorders.

In coming to their Opinion, SCENIHR recognises that dental amalgam is an effective restorative material and, from the perspectives of longevity, the mechanical performance and health economics, may be considered the material of choice for some restorations in posterior teeth, including replacement therapy for existing amalgam fillings. However, because dental amalgam is neither tooth-coloured nor adhesive to remaining tooth tissues, its use has been decreasing in recent years and the alternative tooth-coloured filling materials have become increasingly more popular. This is consistent with the trend towards minimal interventional, adhesive, techniques in dentistry. This trend towards non-amalgam restorations is emphasized by the significant reduction of training in the placement of dental amalgam restorations, and the corresponding increase in training in the use of amalgam alternatives in many dental schools in European countries.

Independent of risk management decisions and of the economic considerations in restorative dentistry, a sustained reduction in the use of dental amalgam in oral health care provision is expected across the European Union, the rate of which is dependant on trends in dental education towards the increasing use of alternative materials in place of amalgam and the possible reduced availability of mercury products in general.

Mercury is the major metallic element used in dental amalgam. It is recognized that mercury in general does constitute a toxicological hazard, with reasonably well defined characteristics for the major forms of exposure, involving elemental mercury, organic and inorganic mercury compounds. It is accepted that the reduction in use of mercury in human activity would be beneficial both for the decrease in indirect human exposure and environmental considerations.

It is recognized that some local adverse effects are occasionally seen with dental amalgam fillings, including allergic reactions and an association with clinical features characteristic of lichen planus, but the incidence is low and normally readily managed. There have been claims of causation with respect to a variety of systemic conditions, particularly neurological and psychological/psychiatric effects, including Alzheimer's, Parkinson's Disease, Multiple Sclerosis and also kidney disease. However, several major epidemiological studies have failed to reveal such effects. These studies have included assessments in children and in pregnant and lactating women. The most recent studies have failed to find any association between the use of amalgam and neuropsychological development in children. It is generally concluded that no increased risks of adverse systemic effects exist and we do not therefore consider that the current use of dental amalgam poses a risk of systemic disease.

The main exposure to mercury in individuals with amalgam restorations occurs during placement or removal of the fillings. The transient mercury release during placement and removal will result in exposure to the patients and also to the dental personnel. It should be noted that the removal of amalgam restorations will increase the exposure of the individual patient to relatively high levels of mercury compared to leaving the amalgam filling intact and there is no clinical justification for removing clinically satisfactory amalgam restorations, except in those patients suspected of having allergic reactions to one of the amalgam constituents.

We note that the alternative materials, which may be very complex chemically, are not without certain clinical limitations and toxicological hazards. They contain a variety of organic substances and undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement. Therefore, it should not be assumed that non-mercury containing alternatives are free from any concerns about adverse effects. With respect to dental composite restorative materials and hybrid systems that incorporate polymerisable resins, it is known that some of the monomers used are highly cytotoxic to pulp and gingival cells in vitro. There is also evidence that some of these are mutagenic in vitro although it is far from clear whether this has any clinical significance. Allergies to some of these substances have been reported, both in patients and in dental personnel.

It is noted that there are very limited scientific data available concerning exposure of patients and dental personnel to these substances that are used in alternative restorative materials. It is recognised that such data are very difficult to obtain.

These alternative materials have now been in clinical use for well over thirty years, initially in anterior teeth and more recently also for restorations in posterior teeth. This clinical use has revealed little evidence of clinically significant adverse events. It is also important to note that the commercially available materials have either changed substantially or been improved considerably over this time, with reduced bioavailability of harmful components through improved polymerisation processes.

We note that the full chemical specification of these alternative restorative materials is not always divulged and it may be difficult to ascertain exactly what they contain. As a result, there is limited toxicological data publicly available for these materials. All dental restorative materials are defined as medical devices according to EU-Directive 93/42/EEC, within which a derogation clause states that when such medical devices are used in teeth they will be in class 2a. When regulatory approval is sought it is not necessary to include a design dossier and therefore the chemical specification does not have to be revealed. In view of the lack of information on the toxicity of the constituents of the materials and relevant exposure data it may not be possible to provide a scientifically sound statement on the generic safety of these materials.

As a general principle, the relative risks and benefits of using dental amalgam or the various alternatives should be explained to patients to assist them to make informed decisions. In view of the controversial nature of this subject, it would also be beneficial for the community in general to be better informed of the recognized benefits and risks.

In the light of the above comments we conclude that dental amalgam is a safe material to use in restorative dentistry with respect to patients. With respect to populations at risk, there is a lack of information about effects in pregnant women. There is no evidence to suggest that pre-existing amalgam restorations pose any risk as far as the health of such women and the developing foetus is concerned, and certainly any removal of restorations during this time would present a greater exposure to mercury. As with any other medical or pharmaceutical intervention, however, caution should be exercised when considering the placement of any dental restorative material in pregnant women. There is no evidence that infants or children are at risk of adverse effects arising from the use of dental amalgam. As far as dental personnel are concerned, it is recognised that they may be at greater risk with respect to mercury exposure than the general population, although the incidence of reported adverse effects is very low.

Far less information is available concerning exposure, toxicity and clinical outcomes for alternative materials. There is some evidence that certain of the low molecular weight substances used in their preparation are associated with local allergic reactions, although the incidence is very low. There is no evidence that there is any association between these materials, as used clinically, and any neurological disorders or any other health disorders. We do emphasise, however, that data is sparse and the continuing evolution of these materials suggests that caution should be exercised before new variations are introduced into the market. As far as dental personnel are concerned, again there is

evidence of limited numbers of cases of allergies to these materials. The pervasiveness of some of the low molecular weight species throughout dental clinics should be noted.

We conclude that dental health can be adequately ensured by both types of material. All the materials are considered safe to use and they are all associated with very low rates of local adverse effects with no evidence of systemic disease. There is, obviously, a greater level of aesthetic appeal with those alternatives that are tooth coloured compared to the metallic amalgam. Furthermore, the use of these alternatives allows the use of minimally interventional adhesive techniques. On a historical basis, amalgam restorations have in general been found to last longer, as restorations using alternatives have had a higher incidence of secondary caries. There are indications, however, that the longevity of restorations of alternative materials in posterior teeth has improved with the continuing development of these materials and the practitioner's familiarity of effective replacement techniques. The alternative materials were originally introduced for the restoration of anterior teeth but their use has now extended towards lesions of all sizes in posterior teeth. Dental amalgam may for the foreseeable future continue to find application in the restoration of large lesions and in the replacement of failed amalgam restorations, but the clinical trends themselves towards the use of adhesive alternatives imply that there will continue to be a sustained reduction in the use of dental amalgams in clinical practice across the European Union.

1. BACKGROUND

Dental amalgam has been used for over 150 years for the treatment of dental cavities and is still used, in particular in large cavities due to its excellent mechanical properties and durability. Dental amalgam is a combination of alloy particles and mercury that contains about 50% of mercury in the elemental form.

Overall, the use of alternative materials such as composite resins, glass ionomer cements, ceramics and gold alloys, is increasing, either due to their aesthetic properties or alleged health concerns related to the use of dental amalgam.

Whereas the toxicity of mercury has been extensively researched, relatively little is known about the safety of alternative materials, possibly because some alternatives are relatively new materials.

In January 2005, the Commission adopted a proposal for a Community Strategy concerning Mercury[2] in order to reduce mercury levels in the environment and human exposure. Pursuant to Action 6 of the Strategy, the use of dental amalgam should be evaluated with a view to considering whether additional regulatory measures are appropriate.

Dental amalgam and its substitutes are regulated under Council Directive 93/42/EEC[3] concerning medical devices, according to which they must comply with the essential requirements laid out in the directive, in particular in relation to the health and safety of the patients.

An Expert Report mandated by the European Commission's DG III and published in 1998[4] concluded that no proven adverse effects could be associated with the presence, placement or removal of dental amalgam fillings in patients and users, based on available science and when used according to manufacturer's instructions.

Subsequently, several Member States have adopted recommendations according to which dental amalgam should not be used in certain patient groups such as pregnant women or young children.

In view of the above and in order to reconcile patients' oral health and the global aim of the Community Strategy concerning mercury, it is necessary to review the safety and performance of dental amalgam and of their substitutes for the treatment of dental cavities.

[2] COM (2005) 20 final

[3] OJ L 00042, 20.11.2003, p.2

[4] Dental Amalgam. A report with reference to the Medical Devices Directive 93/42/EEC from an AD Hoc Working Group mandated by DG III of the European Commission. 1998.

2. TERMS OF REFERENCE

2.1. Human safety

2.1.1. Dental amalgam

In view of mercury exposure level due to the presence, the placing or the removal of dental amalgam, the Scientific Committee is requested to consider the following questions:

1. is there scientific evidence that supports a link between amalgam and allergic reactions, neurological disorders or other health disorders?
2. in view of the above, is the use of dental amalgam safe for patients and users, i.e. dental health professionals? Are certain populations particularly at risk, e.g. pregnant women or children?

2.1.2. Alternative materials

Overall, alternative materials such as composite resins, glass ionomer cements, ceramics and gold alloys, are increasingly used for the restorative treatment of dental cavities. The Scientific Committee is requested to evaluate the safety of these materials when used for dental restorative treatment and to consider the following questions:

1. is there scientific evidence that supports a link between alternative materials and allergic reactions, neurological disorders or other health disorders?
2. in view of the above, is the use of alternative dental restoration treatment safe for patients and dental health professionals? Are certain populations particularly at risk, e.g. pregnant women or children?

2.2. Oral health and safety

In view of the specific properties of dental amalgam and alternatives when used for dental restorative treatment, is dental health equally ensured by dental amalgam and alternatives?

3. SCIENTIFIC RATIONALE

3.1. Introduction

This Opinion concerns one of the oldest unresolved controversies in medicine, that is whether there is a causal relationship between the use of mercury-containing amalgams for the restoration of teeth and the aetiology of a variety of diseases in individuals with amalgam restorations, in dental professionals and in the general population.

Dental amalgam has been used in various forms for the reconstruction of carious teeth for more than 150 years and became common, especially in the USA, in the latter part of the nineteenth century, its formulation and clinical use being rationalised by G V Black at the end of that century. The use of amalgam was almost wholly predicated on the fact that mercury is one of the very few metallic elements that is liquid at room temperature. As a consequence of this it is able to undergo an alloying reaction with other elements at ambient temperatures to form, in a clinically acceptable time, a customised mass that can be adapted to the size and shape of a tooth cavity, where it should be strong enough to resist the forces of occlusion for many years. At the time of the introduction of amalgam into dentistry, gold could be used in some types of dental restoration, but its cost prohibited widespread use. There were no other synthetic materials that had the combination of the required mechanical properties and ease of intra-oral manipulation. As a metallic alloy, amalgam did not have any aesthetic appeal, but the increasing prevalence of dental caries in the late eighteenth and early nineteenth centuries meant that this was a minor consideration. The even more profound increase in caries throughout the early and middle twentieth century, through the ubiquitous use of refined carbohydrates in foodstuffs, resulted in the increased use of dental amalgam fillings.

The essential metallurgical principles of dental amalgam, discussed in detail below in section 3.3, are fairly straightforward. Liquid mercury is able to react with many other metallic elements to produce a series of multi-phase alloys that are solid at room temperature. The key development was to find an element, or a combination of elements, that would allow the amalgamation reaction to occur in a short space of time, with a rapid rate of solidification and development of strength. Although several metallic elements were tried, it was soon realised that an alloy of silver and tin, essentially Ag_3Sn, reacts with liquid mercury to produce a clinically acceptable alloy that would solidify in a few minutes and gradually harden over a few hours.

It had been recognised for a long time that certain forms of mercury and its compounds have toxicological characteristics, and the potential for neurotoxicity had already been discussed at the same time that amalgam was introduced into dentistry. Throughout the twentieth century and even more now at the beginning of the twenty-first century, the potential role of dental amalgam in the causation of disease has been a matter of considerable controversy. The focus has been on the mercury contained within the amalgam, and the potential for it to induce local intra-oral reactions to the amalgam restorations and to cause systemic or remote-site diseases associated with its systemic distribution and accumulation. Both governmental and non-governmental organisations have considered this possibility and many reports have been written on the subject. Many academic studies have been published, including some very recent epidemiological studies, which have attempted to prove conclusively, one way or the other, whether the mercury in amalgam has a causative role in disease, but until now, no clear unequivocal conclusion has been forthcoming. This is of immense importance since, during the last forty years, several types of alternative to amalgam for dental restorations have been developed such that the overall risk – benefit assessments for dental restorations in general have had to be changed. However, it is far from clear whether the use of such alternatives, involving, as they do, their own potentially toxic components, reduces the risk of disease associated with dental restorations.

This Opinion therefore takes into account currently available scientific and clinical evidence concerning mercury and other elements contained within dental amalgam, and

also the components of the alternative materials. These alternatives include resin based composite materials, glass ionomer cements and a variety of hybrid structures. In addition, restorations made of gold-based and other alloys are possible alternatives to dental amalgam. These latter types of restoration are considered as custom-made devices in the context of the Medical Device Directive of the European Commission and are produced by indirect techniques in dental laboratories, which are clearly more time consuming and expensive. With each of the different types of alternative material, it is necessary to consider the chemistry and toxicology of all of the components, including monomers, acids, glasses and ions, taking into account the physico-chemical aspects of the setting process, the techniques for promoting adhesion to the tooth substance and the energies of any light sources used in photo-polymerisation. The clinical and epidemiological evidence has to be analysed in relation both to the patients themselves and to dental personnel, taking into account the phases of use, including placement of the filling, corrosion, degradation or wear in clinical service, and the release of materials during the removal of restorations. With respect to amalgam, it is also necessary to consider the exposure of the general population to mercury derived from the use of dental amalgam, placing this in the context of environmental exposure in general, and the contribution that amalgams make over their whole life cycle, including aspects of waste water treatment in dental offices and the release of mercury into the atmosphere in crematoria. With respect to alternatives to dental amalgam, it is also relevant to consider the life cycle of these materials, although very little data is available.

It is also important to examine the pattern of usage of amalgams and alternatives in dental clinics, since perceived benefits and risks, and the trends in these perceptions may change and this should be taken into account in making recommendations for future usage. For example, in some countries, general environmental considerations and public attitudes and expectations have contributed to a decline (sometimes a very substantial decline) in amalgam use and to a reduction in the use of mercury-containing products in general. Furthermore, dental schools are either reducing or have discontinued teaching the use of amalgams in view of the changing attitudes to restorative dentistry (Roeters et al. 2004). These trends must be placed in the context of the overall performance and longevity of amalgam and non-amalgam restorations, taking into account the size and location of the restorations. It is also important to recognise that the perception of patients may differ to some extent from the views of health care professionals.

3.2. Methodology

This Opinion of SCENIHR is concerned with the analysis of the evidence for the potential for either amalgam or alternatives to amalgam to have adverse effects on human health, from the perspectives of both scientific plausibility and clinical and epidemiological data, and to make observations about the future uses of these materials in dentistry.

The Working Group has considered evidence derived from a wide variety of sources, including peer-reviewed scientific and medical literature and published reports of institutional, professional, governmental and non-governmental organisations. In common with the usual practice of SCENIHR Working Groups, no reliance has been made on unpublished work or publicly available opinions that are not scientifically based. Due to the availability of extensive peer reviewed epidemiological and large scale clinical studies with respect to dental amalgam, it has not been necessary to rely on single case or anecdotal reports in establishing this Opinion. The Working Group has been careful, however, to review as much evidence as possible and, especially where the available data on alternatives is limited, attention has been given to some less rigorous studies where no other information was available. During the course of the deliberations of the Working Group, a Call for Information was issued by the Commission and the replies have all been considered.

In a major review of the evidence for or against causation of disease, it is necessary to take into account the generally accepted criteria for causation. The Working Group has therefore been mindful of such criteria, particularly the Bradford Hill Criteria of Causation

(Bradford Hill 1965). The main features of these criteria are the paramount need to establish a temporal relationship between exposure and outcome, the strength of any effect or association determined statistically, the evidence of a dose-response relationship, the plausibility and specificity of any association, and the coherence of any putative association with existing knowledge. It will become obvious with respect to both dental amalgam and the alternative restorative materials, that some of these questions are difficult to analyse, for example because of the uncertainty over the exposure of individuals to mercury derived from amalgams compared to their exposure to mercury from other sources. Nevertheless, the Working Group is confident that it has been possible to take all factors into account in producing an Opinion that is consistent with these criteria for causation.

3.3. Dental Amalgam

In this Chapter, the essential and relevant characteristics of dental amalgam and the evidence concerning the general exposure and toxicity of mercury based substances are explained and discussed. This is followed by an assessment of the reported adverse effects in individuals with amalgam restorations, the epidemiological and clinical evidence concerning adverse effects in dental personnel, and general observations about the clinical usefulness of dental amalgam restorations.

3.3.1. Metallurgical principles and physical-chemical properties

An amalgam is an alloy of mercury with one or more other metals. Most dental amalgams are called silver amalgams since silver is the principal constituent that reacts with mercury. The kinetics of reactions between mercury and silver are not appropriate for clinical use, so that the silver is provided as an alloy with other elements. This alloy is often referred to as a dental amalgam alloy or, collectively, they are known as 'alloys for dental amalgam' (ISO 1995). There are several types of dental amalgam alloy, all involving tin and most having some copper and, to a lesser extent, zinc. Some of the dental amalgam alloys themselves contain a little mercury to facilitate the amalgamation reaction. A conventional dental amalgam alloy will contain between 67% and 74% silver, with 25-28% tin, and up to 6% copper, 2% zinc and 3% mercury. The so-called dispersion type amalgam alloys have around 70% silver, 16% tin and 13% copper. A further, quite different, group of amalgam alloys may contain up to 30% copper, and are known as high-copper content amalgam alloys. In addition, again being very different, so-called copper amalgams which contained approximately 30% copper and 70% mercury were once used, but these are no longer recommended.

The amalgam alloys are mixed with mercury before clinical placement at a 1 to 1 weight-ratio. The mercury content of a finished dental amalgam restoration is therefore approximately 50% by weight.

In the conventional dental amalgam alloys, the ratio of silver to tin results in a crystal structure that is essentially the intermetallic compound Ag_3Sn, referred to as the gamma (γ) phase. The exact percentage of this phase controls the kinetics of the amalgamation reaction and many properties of the resulting amalgam structure. With the higher copper dispersion alloys, the microstructure is usually a mixture of the gamma phase with the eutectic silver-copper phase.

Different manufacturers present the amalgam alloy in different formats, although they are usually made available as fine particles, either spherical or irregular in shape, with particle sizes around 25-35 microns. Although there are also several different ways of dispensing the liquid mercury and the solid amalgam alloy, this is usually achieved by means of a sealed, compartmentalised capsule, with the alloy in one part and the mercury in the other, the membrane between the two being broken during the process of mixing in a mechanical amalgamator. This is an important point since a major route for exposure to metallic mercury during hand mixing, as carried out until a few decades ago, is eliminated during this process. Nevertheless, exposure certainly does occur during the

next phases of placement, where the setting amalgam is placed into the prepared tooth cavity and condensed, or compressed, firmly within the cavity. During this process, the structure of the amalgam is optimised by this compression, causing excess mercury to rise to the surface, from where it is removed. The properties of the amalgam restoration will depend on the perfection of this technique, the elimination of as much excess mercury as possible being essential.

The metallurgical characteristics of the amalgamation process are very important. With the conventional amalgam alloy, the reaction between the Ag_3Sn (γ) phase and the mercury results in the formation of the γ_1 phase, which is a body-centred cubic mercury - silver phase with a mercury – silver ratio between 3:2 and 8:5, and the γ_2 phase, a hexagonal tin-mercury phase of mercury - tin ratio between 1:6 and 1:8. The reaction does not go to completion and some 30% of the set amalgam consists of un-reacted Ag_3Sn (γ) phase. There will be, as noted above, some retained mercury, the majority of which is removed by the dentist during condensation; much of the remainder continues to react, very slowly, with the Ag_3Sn (γ) phase. It is emphasised that the set amalgam contains about 50% mercury and it will be seen that the majority of this mercury in the amalgam is contained in the γ_1 phase, with a minority in the γ_2. These metallurgical principles of dental amalgam are well established and have been discussed in detail in standard dental textbooks and reference documents (for example, Anusavice 2003).

The mercury in the set amalgam is in a very different form to that in the liquid mercury. According to Okabe (1987), mercury has a vapour pressure of 1.20×10^{-3} Torr at 20°C. It is difficult to compare directly the vapour pressure of liquids and solids, and indeed it is difficult to obtain good and reproducible measurements of very low vapour pressures such as those found with amalgams (Halbach and Welz 2004), but best estimates of the vapour pressure for amalgam surfaces range from 10^{-6} to 10^{-10} Torr (Wieliczka et al. 1996). This implies that the release of mercury vapour from a set amalgam restoration will be many orders of magnitude lower than that from liquid mercury, and the availability of mercury from a solid alloy structure should not be equated with that from the liquid. This subject is considered further in the following sections on exposure levels.

An amalgam restoration will be susceptible to tarnish and corrosion. Tarnish is a process that involves the deposition of substances from the oral environment, especially sulphides, such that the surface loses its metallic lustre, but without any significant chemical reaction involving the underlying alloy. In fact, tarnished alloys have greater protection from corrosion because of the passivating effect of the deposited layer. Nevertheless, the amalgam itself will corrode over time, even though mercury and silver are intrinsically corrosion resistant elements. The main cause is that the γ_2 is significantly more electronegative than either the γ or γ_1 phases so that galvanic corrosion occurs, with the release of the constituents of the γ_2, namely tin and mercury. The corrosion of the higher copper based amalgams is less because little or no γ_2 forms. It is anticipated that the corrosion rate of amalgams will decrease with time as the surface becomes progressively more noble, but this appears to take place more slowly in restorations than predicted by in vitro tests on amalgam samples (Sutow et al. 2007). This latter paper typifies the problems with the assessment of the corrosion rate of amalgams, as most estimates are based on electrochemical tests in vitro, from which it is extremely difficult to extrapolate to reliable, clinically relevant data on the rate of release of mercury from amalgam restorations by corrosion process within the mouth. With respect to this Opinion, it may be stated that corrosion of restorations will occur at a very low rate, which may contribute to overall exposure, but the exact contribution that this makes is unknown.

3.3.2. Exposure to Mercury

Mercury is a metallic element that occurs naturally and also in the form of several types of ore, the mercury burden of the environment being derived predominantly from natural sources. Input into the earth's atmosphere occurs regularly through emissions from volcanoes, soil erosion and the combustion of fossil fuels. Widespread utilisation of

mercury and its compounds in a number of industries over the last several centuries has resulted in the release of large amounts of mercury into the atmosphere, increasing the total amount in the ecosphere. Of special importance has been the accumulation of some mercury compounds in the aquatic food chain and the use of mercury compounds in a variety of medical and cosmetic products including dental amalgam. It is clear that exposure to mercury by individuals will be controlled by several factors, including ambient mercury levels (determined by geographical location and life-style choices), the diet, especially in relation to fish consumption, the possibility of occupational exposure for those who work in mercury-related industries and practices, and the use of mercury containing medical or cosmetic products, including amalgam. The exposure of individuals with amalgam restorations and dental personnel has to be considered in the context of this broader exposure scenario.

3.3.2.1. Major Forms of Mercury

It is also important to note that there are several different forms of mercury. First there is elemental mercury itself, a volatile form of the liquid metal, referred to as Hg^0. Secondly, mercury is stable in two other oxidation states (Hg^{1+} and Hg^{2+}) and is able to form inorganic compounds, of either monovalent or divalent form, including mercuric chloride ($HgCl_2$), mercurous chloride (Hg_2Cl_2), mercuric sulphide (HgS), and mercuric selenide (HgSe). Thirdly, mercury is able to form a variety of organic compounds, including methylmercury. There is a clear connectivity between these forms with respect to the global cycle of mercury (Nielsen et al. 2006). Elemental mercury may be converted to soluble inorganic forms, which may be methylated in water, especially by microorganisms, which enter the food-chain and accumulate in the tissues of large predatory fish. The ratio of methylmercury in these fish to the mercury concentration in the water can be as high as 10^5.

Each form of mercury has its own toxicological profile, although, in general terms, the toxicity of these forms is highest with the organic mercury compounds, followed by elemental mercury and inorganic mercury compounds. This is important when considering different exposure routes to these forms.

3.3.2.2. Evidence of exposure to mercury from dental amalgam restorations

Exposure to Mercury in Adults

Exposure to mercury is difficult to measure. The indications for mercury exposure are therefore normally obtained by measuring mercury levels in urine and blood of individuals. Autopsy/post-mortem studies give an indication of the overall exposure of individuals during their whole lifetime due to all kinds of mercury sources, including dental amalgam. As such, these studies suffer certain unquantifiable limitations. Therefore, data dealing with blood and urine mercury determination were considered more relevant as they reflect actual exposure.

Mercury is distributed ubiquitously in the environment and can therefore be taken up by the general population via food, water and air, potential sources of exposure including the inhalation of mercury vapors in ambient air, the ingestion of drinking water and food, and exposure to mercury through dental and medical treatments. Dietary intake is the most important source of non-occupational exposure to methylmercury, with fish and other seafood products being the dominant source of this highly absorbable form in the diet. Intake of elemental mercury from dental amalgams is another source contributing to the total mercury burden in humans in the general population (WHO 1990, WHO 1991). Tolerable limits for methylmercury content of fish and human consumption have been set by various organisations. In the USA, the Environmental Protection Agency set a limit, the so-called Tissue Residue Criterion, of 0.3 mg methylmercury / kg fish (EPA 2001). In Europe, the 2005 Opinion of the Scientific Panel of the EFSA on contaminants

in the food chain (EFSA 2005) contained detailed reference to methylmercury in fish. In practice, levels range from under 0.1 mg/kg fish up to 0.5 mg/kg. The provisional tolerable weekly intake (PTWI) has been established at 1.6 µg/kg body weight, implying that a high consumption of a predatory fish such as bluefin tuna, which may have a methylmercury level around 0.5 mg/kg, gives up to twice the recommended intake.

Because the two major sources of mercury body burden include dietary intake of methylmercury and intake of elemental mercury from dental amalgams, mercury is inevitably present at low concentrations in human tissues. Mercury has been detected in blood, urine, human milk, and hair in individuals in the general population. The mercury concentrations in whole blood of individuals with or without amalgam fillings are usually below 5 µg/l blood, but these concentrations do depend on dietary habits and the number of amalgam fillings (ATSDR 1999, BAT 1997).

In a study on the influence of fish consumption and number of amalgam fillings, (Schweinsberg 1994), blood mercury concentrations in individuals without fish consumption and dental amalgams were in the range of 0.2 – 0.4 µg/l. Blood mercury concentrations were raised the least in individuals without fish consumption but with more than 6 amalgam fillings, followed by high fish consumers with no amalgam restorations, and highest in high fish consumers with more than six fillings, at 1.5 to 4 µg/l. Average blood mercury levels below 3 µg/l in individuals with amalgam fillings are also reported in several other studies. Barany et al. (2003) studies 245 17-year-old Swedish individuals and found a geometric mean level of 1.1 µg/l in their blood, which were positively correlated with fish consumption and serum mercury was influenced by the number of fillings as well as fish consumption. Dye et al. (2005) found that the average urinary mercury level in women of childbearing age was 1.34 µg/l and it was estimated that an increase of 1.8 µg/l would be seen in the urinary levels for each ten dental surfaces restored with amalgam. Zimmer et al. (2002) reported median mercury levels in blood of 2.35 µg/l in 40 females who had claimed to suffer from serious health damage due to amalgam fillings and 2.40 µg/l in a series of 43 control female subjects.

The mercury concentrations in the urine of persons not occupationally exposed to mercury are usually below 5 µg/l. Again, the urinary excretion may vary considerably depending on non-occupational sources of mercury, such as fish consumption and amalgam fillings. In one study with 380 Italians without occupational exposure to mercury, a mean value of 3.5 µg/l urine was observed, with a range from 0.1 to 6.9 µg/l (BAT 1997). Median values between 1.5 and 1.8 µg/l urine have been reported (Zimmer et al. 2002). In a study of 1127 healthy males, Kingman et al. (1998) found an average total mercury urinary concentration of 2.55 µg/l with a significant correlation between this level and amalgam exposure equivalent to an increase of 1 µg/l of urine for each 10 amalgam surfaces.

As discussed by Barregard (2005) and Barregard et al. (2006) values of urinary mercury expressed in relation to creatinine vary between countries, especially with reference to different food habits and national health care systems. Median levels in subjects with dental amalgams were 1.2 µg/g creatinine in Italy but 0.6 µg/g creatinine in Sweden, corresponding figures for those without amalgams being 0.9 and 0.2 µg/g creatinine respectively. Elevated levels, approximately five times higher than controls are found in individuals who regularly use nicotine chewing gums as a smoking replacement therapy (Sallsten et al. 1996).

In a population of 245 German children, mercury concentrations in urine ranged between <0.1 and 5.3 µg/l, with a mean of 0.25 µg/g creatinine, with some correlation with the number of teeth with amalgam fillings and also the number of defective amalgam fillings (Pesch et al. 2002). Differences were noted between mercury in plasma and erythrocytes by Halbach et al. (2000, 2007). The authors conclude that the integrated daily mercury dose of 7.4 µg for a high amalgam load is well below the tolerable dose of 30 µg (WHO 2003, ATSDR 1999). A recent paper indicated that there may be difference in mercury excretion between boys and girls 8-18 years of age, treated with dental amalgam (Woods 2007).

Exposure during pregnancy and breast-feeding

Mercury is normally present in amniotic fluid. In one study of 72 pregnant women, (Luglie et al. 2005) there was an overall mean mercury concentration in amniotic fluid of 0.37 +/- 0.49 ng/ml. The women were divided into those with a low concentration of less than 0.08 ng/ml (26.4% of the subjects) and those with a high concentration of greater than 0.08 ng/ml, mean 0.49 +/- 0.52 ng/ml (73.6% of subjects). The amniotic fluid concentration was dependent of the number of amalgam fillings and fish consumption; the low concentration group having an average of 2.26 amalgam fillings and the high concentration group having an average of 5.32 fillings. However, no adverse effects were observed throughout pregnancies and in the newborn. Only a small fraction of divalent inorganic mercury is transferred to the fetus, whereas placental transfer of methyl mercury and elemental mercury occurs easily.

Bjornberg et al. (2005) report that infant blood inorganic mercury is similar to maternal blood mercury at delivery but decreases until 13 weeks of age. In breast milk inorganic mercury decreased from day 4 to 6 weeks after delivery, and remained unchanged thereafter. Total mercury in breast-milk was associated with maternal but not infant inorganic mercury. The exposure to both methylmercury and inorganic mercury was low, being higher before birth than during the breast-feeding period. Methylmercury contributes more than inorganic mercury to infant exposure post-natal via breast milk. The median value for methylmercury in maternal blood at delivery is 0.99µg/l, decreasing to 0.38 µg/l by 13 weeks after birth. The median for inorganic mercury concentration was 0.09µg/l in maternal blood at delivery and 13 weeks. The same values were found in infant blood at delivery, reducing to 0.05µg/l at 13 weeks. The child's exposure to methylmercury and inorganic mercury is much greater before birth than during breast-feeding. In breast milk, the mercury level correlated significantly to maternal blood inorganic mercury (0.29µg/l). Gundacker et al. (2002) indicate that the mean concentration of total mercury in human breast milk is 1.59µg/l, which they considered to pose no risk to infants.

Intake estimates for mercury from dental amalgams

Mercury vapour is released from silver amalgam restorations during chewing, tooth brushing, and parafunctional activities including bruxism. The parameters of this release of mercury vapour by amalgam depends of the number of fillings, the filling size and placement, chewing habits, food texture, grinding and brushing teeth, nose-mouth breathing ration, inhalation-absorption, ingestion and body weight, and the surface, composition and age of the amalgam restorations. Therefore, there are large variations in the estimation of daily mercury absorption and release.

Mercury released from dental amalgam distributes in the oral cavity as inhalable mercury vapour, or is dissolved in saliva after oxidation or suspended in it as amalgam particles. There is no evidence that biotransformation of amalgam-derived mercury takes place intra-orally in association with bacterial activity. With respect to systemic exposure assessment, only the inhaled fraction is relevant since elemental mercury and inorganic mercury are poorly absorbed from the GI-tract and therefore have only a very minor contribution to systemic exposure. The daily uptake of mercury from amalgam fillings is estimated to be up to 27 µg/day in individuals with large numbers of fillings. One study shows an intake from 1 to 5 µg/day from dental amalgam for people with 7-10 fillings. The World Health Organization reported a consensus average estimate of 10 µg/day of amalgam derived mercury (range: 3-17 µg/day) (WHO 1991). Weiner and Nylander (1995) estimated the average uptake of mercury from amalgam fillings in Swedish subjects to be within the range of 4-19 µg/day. Skare and Engqvist (1994) estimated that the systemic uptake of mercury from amalgams in middle - aged Swedish individuals with a moderate amalgam load (30 surfaces) was, on average, 12 µg/day.

3.3.2.3. Exposure to mercury in dental personnel

The mercury body burden of dental personnel is normally higher than in the general population. The mean urine mercury levels in dental personnel has been variously reported to range from 3 µg/l to 22 µg/l, compared to 1-5 µg/l as the normal range for non-occupational groups (Hörsted-Bindslev 2004). This increased body burden is attributed to dental personnel mixing and applying dental amalgam and removing amalgam restorations; Ritchie et al. (2004) showed that dentists had, on average, urinary mercury levels over 4 times that of control subjects although all but one dentist had urinary mercury below the UK Health and Safety Executive health guidance value. Dentists were significantly more likely than control subjects to have suffered from disorders of the kidney but these symptoms were not significantly associated with their level of mercury exposure as measured in urine. Over 67% of the 180 surgeries visited had environmental mercury measurements in one or more areas above the Occupational Exposure Standard (OES) set by that Executive. In the majority of these surgeries the high levels of mercury were found at the skirting and around the base of the dental chair. In 45 surgeries (25%) the personal dosimetry measurement (i.e. in the breathing zone of dental staff) was above the OES.

Dental personnel may now be exposed to much less mercury than in the past, in view of the increased use of encapsulated dental amalgam, improvements in amalgam capsule design, the heightened awareness and practice of appropriate dental mercury hygiene measures, and the increasing use of alternative, non-mercury-containing materials (ADA 2003, Hörsted-Bindslev 2004). However, despite trends to reduce exposure to mercury, large, highly statistically significant differences ($P<0.0001$) may be found between dental personnel (in particular dentists) and controls, with respect of mean urinary, hair (head and pubic) and nail (finger and toe) mercury levels, with the reasons for such differences being considered to be multifactorial (Morton et al. 2004)

Since most dental chairside personnel do not touch dental amalgam during mixing and placement, it is considered that the main sources of mercury exposure are aerosols, created in the immediate working environment during and in particular, the removal of restorations of dental amalgam, and the exhaust air from dental vacuum systems. These mercury vapour releases can be substantial and well in excess of human exposure limits (Stone et al. 2007). Immediate working environment aerosols and exhaust air from dental vacuum systems will be inhaled despite the wearing of face masks, which may provide little, if any, barrier to mercury vapour entering the lungs and being absorbed.

Correlations have been found amongst dentists between urinary mercury levels and the number of hours worked in the surgery ($r=0.22$, $P=0.006$) and the number of amalgam restorations placed ($r=0.38$, $P<0.001$) and removed ($r=0.29$, $P<0.001$) in a week, with urine mercury levels in dentists ranging from 0.02 to 20.90 (mean 2.58) nmol mercury per nmol creatinine. A confounding factor in such investigations is the number of amalgam surfaces dentists have in their own mouths (Ritchie et al. 2002, Ritchie et al. 2004).

3.3.2.4. Metrology

While the analytical instruments for the determination of mercury concentrations in biological samples are well developed and sufficiently sensitive, a number of problems with sampling, the determination of mercury speciation, and the interpretation of results are evident. For the determination of total mercury in occupation exposures, the German BAT-commission (which sets limit values for occupational exposures to chemicals and develops and validates analytical methodology) recommended a specific sampling procedure and analytical methods to determine mercury in blood or urine. Sampling procedures for mercury determination are also described by the "Humanbiomonitoring Kommission" of the German UBA (Umweltbundesamt, Federal Environment Agency, Dessau-Rosslau, Germany). These authorities also concluded that the often proclaimed exposure assessment for mercury release from dental amalgams, "dimercaptopropane sulfonate (DMPS) mobilisation test" for mercury, does not provide additional important

information. This mobilisation test uses DMPS to chelate mercury, which results in an increased elimination of mercury with urine for a short time after DMPS-application (BAT 1997, UBA 1999).

Rapid and reliable detection of mercury in blood and urine resulting from environmental and occupational exposure may be carried out in most analytical laboratories, using, for example, atomic fluorescence spectrophotometry (Berglund et al. 2005). Measurements of total mercury in the urine tend to reflect inorganic mercury exposure and total mercury levels in whole blood are more indicative of methylmercury exposure. However other fluids, such as saliva, hairs or nails or faeces have been proposed and used. Total mercury in red blood cells may be a suitable proxy for methylmercury exposure. The mercury concentration in saliva and scalp hair is more controversial. According to Pesch et al. (2002), hairs reflect fish consumption, the age of a child and the smoking habits of parents, with a low correlation between the hair and urine mercury content. Mercury content in saliva ranged between 0.32 and 4.5 µg/l and below the limit of quantification for more than 70% of the samples. Pesch et al. (2002) concluded that saliva does not seem to be a suitable tool to monitor the mercury burden. Although in general no correlation was found between elemental concentration in hairs and internal organs (Yoshinaga et al. 1990) a hair-organ relationship was found by Suzuki et al. (1993) for mercury concentration. More recently, the total mercury levels in hair, toenail and urine were shown to result from fish consumption, but the method was applicable neither to occupational exposure nor to dental filling mercury release (Ohno et al. 2007).

Mercury levels in saliva determined by cold vapour atomic absorption spectrometry did not correlate with the concentration in blood and urine, and therefore is not recommended for a biological monitoring (Zimmer et al. 2002). Faeces reflect the elimination of metallic mercury by abrasion and therefore do not present any usefulness in the context of a potential burden. Generally blood and urine are preferred for the assessment of mercury exposure.

3.3.3. Mercury toxicology

In general, the toxicology of mercury is highly dependent on the route of administration, the exposure conditions and the speciation of the mercury. Since human exposure to mercury from dental amalgams may occur by inhalation of mercury vapour released from the dental fillings into the oral cavity, by ingestion of the released elemental mercury, or swallowing small pieces of amalgam releasing elemental mercury in the alimentary tract, this discussion focuses on the toxicology of elemental mercury.

3.3.3.1. Toxicokinetics

Oral ingestion of elemental mercury results only in a very limited absorption, typically < 0.01 % of the dose (ATSDR 1999, MAK 1999, Klaassen 2001). Dermal absorption of liquid elemental mercury is also very limited. In contrast, approximately 80 % of the inhaled elemental mercury is absorbed in the lungs. Due to the high lipid solubility, elemental mercury rapidly penetrates alveolar membranes and is then distributed to all tissues of the body. Elemental mercury is slowly oxidized in the blood in a saturable process to give Hg^{2+}, probably by catalases. Due to the ease of saturation of the enzymatic oxidation of elemental mercury to Hg^{2+}, the proportion of elemental mercury in blood increases with increasing dose of elemental mercury. A small part of the elemental mercury dose received is also eliminated by exhalation and a small part of the dose is also delivered to the central nervous system. Oxidation of elemental mercury may also occur in the central nervous system and result in an accumulation of Hg^{2+} in the central nervous system since Hg^{2+} is unable to cross the blood-brain barrier and diffuse out of the brain. Hg^{2+} is tightly bound to sulphydryl groups in proteins which represents the principal mode of action for its toxicity and is responsible for the slow elimination from the organism. It may be eliminated by excretion within urine and/or faeces. The elimination of elemental mercury or Hg^{2+} follows complex kinetics with half-lives in the range of 20 – 90 days. Usually, the kidney contains the highest concentration

of mercury following exposure to elemental mercury and Hg^{2+}. After repeated exposures, a steady state level of blood mercury is reached, this being influenced by the average intake of mercury. At the end of the exposure, mercury levels slowly decline.

3.3.3.2. Toxicity of Elemental Mercury

Due to the very low absorption of elemental mercury after oral intake, this section focuses on toxic effects observed after inhalation of elemental mercury. Due to the widespread use of mercury in industrial settings, a large and detailed database on human effects of elemental mercury inhalation is available. A number of reviews addressing the toxicity of elemental mercury have been published (MAK 1999, BAT 1997, UNEP 2002, ATSDR 1999, IRIS 2002)

The assessment of elemental mercury toxicity is mainly based on observations in occupationally exposed humans. Inhalation of extremely high concentrations of elemental mercury, in excess of 10 mg/m^3, may produce bronchitis and pneumonia, in addition to symptoms of the central nervous system. However, such concentrations are many orders of magnitude above those encountered through the release of elemental mercury from dental fillings. After long-term elemental mercury exposure in occupational settings, and under occupational hygiene conditions considered as poor by present standards, the major effects of elemental mercury reported are on the central nervous system. The major manifestations of mercury poisoning from inhalation of elemental mercury are increased excitability and tremors. Characteristic symptoms after long-term high dose exposures (the inhalation of concentrations above 0.5 mg/m^3 for many years) are muscle tremors in fingers, eye lids and lips, which may progress to chronic spasms of the extremities. Early signs of toxicity after inhalation of mercury are less specific and the early phase of toxicity is often referred to as "micromercurialism". Clinical findings in this condition are tremor, enlargement of the thyroid, increased uptake iodine in the thyroid, tachycardia, gingivitis and haematological changes. For diagnosis of the early phase of elemental mercury intoxications, at least three of these findings should be present along with increased mercury concentrations in blood or increased mercury excretion with urine. After chronic occupational exposure to mercury vapour, proteinuria and even a nephritic syndrome have been described in humans. The glomerular damage may progress to an interstitial immune-complex nephritis. Gingivitis and hypersalivation with a strong metallic taste are considered to be further symptoms of chronic inhalation exposure to elemental mercury.

Quantitative data on elemental mercury inhalation exposure, mercury concentrations in blood and urine and early effects of mercury toxicity have been established. The non-specific symptoms of micromercurialism are observed at long term exposures to elemental mercury air concentrations of 0.05 mg/m^3, or at concentrations of mercury of 35 µg/l in blood or 150 µg/l in urine. Overt neurotoxicity (tremor) occurs after long term inhalation of elemental mercury at concentrations between 0.1 and 0.2 mg/m^3 with resulting blood mercury concentrations between 70 – 140 µg/l and urinary mercury in the range of 300 – 600 µg/l (MAK 1999, BAT 1997, UNEP 2002, ATSDR 1999, IRIS 2002).

Occupational allergies to mercury were rare in the past, even with widespread exposures to elemental mercury at the workplace and the use of mercury in medicinal preparations (including the use of Hg^{2+} due to its bactericidal activity) and consumer products (Kanerva et al. 1993).

Regarding animal toxicity studies, no adequately performed studies with elemental mercury inhalation are available for evaluation. However, long term oral administration of Hg^{2+} to rodents causes glomerulonephritis, which was found to have an immune basis, thus being similar to the human disease described after long term elemental mercury inhalation (Bigazzi 1999, Havarinasab and Hultman 2005, Havarinasab et al. 2007).

Mercury compounds are well known for their immunosuppressive activity (Havarinasab and Hultman 2005). Organic mercury compounds such as methylmercury and

ethylmercury are much more potent suppressors of the immune system than inorganic mercury or elemental mercury. In a susceptible genotype of mice, inorganic mercury interacts with the immune system inducing immunostimulation, antinuclear antibodies and systemic immune-complex deposits, a syndrome designated as mercury-induced autoimmunity (Hultman et al. 1989, Reuter et al. 1989). In mice a similar effect was observed for mercury vapour (Warfvinge et al. 1995). In a genetically modified mercury susceptible rat model for autoimmune diseases, the Brown Norway (BN) rat, dental restorations with amalgam induced immune activation with an increase in IgE plasma concentrations, and immune complex deposits in systemic organs including the kidney, whereas this was not observed in BN rats receiving composite resin restorations, or mercury resistant Lewis rats (Hultman et al. 1998). Another model for studying mercury induced autoimmunity is the New Zealand White rabbit in which mercuric chloride treatment results in immune deposits in kidneys and other organs (Roman-Franco et al. 1978).

3.3.4. Toxicology of other metallic elements in amalgam

3.3.4.1. Toxicology of silver

Despite the widespread use of silver and silver ions in industry and for medicinal purposes, only limited information on silver toxicity is available. Silver exposure is ubiquitous in the general population and dietary intake is estimated at 70 – 90 µg/day. Silver ions may be absorbed from the gastrointestinal tract after oral uptake or after inhalation of silver containing dusts. At higher local concentrations, silver ions may produce skin and gastrointestinal tract irritation. The critical effect of excessive silver absorption is argyria, a deposit of silver sulphide resulting in local or generalized impregnation of tissues. Other specific toxic effects of silver in humans or in experimental animals have not been described. Silver does have antimicrobial activity (Drake and Hazelwood 2005).

3.3.4.2. Toxicology of copper

Copper is an essential nutrient that is incorporated into a number of metalloenzymes. Symptoms associated with copper deficiency in humans include anaemia and leucopoenia. Copper released from dental amalgams may be readily absorbed from the stomach and small intestine. After nutritional requirements at the recommended daily intake are met (2 mg/person), excess copper (well above TDI of 0.5 mg/kg bw/day) is absorbed into gastrointestinal mucosal cells and into the liver induces the synthesis of and binds to metallothionein. Bound copper is excreted when the cell is sloughed off or released into bile and excreted in the faeces. Exposure to excessive levels of copper can result in a number of adverse health effects including liver and kidney damage, anaemia, immunotoxicity, and developmental toxicity. One of the most commonly reported adverse health effect of copper in humans is nausea, vomiting, and/or abdominal pain. The observed effects are not usually persistent and gastrointestinal effects have not been linked with other health effects. The liver is also a target of toxicity. Liver damage has been reported in individuals ingesting lethal doses of copper sulphate. Liver effects have also been observed in sensitive subpopulations such as individuals diagnosed with Wilson's disease or Indian childhood cirrhosis, or idiopathic copper toxicosis. These syndromes are genetic disorders that result in an accumulation of copper in the liver or with excessive copper exposure. Inflammation, necrosis, and altered serum markers of liver damage were observed in rats fed diets with copper sulphate levels that are at least 100 times higher than the nutritional requirements (Klaassen 2001).

3.3.4.3. Toxicology of tin

Humans chronically exposed to inorganic tin (e.g., stannic oxide dust or fumes) manifest a benign form of pneumoconiosis known as stannosis, which mainly involves the lower respiratory system. Gastrointestinal effects, such as nausea, vomiting, and diarrhoea

have been reported in subjects ingesting food items containing inorganic tin. Based on the available studies in humans, there is no evidence that inorganic tin affects reproduction or development in humans or that it is neurotoxic, mutagenic, or carcinogenic. Studies in animals have not clearly established potential target organs for inorganic tin toxicity. Of the effects described, signs of anaemia and gastrointestinal distension appear to be tin-related. No adverse reproductive or developmental effects of inorganic tin were reported. Studies in animals have shown that excess dietary tin reduces serum iron and copper levels. Excess doses of tin affects the metabolism of other metals such as copper, zinc, and iron. Due to the altered disposition of these metals, it is difficult to ascertain whether an effect is specific to tin itself or is due to fluctuations in tissue levels of other metals. Feeding a diet with excess tin to rats produced signs of anaemia and individuals with low levels of iron or copper may be at risk of developing signs of anaemia if they consume excessive amounts of tin. (Klaasen 2001).

3.3.4.4. Toxicology of zinc

Zinc is an essential nutrient and zinc deficiency has been associated with dermatitis, anorexia, growth retardation, poor wound healing, impaired reproductive capacity, and depressed mental function; an increased incidence of congenital malformations in infants has also been associated with zinc deficiency in the mothers. Nausea has been reported in humans exposed orally to high doses of zinc chloride. Other gastrointestinal symptoms reported in cases of excess zinc exposure include vomiting, abdominal cramps, and diarrhoea. The limited data suggest that single-dose exposures in the range of 140–560 mg zinc are sufficient to cause these effects, which are consistent with gastrointestinal irritation. Following longer-term exposure to doses of 0.5–2 mg zinc/kg/day, the observed symptoms are indicative of copper deficiency. The most noticeable manifestation of the decreased copper levels due to the interaction with zinc is anaemia, manifesting as decreased erythrocyte number. Long-term consumption of excess zinc may also result in decreased iron stores. Effects of zinc on reproductive or developmental end points have been noted in oral-exposure animal studies, but generally only at very high doses (>200 mg/kg/day) (Klaasen 2001).

3.3.4.5. Conclusions

The elements other than mercury contained with dental amalgam all have their own, different profiles in terms of essentiality and/or toxicology. There is no scientific evidence that any of those elements currently used in dental amalgam restorations constitute a risk of adverse health effects in individuals apart from allergic reactions to the individual elements.

3.3.5. General conclusions concerning correlation between exposure and toxicology (risk assessment)

A number of regulatory limits for mercury exposures have been set by various organisations. When using these regulatory limits describing safe intakes of mercury (safe as defined to be without toxic effects after lifetime exposure) it should be recognised that many of the values are recommended for dietary intake of mercury ions and methyl mercury. Therefore, these limits have only limited use for the assessment of mercury emissions from dental amalgams since the exposure in this case is inhalation or ingestion of elemental mercury. Due to the differences in toxicokinetics as outlined above, the assessment for mercury exposure from dental amalgams therefore should be based on resulting blood levels of mercury and/or urinary excretion of mercury. Toxicologically based limits for both of these media have been developed.

Due to the small dose received by inhalation of mercury from amalgams, a direct comparison of maximal mercury air concentration in the oral cavity of individuals with amalgam fillings and occupational limits for air concentrations of mercury requires consideration of absorbed dose. As shown in table 1, inhalation of mercury at the

occupational exposure limit results in an uptake of more then 300 µg of Hg per day, whereas inhalation of mercury from dental amalgams gives body burdens which are at least 20 fold lower then those resulting from occupational exposures at present limits for air concentrations.

Based on the evaluation of several longitudinal studies involving blood samples to determine mercury content over a prolonged time period, the German MAK-Commission (tasked to set occupational exposure limits which are without health risks) concluded that even many years of mercury exposure to concentrations that result in urinary mercury levels of 100 µg/l or even higher do not cause objective adverse effects. The urinary mercury levels were equivalent to mercury concentrations in blood of approximately 23 µg/l. The BAT-value (maximal permissible concentration of hazardous compounds or their metabolites in body fluids) was therefore set at 100 µg/l of urine or 25 µg/l of blood and is considered a No-adverse-effect-concentration for mercury in humans.

For the general population, the Federal Environment Agency (Umweltbundesamt (UBA)) derived reference values including general background exposure to mercury from various sources (fish and seafood consumption, mercury in other foods) of 1.4 µg/l of urine and of 2 µg mercury/L of blood in adults without amalgam fillings and with low seafood consumption. According to UBA, no adverse effects of mercury are observed at blood levels lower than 5 µg/l (including pregnant women) and urinary mercury concentrations lower than 0.7 µg/l. These assessments included both inorganic mercury and the more toxic methyl mercury (UBA 1999).

Table 1 Estimated average daily intake and retention of total mercury and mercury compounds in the general population.

Sources of exposure	Elemental mercury vapour	Inorganic mercury compounds	Methylmercury
Air	0.030 (0.024)	0.002 (0.001)	0.008 (0.0064)
Food			
Fish	0	0.600 (0.042)	2.4 (2.3)
Non-fish	0	3.6 (0.25)	0
Drinking water	0	0.050 (0.0035)	0
Dental amalgams	3.8 – 21 (3 – 17)	0	0
Total	3.9 – 21 (3 – 17)	4.3 (0.3)	2.41 (2.31)

Note: Values given are the estimated average daily intake (µg/day) for adults in the general population who are not occupationally exposed to mercury; the figures in parentheses represent the estimated amount retained in the body of an adult. In Europe, the intake of total mercury with food was estimated to be below 1 µg/kg body weight/week in adults (1 to 9 µg/person/day), depending on fish consumption (EFSA 2004)

Source: WHO 1990, WHO 1991

Table 2 gives respiratory air concentrations, blood levels and urinary excretion of mercury in individuals with amalgam fillings and compares these to levels of mercury considered safe for occupational exposures. It is clear that, although exposure to individuals with amalgam restorations does occur, the levels of exposure encountered as between 5 and 30 times lower than those permitted for occupational exposure.

Table 2 Respiratory air concentrations, blood levels and urinary excretion of mercury in individuals with amalgam fillings compared to levels of mercury considered safe for occupational exposures.

Medium	Individual with typical number of fillings	Occupational limit
Respiratory air concentration	3 – 17 µg Hg/day	346 µg Hg/day*
Urinary concentration of mercury	3.5 µg Hg/l	100 µg Hg/l
Blood concentration	3 – 5 µg Hg/l	25 µg Hg/l

*Based on an alveolar ventilation of 9 l/min, a retention of 0.8 for elemental mercury. The MAK-value was 0.1 mg/m^3 and 8h of occupational exposure.

3.3.6. Adverse effects in individuals with amalgam restorations

Mercury toxicity associated with methylmercury, elemental and inorganic mercury is well documented (see above). The question remains, however, whether metallic mercury exposure from dental amalgams is the cause of adverse health effects, including multiple sclerosis, autism, CNS and renal damage, chronic fatigue, memory impairment and depression. These conditions and their etiology have been studied extensively and risk factors are well defined (see the review article by Brownawell et al. 2005).

The parameters of the adverse effects may be toxicological, allergic and/or psychological.

3.3.6.1. Localized mucosal reactions

The possibility that restorative dental materials could be responsible for lesions within the mouth associated with direct contact between the material and the oral mucosa is obviously of importance. Such localised reactions are often discussed in the context of allergies and hypersensitivity.

In the dental clinic two reaction patterns are relevant: the delayed reaction (Type IV) and the immediate reaction (Type I). In the type IV reaction, the incomplete allergens (haptens) are brought in contact with tissue proteins by way of the oral mucosa to form complete allergens. Provided that previous sensitisation has taken place, specialised T-lymphocytes now produce inflammatory mediators causing tissue damage, seen as contact mucositis, i.e. intra-oral diffuse, red zones, blisters, or ulceration with pain and burning sensation. The inflammation is not always limited to the exposure site. Contact dermatitis may be observed in the face or more distant locations as urticarial or eczematous reactions. A suspected Type IV reaction may be confirmed with an epidermal patch test (see standard textbook such as Roitt and Delves 2006)

An immediate type (Type I) allergic reaction is based on the release of vasoactive humoral mediators from mast cells or basophilic granulocytes. These mediators are released from the cells upon contact with antigens binding to the IgE antibodies on their surface. The antigen specific IgE antibodies provide the specificity of the allergic response. The released mediators lead to increased capillary permeability and contraction of smooth muscles. The symptoms may consist of urticaria, asthmatic seizures, swelling of the mucosa of throat and eyes and even result in anaphylaxis, all seen within minutes. This immediate type hypersensitivity is in general associated with allergic responses to protein allergens. Potential full allergens encountered in restorative dentistry are mainly limited to the accessories used, including residual proteins from natural rubber latex in gloves, rubber dam, polishing remedies or parts of anaesthetic cartridges.

A chronic inflammatory response of the gingival tissue around restorations may be present, which appears as chronic gingivitis, recurrent necrotic gingivitis and periodontal pockets. When patients with self-diagnosed oral problems (142 women and 76 men)

were examined, the mean concentration of mercury in the whole blood was 17.3 nmol/l and no value exceeded 50 nmol/l. Mental disorder was diagnosed in 93 cases (42.7%), including 41 cases of generalized anxiety disorder and 12 cases of panic disorder. A total of 82 patients (40%) did not work because of medical reasons or unemployment (Herrstrom and Hogstedt 1993). However, no correlation could be demonstrated between the oral symptoms and a generalized toxic effect of amalgam fillings.

Amalgam tattoos, which are occasionally observed, are associated with the iatrogenic introduction of small particles of dental amalgam, inadvertently implanted into oral soft tissues during dental procedures. Tattoos are resistant to protracted conventional therapies. Most of the foreign bodies examined by light and EDAX methods contained amalgam (amalgam dusts) that appears either as fine granular or larger globular structures implanted in gingival tissues. There is no free mercury, but large globular pieces of amalgam, which induce metallothionein expression in adjacent histiocytes. There is no consequence to the presence of tattoo, except the unpleasant dark blue staining of the gingiva (Lau et al. 2001) and currently there is no indication for the surgical removal of these tattoos.

Metals in close contact with skin and mucosa are well-recognized causes of contact dermatitis including mercury (Garner 2004). Oral lichen planus is associated with dental restorations and one of the causes may be contact allergy to constituents of dental amalgam. Khamaysi et al. (2006) examined 134 patients presenting with mucosal reactions, where the most frequent oral manifestations were cheilitis, peri-oral dermatitis, burning mouth, lichenoid reactions and orofacial granulomatosis. Patch testing showed several allergens in this group, including metals such as gold, cobalt, platinum, nickel and mercury. No specific association between any one metal and a specific clinical manifestation was found but mercury was not a significant factor contributing to the pathogenesis of oral lichenoid reactions.

When dental amalgam was removed in a subgroup of patients suspected of amalgam contact hypersensitivity lesions, considerable improvement was seen (Thornhill et al. 2003) Seventy percent of these patients also showed a positive skin patch test for amalgam or mercury. Total or partial replacement of amalgam fillings following a positive skin patch test reaction to ammoniated mercury, metallic mercury, or amalgam is followed by significant improvement, when the lesions are confined to areas in close contact with amalgam fillings. Even if there is no topographic relationship, improvement occurs in nearly all patch test-positive patients (Laeijendecker et al. 2004). If mercury is the allergen, the removal of the filling should lead to complete remission after about 3 months. A total of 51 patients who had oral lichenoid lesions suspected to be related to the dental restorations were investigated. Fifty three per cent (n= 27) of the patients had positive patch test reactions, 24 of them for one or more mercury compounds. Nine months after the removal of the fillings, 42% of the patients were completely healed. Improvement was found in 47% especially when lesions were in close contact with restorations (Issa et al. 2005). This possible adverse effect of dental amalgam is widely recognized and reflected in contemporary contra-indications for the use of this material.

Burning Mouth Syndrome can occasionally be associated with a change in the appearance of the clinically normal oral mucosa. In some case it may be associated with a strong allergy to mercury and a positive patch test supports the removal of the amalgam filling. Full recovery and complete remission of systemic dermatitis may occur after removal of a mercury-containing filling (Pigatto et al. 2004). Patch-test analysis for the determination of mercury allergies was carried out by Wong & Freeman (2003) on a group of 84 patients with reticulate, lacy, plaque-like or erosive oral lichenoid lesions. Thirty three (39%) of the patients had positive patch test findings. The amalgam fillings were removed for thirty of these, and an improvement was seen within 3 months in 28 of these (87%).

3.3.6.2. Systemic reactions

General

There are some epidemiological studies on the health effects of mercury released by dental amalgam fillings. The effects reported may affect the nervous and renal system, and also the immune, respiratory, cardiovascular, gastro-intestinal, haematological, and reproductive systems. Bates (2006) reviewed these studies and concluded that the available studies show little evidence of effects on general chronic disease incidence or mortality.

Reports of effects caused by amalgams have involved many diseases. A few data suggest that the mercury from amalgam reduces lymphocytes responses, compromising immune functions. As a consequence, amalgam has been implicated in the development of Alzheimer‘s disease and there is a long list of heterogeneous diseases that might be due to the accumulation of mercury in the body. However, for many of the claims, scientific investigations have tended to provide either refutation or evidence of a lack of correlation. There is usually little evidence of general chronic disease incidence or mortality associated with dental amalgams. In one New Zealand retrospective cohort study of 20.000 military personnel (84% males) followed up for 20 years, data on dental history was linked with national mortality, hospital discharge and cancer incidence databases. There was no association between dental amalgams and chronic fatigue syndrome or kidney diseases. The number of cases for investigation of Alzheimer’s or Parkinson‘s diseases was insufficient to draw any conclusion (Bates et al. 2004).

No link has been detected between mercury exposure and negative health effects with respect to dentist mortality, although the mercury blood level is higher in dentists than in a control population. The life span of dentists was shown to be three years greater than that for a control non-dentist group. The same type of effect was seen with many other parameters, indicating that the general health of dentists is good (McComb 1997).

In several situations, such as with Alzheimer’s and Parkinson’s diseases, there is no definitive answer concerning causation and caution has to be expressed, bearing in mind that this collection of diseases possibly associated with amalgam restorations bears little comparison with the known characteristics of the occupational toxicology of mercury.

The available evidence is discussed here in relation to specific organ systems.

Urinary system

A few studies have investigated the relation between amalgam and kidney function. Except for a small increase in N-acetyl-β-glucosaminidase, which is not considered to have any clinical significance, no parameters suggest that there is an association between amalgam fillings and kidney diseases. Evidence of renal disease was investigated among dentists, who are exposed to greater levels of mercury vapour than other populations, but no kidney dysfunction has been found. During on-site screening of dentists at annual American Dental Association meetings in 1985 and 1986, the mean urinary values were of mercury were 5.8- 7.6 µg /l , showing that dentists have a much higher mean urinary mercury, but there was no evidence that they exhibited any higher levels of morbidity, mortality and kidney dysfunctions (see for review: Dodes 2001). It is recognized that mercury does induce antinuclear antibodies and the induction of metal-associated autoimmunity in general, with some effects in the renal system (Bigazzi 1999).

Bellinger et al. (2006), in a comprehensive neurophysiological and urological analysis of 534 children followed for five years in a randomized clinical trial, comparing groups with amalgam restorations and alternative composite resins. There were no statistically significant differences between these two groups in renal glomerular function as measured by creatinine adjusted albumin levels.

The overall conclusion of the epidemiological studies suggests that there is no evidence that dental amalgam fillings affect kidney function in human.

Neurological System

Alzheimer's Disease

Inorganic mercury is a neurotoxin at high doses and it has therefore been suspected to play a role in the pathogenesis of neurodegenerative diseases such as Alzheimer's disease. Mercury vapour released by dental amalgam has been suspected of being one of the potential factors relating to this disease. However, when autopsies of subjects with and without Alzheimer's disease were carried out, no significant association of the disease with the number, the surface area or history of dental restorations was found. Retrospective cohort studies provide limited evidence of an association between amalgam and this disease (Bates et al. 2004). There was no significant difference in brain mercury levels between Alzheimer's disease and control subjects (Saxe et al. 1999).

Multiple Sclerosis

Although a few articles have concluded that there is some suggestion of a possible association between amalgam and multiple sclerosis, the evidence is inconclusive. A systematic review and meta-analysis suggests that there is a non-statistically significant difference in the risk of multiple sclerosis between individuals with and without amalgam restorations. However, the small number of subjects, inadequate exposure data, and inadequate control recruitment methods constitute limitations of the available studies. Without any knowledge on the size of the restoration, the surface area, the duration of the exposure, it is not possible to confirm or to rule out any link between amalgam and multiple sclerosis (Aminzadeh and Etminan 2007).

One case control comparison between 132 multiple sclerosis patients and 423 controls failed to demonstrate an association between the number of dental fillings, the duration of the exposure to dental amalgam and the condition (Casetta et al. 2001). However, in one further study a correlation was found between the number of amalgam restorations in the a multiple sclerosis group of 39 females compared to matched 62 controls, although it is impossible to establish any temporal relationship concerning cause and effect in such a situation; in other words it may not be possible to determine whether patients with such a neurological condition are more likely to need dental restorations because of difficulty with oral hygiene (McGrother et al. 1999). In another case-control study (Bangsi et al. 1998) a comparison was made between 143 multiple sclerosis patients and 128 controls, where neither the number nor the duration of exposure to amalgam fillings supported an increased risk of multiple sclerosis.

Parkinson's Disease

Parkinson's disease involves the aggregation of alpha-synuclein forming fibrils, the major constituent of intracellular protein inclusions (Lewy bodies and Lewy neurites) in dopaminergic neurons of the substantia nigra. Aluminium, copper, iron, cobalt and manganese are effective di- and trivalent metals that may be involved in this process; however mercury is also included as a risk factor. Even low concentrations of some metals can directly induce alpha-synuclein formation (Uversky et al. 2001). An analysis of 130 patients with confirmed disease versus matched controls support the view that the disease has a multifactorial etiology, involving genetic, environmental, trauma, and possibly other factors (Semchuk et al. 1993). Consequently, it is very difficult to establish any causal link with a putative agent such as dental amalgam. In one study, occupational mercury exposure was related to an eightfold increase in risk of Parkinson's disease (Schulte et al. 1996), but this is still a matter of debate and there is no scientifically sound report establishing a direct relation with dental fillings.

Paresthesia

Paresthesia is considered to be the most sensitive neurological effect, and is produced by blood mercury concentration in the range of 34 to 97µg/l. A deficit in neurocognitive functions may result from doses below those considered to be the threshold for general clinical effects. Accentuated postural tremor, impaired coordination, positive Romberg sign, and reduced distal sensation suggesting peripheral neuropathy have been reported especially among those occupationally exposed to mercury. Low-dose, long-term exposure to mercury vapour from dental amalgam has been suggested as a risk factor. However, Kingman et al. investigated the relation between amalgam exposure and neurological functions in a cohort of 2038 participants (Kingman et al. 2005). No significant trends between neurological signs (tremor, alternate motion rate, coordination, vibrotactile threshold deficit, proximal and distal strength and station) and the presence of dental amalgam were detected. Therefore, no link could be established between peripheral neuropathy and amalgam exposure.

Autism

Mercury and an infectious agent such as the measles virus may contribute to the immunopathogenesis of autism (Cohly and Panja 2005). Studies showing elevated brain specific antibodies support an autoimmune mechanism. A virus may initiate the process but subsequent activation of cytokines is the damaging factor associated with the disease. Environmental exposure to mercury is suggested to modulate immune homeostasis. These hypotheses have not yet been demonstrated, but their involvement in autism cannot be ruled out (Cohly and Panja 2005). Some data are related to the possible effects of the mercury-containing Thimerosal, included in certain vaccines to protect from bacterial and fungal contamination. One retrospective cohort study did not support the possibility that Thimerosal exposure causes neurodevelopmental disorders (Andrews et al. 2004). The systematic critical review of the articles published between 1966 and 2004 does not support any relationship between the mercury-containing vaccine and clinical findings (Parker et al. 2004). A report for the Food and Drug Administration by the Institute of Medicine (IOM 2004) confirms that no link has been yet established between vaccines, Thimerosal and autism. There is no evidence of a causal relationship between dental amalgam and autism.

Amyotrophic Lateral Sclerosis

There is no evidence for a relationship between Amyotrophic Lateral Sclerosis (ALS) and mercury. A retrospective case-control study was conducted on 66 ALS patients and 66 age- and sex-matched control patients. No association was found between heavy metal exposure and the pathogenesis of ALS (Gresham et al. 1986).

Psychological Conditions

During the past two decades, mercury and heavy metals have been claimed to be responsible for a series of mental health problems, with a variety of symptoms. Between 1978 and 2007, a total of 53 publications in international journals were published and listed in MedLine, with an increased tendency to take into account the psychological and psychiatric aspects of these patients. However, evidence is lacking for a causal link between mercury and human mental health problems or psychological conditions.

A series of self-assessed patients were referred to the Dental Biomaterials Adverse Reaction Unit in Bergen, Norway (Lygre et al. 2005). Patient's complaints were heterogeneous. Many individuals displayed multiple subjective symptoms associated with several organ systems. The most common were fatigue, muscle and joint pain, dizziness and headache. Intra-oral symptoms were related to burning sensations, taste disturbances and dry mouth. After removal of the mercury-containing fillings, a small decrease in the intensity of different symptoms was noted. Intra-oral symptoms were decreased and the decrease was statistically significant for taste disturbances ($p=0.001$),

dry mouth (p=0.034), and stiffness/paresthesia (p=0.05). However, the symptoms were still higher than in a reference group sampled from the general population in Norway.

A psychiatric diagnosis was established in 70% of the patients referred for self-reported complaints, which they had attributed to amalgam restorations; this compared to 14% in the control group. The prevailing symptoms were anxiety, asthenia and depression. Mercury levels were similar in the two groups, and far below the critical levels of mercury intoxication. No positive patch test was found in any of the two groups. As the number of fillings and the mercury level were similar in the two groups, the authors concluded that mercury was not the cause of the impaired health reported by the patients, and that the reported symptoms were parts of a broad spectrum of mental disorders (Bratel et al. 1997a,b).

The psychological/psychiatric, odontological and medical aspects of patients with symptoms attributed to the side effects of mercury-containing dental filings were studied in a total of 67 patients and 64 controls matched for age, sex, and residential area. The high prevalence of psychiatric disorders (89% in the patient group) compared to the control group (6%) seems to constitute the main characteristic of the patients. The clinic and medical data did not provide any explanation on the occurrence of the symptoms (Bagedahl-Strindlund et al. 1997).

General neuropsychological and neurophysiological functions

One epidemiologic study showed no evidence of deterioration of performance associated with amalgam exposure. The evaluation of relationships between amalgam fillings and any decrease of peripheral neurological function did not allow any correlation to be established. The mouths of 2038 US military personnel were examined, the number of oral fillings scored and neurological function assessed (Kingman et al. 2005). Consistent with other studies, no evidence of effects of amalgam fillings on neurological functions was found.

Another study (Factor-Litvak et al. 2003) was carried out on 550 adults, aged between 30 and 49 years. Urinary mercury was 1.7µg/gC (range 0.09-17.8), the mean number of amalgam surfaces was 10.6 (range 0-19). It was concluded that mercury exposure derived from dental amalgam was not associated with any detectable deficit in cognitive or fine motor functioning.

While many individuals consider that their neuropsychological conditions are related to exposure to dental amalgam the literature contains no credible supportive data

Psychological Development

Two randomized, controlled clinical trials have been carried out on the neuropsychological and renal effects of dental amalgam in children (Bellinger et al. 2006 and 2007, DeRouen et al. 2006). In the first study 534 children aged 6 to 10 years living in New England area (USA), were randomly assigned to receive dental restorations using either amalgam (n=267) or resin composites (n=267). They were examined after a 5-year period. No difference appeared in full-scale IQ. No difference was found in the general memory index. Over the 5-year period, a significantly higher mean urinary mercury level was noted, but no renal effect was observed (Bellinger et al. 2006). The latest publication from this group (Bellinger et al. 2006), concludes that the exposure to mercury from dental amalgam was not associated with any adverse neuropsychological effects over a five year period and that the use of dental amalgam is not associated with an increase in children's risk of experiencing neuropsychological dysfunction. Another randomized clinical trial with annual follow-up for 7 years was carried out on 507 children in Lisbon, Portugal. The children received either amalgam restorations (n=253) or resin composites (n=254). The creatinine-adjusted urinary mercury levels were 1.8µg/g in the amalgam group, and 1.9µg/g in the composite group. No statistically significant difference was found in measures of memory, attention, visual function, or nerve conduction velocities over all the 7 years of follow-up. The authors noticed also that the

need for additional restorative treatment was approximately 50% higher in the composite group. These data suggest that exposure to dental amalgam restorations within this age range has no effect on psychological development, with the superior performance of the amalgams compared to alternatives being noteworthy, although of course each procedure with a non-amalgam alternative would normally be less invasive.

As noted above, epidemiological evidence supports the view that low-level mercury exposure is not a cause of autism. Based on a recent meta-analysis, from all the published data, the risk of neurodevelopmental disabilities from low-level methylmercury exposure has not been established (Ng et al. 2007).

There is evidence of *in utero* exposure of mercury to the fetus, or in infancy through the breast milk transfer. The relationship between mercury exposure from dental filling placement during pregnancy and low birth weight risk was investigated on a cohort of 1117 women with low-birth weight infants (< 2.500 g) compared with 4468 women with infants weighting 2.500g or more. The study found no evidence that the mercury-containing dental fillings placed during pregnancy increased low-birth-weight risk (Hujoel et al. 2005).

Immune System

It has already been noted that mercury is able to induce autoimmunity in susceptible strains of rodents and so the question arises as to whether such effects are seen in humans with respect to amalgam related mercury exposure. In man a correlation between plasma mercury and IgE levels has not been demonstrated, while contradictory results have been seen with other immunoglobulins (Langworth et al. 1993, Queiroz et al. 1994, Herrström et al. 1994, 1997). No association was found between the number of fillings in individuals and Henoch-Schönlein purpura and acute glomerulonephritis, which are all autoimmune diseases. With respect to the reduced lymphocyte responses, Mackert et al. (1991) showed no indication that amalgam affects the human immune system. Epidemiologic studies have shown that occupational exposure to mercury does not usually result in autoimmunity.

Mercury does induce antinuclear antibodies, scleroderma-like diseases, lichen planus, or membranous nephropathy in some individuals. Immunogenetic and pharmacogenetic factors are responsible for the induction of metal-associated autoimmunity in general (Bigazzi 1999). In addition to estrogen replacement therapy, other factors including mercuric chloride are putative risk factors for the development of lupus, scleroderma, and Reynaud disease. Mercuric chloride causes complex glomerulonephritis and autoantibodies recognizing a nucleolar protein, fibrillarin. Antibodies directed against fibrillarin are higher in scleroderma patients. Urinary mercury excretion has been reported to be higher in scleroderma patients who are positive for antifibrillarin antibodies. However this level is still in the normal and unexposed ranges, and these patients never develop immune complex glomerulonephritis (Mayes 1999).

Another epidemiological study established that the effects of mercury occur at high doses which are above the levels to which humans would be exposed through fish consumption. The hypothesis was tested that mercury exposure does not cause autoimmune disease directly, but rather interacts with genetic predisposition, or with exposure to antigens or infection, and consequently exacerbates the disease, acting as a co-factor (Silbergeld et al. 2005).

As mentioned above, mercury like other metals is well known for its potency to induce allergic contact dermatitis (Garner 2004, Khamaysi et al. 2006). Indeed a high percentage of patients with localized mucosal reactions (oral lichen planus) shows a positive skin patch test for amalgam or mercury and removal of dental amalgam restorations can result in clinical improvement and even complete remission (see 3.3.6.1).

Reproductive system

Although reproductive effects have been addressed in several of the studies discussed in this Opinion, there is very little data available on this subject. There is no evidence of any association between amalgam restorations and either male of female fertility or obstetric parameters. One study that attempted to examine the question of fertility in detail failed to show any correlation between the mercury burden from amalgam restorations and male fertility disorders (Hanf et al. 1996). No evidence can be found for any relationship between amalgam restorations and birth defects.

Miscellaneous effects

The risk of coronary heart disease in man was studied in 470 cases of coronary heart disease (coronary and artery surgery, non fatal myocardial infarction, and fatal coronary heart disease). The mercury level was significantly correlated with fish consumption, and the level of mercury higher in dentists than in non-dentists. However, the mercury level was not associated with the risk of coronary heart disease (Yoshizawa et al. 2002). However, in a further study of a birth cohort, methylmercury exposure was associated with decreased sympathetic and parasympathetic modulation of the heart rate variability (Grandjean et al. 2004).

Long-term parenteral exposure to mercury may occur in patients with hypogammaglobulinaemia. The patients receive regular long-term replacement therapy with a concentrate of pooled human immunoglobulin G containing an organic mercury compound (Thiomersal) as a preservative. In 26 such patients, the urinary mercury level ranged from 4 to 734mg (mean 152mg) over treatment periods of 6 months to 17 years (mean 6.5 years). The urine concentration was raised in 73%, but without any correlation between urine mercury and the age of the patient, the IgG dose, or the duration of the treatment. No clinical evidence of toxicity was apparent (Haeney et al. 1979).

At the present time we may conclude that there is no epidemiological evidence to support the contention that mercury released by dental amalgam fillings contributes to the etiology of systemic diseases.

3.3.7. Epidemiological and clinical evidence concerning adverse effects of dental amalgam in dental personnel

As with individuals with amalgam restorations, adverse effects of mercury exposure in dental personnel have been the subject of numerous investigations (Hörsted-Bindslev 2004). These investigations have focussed on general reactions to chronic low-level exposure to mercury and atypical mercury body burden.

Jones et al. (2007) reported possible residual adverse effects from occupational mercury exposure in dentistry, Thirty years ago, the all-women exposed group worked with both silver and copper amalgam filling material without protective gloves or a ventilation system, resulting in chronic mercury exposure. The aim of the study was to test the null hypothesis in a survey of general and reproductive health, and a battery of nine neurobehavioral tests. The population was the 115 graduates of one school for dental nurses from 1968 to 1971. The sample was 43 mercury-exposed women and 32 matched controls. Statistical comparisons revealed that the two groups were equivalent on cognitive tasks and four of the six mood subscales. Significant between-group differences were found in current health symptom experience and reproductive health, especially early hysterectomy experience.

Concerning neurobehavioral studies, the review of Hörsted-Bindslev (2004) determined that it was justified to conclude that a risk of subtle neurotoxic changes may occur in dental personnel, who show a urine concentration of mercury below that which is seen when operating within the accepted threshold limit. However, they stressed that other

factors such as the daily exposure to high frequency vibrations (Åkesson et al. 1995) and stress may be equally important for the subtle behavioural changes. Also none of the studies referred to had shown the dental personnel to suffer the classical signs of mercury intoxication. This conclusion is mirrored by others: for example the principal conclusion of Ritchie et al. (2002) indicated that although differences in health and cognitive functioning between dentists and controls could be found, these differences could not be directly attributed to their exposure to mercury. They further recommended that environmental monitoring of dental surgeries should be regularly conducted to ensure that dental personnel were not exposed to mercury concentrations above the occupational exposure standard. The need for such measures will diminish with further reductions in the use of dental amalgam and fewer amalgam restorations being removed in everyday clinical practice. The possible exception may be dental personnel with a brain-derived neutrotrophic factor (BDNF) polymorphism which may be associated with abnormal intracellular trafficking in hippocampal neurons which, in turn, may be associated with episodic memory impairment, as described by Echeverria et al. (2005).

Non-neurological adverse effects of occupational exposure to mercury have been claimed to be many and varied, in a similar fashion to those alleged to occur in patients. Of particular concern to dental personnel have been the possible reproductive effects of occupational exposure to mercury. In contrast to the work of Rowland et al. (1994) which reported that chair-side assistants with a high occupational exposure to mercury were less fertile than unexposed controls, a substantial study in Norway by Dahl et al. (1999) found no difference in fertility between high school teachers and dental surgeons, of whom one-third placed more than 50 restorations of dental amalgam a week. Work by Lindbohm et al. (2007) found a slightly increased risk of miscarriage amongst "dental workers" with occupational exposure to dental amalgam, but no pattern of dose-response was found. Lindbohm et al. (2007) concluded that no strong association or clear dose-response relationship could be observed between occupational exposure to chemical agents or restorative materials (including dental amalgam) and the risk of miscarriage amongst dental personnel. It was acknowledged, however, that the possibility of a slightly increased risk of miscarriage among exposed workers could not be excluded. Concerning cytogenetic damage in dentists exposed to mercury, Atesagaoglu et al. (2006) found that examination of leukocytes from dentists exposed to mercury vapour below concentrations of 0.1mg/m^3 failed to reveal cytogenetic damage.

3.3.8. Life-cycle of mercury in relation to dental amalgam

This Opinion is concerned with the possible direct effects on human health arising from the use of amalgams, relating both to patients and dental personnel. There is an obvious life cycle for the mercury used in these amalgams. This starts with the opening of a packaged amalgam product in the dental clinic, followed by its clinical handling during placement and possible subsequent manipulation or removal, the possible excretion or exhalation of mercury from recipients throughout their lifetime, and culminates with the disposal of the body. Implicit in this life cycle is the exposure of the environment in general and the possibility of indirect effects on human health in general. The detailed discussion of these life cycle factors and environmental effects is outside the scope of this Opinion. It is noted, however, that amalgam waste management, including the disposal of packaging materials and surplus amalgam is take seriously in the dental profession with respect to dental clinics and offices (Jokstad and Fan 2006) and detailed studies have recently been performed on the mercury generation from dental waste amalgam and its potential for both recycling and environmental exposure (Drummond et al. 2003). With respect to disposal of amalgam-containing bodies, no significant information can be found about contamination at burial sites, but it is known that cremation process will yield mercury emissions (Santarsiero et al. 2006). These have been estimated to range from 0.036 to 2.140 g mercury per corpse, with mercury concentrations ranging from 0.005 to 0.300 mg/m^3.

3.3.9. Experience with non mercury-based fillings/amalgams

Mercury is not the only element that is liquid at room temperature and some others have also been considered for use in dentistry. As reported by Hero and Okabe (1994), gallium has been in use, in limited amounts, since 1956, but they did note problems with corrosion resistance and overall biocompatibility. Dunne et al. (2005) have recently published a longitudinal controlled clinical study of a commercially available gallium based restorative material and found the clinical performance so grossly inferior to a control amalgam that its continued clinical use could not be justified. Indium has also been considered, but mostly as an adjunct to mercury, possibly replacing up to 10% of the mercury, but there is little evidence about either performance or safety (Johnson et al. 1992) and its use is not considered significant.

3.3.10. General Observations on Amalgam Efficacy

The efficacy, longevity and general performance of amalgam restorations has been assessed on many occasions in the past, and it is not necessary to review these studies here. Whatever the material chosen, direct restorations may fail, primarily through secondary caries, fracture of the restoration or tooth, marginal deficiencies or wear. The rates at which these failures occur are difficult to compare since they will vary with clinical technique and patient characteristics, and since there have been improvements to the quality of all materials over time. It remains the view, however, that from mechanical functionality and longevity perspectives and resistance to secondary caries, possibly through anti-bacterial activity, amalgam will outlast alternative materials under many circumstances (Mitchell RJ et al. 2007). From such perspectives, it may still be the material of choice with many dental practitioners for large restorations and the replacement of large restorations. It is with respect to their aesthetics and non-adhesive character, which means that larger cavities have to be prepared, often with excessive tooth tissue removal, that amalgams may be seen to be inferior to the alternatives, and it is this, and not overall longevity, that is driving a change to these alternatives.

3.3.11. Conclusions on Dental Amalgam

We emphasise that dental amalgam remains an effective restorative material and, from the several perspectives of performance and economics, may be considered the material of choice for some restorations in posterior teeth. However, because dental amalgam is not tooth-coloured nor does it adhere to remaining tooth tissues, its use has been decreasing in recent years and tooth-coloured filling materials have become increasingly more popular, consistent with the general trend towards more minimal intervention techniques in dentistry. There has been for some years a move towards non-amalgam, adhesive, tooth coloured restorations. This trend shows some variations within and between countries, and is emphasized by the significant reduction of training in the placement of dental amalgam restorations and the corresponding increase in training in the use of amalgam alternatives in a growing number of dental schools. We anticipate there to be a continued and sustained reduction in the use of dental amalgam in oral health care provision across the European Union, the rate of which is dependant on trends in dental education towards the increasing use of alternative materials in place of amalgam and the possible reduced availability of mercury products in general.

It is recognized that mercury which is the major metallic element used in dental amalgam, does constitute a toxicological hazard in general, with reasonably well defined characteristics for the major forms of exposure. It is accepted that the reduction in use of mercury in human activity would be beneficial, both for the general decrease in human exposure and from environmental considerations.

However, with respect to the debate about the possibility of causal relationships between the use of mercury containing amalgam and a wide variety of adverse systemic health effects and taking into account many studies and investigations into this putative causal link, there is no unequivocal evidence to support this possibility. These studies have

included assessments in children and in pregnant and lactating women. It is generally concluded that no increased risks on adverse systemic effects exist and we do not consider that the current use of dental amalgam poses a risk of systemic disease. It is recognized that some local adverse effects are occasionally seen with dental amalgam fillings, but the incidence is low and normally readily managed. It is also recognised that there have been reports of reactions to dental amalgam, which are not supported by scientific evidence, but indicate that very occasionally an individual may have unexplained atypical physical or other reactions attributed to mercury.

The main exposure to mercury in individuals with amalgam restorations occurs during placement or removal of the fillings. The transient mercury release during placement and removal will result in exposure to the patients and also to the dental personnel. It should be noted that the removal of amalgam restorations will result in an acute relatively high exposure of the individual patient to mercury, compared to leaving the amalgam filling intact. We find no evidence of clinical justification to remove clinically satisfactory amalgam restorations with the exception of those patients which are suspected to have allergic reactions and positive patch tests.

3.4. Alternatives

3.4.1. Classification of alternatives according to chemical composition

Increasing use is made of tooth-coloured materials in restorative dentistry. Currently, most attention is focused on direct restorative materials, such as composites, glass ionomer cement, compomers, giomers and sealants, and less on indirect materials, such as dental porcelain. The reason is that the use of indirect materials is costly and time consuming (in terms of procedure) even though these materials show excellent biocompatibility properties and durability, particularly a high resistance to wear and distortion.

A composite is generally defined as a material composed of two or more distinct phases (O'Brien 2002). Dental composites consist of a polymerisable resin base containing a ceramic filler. They may be classified in a number of ways, the normal method being based on the size, distribution, and volume percentage of the ceramic particles. With respect to their size, this classification yields the so-called macrofill, midifill, minifill, microfill and nanofill composites. Macrofill composites contain ceramic particles ranging in size form 10-100 μm, midifill in the range from 1-10 μm, minifill in the range from 0.1-1 μm, microfill in the range from 0.01-1 μm and nanofill in the range from 0.005-0.01 μm. Hybrid composites contain a mix of two particles size fraction of fillers, e.g. midi-hybrids consist of mix of microfillers and midifillers, mini-hybrids or micro-hybrids consist of a mix of microfillers and minifillers and nanohybrids consist of a mix of nanofillers and minifillers.

Filler loading varies significantly between the different composite materials. For example in a macrofill and hybrid composite, the filler material occupies 50-80% of the composite by weight, while in a microfill composite the filler loading is limited to about 35-50% by weight.

Currently, almost all composites are supplied as a pre-packed single-paste system, the curing of the resins occurring by light activation. Different types of commercially available curing units have different light intensities and utilise different light sources. Light-curing units use halogen-based, light-emitting diode (LED), plasma-arc, or laser technology. The energy levels range from 300 to more than 3,000 milliwatts/cm^2.

Glass ionomer cements were introduced in 1972 by Wilson and Kent (1972) and may be considered as a combination of silicate and polyacrylate cement system. Glass ionomer cements bind to dental hard tissues. Polyalkenoate chains enter the molecular surface of dental apatite, replacing phosphate ions, which leads to the development of an ion-enriched layer of cement that is firmly attached to the tooth (Wilson et al. 1983). In

addition to the original concept of glass ionomer cement, certain resin modified cements are now used in order to improve functionality.

Compomers were introduced in the 1990's and combine some of the benefits of composites and glass-ionomer cements. However, compomers do not bond to hard dental tissue. Giomers have been recently introduced and feature the hybridization of glass-ionomer and composite resins. They contain an adhesive promoting monomer and a bonding polymer catalyst, which allow bonding to hard tooth tissues.

Sealants are flowable resins and high viscous glass ionomers that are applied to seal pits and fissures in permanent teeth in order to prevent the occurrence of caries.

3.4.2. Chemical characterisation of alternative materials

3.4.2.1. Composites

Dental composites are composed of a wide variety of components with different chemical composition (O'Brien 2002, Powers and Wataha 2007, Roeters and de Kloet 1998). There is inadequate data on the composition and leachables of these materials, which is sometimes reflected in the material safety data sheets (MSDS) (Henriks-Eckerman and Kanerva, 1997)

Filler material

The filler materials are of inorganic composition, such as silica glass (SiO_2), alumina glass (Al_2O_3), and combinations of glass and sodium fluoride. Silica glass is made of beach sand and ordinary glass, but also of crystalline quartz, pyrolytic silica and specially engineered aluminium silicates (e.g. barium, strontium or lithium aluminium silicate glass). Alumina glass is made of crystalline corundum, while sodium-calcium-alumina-fluorosilicate glass is an example of a combination glass. A combination glass has to be considered as an engineered mixture of various glasses, which can serve as a source of fluoride ions. The radiopacity of composites is obtained by the addition of barium, strontium, lithium or ytterbium fluoride (YF3) to the filler particles.

Matrix material

The matrix is of organic composition. A large group of different aromatic and diacrylate monomers and oligomers is used, such as bisphenol A-glycidylmethacrylate (Bis-GMA), ethoxylated bisphenol A-methacrylate (Bis-EMA), triethyleneglycoldimethacrylate (TEGDMA) and urethane dimethacrylate (UDMA).

Filler particle incorporation

Coating of the filler particles with silane coupling agents (such as trialkoxysilane) ensures covalent coupling between filler and resin matrix. The carbon-carbon bond on silane molecules binds to the filler particles as well as resin monomer during polymerization of the composite.

Composite curing

Chemical agents (self or auto-cure) or, most commonly, light energy (ultraviolet or visible light) ensures polymerization of dental composites. Dual curing, i.e. a combination of chemical and light curing is also possible. For most composite systems in current use, visible light polymerization at 470 ± 20 nm wavelength is used. Depending on the curing method, various polymerisation initiators and accelerators are required. Initiators for chemical curing are usually benzoyl peroxide and benzene sulphinic acid which initiate polymerisation in the presence of an aromatic tertiary amine. For light curing systems,

camphorquinone is normally used in conjunction with an aliphatic tertiary amine as accelerator.

Additional components

Inorganic oxides and organic compounds are pigments that are added to create a range of various composite shades.

Bonding to enamel and dentine

Bonding of the composite material to hard tooth tissues is achieved by use of a bonding system may that incorporates etchants, primers and resins. Chemical etching solutions, such as phosphoric acid, citric acid, and maleic acid are used to demineralise the tooth surface and increase the surface area. Subsequently, after rinsing and drying, a primer solution, composed of a low viscosity resin such as hydroxyethylmethacrylate may be applied to obtain optimal wetting of the surface for the bonding agent. In addition to water based primers, use is also made of acetone based primers, and primers without the addition of resins. Final bonding of the composite material is achieved by the application of a very thin resin layer. Classical bonding agents are composed of unfilled resin of similar composition as the resin matrix of the composite material. Newer bonding systems are composed of two components, one consisting of a resin and the other containing ethanol and a catalyst. Currently, there is a trend to simplify the bonding procedure by combining the etchant and primer and by supplying primer and bonding as one component.

3.4.2.2. Glass ionomer cements

In the original form, the powder component of these cements is a sodium-calcium-alumino-fluoro-silicate glass. The liquid component is composed of polyacrylic acid and tartaric acid. When the powder and liquid are mixed together, a three phase acid-base reaction occurs, involving calcium and aluminium ions leaching as the acid attacks the glass particles, hydrogel formation as the polyacrylic acid molecules crosslink, and polyalkenoate salt gelation as the polyalkenoate salt captures un-reacted glass.

In the resin modified cements, methacrylate monomers have been added to improve functionality with respect to higher strength and water resistance. The materials have been further modified by the addition of photo initiators so that light-curing can occur, but they maintain their ability to set by an acid-base reaction. The setting of resin modified glass ionomer cement is identical to the polymerization of composite resin. During this process, free radical species are generated.

3.4.2.3. Compomers

The main components of compomers are polymerisable dimethacrylate resins, such as urethane dimethacrylate and TCB, which is a reaction product of butane tetracarboxylic acid and hydroxyethylmethacrylate, and ion-leachable glass filler particles such as strontium fluorosilicate glass. The glass particles are partially silanised to achieve bonding with the resin matrix. The setting reaction is based on free radical polymerization using photoinitiators. During the setting reaction HEMA is released while fluoride release occurs after setting. Since compomers do not bind to enamel and dentine directly, a specific priming and bonding system has had to be developed, which includes the use of a tooth conditioner (34% phosphoric acid) and a light curing adhesive consisting of di- and trimethacrylate resins, functionalized amorphous silicon dioxide, dipentaerythritol penta acrylate monophosphate, photoinitiators, stabilizers, cetylamine hydrofluoride and acetone.

3.4.2.4. Giomers

Giomers are based on the technology of a reaction between fluoride containing glass and a liquid polyacid. The reacted glass particles are mixed with resin such as urethane dimethacrylate and hydroxyethylmethacrylate, and a catalyst to initiate polymerization. Bonding of the material is achieved through the use of self-etching primers that modify the smear layer and allow the penetration of the bonding agent into the dentine. The bonding agent releases fluoride. This group of materials may be used for restoration of small cavities, and also for pit and fissure sealing.

3.4.3. Toxicology of components of alternative materials

Clearly these alternative restorative materials are complex chemically, with many different components, setting reaction mechanisms and opportunities to interact with tissues of the individuals in whom they are placed. However, characteristics of exposure are very difficult to determine, bearing in mind that volumes of the materials used are very small, the residence time within the body of chemicals that take part in setting reactions is usually very short and the chemical and toxicological profiles of the set material are usually very different to those of the starting materials. In evaluating the possibilities for adverse effects arising from the clinical use of these materials, it is necessary to consider the evidence about the inherent toxicity of the chemicals used and the performance and behaviour of the restorations over time. Of interest to most investigations here have been the monomers used in polymerisation reactions, which may remain unreacted and therefore present in the set material, the acids used in various phases of the setting and etching processes and ions released from glasses. An extensive evaluation of the acute and chronic toxicity of materials used in various alternatives to dental amalgam was published by IARC (1999).

3.4.3.1. Short-term release of monomers during polymerisation

Unbound monomers and/or additives are eluted within the first hours of placement in the tooth cavity. The very nature of the polymerisation processes, that involve the absorption of light energy by the material, which will vary with depth within the restoration, and the subsequent conversion of monomer molecules into cross-linked macromolecules, inevitably means that some monomer molecules do not have the opportunity to take part because of diffusion limitations. The completeness of the polymerisation process is reflected by the degree of conversion. Between 15 and 50% of the methacrylate groups may remain un-reacted according to Ferracane (1994). Improvements in the material formulations has resulted in increasingly superior degrees of conversion in recent years and currently only 1.5 - 5% of groups should remain un-reacted. However, this is may be enough to contribute to major cytotoxic effects in vitro (Stanislawski et al. 1999). The effects may also be dependent on dentine permeability and residual dentine thickness (Bouillaguet et al. 1998) since dentine may absorb unbound monomers and therefore contributes to decrease the cytotoxicity of the material. This is not directly under the control of the dental surgeon although the formation of reactionary dentine may be stimulated by preparative steps. Dentine permeability may also be modified by calcium phosphate precipitation in the lumen of the tubules leading to sclerotic dentine formation. It has also been shown that the surface of composite resins exposed to oxygen during curing produces a non-polymerized surface layer rich in formaldehyde, which by itself is an additional factor of cell toxicity (Schmalz 1998).

Monomers have been identified in dental composites eluates by gas and liquid chromatography/mass spectrometry. A considerable concentration of the co-monomer triethyleneglycoldimethacrylate and minor concentrations of the basic monomers Bis-GMA and UDMA as well as the co-monomer HDDMA have been detected with these methods (Geurtsen 1998, Spahl et al. 1998). TEGDMA and the photostabiliser 2-hydro-4-

methoxybenzophenone (HMBP) are cytotoxic and inhibit cell growth (Geurtsen and Leyhausen 2001). The intracellular glutathione level may be decreased by 85% by TEGDMA (Stanislawski et al. 1999, Stanislawski et al 2000, Stanislawski et al 2003, Engelmann et al. 2001, Engelmann et al 2002).

An i*n vitro* evaluation of the cytotoxicity of 35 dental resin composite monomers and additives indicated moderate to severe cytotoxic effects (Geurtsen et al. 1998). The effects vary according to the material tested, but also they are strongly depending on the cells used for testing. For example, human periodontal ligament and pulp fibroblasts are more sensitive than 3T3 and gingival fibroblasts (Geurtsen et al. 1998). With the exception of a very few reports, there is a general consensus that resin-containing restorative materials are cytotoxic (Geurtsen et al 1998, Geurtsen 2000, Schmalz 1998), greater effects generally been seen at early intervals after preparation.

3.4.3.2. Leachable substances generated by erosion and degradation

Leachable components are released due to degradation or erosion over time, the leaching process being determined not only by the degradation process itself but also diffusivity through the material. Chemical degradation is caused by hydrolysis or enzymatic catalysis. Non-specific esterases, human saliva derived esterase and pseudocholinesterase may catalyze the biodegradation of composite resins (Geurtsen 2000, Jaffer et al. 2002, Finer et al. 2004). Incubated *in vitro* with cholesterol esterase, the composites may release 2,2-bis [4(2,3-hydroxypropoxy)-phenyl]propane (bis-HPPP) and TEGDMA for up to 32 days, the amount depending on the matrix/filler ratio (Shajii and Santerre, 1999).

It is also assumed that bonds in the pendant side chains of the macromolecule are attacked through the effect of thermal, mechanical and photochemical factors.

Water or other solvents may diffuse into the polymer, facilitating the release of degradation products, including oligomers and monomers. The leaching process is influenced by size and polarity and by hydrophilic and lipophilic characteristics of the released components (Geurtsen 1998). Softening of the Bis-GMA matrix allows the solvents to penetrate more easily and expand the polymer network, a process that facilitates the long-term diffusion of unbound monomers (Finer and Santerre 2004). Differences in the toxicity of monomers leached out in the short-term and long-term are not yet documented.

3.4.3.3. Release of ions

Many of the alternative materials release ions such as fluoride, strontium and aluminium ions. The fluoride is expected to be beneficial and reduce the development of secondary caries. Presumably, the fluoride content of toothpastes and nutriments reload the material so that the resins or resin modified glass ionomer cements do not become porous. Other ions are implicated in the colour of the restorative material, and these metal elements may interfere with the biocompatibility of the resin because they are implicated in the Fenton reaction producing reactive oxygen species that are cytotoxic. The concentration of fluoride and strontium is considered to be too low to produce cytotoxicity. In contrast, however, copper, aluminium and iron may be present in toxic concentrations. The cytotoxic cascade has been shown to be enhanced by metals such as aluminium and iron present in various amounts in some of these materials (Stanislawski et al. 1999, Stanislawski et al.2000, Stanislawski et al.2003).

3.4.3.4. Toxicity of composite resin monomers

Only limited toxicity data for the monomers used for in dental composite systems are available. Major differences in the degrees of cytotoxicity of various composite materials have been found (Schedle et al. 1998, Franz et al. 2003, Franz et al. 2007). Most tested

materials showed only mild cytotoxicity comparable to amalgam or less than amalgam but there were a few exceptions. Most of the available toxicity data have been generated in in-vitro systems that focus on genetic toxicity of the compounds in standard test systems such as the Ames-test, and on cytotoxicity in gingival fibroblasts. TEGDMA, UDMA and HEMA have all been shown to be positive in the COMET assay indicating induction of DNA-damage in mammalian cells. HEMA, BisGMA and TEGDMA also induced gene mutations in mammalian cells by a clastogenic mechanism.

The monomers also caused cytotoxicity in cultured cells with ED_{50} in the low millimolar to submillimolar concentrations (Kleinsasser et al. 2006, Schweikl et al. 2005, Schweikl and Schmalz 1996a, Schweikl and Schmalz 1997, Schweikl et al. 1998a, Schweikl et al. 1996b, Schweikl et al. 1998b, Schweikl et al. 2006). In an in vitro embryotoxicity screening study, BisGMA induced effects at low, non-cytotoxic concentrations suggesting a potential for embryotoxicity or teratogenicity (Schwengberg et al. 2005).

The limited data on these monomers in experimental animals include studies on absorption, distribution, metabolism and elimination (ADME) on HEMA and TEGDMA after oral application of radiolabelled compounds. A rapid absorption of these compounds from the gastrointestinal tract and rapid catabolism by physiological pathways to carbon dioxide, which is exhaled (Reichl et al. 2001a, Reichl et al. 2002a, Reichl et al. 2002b, Reichl et al. 2001b, Reichl et al. 2002c).

No direct data on toxic effects of resin monomers in animals are available from publicly accessible sources. However, since the materials used as a basis for resin generation are derivatives of methacrylic acids and glycidyl ethers, the well studied toxicology of methacrylate and its esters may be used as a basis for structure activity relationships to predict major toxicities.

Methylmethacrylate, as a relevant resin monomer, is rapidly absorbed after oral administration in experimental animals and is rapidly catabolised by physiological pathways to carbon dioxide. The major toxic effects of methylmethacrylate in animals are skin irritation and dermal sensitization. In repeated dose-inhalation studies, local effects on respiratory tissue were noted after methylmethacrylate inhalation. Neurotoxicity and liver toxicity were observed as systemic effects after inhalation of methylmethacrylate in rats and in mice to concentrations above 3000 ppm for 14 weeks. For developmental toxicity of methylmethacrylate a NOAEC > 2000 ppm was observed. Methylmethacrylate is also clastogenic at toxic concentrations (EU-RAR 2002).

A detailed overview of the toxicity of glycidyl ethers compounds is available (Gardiner et al. 1992), although it is based mainly on unpublished study reports. Skin irritation and sensitization were the major toxicities observed. In addition, positive effects in genetic toxicity testing were seen with many glycidyl ethers at comparatively high concentrations.

3.4.4. Exposure

As noted earlier there are very limited data on exposure levels to the components of alternative dental restorative materials. Unlike the situation with amalgam, there are no obvious markers for exposure. Moreover, there are significant limitations to the determination of these exposure levels. The molecules used in any setting reaction, whether that is a polymerisation or an acid – base reaction, are by definition chemically reactive with a potential to exert toxic effects in humans. However, the reaction involves a small amount of material and usually takes place very quickly, following which many of these molecules have been irreversibly changed into far less reactive species or trapped within a solid mass with very limited capacity to diffuse and leach out. It is therefore expected that there will be a low but detectable level of exposure to many of these molecules during placement of the restoration. This is followed by a very much reduced level, possibly an infinitesimally low level, during the lifetime of the restoration. It is difficult to see how such low levels could be measured in a clinical setting.

The monomers used in dental resin-based materials are volatile and it is usually possible to smell them in dental clinics. The exposure of dental personnel to airborne methacrylates was studied during the placing of composite resin restorations in six dental clinics in Finland by Henriks-Eckermann et al. (2001). Both area and personal sampling were performed, and special attention was paid to measurement of short-term emissions from the patient's mouth. The median concentration of HEMA was 0.004 mg/m^3 close to the dental nurse's work-desk and 0.003 mg/m^3 in the breathing zone of the nurse with a maximum concentration of 0.033 mg/m^3. Above the patient's mouth the concentration of 2-HEMA was about 0.01 mg/m^3 during both working stages, i.e., during application of adhesive and composite resins and during finishing and polishing of the fillings. Maximum concentrations of 3-5 times higher than median concentrations were also measured. TEGDMA was released into the air during the removal of old composite resin restorations (0.05 mg/m^3) but only to a minor extent during finishing and polishing procedures. The results showed that, except for short-term emissions from the patient's mouth, the exposure of dental personnel to methacrylates is very low. Measures to reduce exposure were discussed, as the airborne concentrations of methacrylates should be kept as low as possible in order to reduce the risk of hypersensitivity. Except for the data from this paper, there seems to be very limited information about the actual level of exposure to volatile monomers in a clinical situation.

Polymerised resin based materials contain various amounts of residual monomers and polymerisation additives that may leach from restorations. The release may remain on a high level for some days (Polydorou et al. 2007). In addition, as noted above, chemical, microbiological and wear impacts are observed over time, and occlusal or approximal degradation of composites restorations occurs (Groger et al. 2006, Söderholm 2003). Most information on the release of material components is based on laboratory models with solvents such as ethanol, water, saline, artificial saliva or culture media. Gas chromatography and mass spectrometry of the solutes from composites, compomers and resin based glass-ionomers have demonstrated the presence of a number of organic leachables such as monomers, co-monomers, initiators, stabilizers, decomposition products and contaminants Some of them have been identified as the low viscosity monomers EDGMA, TEGDMA and HEMA together with initiator and co-initiators such as hydroquinone, camphorquinone, and DMABEE and an ultraviolet absorber, Tinuvin P (Lygre et al. 1999, Michelsen et al. 2003). Attempts at quantification have shown that elution from different materials differs significantly (Michelsen et al. 2006) and the data are contradictory. Bis-GMA, Bis-EMA, UDMA and various additives have been shown to leach (Rogalewicz et al. 2006), although others have failed to demonstrate BisGMA and UDMA in aqueous extracts, even though TEGDMA-based composites released high amounts of monomers (Moharamzadeh et al. 2007).

It is reasonable to assume that similar leaching reactions take place in patients, depending on the composition of the material, the effectiveness of the polymerisation process and the chemical impact of the oral environment, although limited information is available on the concentration of components from amalgam alternatives in patient saliva or other body fluids. There are some exceptions, such as acrylic monomers from soft liners and phthalates from denture base materials (Lygre et al. 1993, Lygre 2002). In addition, bisphenol A has been indicated in leachables from composites and sealants (Olea et al. 1996, Sasaki et al. 2005).

3.4.5. Potential adverse effects in patients

On the basis of the above comments on the composition of the alternatives to amalgam, the possible exposure levels associated with their components and known in vitro data on their toxicity, a general assessment of potential adverse effects in patients may be made.

3.4.5.1. General

The components released from dental restorative materials comprise a long list of xenobiotic organic substances and metallic elements (Schmalz 2005, Wataha and

Schmalz 2005). The components are subject to oral mucosal, pulpal and gastrointestinal absorption, and, for aerosols, pulmonary absorption, the passive diffusion through cell membranes being guided by factors such as the concentration gradient, molecular size, polarity, lipophilicity, and hydrophilicity.

Toxic effects after inadvertent contact with chemicals associated with restorative dentistry may appear as acute soft tissue injuries among dental patients. Local chronic reactions of irritation, or of combined irritation and hypersensitivity, appear as lichenoid reactions of the gingiva or mucosa. It is generally accepted that the amount of potentially toxic substances absorbed from alternatives to amalgam is too small to cause systemic reactions by dose dependent mechanisms in target organs. However, this statement does not deny that adverse reactions may occur, elicited by minute quantities of released substances, including allergies and genotoxicity. Of these, only allergy has been confirmed among dental patients.

The cytotoxicity and genotoxicity of substances leached from resin based materials and metallic elements have been the subject of extensive studies using cell culture techniques and bacterial mutation test (Ames test). Substances such as TEGDMA and HEMA cause gene mutations in vitro. Studies on the intracellular biochemical mechanisms have clarified various effects such as cell membrane damage, inhibition of enzyme activities, protein or nucleic acid synthesis etc. (Schweikl et al. 2006). At present, the clinical relevance of these in vitro studies is uncertain.

The release of Bisphenol A from Bis-GMA based materials such as fissure sealants and composites into saliva has been of special interest because of its potential estrogenic effect (Joskow et al. 2006). The concentration of released Bis-GMA from certain types of sealants has been reported to be within the range at which estrogen receptor-mediated effects were seen in rodents (Schmalz et al. 1999). However, the release from resin based restoratives is much lower. The conversion of Bis-GMA to Bis-MA is minimal in resin based materials if pure base monomers are used (Arenholt-Bindslev and Kanerva 2005). However, the minute concentration in resin based amalgam alternatives is not considered to be a problem.

It must be noted that there are other alternatives to amalgams in addition to these resin and cement based materials. These primarily include gold alloys and ceramics used for indirect restorations. These, however, do not represent clinically relevant options for the treatment of the vast majority of teeth and are only used when direct restorations are contra-indicated. Although idiosyncratic responses may be encountered with most materials (Ahlgren et al. 2002), and there may be exposure even to gold from such restorations (Ahlgren et al. 2007), there are very few indications that such materials have the potential for adverse effects and they are not considered further in this Opinion.

3.4.5.2. Allergy

Potential allergens among amalgam alternatives

There is limited possibility to predict the allergenic potential for a foreign substance on the basis of chemical composition using Quantitative Structure-Activity Relationship (QSAR) analysis. However, experimental testing such as the Guinea Pig Maximisation Tests or the murine Local Lymph Node Assay, and empirical results after years of testing substances causing allergies, have given some leads: the strongest allergens are often low molecular weight, aromatic, lipid soluble substances, or otherwise chemically active substances that react with proteins. Metal and metal salts are also high ranking haptens. On this basis, monomers, cross-linking agents, chemicals associated with the polymerisation process, and degradation products, all associated with resin based materials, are important candidates for allergic responses among users of these alternatives, including dental patients and professionals. A short list of allergens relevant to resin based amalgam alternatives is presented in Table 3.

Although an allergic reaction may be provoked by haptens derived from dental materials, the sensitisation process may be caused by substances unrelated to dentistry. Plastics are met with in everyday life and in occupations such as construction work and printing. For anatomical reasons both the allergic sensitisation and the allergic response are more easily obtained on skin than in the oral tissues. Epidermal tests are therefore adequate also for observations of intraoral adverse effects. A positive patch test is an indication of a causal relationship between the substance and the suspected allergic reaction, but does not provide definitive evidence without other criteria of causality, which often cannot be performed for practical and ethical reasons.

Table 3 Some allergens in resin based amalgam alternatives (primers, bonding agents, composites, glass ionomers, resin modified glass-ionomers, compomers etc).

Methacrylate monomers
2-hydroxy ethyl methacrylate
Triethylene glycol dimethacrylate
Pyromelilitic acid dimethylmethacrylate
Bisphenol-A glycidyl methacrylate
Urethane dimethacrylate
Bis-phenol-A polyethylene glycol diether dimethacrylate
Ethylene glycol dimethacrylate (EGMDA)
Other substances
Benzoyl peroxide, camphoroquinone (initiators)
Tertiary aromatic amine (activator)
Methylhydroquinone (inhibitor)
2-hydroxy-4-methoxy benzophenones, (UV absorber)
2-(2-hydroxy-5 methylphenyl) benzotriazole (Tinuvin P)

3.4.5.3. The role of bacteria

The presence of bacteria located at the interface between composite materials and dental tissues may be important (Hansel et al. 1998). EGDMA and TEGDMA promote the proliferation of cariogenic microorganisms such as *Lactobacillus acidophilus* and *Streptococcus sobrinus*; TEGDMA stimulates the growth of *S mutans* and *S salivarius* in a pH dependent manner (Khalichi et al. 2004). This provides one explanation for caries that develops beneath restorations of resin-containing materials. In addition, bacterial exotoxins have harmful effects on pulp cells after diffusion throughout dentine tubules.

It is also important to note that effects on dental pulp associated with restorations may be caused by bacterial contamination rather than the materials themselves (Bergenholtz et al. 1982, Bergenholtz 2000). This is still a matter of controversy and a few reports still consider that the pulp reaction to adhesive systems is generally minimal (Murray et al. 2002, Murray et al. 2003). Improvements of resin-containing materials and bonding agents and techniques have reduced the significance of shrinkage and gaps at the interface, which may be less than 1µm (Hashimoto et al. 2004). However this is still a large gap for many microorganisms such as lactobacilli that are less than 0.1µm in diameter, and therefore the microbial parameter cannot be ignored.

3.4.6. Epidemiological and clinical evidence concerning adverse effects of alternatives in patients

3.4.6.1. Case reports

Several cases of confirmed allergic reactions caused by tooth coloured restorative materials have been published. For example, an early case report described a female patient who developed a rash and hives on her chest, arms and legs after treatment with a composite (Nathanson and Lockhart 1979). Patch testing indicated that Bis-GMA was the provoking agent, whereas the sensitisation might have taken place by contact with a cross-reacting epoxy product. Patch tests also indicated Bis-GMA in a case of peri-oral erythema and crusting of cheeks following the application of a bonding agent for composite and glass ionomer fillings (Carmichael et al. 1997). Moreover, stomatitis and peri-oral dermatitis was attributed to Bis-GMA in a filling material (Kanerva and Alanko 1998). Local lichenoid reactions similar to those described for amalgam, have also been attributed to composite fillings. In one case patch testing indicated EGDMA as the allergen (Auzeerie et al. 2002), other cases indicated formaldehyde derived from the resin (Lind 1988). Ulcerating gingivitis localised to composite fillings was explained as a delayed reaction to the UV-absorber Tinuvin P (Björkner and Niklasson 1979).

3.4.6.2. Reports from adverse reaction registry units

In the years 1999-2002 the Norwegian Dental Biomaterials Adverse Reaction Unit received an increasing number of reports of adverse reactions associated with composite materials, although these were still outnumbered by reactions to amalgam and other alloys (Lygre et al. 2003, Vamnes et al. 2004). Swedish data showed a similar tendency. Patch testing of referred patients demonstrated positive reactions to methacrylates and additives relevant to resin based materials, although the most frequent allergens were nickel, gold, cobalt, palladium, mercury, and chromium. A survey by the UK registry indicated that the number of adverse reactions caused by resin based materials, amalgam alternatives included, was about 14 % of the total number of patient reactions (Scott et al. 2004).

Since all dental materials pose a potential risk to patients and members of the dental team, the post-market monitoring of adverse reactions caused by dental materials should be considered essential. Van Noort et al. (2004) reviewed the current status of post-market monitoring of adverse reactions to dental materials and highlights some of the issues that arise in trying to establish an evidence base on the characteristics of adverse reactions to dental materials. Norway, Sweden and the UK have sought to monitor adverse reactions to dental materials systematically and proactively in an effort to add to the evidence base on the safety of dental materials. Their experience in undertaking post-market surveillance was combined. The Norwegian, Swedish and the UK projects had received 1268 reports over 11 years, 848 reports over 5.5 years and 1117 reports over 3 years, respectively, relating to adverse reactions seen or experienced by dental personnel and patients. There are no harmonized criteria for what can be classified as an adverse reaction related to dental materials. Under-reporting was a recognised problem and lack of awareness and lack of clarity as to what constitutes an adverse reaction may be contributory factors. A pro-active reporting system takes a considerable time to become established, but can generate a lot of potentially useful information. Van Noort et al. (2004) concluded that there is a need to raise the awareness among dental professionals of the potential for adverse reactions due to dental materials and to develop an internationally accepted system of data gathering that can produce the evidence that reflect the extent, severity and incidence of adverse reactions to dental materials.

3.4.6.3. Reports from dermatological units

A Finnish multicentre study based on dental screening allergens on 4000 patients concluded that methacrylates, particularly HEMA, were responsible for 2.8 % of

reactions, which were otherwise dominated by metal salts (Kanerva et al. 2001). A Swedish investigation showed positive patch tests to methacrylate allergens in 2.3 % of the patients (Goon et al.2006). The most common of these allergens was HEMA, followed by EDGMA, TEGDMA, and MMA. Simultaneous positive reactions were frequent. Only one patient reacted to Bis-GMA, whereas reactions to HEMA alone were seen in most patients. Data from Israel after testing of patients with oral manifestations such as cheilitis, burning mouth, lichenoids, and orofacial granulomatosis also ranked HEMA as the most frequent dental allergen after the metal salts (Khamaysi et al. 2006).

3.4.6.4. Questionnaire studies

A few attempts have been made to estimate the incidence of adverse effects of dental materials among dental patients. However, no studies have focussed specifically on alternatives to amalgam. After about 10 000 dental treatments, one fifth of which were composite restorations, 22 adverse reactions were observed, none of them being related to tooth coloured restorative materials. Thirty-one dentists, representing a collective practice time 387 years, recollected 70 cases of adverse effects, of which two were attributed to temporary resin based and denture base materials, and 5 to copper cement, but none to alternatives to amalgam (Kallus and Mjør 1991).

Other questionnaire studies have aimed at obtaining incidence rates of materials related side effects in dental specialty practices such as paedodontics, orthodontics, and prosthodontics. Data from paedodontics indicated one reaction in 2400 patients, but only a minimal part was attributed to alternatives to amalgam (Jacobsen et al. 1991). Orthodontics and prosthodontics do not regularly include the placement of restorative amalgam alternatives, but resin based materials of similar composition are used. In orthodontics, only one of 41 000 patients showed an intra-oral reaction to an orthodontic composite, but 9 others reacted to resin based removable appliances, retention appliances, activators, and polymeric brackets (Jacobsen and Hensten-Pettersen 2003). However, some of these appliances are often made by chemically polymerised methacrylates, containing relatively higher concentration of potentially allergenic residual monomers as compared to well-cured restorative composites. Questionnaire data from prosthodontics could be interpreted to indicate a reaction rate of one per 600 patients for resin-based prosthodontic materials (Hensten-Pettersen and Jacobsen 1991).

3.4.6.5. General Comments

Case reports and reports from dermatological units highlight the possibility of adverse effects related to identified dental materials. Information from these sources is helpful in a field where these events are infrequent. The adverse reaction registry units in some countries contribute data on the relative frequency of the different adverse reactions, including those to amalgam alternatives. However, since participation by dental personnel is voluntary, the amount of under-reporting of patient reactions is unknown. The existing epidemiological studies offer an impression of the different materials related adverse effects as perceived by dental personnel. However, none of these studies are well suited as a basis for estimation of the prevalence of reactions caused by specific allergens associated with amalgam alternatives or other materials.

In spite of these drawbacks, an attempt to rationalise the risk of materials related adverse effects in dentistry on the basis of published reports has appeared recently (Schedle et al. 2007). Large variations were found, ranging between 1:10 000 and 1:100 for dental patients. A recent FDI-report also points to the fact that the vast majority of patients have encountered no adverse reactions, but dentists were advised to be aware of the possibility of reactions to resin based materials (Fan and Meyer 2007). The importance of satisfactory curing of these materials was specifically underlined. It is assumed that the most frequent potential allergens associated with resin based amalgam alternatives are found in Table 3.

3.4.7. Epidemiological and clinical evidence concerning adverse effects of alternatives in dental personnel

The potential for adverse effects to alternative restorative materials amongst dental personnel is widely recognised (Hume and Gerzina 1996). Most of the evidence of adverse effects takes the form of case reports, findings from surveys (Örtengren 2000) and reports from national reporting systems (van Noort et al. 2004). Given the extent of the use of alternative restorative materials, hundred of millions of restorations annually, and the possibility that <7% of dental personnel may report skin symptoms when working (Örtengren 2000), it is surprising that the reported incidence of adverse effects to alternative restorative materials is low (van Noort et al. 2004). The prevalence of verified allergic contact dermatitis amongst dental personnel (<1%) is much lower than the prevalence of self-reported skin symptoms (<7%) (Örtengren 2000).

Most of the adverse reactions reported take the form of contact dermatitis, which in severe cases may be associated with paresthesia of the finger tips (Kanerva et al. 1998). Reactions around the eyes, generalised skin itching and bronchial problems have been reported, but these are rare (Hume and Gerzina 1996).

HEMA appears to be a common sensitizer, although a small minority of dental personnel may have positive patch-tests to BisGMA and/or TEGDMA (Kanerva et al. 2001). It is relevant that relatively low molecular weight resin monomers, including HEMA and TEGDMA take only a few minutes to diffuse through latex gloves of the type worn by dental personnel, while higher molecular weight monomers, such as BisGMA, take a little longer to pass through the relatively thin latex of treatment gloves (Jensen et al. 1991, Munksgaard 1992). These findings emphasise the importance of a "no-touch" technique when handling resin-based restorative materials, even when wearing gloves. This approach to the handling of resin-based restorative materials is highlighted in manufacturers' directions for use.

Regarding the lower incidence of allergic responses to resin-containing alternative restorative materials in patients relative to dental personnel, Kallus and Mjör (1991) and Hensten-Pettersen and Jacobsen (1991) suggest that this may be related to the fact that the principal exposure of dental personnel is to methacrylates as monomers during the handling of uncured materials. Adverse effects of alternative restorative materials in dental personnel may, as a consequence, be minimised by the avoidance of contact with, in particular, low molecular weight monomer during the handling and placement of uncured materials. The effects may be further reduced by the use of effective face protection, water cooling and suction, as appropriate, in all operative procedures involving both cured and uncured resin-based materials and associated systems.

Between 1995 and 1998, 174 dental personnel were referred as patients to the Department of Occupational and Environmental Dermatology, Stockholm (Wrangsjö et al. 2001). After clinical examination, 131 were patch tested with the Swedish standard series and 109 with a dental screening series. Furthermore, 137 were tested for IgE-mediated allergy to natural rubber latex. Hand eczema was diagnosed in 109/174 (63%), 73 (67%) being classified as irritant contact dermatitis and 36 (33%) as allergic. Further diagnoses included other eczemas, urticaria, rosacea, psoriasis, tinea pedis, bullous pemphigoid or no skin disease. 77/131 (59%) had positive reactions to substances in the standard series and 44/109 (40%) to substances exclusive to the dental series. 24/109 (22%) patients had positive reactions to (meth)acrylates, the majority with reactions to several test preparations. Reactions to HEMA, EGDMA and MMA were most frequent. Nine of the 24 were positive only to (meth)acrylates, the remaining 15 also had reactions to allergens in the standard series. Irritant hand dermatitis was the dominant diagnosis. Contact allergy to (meth)acrylate was seen in 22% of the patch tested patients, with reactions to 3 predominant test substances. In one third of these cases the (meth)acrylate allergy was seen together with atopy and/or further contact allergies.

Also less severe allergic skin reactions among dental personnel have been diagnosed as caused by methacrylates, secondary in frequency only to chemicals related to natural

rubber latex (Alanko et al. 2004). Hand dermatoses, together with eye-, nose-, and airways reactions are consistent findings among dental personnel, although the role played by amalgam alternatives is undecided (Sinclair and Thomson 2004, Andreasson et al. 2001).

The Finnish Register of Occupational Diseases diagnosed 24 cases of occupational asthma or rhinitis caused by methacrylates during the years 1990-98 .The incidence rate of occupational respiratory disease was considered greater than in the whole population (Piirilä et al. 2002)

Preventive actions such as change in hygiene factors, use of no-touch techniques when working with methacrylates, less use of latex and awareness of risk factors seems to keep the prevalence of skin and respiratory symptoms low among dental personnel (Schedle et al. 2007).

3.4.8. Potential adverse effects of ancillary items and equipment

3.4.8.1. Photopolymerisation energy sources

Light sources are used to activate photoinitiators, by absorption of photons, in order to initiate polymerisation in many restorative materials (Small 2001). The applied energy depends on the light source used. Photoinitiator activation occurs at specific wavelengths. The most common photoinitiator is camphoroquinone, the activity of which peaks between 470 and 480 nm. The main advantages of light-cured composites compared to chemically cured products are based on the fact that mixing of components in the clinic is not required, resulting principally in less porosity and increased strength.

Types of curing lamps

Dental curing systems use light sources such as quartz-tungsten-halogen lamps (QTH), light-emitting diodes (LEDs), xenon-plasma arcs and lasers. The lamps are discussed here in the conventional order of lowest to highest intensity, although this has changed recently since some of the LED lamps now claim to have much higher energy output than the QTH lamps.

LED dental curing lamps, using a solid-state, electronic process emit radiation only in the blue part of the visible spectrum, between 435 and 495 nm and do not require filters. The irradiance of 13 products measured in the 400 to 515 nm range varied from 454 - 1456 mW/cm^2 (Bruzell and Wellendorf 2007). Some LED lamps marketed in 2007 claim irradiance values up to 3000 mW/cm^2.

QTH lamps with halogen inside quartz bulbs generate light through the heating of a tungsten filament to high temperatures. A small percentage (less than 1 %) of the energy is given off as light, most of the energy being in the form of heat. A drawback of halogen bulbs is that the generation of heat causes a degradation of the components of the curing unit over time. The result can be a decline in the irradiance, which compromises the curing ability of the unit. The light is filtered to remove heat and all wavelengths except those in the violet-blue range (400-515 nm). The irradiance varies from 366 to 1360 mW/cm^2, depending on the product.

Plasma-arc lights are made up of two electrodes in a xenon-filled bulb. The plasma is heated to several thousand degrees Celsius and gives off light (less than 1 percent of the energy) and heat. The high intensity white light is filtered to remove heat and to allow blue light (400-500 nm) to be emitted.

Lasers can emit light at specific wavelengths as a result of the excitation of atoms of suitable gases/liquids/solids to specific energy levels. Argon lasers currently available emit at 488 nm and have the highest energy output of the dental curing units, up to 5 W. Lasers are reported to require less time to adequately polymerise composites although these units are large, expensive and not widely used.

Light-curing of composites

The dental curing lights initiate polymerization of resin-based dental restorative materials by transmission of light through a fibre optic tip into to the material. For maximum curing, a radiant energy influx of about 16 J/cm^2 is required for a 2 mm thick layer of resin. This can be delivered by a 40 second exposure from a lamp emitting 400 mW/cm^2 or by using higher intensity energy output and shorter exposure times. Curing depths equivalent to that of a 500 mW/cm^2 QTH lamp have been demonstrated using an exposure time of 10 seconds with certain PAC lamps and 5 seconds with an argon laser (Rawls and Esquivel-Upshaw 2003).

Hazards

The light intensity and energy output may be hazardous per se. The light emitted by curing lamps can cause retinal damage if a person looks directly at the beam. Laser light sources require the use of special protective glasses.

Exposure of the eyes

The eyes of the lamp operators are at risk from acute and cumulative effects, mainly due to back-reflection of the blue light. Exposure to intense visible light radiation sources in a dental clinic necessitates the use of eye protective filters to avoid blue-light photochemical retinal damage. Bruzell et al. (2007) measured the visible light transmittance of protective filters; nine of the 18 tested filters had adequate filtering capacity.

Exposure of the eyes of patients and professional persons with ocular diseases

Most manufacturers state in the instructions for use that the exposure to light from dental curing units should be avoided in persons who have undergone cataract surgery, with other cataract problems or who have other types of impaired eyesight.

Exposure of skin

The visible light wavelengths and intensity of the dental curing lights do not appear to cause damage to healthy skin. The quartz-halogen lamps may emit some radiation in the UV-region. Chadwick et al. (1994) assessed the level of UVA-I (340 to 400 nm) emitted from three commonly used QTH-radiation sources and assessed the level of protection afforded by six brands of surgical gloves. It was concluded that the risk of initiating adverse dermatological consequences as a result of exposure to UVA-I, is minimal in normal usage. Irradiation with a QTH dental curing light on human stratified epithelium in heterotransplanted skin on nude mice showed that 72 hours after exposure, there was epithelial hyperplasia and reduced reactivity for OKT6 cells. After 4 min of exposure OKT6 positive cells were completely absent from the epithelium after 72 hours. The results indicated that emission from dental light curing units can affect Langerhans cells and could thus modify the local immunological response (Bonding et al. 1987). There does not seem to be any scientific studies on the possibility of adverse reactions in the oral mucosa after exposure to high intensity visible blue light.

Exposure of teeth

The curing lamps with high energy output intensity may cause local thermal emission. Laboratory studies show temperature rises, at 3 mm distance from the light source, from 4.1°C to 12.9°C, and from 17.4°C to 46.4°C for LED and QTH lamps, respectively (Yap and Soh 2003). In vitro studies with thermocouples placed in pulp chambers of extracted teeth show a moderate rise in pulpal temperature. In a vital tooth this does not seem to be a problem, possibly due to the effects of the blood circulation. However, the recent introduction of the high-intensity LED-lights might change this situation.

Light as cofactor in photobiological reactions

Most manufacturers state in the instructions for use that dental curing lights should not be used in patients with a history of photobiological reactions – or who are currently on photosensitising medication, including 8-methoxypsoralen or dimethylchlorotetracycline. Phototoxic and photoallergic reactions are potential problems, but there does not seem to be any case reports on this issue. The dose or output from the high intensity lights are in the same range of what is used for dermatological skin testing of photobiological reactions. Phototoxic or photoallergic reactions have not been documented in the context of oral medicine. The possibility of photo-related reactions should be taken into account in evaluation of dermatological conditions in dental personnel.

Electromagnetic compatibility (LED, QTH)

The instructions for use for some QTH and LED lights warn that the devices must not be used in patients, or by users, with heart pacemaker implants, who have been advised to be cautious about their exposure to small electrical devices. A 59-year-old male with Parkinson's disease had stimulator electrodes implanted in the brain. During curing of composites with a LED curing unit the patient felt immediate headache which he associated with the use of the curing light. Although the cause-and-effect relationship was questionable, an incidence report was submitted to the Norwegian Board of Health (Vangstein 2003).

Cross-contamination

The routines for infection control procedures as written in the instructions for use for the dental curing light units vary greatly. Some have no recommendations, one states that it should be sterilized before using it the first time, many have elaborate descriptions for cleaning and disinfection procedures.

Ineffective treatment/inferior quality of restoration

Most of the dental curing lights have an integrated photometer to check that the energy output is sufficient for the intended use. Others recommend the use of a separate photometer or to use a device for checking that the depth of cure for the various composites is sufficient. The latter method checks both the quality of the light source and the quality of the composite material. This is an important aspect, since the resin-based materials have a limited shelf life. It is also an issue with some of the very light shades of tooth-coloured resin-based materials that use phenyl propanedione as photo-activator, which requires radiation in the lower part of the spectrum of lower wavelengths than does camphorquinone (absorption peak at about 390 nm).

Overall risk assessment

There are inherent problems in the assessment of adverse effects of light exposure from dental curing lamps. Spectral characteristics vary among the different products, tissues treat radiation differently and the repair mechanisms for photo-induced damage may mask any adverse effect.

The dental curing lights, when used according to the manufacturer's instructions and with proper eye protection, seem to be safe for use in most patients and users. However, the potential for adverse reactions to occur are definitely present and the manufacturer's cautionary statements about not using them in specific situations should be heeded (Bruzell Roll et al. 2004).

3.4.8.2. Glove use

The wearing of gloves, often of latex, but increasingly of non-latex alternatives, has become routine in the everyday dental practice. Although not advised, should alternative resin-based filling materials be handled during use, low molecular weight components

may quickly pass through the glove (Jensen et al. 1991, Munksgaard 1992) and will remain in contact with the moist skin of the clinician until the gloves are removed and the hands washed at the conclusion of the treatment. With practitioners who are sensitive to such constituents, or in the presence of skin conditions, cuts or abrasions, an adverse reaction may occur. Such reactions may be avoided by strict adherence to the no-touch techniques recommended by manufacturers of alternative restorative materials.

3.4.9. General Observations on Efficacy of Alternatives

The general observations on the efficacy of amalgam restorations (Section 3.3.10) may be reinforced here. Alternatives to amalgam have been in clinical use for well over 30 years. They have not only addressed the issues on the aesthetics of amalgams but have facilitated a radical change in the concepts of restorative dentistry through the introduction of more minimally invasive techniques and the associated retention of more tooth substance when treating caries. This has been achieved through the use of tooth coloured materials that are themselves adhesive to tooth substances or that can achieve adhesion through the use of intermediary agents. It is recognised that their use may be technique sensitive and that the procedures for their placement may take longer and therefore be more expensive. It is also true that they may be more susceptible to secondary caries and, in some situations, have less longevity than amalgams. In general therefore these tooth coloured alternatives offer an effective modality for the treatment of dental caries in most situations.

3.4.10. Conclusions on Alternatives

We note that the materials used as alternatives to dental amalgam for direct restorations are usually very complex chemically, and are not without certain clinical limitations or toxicological hazards. They frequently contain a variety of organic substances and they undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement. It should not be assumed that non-mercury containing alternatives are free from any concerns about adverse effects (Goldberg 2007).

With respect to those materials that incorporate polymerisable resins, it is known that some of the monomers involved in their intra-oral placement and polymerisation are highly cytotoxic to pulp and gingival cells in vitro and there is also evidence that some of them are mutagenic, although it is far from clear whether this has any clinical significance. Some of these substances are irritants when used by themselves in various situations and the occupational hazards associated with their use are similar to those hazards found in the printing and automotive industries. Allergies to a few of these substances have been reported, both in patients and in dental personnel. We note that the full chemical specification of these alternative restorative materials is not always divulged and it may be difficult to ascertain exactly what they contain. In the absence of data, it may not be possible to provide a scientifically sound statement on the safety of individual products. It is also noted, however, that there are very limited scientific data available concerning exposure of patients and dental personnel to these substances.

Nevertheless, these alternative materials have now been in clinical use for well over thirty years, and this use has revealed little evidence of clinically significant adverse events. The commercially available materials have either changed substantially or been improved considerably during this time, with reduced bioavailability of harmful components through improved polymerisation processes. It is recognised that many of the new forms of these alternative materials lack long-term clinical data and as such, need to be monitored for possible risks to patients and dental personnel.

As a separate issue, it should be borne in mind that these photo-polymerisable systems require activation and that the powerful light sources now used for this purpose may constitute an additional risk for adverse effects, both to patients and dental personnel. Eye protection is extremely important.

4. OPINION

We discuss here the general observations that constitute the scientific opinions concerning the safety of dental amalgams and alternative dental restorative materials and then provide answers to the questions posed in the mandate.

4.1. The scientific and clinical evidence

Dental amalgam remains an effective restorative material and, from the perspectives of longevity, the mechanical performance and economics, may be considered the material of choice for some restorations in posterior teeth, including the replacement therapy for existing amalgam fillings.

However, because dental amalgam is not tooth-coloured nor does it adhere to remaining tooth tissues, its use has been decreasing in recent years and tooth-coloured filling materials have become increasingly more popular. This is consistent with the significant trend towards more minimal intervention techniques in dentistry, especially those that involve materials with adhesive properties.

There is an increasing trend towards non-amalgam restorations, which shows some variations within and between countries, and is emphasized by the significant reduction of training in the placement of dental amalgam restorations and the corresponding increase in training in the use of amalgam alternatives in a growing number of dental schools in European countries.

Independent of risk management decisions, and of the economic considerations in restorative dentistry, a sustained reduction in the use of dental amalgam in oral health care provision is expected across the European Union, the rate of which is dependant on trends in dental education towards the increasing use of alternative materials in place of amalgam and the possible reduced availability of mercury products in general.

Mercury is the major metallic element used in dental amalgam. It is recognized that mercury in general does constitute a toxicological hazard, with reasonably well defined characteristics for the major forms of exposure, involving elemental mercury, organic and inorganic mercury compounds. It is accepted that the reduction in use of mercury in human activity would be beneficial, both for the decrease in indirect human exposure and environmental considerations.

For many decades, going back to the introduction of amalgam into clinical practice over 150 years ago, there has been a debate about the possibility of causal relationships between the use of mercury containing amalgam and a wide variety of adverse systemic health effects. In spite of many studies and investigations into this putative causal link, there is no unequivocal evidence to support this possibility.

It is recognized that some local adverse effects are occasionally seen with dental amalgam fillings, including allergic reactions and an association with clinical features characteristic of lichen planus, but the incidence is low and normally readily managed. There have been claims of causation with respect to a variety of systemic conditions, particularly neurological and psychological/psychiatric effects, including Alzheimer's, Parkinson Disease, Multiple Sclerosis and also kidney disease. However, several major epidemiological studies have failed to reveal such effects. These studies have included assessments in children and in pregnant and lactating women. It is generally concluded that no increased risks on adverse systemic effects exist, and indeed the most recent studies have failed to find any association between the use of amalgam and neuropsychological development in children. We do not therefore consider that the current use of dental amalgam poses a risk of systemic disease.

The main exposure to mercury in individuals with amalgam restorations occurs during placement or removal of the fillings. Exposure does occur through the lifetime of a restoration, but the rates of mercury release are extremely low. The transient mercury release during placement and removal will result in exposure to the patients and also to

the dental personnel. However, this may be minimized by the use of appropriate clinical techniques. In particular it should be noted that the removal of amalgam restorations will increase the exposure of the individual patient to relatively high levels of mercury compared to leaving the amalgam filling intact. Although there is the possibility of some alleviation of subjective symptoms such as burning or dry mouth and taste disturbance, we find no evidence of clinical justification to remove clinically satisfactory amalgam restorations with the exception of those patients which are suspected to have allergic reactions and positive patch tests.

The use of dental amalgam results in environmental exposure to mercury, primarily through its release during amalgam placement and removal, and the handling and disposal of amalgam waste products in general. Improvements in the treatment of waste water from dental clinics and amalgam waste has generally reduced this exposure. A further source of environmental exposure occurs through the burial or cremation of individuals with dental amalgam fillings. It should be noted that a significant increase in amalgam usage occurred between 1950 and 1990 that may result in a rise in environmental exposure over the next few decades as these individuals die.

The general reduction in the use of dental amalgam in clinical practice has been coincident with an increasing use of alternative restorative materials, usually referred to as tooth-coloured materials, principally composites, cements and their hybrids. We note that these materials, which may be very complex chemically, are not without certain clinical limitations and toxicological hazards. They frequently contain a variety of organic substances and they undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement.

It should not be assumed that non-mercury containing alternatives are free from any concerns about adverse effects. With respect to dental composite restorative materials and hybrid systems that incorporate polymerisable resins, it is known that some of the monomers involved in their intra-oral placement and polymerisation are highly cytotoxic to pulp and gingival cells in vitro. There is clear evidence that some of these substances are mutagenic in vitro although it is far from clear whether this has any clinical significance. Some of these substances are irritants when used by themselves in various situations and the occupational hazards associated with their use are similar to those hazards found in the printing and automotive industries. Allergies to a few of these substances have been reported, both in patients and in dental personnel.

It is noted that there are very limited scientific data available concerning exposure of patients and dental personnel to those substances that are used in alternative restorative materials. It is recognised that such data are very difficult to obtain.

These alternative materials have now been in clinical use for well over thirty years, initially in anterior teeth and more recently also for restorations in posterior teeth. This use has revealed little evidence of clinically significant adverse events, even taking into account the fact that the quality of evidence concerning clinical outcomes is limited, with a reliance on case reports. It is also important to note that the commercially available materials have either changed substantially or been improved considerably during this time, with reduced bioavailability of harmful components through improved polymerisation processes.

As a separate issue, it should be borne in mind that these photo-polymerisable systems require activation and that the powerful light sources now used for this purpose may constitute an additional risk for adverse effects, both to patients and dental personnel. Eye protection is extremely important.

We note that the full chemical specification of these alternative restorative materials is not always divulged and it may be difficult to ascertain exactly what they contain. As a result, there is limited toxicological data publicly available for these materials. All dental restorative materials are defined as medical devices according to EU-Directive 93/42/EEC. They are surgically invasive medical devices intended for long-term use which according to rule 8 defines them as class 2b medical devices. However, the

directive has a derogation clause which states that when such medical devices are used in teeth they will be in class 2a. As such when regulatory approval is sought from a notified body it is not necessary to reveal a design dossier including a risk analysis and therefore the chemical specification does not have to be revealed. In view of the lack of information on the toxicity of the constituents of the alternatives and relevant exposure data it is not possible to provide a scientifically sound statement on the safety of these materials.

As a general principle, the relative risks and benefits of using dental amalgam or the various alternatives should be explained to patients to assist them to make informed decisions. This may have implications concerning the provision of product information. In view of the controversial nature of this subject, which has existed for very many years, it would also be beneficial for the community in general to be better informed of the recognized benefits and risks.

It is noted that indirect restorative techniques, involving the use of gold alloys and ceramics may also be used when direct restorations are contra-indicated. Their use, which is both time-consuming and expensive, has remained at a comparatively low level in recent years. This use is not seen as a health concern.

4.2. Human Safety of Dental Amalgam

4.2.1. Is there scientific evidence that supports a link between amalgam and allergic reactions, neurological disorders or other health disorders?

With respect to allergic reactions, many metals in close contact with the skin or mucosal surfaces can be the cause of contact dermatitis and equivalent conditions, and mercury is no exception. Oral lichen planus is sometimes associated with dental amalgam restorations, and one of the possible causes is allergy to constituents of dental amalgam. Whilst the incidence is low, it is recognised that many of the patients affected will show a positive skin patch test for either amalgam or mercury, and removal of restorations from patients with such conditions and positive patch tests often results in the alleviation of symptoms.

With respect to all other putative links between dental amalgam and health disorders in recipients of amalgam restorations, there is no scientific evidence to support such links. It is accepted that elemental mercury does have a specific toxicological profile and that the presence of amalgam restorations in an individual is likely to lead to raised blood and urine mercury levels. However these raised levels appear to be lower than those necessary to cause adverse effects in general, and the overwhelming clinical and epidemiological evidence does not support any causal link between mercury and any of the diseases that have been suggested as being associated with dental amalgam. This analysis has taken into account the possibilities of effects within the urinary, neurological, reproductive and immune systems and also associations with psychological conditions.

4.2.2. Is the use of dental amalgam safe for patients and users, i.e. dental health professionals? Are certain populations particularly at risk, e.g. pregnant women or children?

In the light of the above comments we conclude that dental amalgam is a safe material to use in restorative dentistry with respect to patients. Dental health is an extremely important component of general health care and the benefits of amalgam to individuals presenting with dental caries far outweigh the very low level of risk associated with allergies. With respect to populations at risk, there is a lack of information about effects in pregnant women. There is no evidence to suggest that pre-existing amalgam restorations pose any risk as far as the health of such women and the developing foetus

is concerned, and certainly any removal of restorations during this time would present a greater exposure to mercury. As with any other medical or pharmaceutical intervention, however, caution should be exercised when considering the placement of any dental restorative material in pregnant women. There is no evidence that infants or children are at risk of adverse effects arising from the use of dental amalgam, the most recent studies failing to find any association between the use of amalgam and neuropsychological development in children. We emphasise that we find no evidence of clinical justification to remove clinically satisfactory amalgam restorations on the grounds of patient safety, with the exception of those patients which have a positive patch test and local alterations of the oral mucosa or systemic allergic reactions. It should be noted that the removal of amalgam restorations will result in an acute relatively high exposure of the individual patient to mercury, compared to leaving the amalgam filling intact.

As far as dental personnel are concerned, it is recognised that they may be at greater risk with respect to mercury exposure than the general population. However, the incidence of reported adverse effects is very low and this possibility has decreased substantially with improvements to dental amalgam delivery and amalgam hygiene practices in general.

4.3. Human Safety of Alternatives

4.3.1. Is there scientific evidence that supports a link between alternative materials and allergic reactions, neurological disorders or other health disorders?

Far less information is available concerning exposure, toxicity and clinical outcomes for alternative materials compared with dental amalgam. The materials themselves are far more complex chemically and there are no simple surrogates as markers for either exposure or toxicity, equivalent to the mercury in amalgams.

There is some evidence that certain of the low molecular weight substances used in the preparation of these alternatives are associated with local allergic reactions, although the incidence is very low.

There is no evidence that there is any association between these materials as used clinically and any neurological disorders or any other health disorders.

4.3.2. Is the use of alternative dental restoration treatment safe for patients and dental health professionals? Are certain populations particularly at risk, e.g. pregnant women or children?

Although there are well recognised cytotoxicity and mutagenicity profiles for some of the chemical substances used in alternative materials, there is no evidence of any adverse clinical effects associated with such substances, apart from a very low incidence of allergies. Notwithstanding the observation that complete chemical compositions and risk analyses do not have to be revealed during the regulatory approval process so that some uncertainties may exist, these materials can be considered safe for patients. Since there is no evidence of any systemic bioavailability of these substances in the body, there would be no expectation that any particular population would be at risk. Again, as with any other medical or pharmaceutical intervention caution should be exercised when considering the placement of any dental restorative material in pregnant women. We do emphasise, however, that data is sparse and the continuing evolution of these materials suggests that caution should be exercised before new variations are introduced into the market.

As far as dental personnel are concerned, again there is evidence of limited numbers of cases of allergies to these materials. The pervasiveness of some of the low molecular weight species throughout dental clinics should be noted.

4.4. Oral Health and Safety - In view of the specific properties of dental amalgam and alternatives when used for dental restorative treatment, is dental health equally ensured by dental amalgam and alternatives?

It is difficult to make direct comparisons between dental amalgam and the alternative materials since they are not used in the same way. Dental health can be adequately ensured by both types of material. All the materials are considered safe to use and they are all associated with very low rates of local adverse effects with no evidence of systemic disease. There is, obviously, a greater level of aesthetic appeal with those alternatives that are tooth coloured compared to the metallic amalgam. Furthermore, the use of these alternatives allows the use of minimally interventional adhesive techniques.

In clinical practice, amalgams usually require more extensive cavity preparation, with the removal of more tooth substance, than is necessary with the adhesive alternative systems. The composite resins, cements and various hybrids are associated with more minimally invasive operative techniques, and this trend in dental practice is seen to be very important and valuable as far as patients are concerned, being consistent with the general principles of contemporary dentistry. It is true, nevertheless that on a historical basis amalgam restorations have in general been found to last longer, as restorations using alternatives have had a higher incidence of secondary caries. This may change with continuing improvements to the alternative materials. Patients in general have had needed more frequent interventions when treated with alternatives, but each intervention involves much less tooth removal than required for amalgam restorations. Although the alternative materials were originally introduced for the restoration of anterior teeth, primarily with small and moderate size initial lesions, in recent years their use has extended towards lesions of all sizes in posterior teeth. Dental amalgam may still be used for large lesions, and for the replacement of failed existing amalgam restorations, especially those associated with secondary caries. It is recognised that there are alternative indirect restorative materials, including gold alloys and ceramics, which are used in situations where direct restorative treatments are contra-indicated.

As a general principle, the relative risks and benefits of using dental amalgam or the various alternatives should be explained to patients to assist them to make informed decisions. This may have implications concerning the provision of product information. In view of the controversial nature of this subject, which has existed for very many years, it would also be beneficial for the community in general to be better informed of the recognized benefits and risks.

Finally, independent of risk management decisions and of the economic considerations in restorative dentistry, a reduction in the use of dental amalgam in oral health care provision is expected across the European Union. The rate at which this takes place is dependent on the trends in dental education towards the increasing use of alternative materials in place of amalgam, and the possible reduced availability of mercury products in general. This is a process that can be readily managed by the dental profession with no detriment to patient oral health. In view of the opinions expressed above, we see few if any advantages to carrying out further research on aspects of the safety of dental amalgam restorations. The lack of data on the toxicity, exposure and health effects of the alternative materials does imply, however, that more experimental, clinical and epidemiological research is required to guarantee patient safety in the future.

5. Comments received from the Public Consultation

Information about the public consultation has been broadly communicated to national authorities, international organisations, and other stakeholders. The relevant web site was opened for comments on 14 January 2008 and the deadline for submission was 22 February 2008. In total, 26 contributions were received from which 14 were from organisations and 12 from individuals. Of the organisations, 6 were non governmental, 4 public authorities and 4 other institutions, including dental associations.

In evaluating the responses from the consultation, submitted material has only been considered for revision of the opinion if

1. it is directly referring to the content of the report and relating to the issues that the report addresses,
2. it contains specific comments and suggestions on the scientific basis of the opinion,
3. it refers to peer-reviewed literature published in English, the working language of the SCENIHR and the working group,
4. it has the potential to add to the preliminary opinion of SCENIHR.

Each submission which meets these criteria has been carefully considered by the Working Group. Overall, many of the comments were of good quality. The scientific rationale of the report has been revised to take account of relevant comments. The literature has been updated with relevant publications. The Opinion, however, remained essentially unchanged, but was, in certain respects, clarified by the amendments to the scientific rationale.

Epidemiological studies on dental amalgam do not indicate that this material induces systemic adverse effects in patients, other than the recognised local irritation and allergic responses. However, it is recognised that very occasionally an individual may have unexplained atypical physical or other reactions attributed to mercury.

As indicated in the opinion, the information on adverse effects on alternatives is limited. During the public consultation, limited additional information became available regarding the alternative restorative materials.

6. MINORITY OPINION

none

7. LIST OF ABBREVIATIONS

ADME	Absorption, distribution, metabolism and elimination
ALS	Amyotrophic Lateral Sclerosis
ATSDR	Agency for Toxic Substances Disease Registry
BAT	Biologischer Arbeitsplatz Toleranzwert (biological tolerance value at the workplace)
BDNF	Brain derived neurotrophic factor
Bis-EMA	Ethoxylated bisphenol A-methacrylate
Bis-GMA	Bisphenol A - glycidylmethacrylate
Bis-HPPP	2,2-bis[4(2,3-hydroxypropoxy)-phenyl]propane
DMABEE	4-N,N-Dimethyl amino benzoic acid ethylester
DPMS	Dimercaptopropane sulfonate
EFSA	European Food Standards Agency
EGDMA	Ethyleneglycoldimethacrylate
EPA	Environmental Protection Agency
HDDMA	Hexanediol dimethacrylate
HEMA	Hydroxyethylmethacrylate
HMBP	2-Hydroxy-4-methoxybenzophenone
IRIS	Integrated Risk Information System
ISO	International Standards Organisation
LED	Light-emitting diode
MAK	Maximale Arbeitsplatz Konzentration (maximum concentration at the workplace
MMA	Methylmethacrylate
MRL	Minimal Risk Level
MS	Multiple Sclerosis
NOAEL	No Observable Adverse Effect Level
OES	Occupational Exposure Standard
PTWI	Provisional Tolerable Weekly Intake
QTH	Quartz – tungsten – halogen
TEGDMA	Triethyleneglycoldimethacrylate
UBA	Umweltbundesamt (German Federal Environment Agency)
UDMA	Urethane dimethacrylate
UNEP	United Nations Environment Programme
WHO	World Health Organisation

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Scientific Committee on Health and Environmental Risks

SCHER

Opinion on the environmental risks and indirect health effects of mercury from dental amalgam (update 2014)

SCHER adopted this opinion by written procedure on 10 March 2014

About the Scientific Committees

Three independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to new or emerging issues which may pose an actual or potential threat.

They are: the Scientific Committee on Consumer Safety (SCCS), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and are made up of external experts.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Agency (EMA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCHER

Opinions on risks related to pollutants in the environmental media and other biological and physical factors or changing physical conditions which may have a negative impact on health and the environment, for example in relation to air quality, water, waste and soil, as well as on life cycle environmental assessment. It shall also address health and safety issues related to the toxicity and eco-toxicity of biocides.

It may also address questions relating to examination of the toxicity and eco-toxicity of chemical, biochemical and biological compounds whose use may have harmful consequences for human health and the environment. In addition, the Committee will address questions relating to the methodological aspect of the assessment of health and environmental risks of chemicals, including mixtures of chemicals, as necessary for providing sound and consistent advice in its own areas of competence as well as in order to contribute to the relevant issues in close cooperation with other European agencies.

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All Declarations of Working Group members and supporting experts are available at the following webpage:
http://ec.europa.eu/health/scientific_committees/environmental_risks/members_committee/index_en.htm

ABSTRACT

In the 2008 Opinion on the environmental risks and indirect health effects of mercury in dental amalgam the Scientific Committee on Health and Environmental Risks (SCHER) concluded that only a preliminary screening risk assessment was possible, based on existing knowledge at the time. As new evidence has become available, this has been evaluated to determine whether the risk assessment provided in 2008 opinion needs to be updated.

The concentration of mercury in surface water has been estimated considering three possible scenarios (worst, average and best case, as detailed in the main text). The Predicted Environmental Concentrations (PECs) calculated in the three scenarios have been compared with the Water Framework Directive (WFD) Environmental Quality Standards (Annual Average (AA) EQS and Maximum Allowable Concentration (MAC) EQS) that have been set for mercury. The comparison enables the conclusions stated below:

- best case scenario: the PEC is negligible in comparison to both EQS;
- average case scenario: the PEC is one order of magnitude below the AA EQS;
- worst case scenario: the PEC is substantially above both AA and MAC EQS.

Methylation in the aquatic ecosystem and mercury accumulation in fish have also been estimated. According to the three proposed scenarios and based on five hypothetical values for the methylation rate (between 0.0001 and 1 %), the following conclusions are derived:.

- best case scenario: all the calculated concentrations are far below the acceptable level in fish as well as the WFD threshold for secondary poisoning;
- average case scenario: all the calculated concentrations are far below the acceptable level in fish, however, the WFD proposed threshold for secondary poisoning is exceeded at methylation rates higher than 0.05%;
- worst case scenario: the acceptable level in fish is exceeded (or at least approached) at methylation rates higher than 0.1 %, while the WFD threshold for secondary poisoning is also exceeded at methylation rates higher than approximately 0.005%.

SCHER concludes that, in the worst case scenario, under extreme local conditions (maximal dentist density, maximal mercury use, absence of separator devices), a risk of secondary poisoning due to methylation cannot be excluded. These risks depend on the methylation rate of inorganic mercury which may differ with exposure conditions.

For the soil and air compartment a quantitative PEC cannot be estimated and an assessment of local risk is not possible.

Regarding the risk for human health due to environmental mercury in soil and air originating from dental amalgam use, it can be concluded that this emission fraction of Hg represents a very minor contribution to total human exposure from soil and through inhalation.

Regarding the contribution of amalgam use to the concentrations of methyl mercury in fish, any calculation is affected by a high degree of uncertainty and based on a number of assumptions. However, a screening assessment was undertaken using a provisional risk assessment for surface water based on five hypothetical values for the methylation rate in three possible scenarios (worst, average and best case). In the best and the average cases, the expected methyl mercury concentrations in fish related to contributions of dental amalgam uses are well below maximum tolerable content of methyl mercury in fish. In the worst case scenario, the values obtained with the two highest methylation rates exceeded the threshold. Thus, in the worst case, mitigation

measures are expected to be needed to reduce the risk. Further, the WFD's threshold for secondary poisoning is exceeded at methylation rates higher than 0.005 %. Therefore, compliance with the WFD threshold would contribute to the prevention of human health effects.

The information available on the Hg-free alternatives does not allow a sound risk assessment to be performed.

With regard to human health, SCHER is of the opinion that the conclusions of the 2008-opinion are still valid. For health effects due to alternative materials particularly the potential leakage of bisphenol A (Bis-DMA), SCHER recommends referring to the SCENIHR opinion on the use of bisphenol A in medical devices.

For the environment, considering the probably low level of emissions and the relatively low toxicity of the chemicals involved, it is reasonable to assume that the ecological risk is low. However, it is the opinion of the SCHER that, at present, there is no scientific evidence for supporting and endorsing these statements. Therefore, more research on alternative materials is recommended.

Keywords:

SCHER, scientific opinion, dental amalgam, mercury

Opinion to be cited as:

SCHER scientific opinion on the environmental risks and indirect health effects of mercury from dental amalgam (update 2014), 10 March 2014

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1. BACKGROUND

Dental amalgam and its substitutes are regulated under Council Directive 93/42/EEC[1] concerning medical devices, according to which they must comply with the essential requirements laid out in the directive, in particular in relation to the health and safety of patients.

Dental amalgam has been used for over 150 years for the treatment of dental cavities and is still used, in particular, for the treatment of large cavities due to its excellent mechanical properties and durability. Dental amalgam is a combination of alloy particles and mercury and contains about 50% of mercury in the elemental form. Overall, the use of alternative materials such as composite resins, glass ionomer cements, ceramics and gold alloys, is increasing, either due to their aesthetic properties or alleged health concerns in relation to the use of dental amalgam.

On 28 January 2005, the Commission adopted the Communication to the Council and the European Parliament on a Community Strategy Concerning Mercury[2]. The Strategy addresses most aspects of the mercury life cycle. Its key aim is to reduce mercury levels both in relation to human exposure and the environment. It identifies twenty priority actions to be undertaken, both within the EU and internationally. The Strategy was welcomed by Council Conclusions on 24 June 2005 as well as by a European Parliament Resolution on 14 March 2006. Pursuant to Action 6 of the Strategy, the use of dental amalgam should be evaluated with a view to considering whether additional regulatory measures are appropriate. The Commission services consulted two Scientific Committees on the use of dental amalgam, the Committee for Environmental and Health Risks (SCHER) and the Committee for Emerging and Newly Identified Health Risks (SCENIHR). The opinions[3,4] of both Committees were not conclusive regarding the appropriateness of additional regulatory measures to restrict the use of dental amalgam.

Concerning the environmental aspects, the SCHER opinion concluded that on the basis of the information available, it was not possible to "comprehensively assess the environmental risks and indirect health effects from use of dental amalgam in the Member States of the EU 25/27", and identified a number of gaps that need to be addressed.

In the 2005 communication, the Commission had already expressed its intention to undertake a review of the Mercury Strategy by the end of 2010. To this effect, the Commission requested an external contractor, Bio Intelligence Service, to prepare a study, examining the progress of its implementation, assessing the success of the policies and corresponding measures, and proposing additional actions, if needed. The report produced, "Review of the Community Strategy Concerning Mercury"[5], identified

Actions 4 and 6 of the Mercury Strategy, both linked to dental amalgam, as areas where substantial improvement could still be achieved.

The Commission issued a new Communication[6] to the European Parliament and the Council on the review of the Community Strategy Concerning Mercury on 7.12.2010. Given that some Member States have already substantially restricted the use of dental amalgam in their national health care systems and given that dental amalgam represents the second largest use of mercury in the EU, the Commission expressed its intention to further assess the use of mercury in dental amalgam with due consideration of all aspects of its lifecycle.

This assessment has been concluded under a contract with Bio Intelligence Service, including a stakeholder consultation in March 2012. The final report[7] focuses mainly on the environmental impacts of dental amalgam use and also seeks to address, to the extent possible, the gaps identified in the SCHER 2008 opinion.

There is an international dimension that needs to be considered too. In 2009 the Governing Council of the United Nations Environment Programme (UNEP) established an intergovernmental negotiating committee (INC) with the mandate to prepare a global legally binding instrument on mercury. The Committee started its work in 2010 and completed it, as planned, prior to the 27th regular session of the UNEP Governing Council in January 2013. The Commission represented the European Union in these negotiations and strived for a comprehensive multilateral environmental agreement. Dental amalgam is among the products to be regulated under the UNEP Convention on mercury, which the European Union signed in October 2013. The Convention foresees a number of measures to be taken by the Parties in relation to dental amalgam in order to phase down its use, such as:

(i) Setting national objectives aiming at dental caries prevention and health promotion, thereby minimizing the need for dental restoration;

(ii) Setting national objectives aiming at minimizing its use;

(iii) Promoting the use of cost-effective and clinically effective mercury-free alternatives for dental restoration;

(iv) Promoting research and development of quality mercury-free materials for dental restoration;

(v) Encouraging representative professional organizations and dental schools to educate and train dental professionals and students on the use of mercury-free dental restoration alternatives and on promoting best management practices;

(vi) Discouraging insurance policies, and programmes that favour dental amalgam use over mercury-free dental restoration;

(vii) Encouraging insurance policies and programmes that favour the use of quality alternatives to dental amalgam for dental restoration;

(viii) Restricting the use of dental amalgam to its encapsulated form;

(ix) Promoting the use of best environmental practices in dental facilities to reduce releases of mercury and mercury compounds to water and land

In light of the above, the Scientific Committee on Health and Environmental Risks (SCHER) is asked to update, if appropriate, the opinion adopted in 2008.

2. TERMS OF REFERENCE

Taking into consideration recent developments, the SCHER is requested to review and update, if appropriate, the scientific opinion adopted in May 2008 on "The environmental risks and indirect health effects of mercury in dental amalgam ".

In particular, the Scientific Committee is requested to consider the following questions:

- Are mercury releases caused by the use of dental amalgam a risk to the environment? The fate of mercury released from dental clinics as well as the fate of mercury released to air, water and soil from fillings placed in patients should be taken into account.

- Is it scientifically justified to conclude that mercury in dental amalgam could cause serious effects on human health due to mercury releases into the environment?

- Comparison of environmental risk caused by the use of mercury in dental amalgam and that of the use of alternatives without mercury.

3. Opinion

3.1. Introduction

In the 2008 SCHER Opinion on risks of mercury in dental amalgam a number of issues were raised leading to the conclusion stated below.

"… *a comprehensive EU wide assessment of the human health and environmental risks of the Hg used in dental amalgam is – as far as could be established – not available*".

In particular the lack of "*detailed quantitative information on the use and release pattern in all EU-27 countries, possible country-specific abatement measures, and differences in the fate of mercury due to regional-specific municipal wastewater treatment and sludge application practices*" was recognized.

Moreover, it was stated that the results of the use of the European Union System for the Evaluation of Substances (EUSES) model for calculating environmental concentrations of a metal must be taken with caution, EUSES being developed for organic chemicals.

Therefore, the SCHER concluded that only a preliminary screening risk assessment was possible on the basis of the available information.

The aim of the present opinion is to evaluate if, in light of the new information available, a more scientifically sound assessment on the environmental risks and indirect health effects of mercury in dental amalgam, at local, regional and continental scale, is possible.

3.2. First question

Are mercury releases caused by the use of dental amalgam a risk to the environment? The fate of mercury released from dental clinics as well as the fate of mercury released to air, water and soil from fillings placed in patients should be taken into account.

3.2.1. Exposure assessment

In the 2008 SCHER Opinion several studies were examined on a mass flow analysis of Hg in the environment assessing the consumption and release of mercury used in dental amalgam. That original information has been updated with the results of some recent studies. In particular:

- AMAP/UNEP, 2013
- E-PRTR (European Pollutant Release and Transfer Register) 2011
- BIO Intelligence Service report (BIO Intelligence Service, 2012)

In order to provide an idea of the relevance of large scale emissions of mercury (global, continental), a synthesis is given in Table 1.

From the literature available, it may be concluded that nowadays dental amalgams may represent one of the major intentional uses of Hg. Emissions from the use of mercury in dental amalgam fillings can occur during the preparation of the amalgams and their subsequent removal and disposal in wastes. They can also occur when human remains with amalgam fillings are cremated. A mass balance of mercury emissions, in air, water and soil, from dental amalgam has been proposed by Bio Intelligence Service (2012).

This type of mass balance contributes to the understanding of the magnitude and sources of mercury contamination caused by dental applications. However, it does not allow to quantatively assess the risks of Hg in amalgam, particularly if one considers that a non-

negligible risk from mercury in dental amalgam is likely to occur only at a local scale, close to relevant emission sites. (Bio Intelligence Service, 2012)

Table 1. Synthesis of the data on mercury emissions

Activity of Hg release	Amount	Reference
Worldwide release of Hg to the atmosphere from anthropogenic sources (year 2010)	1960 (1010 - 4070) tons	AMAP/UNEP, 2013
Worldwide release of Hg to the atmosphere from natural sources (year 2010)	825-1335 tons	AMAP/UNEP, 2013
Worldwide release of Hg to water from anthropogenic sources (year 2010)	185 (42.6 – 582) tons	AMAP/UNEP, 2013
Total Hg emissions to the atmosphere from intentional uses in Europe (year 2010)	141.6 (68.2 - 253.4) tons	AMAP/UNEP, 2013
Total Hg natural emissions to the atmosphere in Europe (27) (year 2010)	87.2 (44.5 - 226) tons	AMAP/UNEP, 2013
Hg releases to soil from anthropogenic sources in the USA (year 2000)	2700 tons	Cain et al. 2007
Hg releases to soil from dental amalgams in the USA (year 2000)	28 tons	Cain et al. 2007
Total EU-27 emissions in air of Hg from dental practices	19 tons/y	Biointell., 2012
Total EU-27 emissions in soil of Hg from dental practices	20 tons/y	Biointell., 2012
Total EU-27 emissions in water of Hg from dental practices	2 tons/y	Biointell., 2012

The quantification of mercury emissions from the use in dental amalgam fillings should take into account detailed information on specific issues, such as the density of dentists in a country, the specific amount of mercury used, the effectiveness of recovery through separation devices, etc.

Estimates have been reported for Canada (Richardson, 2000; Van Boom et al., 2003) and for the global scale (Pacyna et al, 2010). The latter report was prepared for the UNEP Governing Council. Collecting this amount of information for different European countries and situations in order to convert the mass balance analysis to an environmental concentration is impossible within the deadline proposed for this opinion. Too many site-specific factors influence the ultimate concentration of mercury originating from dental amalgam in WWTP receiving waters, to make the estimation of a single concentration feasible and/or realistic. However, considering the differences among EU-27 countries in terms of socio-economic and demographic conditions, presence of amalgam separators, WWTP facilities, etc., three possible extreme scenarios (worst, average and best case) may be developed in order to propose a range of possible environmental concentrations.

3.2.1.1. Concentration in surface water

Sufficient data are available for SCHER to perform an estimation of the concentration of mercury in the surface water compartment from the use of dental amalgam. Also in the SCHER Opinion only for this compartment an estimation of Hg water concentration was carried out (SCHER, 2008). SCHER has used the same calculation method as that used in 2008; several assumptions were replaced by new data that have become available. The current version of the calculation method has been added as an Annex 1 to this opinion. SCHER distinguished three scenarios to estimate the Hg concentration in surface water. Table 2 gives an overview of the 3 scenarios.

Table 2. Overview of assumptions used for estimating Hg surface water concentrations due to the emission of mercury used in dental amalgam.

	Worst case situation	Average case situation	Best case situation
Dentist discharge (g/dentist/y)	460*	160**	0.65*
Percentage of separators (%)	0 (in some countries no separation occurs)	75**	95 (estimated value since 100% can hardly be reached)
Efficiency of separator (%)	-	70**	95**
Number of dentists (N/10000 inhabitants)	12**	7**	3**
Average use of drinking water (L/d)	200***	200***	200***
Percentage in effluent water	10*	10*	10*
Dilution factor to surface water (-)	10***	10***	10***
Effluent concentration based on measurements (µg/L)	1*	0.05*	0.001*

* Richardson et al., 2011
** Bio Intelligence Service report, 2012
*** No change from 2008 (TGD 2003)

The meaning and the probability of occurrence of the three scenarios may be explained considering the range of variability of the three major factors affecting Hg emissions: the amount of Hg discharged per dentist, the percentage of installed separators and the number of dentists per inhabitants. For all these factors the actual range of variability has been taken from literature data. The three scenarios have been defined as described below.

For the worst case scenario, the less favourable end of the range of variability for all the three factors has been selected. This situation is possible at local level in some EU

countries or in some site-specific conditions. However, the probability of the presence of these three factors at the same time is difficult to quantify.

For the best case scenario, the more favourable end of the range of variability for all the three factors has been selected. As for the worst case, this situation is possible in some EU countries or in some site-specific conditions. Moreover, at least for the first two factors, it should represent the objective to be reached in the EU.

The average case scenario is based on realistic average values of the three factors. Though the probability of occurrence of this scenario in site-specific conditions cannot be quantified, it represents a realistic indication of the overall risk at EU level.

The results of the calculation are given in Table 3.

Table 3. Estimated Hg concentrations due to the emission of mercury used in dental amalgam and measured Hg effluent concentrations.

	Calculated in effluent (µg/L)	Measured in effluent* (µg/L)	Calculated Concentration in surface water after dilution** (µg/L)	
			From modelling	From measured data
Worst case scenario	1.2	1	0.12	0.1
Average case scenario	0.102	0.05	0.010	0.005
Best case scenario	3.6E-5	0.001	3.6E-6	0.0001

* Based on Richardson (2000).

** Assuming a dilution factor of 10

As Table 3 shows, the estimated Hg concentration due to the emission of mercury used in dental amalgam, including the calculated levels extrapolated from measured levels in the effluent match quite well, except for the best case scenario. This is due to the fact that conditions for the best case scenario are not fully implemented at the moment and therefore corresponding real values cannot be measured yet. Based on future developments, especially in the percentage of separators in use, the concentration in surface water is expected to reduce by a factor of about 50.

In section 3.2.2 the calculated Hg values in surface water presented in Table 3 will be used for further risk assessment.

Methylation and bioaccumulation

In the sheets in Annex 1, 2 and 3 the calculation results of the concentration for methyl mercury and its bioaccumulation in fish are also shown. The results are compilated in Table 4 for the three scenarios.

Table 4. Estimated concentrations of methyl mercury in surface water related to hypothetical methylation rates in 3 scenarios.

Methylation (%)	Mercury concentration in surface water (µg/L)	Mean BAF* (-)	Methyl mercury concentration in fish (µg/kg fish)
Worst case scenario			
0.0001	1.2E-07	3.6E+06	4.2E-01
0.001	1.2E-06	3.6E+06	4.2E+00
0.01	1.2E-05	3.6E+06	4.2E+01
0.1	1.2E-04	3.6E+06	4.2E+02
1	1.2E-03	3.6E+06	4.2E+03
Average case scenario			
0.0001	1.0E-08	3.6E+06	3.7E-02
0.001	1.0E-07	3.6E+06	3.7E-01
0.01	1.0E-06	3.6E+06	3.7E+00
0.1	1.0E-05	3.6E+06	3.7E+01
1	1.0E-04	3.6E+06	3.7E+02
Best case scenario			
0.0001	3.6E-12	3.6E+06	1.3E-05
0.001	3.6E-11	3.6E+06	1.3E-04
0.01	3.6E-10	3.6E+06	1.3E-03
0.1	3.6E-09	3.6E+06	1.3E-02
1	3.6E-08	3.6E+06	1.3E-01

* BAF = Bioaccumulation Factor.

In section 3.2.2 the calculated methyl mercury concentrations in fish will be used for further risk assessment.

3.2.1.2. Concentration in soil

According to the Bio Intelligence report (2012), emissions patterns and quantities of Hg in soil from dental amalgam in the EU are:

- Spreading of sewage sludge on farmland or landfilled: 8 t/y
- Disposal of solid wastes: 8.5 t/y
- Burial: 4 t/y

In the 2008 SCHER Opinion, a preliminary assessment of the potential risk for soil dwelling organisms of mercury released from dental practice was performed based on the generic TGD scenarios and default values. Based on a default average production of 0.071 kg of sludge per person per day at the WWTP, the concentration of mercury in sludge, resulting from dental clinics is calculated to range between 0.01 and 2.4 mg Hg/kg dw with and average value of 0.42 mg/kg dw. These values are consistent with the mercury content of sewage sludge reviewed by BIO Intelligence Service (2012), ranging from 0.2 to 4.6 mg/kg dw (average value = 1.53 mg/kg dw). This range and average mercury concentration in sewage sludge is also consistent with observations made in the USA (US EPA 2009).

The added PEC_{soil} resulting from the contribution of dental clinic emissions - following the TGD default values - ranges from 0.016 to 4.1 µg Hg/kg dw. The same calculation when applied to the concentration in sludge reported by the BIO Intelligence report led to Hg concentrations in soil of about 2.6 and 7.9 µg/kg dw, using average and maximum concentrations in sludge, respectively.

The Bio Intelligence Services report (2012) estimated a discharge of about 1.5 g Hg per person buried and the same value for cremations. For dental waste a total discharge was estimated to be 52 t Hg/y. These values cannot be used without many additional assumptions for a risk assessment purposes. Therefore, with respect to burial and waste containing mercury from dental amalgam, SCHER concludes that insufficient specific information is available to carry out a risk assessment.

3.2.1.3. Concentration in air

According to the Bio Intelligence report (2012), emissions patterns and quantities of Hg in air from dental amalgam in the EU are:

- Losses during application and separation: 3.5 t/y
- Losses from sewage sludge: 6 t/y
- Losses from solid wastes: 4.5 t/y
- Cremation: 3 t/y
- Losses from fillings in use: 2 t/y

In the on-going work to develop a global emission inventory for UNEP/AMAP (2012) the emissions from crematories in the EU were estimated to be 343 kg/y, ranging from 89 to 1130 kg/y. Note that this value only represents cremation and not the handling, production and disposal of dental Hg. The same study estimated the global emissions from crematories at 3.3 tonnes (range 1-12), corresponding to 0.2% of total Hg emissions. This last figure was in reasonable agreement with those reported by the Bio Intelligence report (2012), indicating a value of about 2.8 tonnes for EU-27.

The atmospheric emissions of Hg from crematoria and further deposition close to these installations should be considered as an additional contribution of mercury from dental amalgams.

SCHER concludes that with the scarce information available no estimation of the concentration in air due to the emission of dental amalgam is possible.

3.2.2. Environmental risk assessment

3.2.2.1. Direct risk for aquatic organisms: inorganic mercury

According to the Water Framework Directive, the following Environmental Quality Standards have been set for mercury for all typologies of surface waters:

Annual Average EQS:	50 ng/L
Maximum Allowable Concentration EQS:	70 ng/L

The comparison of these EQS with the calculated exposure estimations in surface waters allows the following conclusions:

- average case scenario: the estimated concentration of 10 ng/L is 5 times less than the AA EQS values;
- best case scenario: the estimated concentration of about 0.004 ng/L is negligible in comparison to EQS values;
- worst case scenario: the estimated concentration of about 120 ng/L is above both AA and MAC EQS values.

It is clear that the contribution of Hg originating from dental amalgam use should be added to the natural and historical background concentrations as well as to the contribution from other anthropogenic Hg sources, to fully assess the risks of Hg to the environment. However, it can be concluded that mercury from dental amalgam does not represent an overall risk for European surface waters. Nevertheless, in particular local conditions, a risk for the aquatic ecosystem is possible and the WFD EQS may be exceeded.

One must be aware that the latter scenario represents an extreme worst case (maximal dentist density, maximal mercury use, absence of separator devices). Although improbable, its occurrence is not impossible at local level in some European countries or regions. In these cases, mitigation measures are needed to reduce the risk.

3.2.2.2. Direct risk for soil organisms: inorganic mercury

The estimated concentrations of mercury in sewage sludge (0.01 and 2.4 mg Hg/kg dw) are far below the limit value for mercury concentration in sludge for use in agriculture (16 to 25 mg Hg/kg dw, Directive 86/278/EEC).

Moreover, the calculated added PEC_{soil} resulting from the contribution of amalgam to sewage sludge (from 0.016 to 4.1 µg Hg/kg) as well as those calculated using the maximum value reported by the Bio Intelligence Service report (7.6 µg Hg/kg) are well below the reported NOECs for soil dwelling organisms (e.g. Verbruggen et al., 2001; de Vries et al., 2007), which are all stated to be above 1.4 mg/kg. Thus, a negligible direct risk to the soil compartment is expected from the contribution of dental Hg in sewage sludge."

As to the two additional sources of contribution to soil (disposal of solid wastes and burial), an estimate of the total European emission is available (Bio Intelligence Service, 2012), but no information is available on the distribution patterns at the local scale. Therefore, a quantitative PEC cannot be estimated and an assessment of local risk is impossible.

3.2.2.3. Direct risk for the air compartment: inorganic mercury

Total European emissions in the atmosphere from different patterns (sludge application, solid waste disposal, cremation) have been also estimated (Bio Intelligence Service, 2012). However, as for soil, no information is available on the distribution patterns at the local scale. Therefore, a quantitative PEC cannot be estimated and an assessment of local risk is impossible.

3.2.2.4. Risks associated with methylation of inorganic mercury.

The main concern related to the anthropogenic emissions of mercury into the environment is related to the well-known potential of this metal to bioaccumulate and biomagnify through the food chain resulting in high levels of exposure for top predators (including humans) and associated risk for secondary poisoning. The bioaccumulation of inorganic mercury in biota - although significant and described even for the mercury present in dental amalgams (Kennedy, 2003) - is generally regarded to be of low relevance compared to that of organic forms of mercury. The potential for biomagnification is, therefore, related to the methylation of inorganic mercury which may result from both abiotic and biotic processes. The later seems to be the most relevant under environmental conditions.

Methylation of inorganic mercury may occur through two different patterns:

- direct emission of methyl mercury from dental practice
- environmental methylation.

The concerns related to mercury in dental amalgams have been enhanced by the identification of methyl mercury in wastewater from dental units in the USA. The measured concentrations were particularly high in tanks from large clinics (up to 0.2% of the total mercury) suggesting methylation to occur within the tank. This may be the result of the activity of sulphate reducing bacteria, which are present in the oral cavity of humans, and can therefore be released during dental intervention. However, methyl mercury levels measured in the chair side wastewater were at least one order of magnitude lower that those measured in the tanks (Stone et al., 2003). In individuals with dental amalgam fillings, Hg-release may occur with time, influenced by individual

factors (i.e. gum chewing, tooth brushing, bruxism, dietary habits, and different rates of Hg releases from different amalgam types). In this situation, methylation may also occur in the human oral cavity as well in the gut, but the extent to which this happens and results in increased methyl mercury exposure is unclear.

A significant association has been found between annual urinary mercury levels and amalgams (Bellinger et al., 2006). The presence of dental amalgam fillings increases Hg excretion up to 3 µg (approximately 3.6 µg Hg/L) with respect to individuals with no amalgam fillings. It has been estimated that each amalgam filling will contribute an increase of around 0.1 µg Hg/L in urinary excretion. To put this value into context, this means that, at the German reference value of 1.4 µg Hg/L (reference value is mean Hg concentration in urine in the general population), up to 36 fillings may be necessary to exceed the HBM-I (defined as a urinary concentration without health risks based on presently available knowledge and applies to the general population).

It has been reported that the probability of exceeding the limits of mercury permitted in wastewater increased proportionally as the number of amalgam-filled surfaces increased and consequently that humans, especially in populated areas, can be a significant source of mercury pollutants (Leistevuo et al, 2002). However, the estimate was based on data coming from urinary excretion of total Hg, a marker which is strongly affected by dietary habits. Indeed, methyl mercury and even demethylated methyl mercury from seafood may significantly contribute to the mercury excreted in the urine (Johnnson et al., 2005;Sherman et al., 2013). By using an Hg isotope, Sherman et al. (2013) identified that while hair-mercury from dental professionals reflect isotope ratios typical for seafood, the urinary mercury differed from the ratio in the amalgam and tended to approach ratios in seafood as well, though with a wide variability that probably reflect differences in dietary habits.

The main environmental concern for methyl mercury is its potential for bioaccumulation and food web biomagnification resulting in a risk for secondary poisoning in ictivorous vertebrates. Consumption of fish and seafood as well as products for special nutritional uses are the most important sources for dietary exposure to mercury and methyl mercury, while other food products and drinking water are of minor relevance (EFSA, 2012). As a threshold level, the EC proposal (within the WFD) of 20 µg methyl mercury/kg in the prey of birds and mammals may be used for safety evaluation. This threshold is much more conservative than the maximum acceptable concentration in food of 0.5 mg/kg ww (EC, 2006). It must be noted that the threshold in food refers to total mercury. However, it is reasonable to assume that most of mercury in fish is in the methylated form.

The comparison with the calculated value of methyl mercury accumulation in fish according to the three proposed scenarios allows the following conclusions:

- average case scenario: all the calculated concentrations are far below the acceptable level in fish, however, the WFD proposed threshold (20 µg Hg/kg) for secondary poisoning is exceeded at methylation rates higher than 0.05 %;
- best case scenario: all the calculated concentrations are far below the acceptable level in fish as well as the WFD threshold for secondary poisoning;
- worst case scenario: the acceptable level in fish is exceeded (or at least approached) at methylation rates higher than 0.1 %, while the WFD threshold for secondary poisoning is also exceeded at methylation rates higher than approximately 0.005 %.

SCHER concludes that, in the worst case scenario, under extreme local conditions (maximal dentist density, maximal mercury use, absence of separator devices in the water treatment process), a risk of secondary poisoning in ictivorous vertebrates due to methylation cannot be excluded. These risks depend on the methylation rate of inorganic mercury which may differ with exposure conditions.

3.3. Second question

Is it scientifically justified to conclude that mercury in dental amalgam could cause serious effects on human health due to mercury releases into the environment?

Mercury coming from dental amalgam as well as from many other sources is ubiquitously distributed in the environment and can be taken up by the general human population via food, water and air.

Potential sources of exposure to mercury, next to the direct exposure to mercury through dental treatments (which is out the scope of this opinion and will be specifically dealt with in the upcoming SCENIHR opinion), include inhalation of mercury vapours in air which is mainly confined to closed ambient air, ingestion of drinking water and food contaminated with mercury. Dietary intake is the most important source of non-occupational exposure to methyl mercury, with fish and other seafood products being the dominant source of mercury in the diet. Most of the mercury present in fish or other seafood is methyl mercury (WHO 1990, 1991).

Taking these exposure considerations into account, for indirect intake of mercury from the environment due to the uses of dental amalgams, the toxicology of both inorganic mercury and methyl mercury is relevant for risk assessment. The toxicological profile of mercury is highly dependent on the route of administration and speciation of mercury (elemental mercury; inorganic salts of mercury; or methyl mercury). Indeed, the main concern related to the anthropogenic emissions of mercury into the environment is related to the potential of the organic forms of mercury to bioaccumulate and biomagnify through the food chain.

Aspects of the hazard assessment for inorganic and elemental mercury have been summarized in previous SCHER opinions on mercury (SCHER, 2010; 2012) and are described in detail in a number of monographs (ATSDR, 1997-1999; Clarkson and Magos, 2006; EFSA, 2012; IRIS, 2002; UBA, 2011; US-EPA, 2010; WHO/IPCS, 2002). Oral ingestion of elemental mercury results only in a very limited absorption (< 0.01 % of dose). Dermal absorption of liquid elemental mercury is also very limited. In contrast, approximately 80 % of the inhaled elemental mercury is absorbed in the lungs. Due to the high lipid solubility, elemental mercury rapidly penetrates alveolar membranes and is then distributed to all tissues of the body. Absorbed elemental Hg is oxidized in blood to Hg-ions, which cannot readily penetrate biological membranes. The potential exposure of humans to drinking water is explicitly included in EFSA (2012).

After consumption of inorganic mercury (Hg^{2+}), only a small part of the dose ingested is absorbed from the gastrointestinal tract. Hg^{2+} absorbed or formed by oxidation of elemental Hg may be eliminated by excretion with urine and/or faeces. The elimination of elemental mercury or Hg^{2+} follows complex kinetics with half-lives in the range of 20 to 90 days. The major target organ for the toxicity of inorganic mercury is the kidney. Ingestion of high doses of Hg^{2+} results in kidney damage characterized by proximal tubular injury. In contrast, long term oral administration of Hg^{2+} to rodents causes glomerulonephritis as the most sensitive endpoint. Higher doses of inorganic mercury also cause neurotoxicity. IPCS has set a tolerable (oral) daily intake (TDI) for lifetime exposure to elemental and inorganic mercury of 2 µg/kg bw/day. The TDI also covers sensitive subgroups such as children (WHO/IPCS, 2002). Recently the EFSA CONTAM Panel established a tolerable weekly intake (TWI) for inorganic mercury of 4 µg/kg bw, expressed as mercury (EFSA, 2012).

Methyl mercury is highly toxic. The diet is the most relevant source of exposure to methyl mercury, with fish meat being the main contributor to methyl mercury dietary exposure for all age classes, followed by other fish products. The middle bound (MB) methyl mercury dietary exposure in Europe varies from the lowest minimum of 0.06

µg/kg bw per week seen in elderly people to the highest maximum of 1.57 µg/kg bw per week in toddlers (EFSA, 2012). It is absorbed from the gastrointestinal tract and subsequently rapidly and evenly distributed in the organism. The biological half-life of methyl mercury in blood is around 70 days. The faeces are the most important route of excretion (approximately 90% of a single oral dose of methyl mercury is excreted in the form of mercuric mercury). Urinary total mercury might be a suitable biomarker of inorganic (and elemental) mercury, but not for methyl mercury exposure. Methyl mercury elimination in humans mainly occurs via the biliary route after conjugation with liver glutathione S-transferases (GSTs), which produce a stable glutathione–metal conjugate which is then eliminated mainly via faeces (Ballatori and Clarkson, 1985; Dutczak WJ, Ballatori N., 1994). GSTs are highly polymorphic in humans and an association between null GSTM1 and GSTT1 genotypes and the retention of the metal has been established (Mazzaron Barcelos et al., 2012). This genetic make up, together with allelic variants of metallothionein (MT) and the heme pathway enzyme coproporphyrinogen oxidase (CPOX) are reported to affect Hg toxicokinetics and individual susceptibility to mercury in adults. Two randomized, controlled, clinical trials evaluated the neurobehavioral effects of Hg from dental amalgam tooth fillings, one in New England that followed 534 children over 5 years (Bellinger et al. 2006) and one in Portugal (DeRouen et al. 2006)that followed 507 children, 8-12 years of age at baseline. Associations between Hg exposure, genetic variants and test performance in boys were in the direction of impaired performance. However, since urinary Hg reflects a composite exposure index that cannot be attributed to a specific source, the authors concluded that the findings do not support an association between Hg in dental amalgams specifically and the adverse neurobehavioural outcomes observed (Woods et al, 2012; 2013. Indeed, other factors, such as variants of Apolipoprotein E, a major protein transporter expressed in the brain, have been postulated to cause genetic predisposition to Hg-induced effects (Ng et al, 2013).

In humans, high dose poisonings resulted in effects that included mental retardation, and sensory and motor impairment: due to the developing stage of their nervous system, children may be particularly susceptible to this effect. Long term, low dose prenatal exposures to methyl mercury due to maternal fish consumption have been associated with more subtle endpoints of neurotoxicity. Results from animal studies also show effects on cognitive, motor and sensory functions indicative of neurotoxicity.

Health based reference values for human exposures to methyl mercury have been established by US EPA in 2001; i.e. US EPA Reference Dose for Chronic Oral Exposure (RfD) 0.1 µg/kg bw/d and by WHO; i.e. TDI = 0.47 µg/kg bw/d [see: http://www.inchem.org/documents/jecfa/jecmono/v52je23.htm]

More recently EFSA (2012) identified a TWI for methyl mercury of 1.3 µg/kg bw/w, expressed as mercury. Data from human studies in children (NOEL from Seychelles Child Developmental Study and $BMDL_{05}$ from Faroese cohort 1 at age seven years) were used as the basis for the derivation of the TWI, by using toxicokinetic modelling and applying a total uncertainty factor of 6.4 (2 to account for variation in the hair to blood ratio 3.2 to account for interindividual variation in toxicokinetics) (EFSA 2012).

The mean dietary exposure does not exceed the EFSA derived TWI for methyl mercury, with few exceptions (i.e. toddlers in some surveys). Concentrations of mercury in blood and hair that correspond to the US EPA RfD and the WHO TDI can be calculated (FAO/WHO, 2003; NRC, 2000; Grandjean *et al.*, 2007). Recent biomonitoring data on mercury concentrations in hair from mothers and children recruited from the general population of 17 European countries indicate that methyl mercury exposure is generally below the EFSA derived TWI (EFSA, 2012) but more than 1.8 million children are born every year with MeHg exposures above the limit derived by US EPA, and about 200,000 births exceed the higher limit proposed by the WHO (Bellanger *et al.*, 2013).

In a detailed analysis of studies on effects of methyl mercury in humans and average fish consumption in the US, the US EPA has developed a fish tissue residue criterion (concentration in fish that should not be exceeded) of 0.3 mg methyl mercury/kg fish

(regarding human consumption) which is similar to a maximum tolerable content of 0.5 mg methyl mercury/ kg fish for many fish species set by EU (EC, 2006). It must be noted that the EU threshold in food refers to total mercury, although it is expected that most of mercury in fish is in the methylated form.

Regarding the contribution of environmental mercury coming from dental amalgam use, it can be concluded that emissions of Hg to soil are not considered as a concern for human health. Indeed, the consideration of the calculated concentrations of 0.016 to 4.1 µg Hg/kg or the estimation that the emission of dental amalgam is about 1% of the total emission of Hg to soil as in the USA (Cain et al, 2007), support the conclusion that dental amalgam represents a negligible contribution to total human exposure from soil.

Regarding inhalation, amalgam use will make only a limited contribution (around 1%) to the overall human inhalation exposure to Hg from anthropogenic sources (22%). Thus, this can also not be considered as a health concern.

The contribution of amalgam use to the concentrations of methyl mercury found in fish and formed from Hg^{2+} dissolved in the oceans from non-anthropogenic sources is not known and consequently no clear conclusion on possible health risks is possible. Any calculation would be indeed affected by a high degree of uncertainty and based on a number of assumptions. However, a screening assessment can be attempted based on the provisional risk assessment for surface water, shown in Table 4, for which only the contribution of the emission of dentists was taken into account. Different situations can be evaluated on the basis of 5 hypothetical values for the methylation rate in three possible scenarios (worst, average and best case), with values spanning 4 -orders of magnitude. In the best and the average cases, the expected methyl mercury concentrations in fish related to contributions of dental amalgam uses are well below the thresholds of 0.3 – 0.5 mg methyl mercury/kg fish set by the US EPA and the EU. In the worst case scenario, those values obtained with a 0.1 % methylation rate exceed the US maximum tolerable content of 0.3 mg methyl mercury/kg fish and those obtained with1% methylation rate exceed the EU maximum tolerable content of 0.5 mg methyl mercury/kg fish . Thus, the 'average' predicted indirect exposures of humans to methyl mercury resulting from emissions due to dental amalgams are much lower than the tolerable limits, although in the unlikely but not impossible worst case, mitigation measures are expected to be needed to reduce the risk. Therefore, compliance to the WFD threshold would prevent human health effects. On the other hand, methyl mercury in fish is the major contributor to the methyl mercury concentration in humans. It exceeds in a considerable proportion of children, safe limits, e.g. the limits set by US-EPA RfD and WHO-TDI, but not the limits set by EFSA. All additional sources which add to the methyl mercury burden in humans may increase the number of people at risk, Respecting the more conservative WFD threshold would contribute to the prevention of human health effects.

3.4. Third question

Comparison of environmental risk from the use of mercury in dental amalgam and the use of alternatives without mercury

Currently, Hg-free materials are used more often than dental amalgam in the EU27. These materials are used in approximately 66% of all dental restorations and their use is growing (Biointelligence Service, 2012). Therefore, assessing the potential risks for these alternatives is a major issue.

The composition of the most commonly used alternatives to dental amalgam is highly variable, represented by a matrix (e.g. a polymeric resin) and by several inorganic materials used as fillers (e.g. Al_2O_3, SiO_2, metal oxides, metal fluorides, etc.).

Erdal (2012) divides materials into the following five main classes.

1. *Composite resins*. They are composed of a polymerisable resin matrix, binding filler inorganic particles. The resin is initially a fluid monomer, which is converted into rigid polymer by a radical addition reaction. The most common resins used now are based on dimethacrylate (bisphenol A-glycidyl methacrylate: Bis-GMA and bisphenol A dimethylacrylate: Bis-DMA) or urethane dimethacrylate (UDMA). The inorganic materials used as fillers are silica-based glass fillers (SiO_2), alumina glass (Al_2O_3), and combinations of glass and sodium fluoride. They may also contain barium, strontium and boron.

2. *Glass ionomer (Glass polyalkenoate) cements.* They are a product of an acid-based reaction between basic fluoro-alumino-silicate and water-soluble polycarboxylic acid consisting of an organic-inorganic complex with high molecular weight (Wilson and McLean 1988; Davidson and Mjör 1999). The filler particles contain alumina (Al_2O_3), silica (SiO_2), metal oxides, metal fluorides, and metal phosphates. The metal ions usually selected are: aluminium (Al), calcium (Ca), strontium (Sr), zinc (Zn), sodium (Na), potassium (K), barium (Ba) and lanthanium (La).

3. *Resin-Modified Glass Ionomer Cement.* They are similar to the previous one, but water-soluble resin monomers (e.g., 2-hydroxyethylmethacrylate), capable of free radical polymerization, are added. Thus, resin-modified glass ionomer cement is a material that undergoes both the polymerization reaction and acid-base reaction.

4. *Compomers.* They are single-paste formulations consisting of fillers and a matrix, similar to a composite resin. The filler usually contains fluoro-alumino-silicate glass powder. Metal fluoride is also included in some materials for the same purpose. The glass powder contains strontium or some other metal. A compomer undergoes an acid-base reaction between the acidic monomer (e.g., polymerisable dimethacrylate resins such as urethane dimethacrylate) and ion-leachable basic glass filler in the presence of water from the saliva.

5. *Giomers.* They feature the hybridization of glass-ionomer and composite resins. They contain an adhesive promoting monomer and a bonding polymer catalyst, which allow bonding to hard tooth tissues.

The detailed composition of some of the most frequently used alternatives is described by Erdal (2012). This report concludes for the alternatives of amalgam that "there is no current evidence of significant personal or environmental toxicity".

Human health

From the human health point of view, there is no new relevant data available on alternatives compared to the opinion of SCHER in 2008 (SCHER, 2008). Therefore, SCHER confirms its position taken in the 2008 Opinion, except for alternative materials included in group 1. For dental materials, the leakage is limited to resins composed of Bis-DMA which has an ester linkage that can be hydrolysed to BPA, whereas the ether linkage in Bis-GMA was found to be stable. Indeed, the possible effects related to the use of bisphenol A-containing dental resins are included in the ToR of an on-going SCENHIR mandate on the the use of bisphenol A in medical devices. SCHER refers the reader to that opinion.

Environment

For the environmental assessment, the statement of the Erdal report is not supported by SCHER. No attempt is made to estimate concentrations of different components in various environmental compartments and no ecotoxicological data is reported. Therefore, the available information is too limited for conducting a proper comparative risk assessment of the amalgam alternatives. However, it is reasonable to consider the risk determined by the polymeric resin as negligible or practically absent. Environmental risks associated with the release of monomers and from the leakage of filling materials cannot

be excluded. However, regarding the possible contribution of BPA leakage from dental material, two recent reports indicate that environmental exposure to BPA is very limited and the major contribution for human exposure is at present represented by food and beverage consumption, from the use of BPA-containing medical devices and thermal paper (EFSA, 2013; SCENIHR, 2014).

Therefore, the first questions to be answered for the development of an environmental risk assessment refer to exposure issues:

- What is the amount of monomers released during the treatment before the polymerisation process?
- Can monomers be released after dental filling disposal?
- What is the amount of inorganic fillers (e.g. metals) leached from the amalgam alternative?

Referring to effects, ecotoxicological information on the products in dental resins is practically absent.

Table 5 gives a list of chemicals (resin monomers or organic and inorganic additives) used in commercially available products (taken from Erdal 2012). Literature data on physical chemical properties (water solubility and log Kow) are available only for a few compounds. Most reported values have been estimated using the EPISUITE software[8]. The few acute toxicity data available for aquatic organisms reported in Table 5 are taken from the ECOTOX[9] database. Other ecotoxicity data were were calculated using the QSAR equations for narcotic type chemicals (TGD EC, 2003).

The chemicals can be divided in five groups:

1. Monomers group 1 are the components of polymeric resins used in a large number of commercial products (more than 15 from the list of Erdal 2012), often in high percentages (even more than 70%);
2. Monomers group 2 are the components of polymeric resins used in a small number of commercial products (less than 5 from the list of Erdal 2012), in medium high percentages;
3. Monomers group 3 are the components of polymeric resins used only in one commercial product in medium low percentages (usually less than 10%);
4. Organic additives are organic chemicals added before the polymerization process with various functions (initiation, catalysis, etc.); they are usually present in relatively small amount (<5%); low toxicity solvents often present in the composition (e. g. ethanol, acetone) are not included in the list;
5. Inorganic additives are some metals that may be added as fillers (as oxides and fluorides) are listed; fluorine is also listed.

For many of the organic chemicals the estimated values show relatively low toxicity, often with E/LC50 values of some hundreds of mg/L. Among the monomers, the more toxic are those derived from bisphenol A. However, the uncertainty associated with these ecotoxicity data must be highlighted: they are estimated values calculated on the basis of estimated values of log Kow.

In many reports it is concluded that the ecological risk of the available alternatives to amalgam is very low, in any case lower than those of amalgam. A synthesis of these opinions is provided by a document of the World Alliance for Mercury-Free Dentistry (2012).

Considering the relatively low toxicity of the chemicals involved, these views may be considered reasonable. However, it is the opinion of the SCHER that, at present, there is insufficient scientific evidence to support these statements.

Therefore the SCHER agrees with the conclusions of the Council of European Dentists (CED, 2012):

1. The scientific community is not yet fully able to demonstrate the relative emerging risks of the use of alternative materials;
2. Evidence about the toxicology of the alternative materials is a work in progress
   The profession should urge manufacturers to fully declare the chemical composition of the alternative materials;
3. The environmental data regarding the use of alternative materials is lacking and the profession should urge the decision-makers to know more;
4. More research on alternative materials is highly recommended.

Finally, it should be noted that the assessment of environmental impacts of the substitutes would require two complementary studies: a comparative risk assessment for the relevant environmental compartments, and a life-cycle assessment covering non ecotoxicological impacts such as those related to energy and natural resources consumption, atmospheric emissions including greenhouse gases, waste production, etc.

Table 5. Physical-chemical and ecotoxicological characteristics of substances frequently used in commercially available products (from Erdal 2012). Figures in italics are estimated using EPISUITE or QSAR equations.

					Ecotoxicology (E/LC50 mg/L)		
			WS		algae	Daphnia	fish
	CAS	MW	mg/L	Log Kow	72h EC50	48h EC50	96h EC50
Monomers group 1							
2-hydroxyethyl methacrylate	868-77-9	130.14	misc	0.47	*2596*	*2228*	227
bisphenol A diglycidyl methacrylate (Bis-GMA)	1565-94-2	512.61	*356*	*4.94*	*0.347*	*0.50*	*1.32*
triethyleneglycol dimethacrylate.	109-16-0	286.33	*366*	*1.88*	*222*	*224*	*294*
urethane dimethacrylate (UDMA)	72869-86-4	470.57	*0.11*	*4.69*	*0.57*	*0.79*	*1.98*
Monomers group 2							
3-trimethoxysilylpropyl methacrylate	2530-85-0	248.35	*5490*	*0.75*	*2600*	*2304*	*2331*
bisphenolA polyethyleneglycoldietherdimethacryl.	41637-38-1	310.44	*612*	*6.14*	*0.013*	*0.02*	*0.08*
glycerol 1,3-dimethacrylate	1830-78-0	228.25	*10350*	*1.16*	*930*	*864*	*960*
methyl methacrylate	80-62-6	100.12	10500	*1.38*	*246*	*234*	276
1,6-hexanediol dimethacrylate	6606-59-3	254.33	*6.1*	3.6	*3.8*	*4.6*	*9.0*
trimethylolpropane trimethacrylate	3290-92-4	338.4	*1.3*	*4.39*	*0.81*	*1.09*	*2.56*
Monomers group 3							
(dimethylamino)ethyl methacrylate	2867-47-2	157.21	50000	0.81	42	33	19
tetrahydrofurfuryl methacrylate	2455-24-5	170.21	*1790*	*1.8*	*159*	*159*	35
bisphenol A dimethacrylate	3253-39-2	364.44	*834*	*5.6*	*0.054*	*0.08*	*0.26*
decamethylene dimethacrylate	6701-13-9	310.44	*612*	*5.4*	*0.073*	*0.11*	*0.33*
ethoxylated bisphenol-A-dimethacrylate	56744-60-6	540.66	*2500*	*6.08*	*0.026*	*0.04*	*0.15*
1-propanol-3,3'-[isopropylidenebis(p-phenyleneoxy)]di-dimethacrylate	27689-12-9	480.61	*29900*	*6.01*	*0.028*	*0.045*	*0.153*
tricyclodocandimethanol dimethacrylate	43048-08-4	332.44	*0.21*	*5.35*	*0.087*	*0.13*	*0.38*
dl-camphorquinone	10373-78-1	166.22	*3230*	*0.75*	*1741*	*1542*	*1560*
Organic additives							
2,2-bis[4-(2-methacryloxy)ethoxy)phenyl]propane	24448-20-2	452.55	*0.03*	*6.63*	*0.01*	*0.01*	*0.04*
2,4,4'-trichloro-2'-hydroxydiphenyl ether	3380-34-5	289.55	*4.6*	*4.76*	*0.30*	*0.42*	0.30
2,4,6-trimethylbenzoyldiphenylphosphine	75980-60-8	348.38	*3.1*	*3.87*	*2.77*	*3.51*	*7.29*

oxide							
2,6-di-tert-butyl-p-cresol (BHT)	128-37-0	220.36	1.1	5.1	*0.10*	>0.17	>0.57
2-benzotriazolyl-4-methylphenol	2440-22-4	225.25	*338*	*3*	*13.3*	*15.2*	*25.9*
acrylamidosulfonic acid	15214-89-8	207.25	misc	*-2.19*	*1890142*	*11939 73*	*6137 54*
dl-camphorquinone	10373-78-1	166.22	*3230*	*0.75*	*1741*	*1542*	*1560*
glutaraldehyde	111-30-8	100.12	misc	*-0.18*	*8923*	*7104.29*	10.50
maleic acid	110-16-7	116.07	788	-0.78	*41183*	*30600*	*21760*
Inorganic additives							
aluminium					0.04	1.6	0.18
lantanium					-	0.08	0.01*
strontium					-	41.5	0.124*
titanium					8.7	3.3	2.3
zinc					0.14	0.37	0.22

* 28d LC50

4. COMMENTS RECEIVED DURING THE PUBLIC CONSULTATION

A public consultation on this opinion was opened on the website of the EU non-food scientific committees from 25 September to 20 November 2013. A public hearing took place on 6 November 2013 in Luxembourg to receive contributions on the topic of the preliminary opinion.

Information about the public consultation was broadly communicated to national authorities, international organisations and other stakeholders. Fifteen organisations and five individuals participated in the public consultation providing input to the three main scientific questions (in total 60 contributions were received). Out of the 15 organisations participating in the consultation, there were six NGOs, three public authorities, three dentist associations, two businesses and one trade union.

Each submission was carefully considered by the Working Group and the scientific opinion has been revised to take account of relevant comments. The literature has been updated with relevant publications. The scientific rationale and the opinion section were clarified and strengthened.

All contributions received and the reaction of the Scientific Committee on Health and Environmental Risks (SCHER) can be downloaded at: http://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scher_cons_06_en.htm

5. MINORITY OPINION

None

6. LIST OF ABBREVIATIONS/ACRONYMS

BAF	Bio-Accumulation Factor
Bis–DMA	bisphenol A dimethacrylate
Bis-GMA	bisphenol A-glycidyl methacrylate
BMD	Benchmark Dose (An exposure due to a dose of a substance associated with a specified low incidence of risk, generally in the range of 1% to 10%, of a health effect; or the dose associated with a specified measure or change of a biological effect).
BMDL	A lower one-sided confidence limit on the BMD
bw	Body weight
CAS	Chemical Abstract System
CSTEE	Scientific Committee on Toxicity, Ecotoxicity and the Environment
dw	dry weight
EC	European Commission
EC50	Median effect concentration (in relation to specific endpoint)
ECDC	European Centre for Disease prevention and Control
ECHA	European Chemicals Agency
EEB	European Environmental Bureau
EFSA	European Food Safety Authority
EMA	European Medicines Agency
EPA	Environmental Protection Agency
EQS	Environmental Quality Standard
EQS AA	Annual Average Environmental Quality Standard
EQS-MAC	Maximum Allowable Concentration Environmental Quality Standard
EU	European Union
EUSES	European Union System for the Evaluation of Substances
Hg	Mercury
INC	Intergovernmental Negotiating Committee
Kow	Octanol-water partition coefficient
LC50	Mean lethal concentration
MW	molecular weight
NO(A)EC	No Observed (Adverse) Effect Concentration
NOEL	No Observed Adverser Effect Level
PEC	Predicted Environmental Concentration
QSAR	Quantitative Structure Activity Relationship
RAR	Risk Assessment Report
RfD	Reference Dose
SCCS	Scientific Committee on Consumer Safety
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks ()
SCHER	Scientific Committee on Health and Environmental Risks
TGD	Technical Guidance Document
TDI	Tolerable Daily Intake
ToR	Terms of reference
TWI	Tolerable Weekly Intake
UNEP	United Nations Environment Programme (established an (INC)

WFD	Water Framework Directive
WHO	World Health Organisation
US	United States
US EPA	US Environmental Protection Agency
WFD	Wtaer Framework Directive
ww	Wet weight
WWTP	Waste Water Treatment Plant

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ANNEXES

Sheets for calculation of PECs in surface water

Annex 1 Average case scenario

Annex 2 Best case scenario

Annex 3 Worst case scenario

Annex 1 Average case scenario

Assumptions					Remark										
0.05	µg/L	Better case concentration in effluent			Assume all Hg comes from dental amalgam										
160	g Hg/dentist/y				Richardson, 2011 and applying 75% separators										
70	dentists/100000 inhabitant				Average (BIO, 2012)										
75	%	percentage amalgam separators			BIO, 2012										
70	%	efficiency of separators			BIO, 2012										
	mercury	dentist/10,000 inhabitants	input WWTP	mercury	water	mercury inflow	% water	mercury outflow	dilution	mercury river					
	g Hg/dentist/y		g/y	mg/d (260d/y)	L/person/d	mg/L		ug/L		ug/L	ng/L				
mean	7.6E+01	7	5.3E+02	2.0E+03	200	1.0E-03	10	1.0E-01	10	1.0E-02	1.0E+01				
								0.05	10	0.005	5				
	methyl mercury									methyl mercury river		mean BAF	methyl mercury fish		
										ug/L	ng/L		ug/kg		
mean										1.0E-08	1.0E-05	3.6E+06	3.7E-02		
	% methylation	field BAF fish													
	1.0E-04	2.2E+04								1.0E-08	1.0E-05	3.6E+06	3.7E-02	Methylation rate 0,0001%	
	1.0E-03	1.0E+05			input value					1.0E-07	1.0E-04	3.6E+06	3.7E-01	Methylation rate 0,001%	
	1.0E-02	1.6E+06			assumption					1.0E-06	1.0E-03	3.6E+06	3.7E+00	Methylation rate 0,01%	
	1.0E-01	6.8E+06								1.0E-05	1.0E-02	3.6E+06	3.7E+01	Methylation rate 0,1%	
	1.0E+00	3.3E+04								1.0E-04	1.0E-01	3.6E+06	3.7E+02	Methylation rate 1%	
	5.5E-02	1.2E+05								5.6E-06	5.6E-03	3.6E+06	2.1E+01	Methylation rate 0.055%	
		6.8E+05													
		2.7E+07													
		7.1E+05													
		2.0E+05													
		2.0E+05													
		6.3E+06													

Annex 2 Best case scenario

Assumptions															
0.001	µg/L	Best case concentration in effluent			Remark										
0.64	g Hg/dentist/y				Richardson, 2011										
3	dentists/10000 inhabitants				Poland (BIO, 2012)										
95	%	percentage amalgam separators			BIO, 2012										
95	%	efficiency of separators			BIO, 2012										
	mercury	dentist/10,000 inhabitants	input WWTP	mercury	water	mercury inflow	% water	mercury outflow	dilution	mercury river					
	g Hg/dentist/y		g/y	mg/d (260d/y)	L/person/d	mg/L		ug/L		ug/L	ng/L				
mean	6.2E-02	3	1.9E-01	7.2E-01	200	3.6E-07	10	3.6E-05	10	3.6E-06	3.6E-03				
								0.001	10	0.0001	0.1				
	methyl mercury									methyl mercury river		mean BAF	methyl mercury fish		
										ug/L	ng/L		ug/kg		
mean										3.6E-12	3.6E-09	3.6E+06	1.3E-05		
	% methylation	field BAF fish													
	1.0E-04	2.2E+04								3.6E-12	3.6E-09	3.6E+06	1.3E-05	Methylation rate 0,0001%	
	1.0E-03	1.0E+05			input value					3.6E-11	3.6E-08	3.6E+06	1.3E-04	Methylation rate 0,001%	
	1.0E-02	1.6E+06			assumption					3.6E-10	3.6E-07	3.6E+06	1.3E-03	Methylation rate 0,01%	
	1.0E-01	6.8E+06								3.6E-09	3.6E-06	3.6E+06	1.3E-02	Methylation rate 0,1%	
	1.0E+00	3.3E+04								3.6E-08	3.6E-05	3.6E+06	1.3E-01	Methylation rate 1%	
		1.2E+05													
		6.8E+05													
		2.7E+07													
		7.1E+05													
		2.0E+05													
		2.0E+05													
		6.3E+06													

Annex 3 Worst case scenario

Assumptions															
1	µg/L	Worst case concentration in effluent			Remark										
460	g Hg/dentist/y				Richardson, 2011										
13	dentists/10000 inhabitants				Greece (BIO, 2012)										
0	%	percentage amalgam separators			BIO, 2012										
0	%	efficiency of separators			BIO, 2012										
	mercury	dentist/10,000 inhabitants	input WWTP	mercury	water	mercury inflow	% water	mercury outflow	dilution	mercury river					
	g Hg/dentist/y		g/y	mg/d (260d/y)	L/person/d	mg/L		ug/L		ug/L	ng/L				
mean	4.6E+02	13	6.0E+03	2.3E+04	200	1.2E-02	10	1.2E+00	10	1.2E-01	1.2E+02				
								1	10	0.1	100				
	methyl mercury									methyl mercury river		mean BAF	methyl mercury fish		
										ug/L	ng/L		ug/kg		
mean										1.2E-07	1.2E-04	3.6E+06	4.2E-01		
	% methylation	field BAF fish													
	1.0E-04	2.2E+04								1.2E-07	1.2E-04	3.6E+06	4.2E-01	Methylation rate 0,0001%	
	1.0E-03	1.0E+05			input value					1.2E-06	1.2E-03	3.6E+06	4.2E+00	Methylation rate 0,001%	
	1.0E-02	1.6E+06			assumption					1.2E-05	1.2E-02	3.6E+06	4.2E+01	Methylation rate 0,01%	
	1.0E-01	6.8E+06								1.2E-04	1.2E-01	3.6E+06	4.2E+02	Methylation rate 0,1%	
	1.0E+00	3.3E+04								1.2E-03	1.2E+00	3.6E+06	4.2E+03	Methylation rate 1%	
	5.0E-03	1.2E+05								5.8E-06	5.8E-03	3.6E+06	2.1E+01	Methylation rate 0,005%	
		6.8E+05													
		2.7E+07													
		7.1E+05													
		2.0E+05													
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Scientific Committee on Emerging and Newly Identified Health Risks

SCENIHR

Opinion on

The safety of dental amalgam and alternative dental restoration materials for patients and users

The SCENIHR adopted this opinion at the 10th plenary meeting on 29 April 2015

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SCENIHR

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All Declarations of Working Group members and supporting experts are available at the following webpage:
http://ec.europa.eu/health/scientific_committees/emerging/members_wg/index_en.htm

ABSTRACT

In the light of new developments and studies on dental amalgam a request was submitted by the Commission to update the SCENIHR opinion produced in 2008 on the safety and performance of both dental amalgam and possible alternatives, such as resin-based composites, glass ionomer cements, ceramics and gold alloys.

This updated 2015 Opinion evaluates the scientific evidence on the potential association between amalgam and possible alternatives and adverse health effects, such as allergies and neurological disorders.

The SCENIHR recognises that dental amalgam is an effective restorative material and is a material of choice for specific restorations.

Currently in the EU, there is a shift away from the use of dental amalgam in oral health care towards an increased use of alternative materials. Because dental amalgam is neither tooth-coloured nor adhesive to remaining tooth tissues, alternative tooth-coloured filling materials have become increasingly used. The change is indicated by trends in education on dental treatment towards an increased use of alternative materials instead of amalgam. This reduction is in line with concern about the use of mercury, the metallic element used in dental amalgam and the general aim to reduce mercury use within the European Union.

The exposure of the general population to mercury is mainly due to fish consumption (organic mercury, methyl mercury) and dental amalgam (elemental mercury, inorganic mercury). The present Opinion reviews only the toxicology of elemental and inorganic mercury being relevant to amalgam safety considerations.

Local adverse effects in the oral cavity are occasionally seen with dental amalgam fillings, including allergic reactions and an association with clinical features characteristic of lichen planus, but the incidence is low (< 0.3% for all dental materials in general) and usually readily managed. Regarding systemic effects, elemental mercury is a well-documented neurotoxicant, especially during early brain development. Inorganic mercury also constitutes a hazard to kidney function. In some scientific reports the presence of dental amalgam has been suggested to be associated with a variety of systemic adverse effects, particularly developmental neurotoxicity as well as neurological and psychological or psychiatric diseases. However, the evidence for such effects due to dental amalgam is weak.

The most recent *in vitro* evidence provides new insight into the effects of mercury on developing neural brain cells at concentrations similar to those accumulated in human brain and found in post mortem specimen. The effects of genetic polymorphism concerning mercury kinetics may influence the degree of individual susceptibility with regard to mercury internal exposure and consequently toxicity. This may raise some concern for possible effects on the brain of mercury originating from dental amalgam. However, so far such effects have not been documented in humans, although some evidence on alteration of mercury dynamics have been reported.

Placement and removal of dental amalgam fillings results in transient short-time exposure to the patients compared to leaving the amalgam intact. There is no general justification for unnecessarily removing clinically satisfactory amalgam restorations, except in those patients diagnosed as having allergic reactions to one of the amalgam constituents. However, as with any other medical or pharmaceutical intervention, caution should be exercised when considering the placement of any dental restorative material in pregnant women.

The mercury release during placement and removal also results in exposure of dental personnel. Recent studies do not indicate that dental personnel in general, despite somewhat higher exposures than patients, suffer from adverse effects that could be attributed to mercury exposure due to dental amalgam. However, exposure of both patients and dental personnel could be minimised by the use of appropriate clinical techniques.

The alternative materials also have clinical limitations and toxicological hazards. They contain a variety of organic and inorganic substances and may undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement. The SCENIHR Opinion "The safety of the use of bisphenol A in medical devices" (2015) concluded that release of BPA from some

dental materials was associated with only negligible health risks. A similar detailed risk assessment has not been performed for other compounds released from other alternative dental materials. Some of the monomers used are cytotoxic to pulp and gingival cells *in vitro*. There is *in vitro* evidence that some of these alternatives are also mutagenic although long-term health consequences are unclear. Allergies to some of these substances have been reported, both in patients and in dental personnel. However, information on the toxicological profile of alternative materials and clinical data on possible adverse effects of alternatives are very limited.

The SCENIHR concludes that current evidence does not preclude the use of either amalgam or alternative materials in dental restorative treatment. However, the choice of material should be based on patient characteristics such as primary or permanent teeth, pregnancy, the presence of allergies to mercury or other components of restorative materials, and the presence of impaired renal clearance.

The SCENIHR recognises that there is a need for further research, particularly relating to (i) evaluation of the potential neurotoxicity of mercury from dental amalgam and the effect of genetic polymorphisms on mercury toxicity and (ii) to expand knowledge of the toxicity profile of alternative dental restorative materials. Furthermore, there is a need for the development of new alternative materials with a high degree of biocompatibility.

Keywords: Dental amalgam, mercury, toxicology, exposure, resin-based composites, glass ionomer cements, allergy, systemic health effects, SCENIHR.

Opinion to be cited as: SCENIHR (Scientific Committee on Emerging and Newly-Identified Health Risks), Scientific opinion on the Safety of Dental Amalgam and Alternative Dental Restoration Materials for Patients and Users (update), 29 April 2015.

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EXECUTIVE SUMMARY

In the light of new developments and studies on dental amalgam, a request was submitted to update the previous Opinion of SCENIHR from 2008 on the safety and performance of both dental amalgam and possible alternatives, such as resin-based composites, glass ionomer cements, ceramics and gold alloys.

This updated 2015 Opinion evaluates the scientific evidence about any links that may exist between either amalgam or possible alternatives and allergies, neurological disorders or other adverse health effects.

The SCENIHR recognises that dental amalgam is an effective restorative material for the general population. From the perspectives of longevity, mechanical performance and economics, amalgam has long been considered the material of choice, especially for certain types of restorations in posterior teeth, including replacement therapy for existing amalgam fillings. However, dental amalgam is neither tooth-coloured nor can it adhere to remaining tooth tissues. It is retained in the tooth by mechanical means, such as undercuts in the cavity preparation. Its use has been decreasing in recent years and the alternative tooth-coloured filling materials are increasingly used. There is a trend towards minimal interventional, adhesive, techniques in dentistry, which are based on adhesion to tooth structure by chemical interaction and/or micromechanical retention. At the same time, the quality and durability of alternative materials have improved.

The exposure of the general population to mercury is mainly due to fish consumption (organic mercury, methyl mercury) and dental amalgam (elemental mercury, inorganic mercury). Mercury is the metallic element of concern used in dental amalgam. Mercury is a well-documented toxicant, with reasonably well-defined characteristics for the major forms of exposure, involving elemental mercury as well as organic and inorganic mercury compounds. This Opinion does not address the issues of organic mercury or methyl mercury.

Local adverse effects in the oral cavity are occasionally seen with dental materials in general, including allergic reactions and an association with clinical features characteristic of lichen planus. These reactions occur at an incidence below 0.3% and are usually readily managed.

Regarding systemic effects, elemental mercury is a well-documented neurotoxicant, especially during early brain development, and inorganic mercury also constitutes a hazard to kidney function. EFSA (2012) has recently evaluated inorganic mercury in food and recommended a tolerable intake limit (tolerable weekly intake of inorganic mercury of 4 µg/kg body weight, expressed as mercury). Several studies have explored the possible association of mercury derived from dental amalgam with a variety of adverse effects, particularly neurological and psychological or psychiatric diseases, including Alzheimer's disease, Parkinson's disease, and multiple sclerosis as well as kidney diseases. The causality evidence for such effects due to dental amalgam is weak because of contradictory reports and major challenges in exposure assessment, which is generally expressed as total mercury in body fluids (mainly urine), without differentiating between organic vs. inorganic forms as well as between sources (dietary vs. dental amalgam or others).

Mercury concentration in the adult brain is associated with the number of amalgam fillings. In the foetus, mercury concentration in the kidney (but not in the foetal brain) has a tendency to be associated with the mothers' number of amalgam fillings. Because the estimated elimination half-life for inorganic mercury in the brain exceeds 10 years, mercury is likely to accumulate in the central nervous system. The accumulated concentrations in brain tissue (as measured in post-mortem specimen) may reach values that are similar to those inducing neurochemical changes in experimental models *in vitro*. Such effects have not been convincingly demonstrated in humans as caused by dental amalgam.

So far, studies in children of school age did not convincingly demonstrate amalgam-associated neuropsychological deficits. However, recent studies suggest that genetic polymorphisms may influence the degree of individual susceptibility with regard to mercury internal exposure and consequently toxicity in children as well in adults.

The transient mercury release during placement and removal will result in transient exposure to the patients (resulting in a transient increase in plasma mercury levels) and also to the dental personnel. There is no justification for removing clinically satisfactory amalgam restorations as a precaution, except in those patients diagnosed as having allergic reactions to amalgam constituents.

Recent studies do not indicate that dental personnel in general, despite somewhat higher exposures than patients, suffer from adverse effects that could be be attributed to mercury exposure due to dental amalgam. Exposure of both patients and dental personnel could be minimised by the use of appropriate clinical techniques.

Respiratory air concentrations, blood levels and urinary excretion of mercury in individuals with amalgam fillings indicate that the levels of exposure encountered are 5 to 30 times lower than those permitted for occupational exposure. Tolerable limits for dietary exposures to mercury are relevant to amalgam safety considerations, as inhaled elemental mercury may add to the body burden of inorganic mercury. Recently the European Food Safety Agency reported that the tolerable weekly intake for inorganic mercury might be exceeded due to the additional inhalation exposure in people with a high number of amalgam fillings. However, evidence is weak and the data are mainly derived from model-based calculations. Studies on large patient collectives did not show any clear correlation of health effects with the number of dental amalgam restorations.

The SCENIHR notes that alternative materials to amalgam are chemically very complex and also have clinical limitations and may represent toxicological risks. They contain a variety of substances including organic solvents, may undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement and may also degrade *in situ*. The SCENIHR Opinion "The safety of the use of bisphenol A in medical devices" (2015) concluded that release of BPA from some dental materials was associated with only negligible health risks. A similar extensive risk assessment has not been performed for other compounds released from alternative dental materials. Non-mercury containing alternatives are not free from any concerns about adverse effects. With respect to resin composite restorative materials and hybrid systems that incorporate polymerisable resins, there is *in vitro* evidence that some of the monomers used are highly cytotoxic to pulp and gingival cells. There is also *in vitro* evidence that some monomers are mutagenic although it is not known whether this has any clinical significance. Allergic reactions to some of these substances have been reported, and to a higher degree, both in patients and in dental personnel. Similar to treatment with dental amalgam, the use of these materials in pregnant women is discouraged.

It is noted that there are very limited scientific data available concerning exposure of patients and dental personnel to substances that are used in alternative restorative materials. Many of the monomers and other organic solvents used in them are volatile and need to be better identified and quantified. Further toxicological research on the various components of these alternative dental materials is warranted.

Alternative materials have now been in clinical use for well over thirty years, initially in anterior teeth and more recently also for restorations in posterior teeth. Existing clinical experience has revealed little evidence of clinically significant adverse events. It is also important to note that the composition of available materials has changed substantially in recent years with reduced bioavailability of harmful components from use of improved polymerisation processes and particular improvement in the adhesive systems and the filler parts. There is no evidence that infants or children are at risk of adverse effects arising from the use of alternatives to dental amalgam. However, similar to mercury, genetic polymorphisms may also exist for toxicokinetics of some constituents of these alternative materials. Cellular reactions towards resin monomers are regulated by the genes that are also involved in the reaction towards mercury and therefore genetic variability is also relevant for resin-based materials.

The SCENIHR notes that the full chemical specification of these alternative restorative materials is not always divulged, and it may be difficult to know exactly what they contain. As a result, there are limited toxicological data publicly available for these materials. Dental restorative materials are defined as medical devices according to the Council Directive

93/42/EEC concerning medical devices and belong to class IIa. Consequently, the certification process does not include examination of the design dossier and, therefore, the chemical specification does not have to be revealed to the third party. Although manufacturers are obliged to assess biocompatibility and the risk from unintended side effects, accessible information on the toxicity of the constituents of the materials as well as relevant exposure data is lacking. Therefore, the SCENIHR notes that it is not possible to provide a scientifically sound statement on the safety of these materials.

As a general principle, the relative risks and benefits of any dental treatment need to be explained to patients to assist them to make informed decisions. Better information concerning the relative risks of dental restorative materials requires more data. Therefore, it is recommended that manufacturers should provide this information.

More publicly available research data are also needed to have a broader basis for risk evaluation. In view of the controversial nature of this subject, it would also be beneficial for the community in general to be better informed of the recognised benefits and risks.

In the light of the above comments the SCENIHR concludes that dental amalgam already in place is not considered a health risk for the general population. Consequently, pre-existing amalgam restorations should not be removed as a preventive measure. As far as dental personnel are concerned, it is recognised that they may be at greater risk with respect to higher mercury exposure from dental amalgam than the general population, although the incidence of reported adverse effects seems to be in the same order of magnitude.

Information on exposure, toxicity and clinical outcomes for alternative materials is much scarcer than for dental amalgam. There is some evidence that some of the low molecular weight substances used in their preparation are associated with local allergic reactions. There are insufficient data to draw firm conclusions about associations between these alternative materials and neurological or other health disorders. The continuing evolution of these materials suggests that caution should be exercised before new variations are introduced into the market. As far as dental personnel are concerned, there are reports of small numbers of cases of induced allergies to these materials. Their volatile organic solvent species that are pervasive in dental clinics should be identified and quantified to enable proper risk assessment.

The SCENIHR concludes that dental restorative treatment can be adequately ensured by amalgam and alternative types of restorative material. The longevity of restorations of alternative materials in posterior teeth has improved with the continuing development of these materials and the practitioner's familiarity with effective placement techniques, but is in certain clinical situations (e.g. large cavities and high caries rates) still inferior to amalgam.

The choice of material should be based on patient characteristics such as primary or permanent teeth, pregnancy, presence of allergies to mercury or other components of the restorative materials, and presence of decreased renal clearance. The clinical trend towards the use of adhesive alternatives is considered advantageous as it implies that a sustained reduction in the use of dental amalgam in clinical practice will continue across the European Union.

The SCENIHR recognises a lack of knowledge and a need for further research, in particular in regard to genetic susceptibility related to mercury effects and to the constituents of alternative restorative materials. Furthermore, there is a need for the development of new alternative materials with a high degree of biocompatibility.

1. BACKGROUND

Dental amalgam and its substitutes are regulated under Council Directive 93/42/EEC concerning medical devices, according to which they must comply with the essential requirements laid out in the directive, in particular in relation to the health and safety of the patients.

Dental amalgam has been used for over 150 years for the treatment of dental cavities and is still used, in particular in large cavities, due to its excellent mechanical properties and durability. Dental amalgam is a combination of alloy particles and mercury that contains about 50% of mercury in the elemental form. Overall, the use of alternative materials such as composite resins, glass ionomer cements, ceramics and gold alloys, is increasing, either due to their aesthetic properties or alleged health concerns related to the use of dental amalgam.

In January 2005, the Commission adopted a proposal for a Community Strategy concerning Mercury in order to reduce mercury levels in the environment and human exposure. Pursuant to Action 6 of the Strategy, the use of dental amalgam should be evaluated with a view to considering whether additional regulatory measures are appropriate.

In view of the above, the Commission requested the Opinion of the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) on the safety of dental amalgam and alternative dental restoration materials. According to the SCENIHR Opinion adopted in May 2008, dental amalgam is a safe material to use in restorative dentistry for patients. No health risk other than allergic reaction in certain individuals can be associated with the use of dental amalgam. The alternatives are not without clinical limitations and toxicological risks, and less is known about these alternatives for which available scientific data are more limited.

In 2010 a report of the meeting convened by WHO on "Future Use of Materials for Dental Restoration" was published, in which a 'phase-down' of the use of dental amalgam at the global level was suggested. According to the report, this may be achieved effectively by strengthening the prevention of dental caries and by encouraging better use of quality alternatives to dental amalgam. More quality studies and systematic reviews are needed in the case of dental materials alternatives to amalgam. A recent "Study on potential for reducing mercury pollution from dental amalgam and batteries" (May 2012) addresses the environmental impacts of dental amalgam use (http://ec.europa.eu/environment/chemicals/mercury/pdf/BIO_Draft%20final%20report.pdf). The study did not evaluate the health aspects.

2. TERMS OF REFERENCE

In the light of recent developments and studies on dental amalgam we would like to ask the SCENIHR to update, if appropriate, the Opinion adopted in 2008. In view of possible safety concerns linked to the use of dental amalgam and its substitutes, it is essential to review and evaluate available scientific data related to the safety of these substances for patients and in particular for high risk groups.

In particular, the SCENIHR is asked the following questions:

1. Is there any new scientific evidence that justify reasons for concern from the health point of view in the use of dental amalgam as dental restoration material?

2. In view of the above, is the use of dental amalgam safe for patients and users, i.e. dental health professionals? Are certain populations particularly at risk, e.g. pregnant women or children? Is it possible to recommend certain practices to minimise patient's and user's exposure to dental amalgam?

3. Is there new scientific evidence on the safety and performance of alternative materials?

4. Is it possible to recommend alternative materials and certain practices related to these materials to reduce potential risks for patients and users?

5. In case there is not enough scientific data to answer these questions, the SCENIHR is asked to formulate recommendations for research that could help to provide the necessary data.

3. SCIENTIFIC RATIONALE

3.1. Introduction

This Opinion is an update of the safety issues of dental amalgam and alternative materials that have been previously considered in an Opinion published in 2008. Since then, additional information has been published, including clinical epidemiological studies. The present document therefore highlights new information, and it supplements and updates the previous opinion. While occupational exposures are included, this Opinion does not consider environmental aspects of amalgam use. It is recognised that both at European and United Nations level there are on-going efforts to reduce the exposure to mercury. The Scientific Committee on Health and Environmental Risks (SCHER) has recently adopted an Opinion regarding the contribution of dental amalgam to the environmental burden of mercury and the possible health effects deriving from environmental exposure to Hg coming from dental amalgam (SCHER, 2014).

One of the major components of the dental amalgam restoration is elemental mercury. The essential metallurgical principles of dental amalgam are fairly straightforward. Liquid mercury is able to react with many other metallic elements to produce a series of multi-phase alloys that are solid at room temperature. The present Opinion will focus on these mercury species. In the body, elemental mercury is oxidised to inorganic mercury, which also occurs as a food contaminant. EFSA (2012) has recently evaluated inorganic mercury in food and recommended a tolerable intake limit (tolerable weekly intake of inorganic mercury of 4 µg/kg body weight, expressed as mercury). Thus, the present Opinion will review the toxicology of elemental and ionic (mercuric) mercury as deemed appropriate in regard to amalgam safety considerations. Once released into saliva, inorganic mercury might be methylated by bacteria in the periodontal pocket and gastrointestinal tract, but the rate is not clear (Langendijk *et al.*, 2001, Leistevuo *et al.*, 2002, van der Hoeven *et al.*, 2007). However, the contribution of this reaction when compared to the intake of methyl mercury from the food is expected to be limited.

The alternatives for dental amalgam in dental restorations include resin-based composite materials, glass ionomer cements, ceramics, gold-based and other alloys, and a variety of hybrid structures. Many of them have been in use only for a limited number of years, and the toxicological database is limited, also in regard to reaction products. Thus, the data base is much more limited in regard to these dental materials, and some conclusions regarding toxic risks and long-term stability must therefore be tentative at this point. As amalgams are phased out, further documentation on new dental restoration materials must be secured so that the present high quality of care and high degree of safety can be maintained.

A changing scenario

Placing restorations due to dental caries is still a commonly performed treatment, but there are great variations in decision-making about the threshold for intervention with restorative treatment. This is a global issue.

Questionnaire surveys have been carried out, asking the practitioners whether they would operatively treat an occlusal lesion confined to the enamel in a patient with low risk of developing caries. In Iran 32 % (Ghasemi *et al.*, 2008), in France more than one half (Doméjean-Orliaguet *et al.*, 2004) and in the USA 63 % would do so (Gordan *et al.*, 2010). Of the Scandinavian respondents only 2.6% said that they would intervene that early (Gordan *et al.*, 2010). A survey based on questionnaires revealed that in 2009, 7 % of Norwegian dentists would restore approximal lesions confined to enamel, compared with (in similar studies) 18% in 1995 and 66 % in 1983. These changes in treatment threshold criteria indicate that many dentists have taken into account that caries is a slowly progressing disease and that especially initial carious lesions can be arrested (Vidnes-Kopperud *et al.*, 2011).

3.2. Methodology

This Opinion of the SCENIHR is concerned with the analysis of the evidence for the potential for either amalgam or alternatives to amalgam to have adverse effects on human health, from the perspectives of both scientific plausibility as well as experimental, clinical and epidemiological data. Recent scientific evidence is reviewed to determine whether it justifies any reason for concern in regard to health risks associated with the use of dental amalgam and currently available alternative materials. In this context SCENIHR refers to the definition of risk as mentioned in different ISO-EN standards (ISO EN 10993-1 and ISO-EN 14971).

The SCENIHR has considered evidence derived from a wide variety of sources, including peer-reviewed scientific and medical literature and published reports of institutional, professional, governmental and non-governmental organisations. In coherence with the usual practice of the SCENIHR, less weight has been given to work not freely available in the public domain.

The SCENIHR has reviewed as much evidence as possible and, especially where the available data on alternatives is limited, attention has been given to some less well-controlled studies where no other information was available. During the course of the deliberations of the Working Group, a Call for Information was issued by the Commission (8 August 2012 to 10 October 2012) and all of the responses have been considered. An extensive literature search was performed in 2012 (covering the period 2008-2012) by an external contractor with the following search terms:

Dental amalgams/mercury amalgams implants/fillings and:

- mercury exposure/levels/ blood/body burden/brain
- leaching/ loss/release/mobilisation/stability
- risk assessment/hazard/adverse effects/disorders/ neuro* effects/safety/risk benefits
- removal, health effects/implications/risk/risk benefit/safety
- cremation
- life cycle analysis/ manufacturing/use/disposal

Non –mercury/ceramic/implants/fillings and:

- leaching/ loss/release/mobilisation/stability
- risk assessment/hazard/adverse effects/disorders/ neuro* effects/safety/risk benefits
- removal, health effects/implications/risk/risk benefit/safety
- life cycle analysis/ manufacturing/use/disposal

In addition, during the writing of the Opinion, additional relevant literature up to 2014 was provided by both members of the working group and of SCENIHR. Literature published before 2008 that was not included in the previous Opinion but was considered relevant was also assessed. Furthermore relevant references provided via the public consultation were included as well.

In a review of the evidence for or against causation of disease, it is necessary to take into account the generally accepted criteria for causation. The SCENIHR published a memorandum on the weight-of-evidence approach to the evaluation of risks and hazards (SCENIHR, 2012). The criteria considered are: (i) the establishment of temporal relationship between exposure and outcome; (ii) the statistical evaluation of an effect; (iii) the evidence of a dose-response relationship; (iv) the plausibility and specificity of any association; and (v) the coherence of any putative association with existing knowledge.

On the other hand, these criteria, which build upon Hill's original 'aspects' are not symmetrical. That is, if one of the conditions is fulfilled, then it supports causality, but it does not necessarily speak against it if not (or not yet) fulfilled (Kaufman and Poole, 2000).

In the weight of evidence approach, lines of evidence or hypothesis for causality are evaluated based on the supportive studies. When a line of evidence is consistently supported by various studies (i.e. evidence is independently reproduced in different studies) causality is likely

between the observed effect and exposure to the substance. Strength and weaknesses of the studies evaluated are considered. The weight of evidence can be categorised as follows:

Strong overall weight of evidence: Coherent evidence from human and one or more other lines of evidence (in particular model/ mechanistic studies) in the absence of conflicting evidence from one of the other lines of evidence (no important data gaps).

Moderate overall weight of evidence: Good evidence from a primary line of evidence but evidence from several other lines is missing (important data gaps).

Weak overall weight of evidence: Weak evidence from the primary lines of evidence (severe data gaps).

Uncertain overall weight of evidence: Due to conflicting information from different lines of evidence that cannot be explained in scientific terms.

Weighing of evidence not possible: No suitable evidence available.

A major problem in many of the reviewed epidemiological studies was the quantitative evaluation of the contribution of mercury exposure coming from dental amalgam.

The evidence for the presence of a causal relationship between exposure to dental amalgam and/or alternative restoration material, and adverse health effects are discussed in the chapters below.

3.3. Dental Amalgam

In this Chapter, the essential and relevant characteristics of dental amalgam and the evidence concerning the general exposure and toxicity of mercury-based substances are explained and discussed. This is followed by an assessment of the reported adverse effects in individuals with amalgam restorations, the epidemiological and clinical evidence concerning adverse effects in dental personnel, and general observations about the clinical usefulness of dental amalgam restorations.

3.3.1. Metallurgical principles and physical-chemical properties

The principles and physical-chemical properties of dental amalgams are described in the previous Opinion (2008). The SCENIHR is not aware of new developments in amalgam metallurgy.

Mercury is a metallic element that occurs naturally and also in the form of several types of ore, the mercury burden of the environment being derived in part from natural sources, in part from accumulated anthropogenic emissions.

3.3.1.1. Major Forms of Mercury

Each form of mercury has its own toxicological profile and shows major differences in toxicokinetics.

3.3.1.2. Background exposure to mercury

<u>Exposure to Mercury in Adults</u>

As described in the previous Opinion (SCENIHR, 2008), background exposure to mercury by inhalation is very low in the general population. The main source for mercury inhalation is dental amalgam as indicated by relatively old data published by WHO in 1990.

The major sources of mercury intake in the diet is methyl mercury, essentially in fish and also inorganic mercury coming from non-fish diet sources. Table 1 shows current estimates for dietary exposures to inorganic mercury (EFSA, 2012).

Table 1: Summary statistics of the chronic dietary exposure to inorganic mercury (µg mercury /kg b.w. per week) by age class (gyEFSA, 2012)

Age group	Minimum			Median			Maximum		
	LB	MB	UB	LB	MB	UB	LB	MB	UB
Mean dietary exposure in total population									
Toddlers	0.27	0.79	1.31	0.37	1.13	1.71	0.59	1.36	2.16
Other children	0.24	0.59	0.89	0.38	0.84	1.24	0.76	1.13	1.75
Adolescents	0.16	0.39	0.59	0.25	0.44	0.68	0.51	0.73	0.94
Adults	0.14	0.26	0.38	0.23	0.41	0.55	0.40	0.53	0.70
Elderly	0.13	0.23	0.33	0.22	0.35	0.48	0.30	0.42	0.55
Very elderly	0.14	0.25	0.35	0.19	0.33	0.47	0.24	0.38	0.52
P95 dietary exposure in total population									
Toddlers	0.67	1.35	2.18	0.84	1.77	2.83	1.07	2.30	4.06
Other children	0.50	1.12	1.66	0.86	1.62	2.20	1.85	2.27	3.37
Adolescents	0.31	0.71	1.00	0.62	0.88	1.26	1.70	1.85	2.33
Adults	0.36	0.53	0.72	0.59	0.78	1.02	1.52	1.66	1.83
Elderly	0.25	0.40	0.55	0.54	0.72	0.92	0.77	0.94	1.12
Very elderly	0.25	0.40	0.54	0.47	0.62	0.82	0.64	0.81	1.01

The minimum, median and maximum of the mean and the 95th percentile exposure values across European countries and dietary surveys are shown.
LB, UB, MB, respectively lower bound, upper bound and middle bound exposure estimates.

In line with JECFA, the EFSA CONTAM Panel (2012) established a tolerable weekly intake (TWI) for inorganic mercury of 4 µg/kg b.w., expressed as mercury. TWI for methyl mercury of 1.3 µg/kg b.w., expressed as mercury was established, which is somewhat lower than the TWI JECFA level of 1.6 µg/kg b.w. It was concluded that mean dietary exposure across age groups does not exceed the TWI for methyl mercury, with the exception of toddlers and other children in some surveys. The 95th percentile dietary exposure is close to or above the TWI for all age groups. High fish consumers may exceed the TWI by up to approximately six-fold. Unborn children constitute the most vulnerable group. The EFSA stated that dietary inorganic mercury exposure in Europe does not exceed the TWI. Inhalation exposure of mercury vapour from dental amalgam is likely to increase the internal inorganic mercury exposure. The TWI might be exceeded when a high number of dental amalgam fillings is present, but no further indication is given.

Exposure during pregnancy and breast-feeding

Mercury vapour, like methyl mercury, is capable of passing the placental barrier. Thus, in a study of 99 mother-child pairs, a strong positive correlation between maternal and cord blood total Hg levels was found (ρ=0.79; P<0.001). Levels of Hg in the cord blood were significantly associated with the number of maternal amalgam fillings (ρ=0.46, P<0.001) and with the number of years since the last filling (ρ=−0.37, P<0.001); these associations remained significant after adjustment for maternal age and education. The median values of total Hg

concentrations were 0.63 µg/L (range 0.14-2.9 µg/L) and 0.80 µg/L (range 0.15-2.54 µg/L) for maternal and cord blood, respectively (Palkovicova *et al.,* 2008).
Mercury is usually present in amniotic fluid. In one study of 72 pregnant women (Luglie *et al.*,2005) there was an overall mean mercury concentration in amniotic fluid of 0.37 ± 0.49 ng/ml. The women were divided into those with a low concentration of less than 0.08 ng/ml, the detection limit of their analytical method (26.4% of the subjects) and those with a concentration of greater than 0.08 ng/ml, mean 0.49 ±- 0.52 ng/ml (73.6% of subjects). A dependence of mercury concentration in amniotic fluid on number of amalgam fillings ($p=0.03$) and fish consumption ($p=0.04$) was observed, but not significant at their preset level ($p<0.01$).

Björnberg *et al.*,(2005) reported that infant blood inorganic mercury was similar to maternal blood mercury at delivery (median =0.09 µg/L) but decreased until the end of follow-up at 13 weeks of age (0.05 µg/L), while remaining unchanged in maternal blood. The exposure of the infants to inorganic mercury was low being higher at birth than during the breast-feeding period. In breast milk the authors could not differentiate between inorganic and organic mercury. They concluded that the exposure to both forms of mercury is higher before birth than during the breast-feeding period, and that methyl mercury seems to contribute more than inorganic mercury to postnatalnfant exposure via breast milk.

In addition, mercury has been detected in foetal brain and kidneys. The concentrations in the kidneys (but not in the brain) showed a tendency to increase with the number of amalgam fillings of the mother, with no statistical significance. Brain levels were in the range of 2-23 µg/kg wet weight, and kidney levels in the range of 5-34 µg/kg (Lutz *et al.,* 1996).

Brain tissue obtained from 18 foetuses and 35 children below 5 years of age showed mercury concentrations up to 6 and 20 µg/kg, respectively. A significant correlation ($p< 0.05$) with the mother's number of amalgam fillings (grouped as less than 2 or more than 10 fillings), was evident only for older children and not for foetuses. In foetuses and older infants significantly higher mean mercury concentrations in the liver and the renal cortex were found, if the mothers had more than 10 teeth with dental amalgam (Drasch *et al.,* 1994).

Da Costa *et al.*,(2005) reported on a correlation between breast milk mercury and the number of amalgam surfaces. However, Drasch *et al.*(1998), compared mercury in breast milk and in cow's-milk-based formulas and concluded that even for mothers with large numbers of dental amalgam, these fillings should pose little danger to breast-feeding infants. Indeed, during the first 2 mo, it is uncertain if any correlation between milk mercury concentrations and maternal amalgam filling exists.

Drexler and Schaller (1998) concluded that Hg exposure in breast-fed babies from maternal amalgam is of no significance to foetal and neonatal Hg blood. Stoz *et al.*,(1995) also reported that newly made tooth fillings during pregnancy had no influence on Hg concentrations in newborns.

Overall, the evidence provided by the available studies seems not to indicate a strong relationship between amalgam fillings and mercury concentration in breast milk.

3.3.1.3. Intake estimates for mercury from dental amalgams

Mercury vapour is released from silver amalgam restorations during chewing, tooth brushing, and parafunctional activities including bruxism. The parameters of this release of mercury vapour by amalgam depends on the number of fillings, the filling size and placement, chewing habits, food texture, grinding and brushing teeth, nose-mouth breathing ratio, inhalation, ingestion and body weight, and the surface, composition and age of the amalgam restorations. Therefore, there are large variations in the estimation of daily mercury release from the restorations. Accordingly, exposure assessment is complicated and inherently imprecise. Feasible assessment of the recent mercury exposure from amalgam restorations is routinely recorded as dose parameters in terms of mercury concentrations in urine and blood (EFSA,

2012; Grandjean and Yorifuji, 2012).Although mercury is also released in saliva, due to the low gastrointestinal absorption, the mercury uptake through saliva was considered to be low (0.2 and 3 µg/kg b.w. per week) (Björkman *et al.*,1997).

As discussed in the previous Opinion, the World Health Organization (WHO) reported a consensus average estimate of 10 µg/day of amalgam derived mercury (range: 3-17 µg/day) (WHO 1991). The daily uptake of mercury from amalgam fillings has been estimated by other Authors to range between 3.8 and 17 µg/day, and results in a steady-state level of mercury in body fluids (Sandborgh-Englund 1998a and 1998b). In case of individuals with a large number of amalgam fillings, dental amalgam may account for 87% of the absorbed inorganic mercury (WHO 1991). In individuals with only a few amalgam fillings, this source may account for about 50% of the absorbed inorganic mercury (summarised in ATSDR, 1999). Unfortunately, many of the older papers only use the arbitrary system of "few" and "large" numbers of restored teeth or surfaces. There are 20 teeth (premolars and molars) with 100 surfaces that may potentially be restored with dental filling materials.

More recently the assessment of exposure from dental amalgam was estimated as 0.2 to 0.4 µg/day per amalgam-filled tooth surface or 0.5 to 1 µg/day per amalgam filled tooth (Richardson *et al.*, 2011); each amalgam-filled surface results in an increase of mercury in urine of 0.1 µg Hg/L or 0.06 to 0.07 µg Hg/g creatinine (summarised in Richardson *et al.*, 2011). However, this calculation has been criticised by Nicolae *et al.*,(2013), arguing that not every aspect of mercury exposure, toxicity or pharmacokinetics was considered in the calculations made by Richardson *et al.*,(2011). Data obtained by measuring urinary mercury levels in the Canadian population show values of 0.12 µg Hg/L and 0.31 µg Hg/L (Nicolae *et al.*, 2013). It was estimated that for the vast majority of the Canadian population (up to 98.23%) this mercury level was below levels associated with any health risks. For the same exposure level the absorption values of inorganic mercury from dental amalgam was estimated six times lower compared to the absorption of organic mercury from food (Jones 1999; Nicolae *et al.*, 2013).

Similar results for blood and urine concentrations have been obtained for amalgam-bearers in the UK (Eyeson *et al.*, 2010) and Canada (Dutton *et al.*, 2013). Dye *et al.*,(2005) found that the average urinary mercury level in women of childbearing age was 1.3 µg/L and an increase of 1.8 µg/L was seen for each ten dental surfaces restored with amalgam. Levels of 1-5 µg/L were described as the normal range for non-occupational groups (Hørsted-Bindslev 2004). Similarly, in a study of 1127 healthy males, Kingman *et al.*,(1998) found an average total mercury urinary concentration of 2.55 µg/L. There was a significant correlation between this level and amalgam exposure equivalent to an increase of 1 µg/L of urine for each 10 amalgam surfaces. Substantially elevated urine levels, i.e. approximately five times higher than controls, have been reported in individuals who regularly used nicotine chewing gums (Sällsten *et al.*,1996).

In a prospective study of adolescents in the Casa Pia study in Portugal, the urinary mercury excretion was averaged approximately 3 µg/L in those with amalgam fillings, compared to 2 µg/L in controls at age 18 years. There was a statistically significant dose-dependent correlation between cumulative exposure to Hg from dental amalgams and urinary Hg levels, after covariate adjustment. When urine values in children of 8 years with amalgam and without were compared, they found 2.77 µg Hg/L without and 3.28 µg Hg/L with amalgam restorations (Geier *et al.*, 2012).

Due to the reduction of use of dental amalgam in children, the mercury levels in that population are significantly decreased as indicated by a study in Germany (Link *et al.*, 2012).

The removal of amalgam fillings causes an additional transient Hg-exposure and results in a transient increase in plasma Hg levels. The mercury-dose from removal of 16 amalgam filled surfaces is estimated to be around 40 µg mercury, based on data from Sandborgh-Englund (1998a and 1998b). This single-dose exposure is equal to the integrated chronic mercury dose from amalgam restorations over 2.3-10 days.

Greater plasma Hg-peaks have been shown in conjunction to amalgam removal in the studies by Molin *et al.*,(1990) and Berglund and Molin (1997), whereas later studies show plasma peaks in parity with Sandborgh-Englund *et al.*,(1998b) (Halbach *et al.*, 1998; Halbach *et al.*,

2000; Kremers *et al.*,1999). The number of fillings removed and the working technique (water spray, suction efficiency, rubber dam use) affects the amount of mercury released.

Retention data are available from analyses of autopsy specimens. Brain tissue generally shows average total mercury concentrations below 10 µg/kg, with a highly significant association between number of amalgam fillings and surfaces on the one hand and the mercury concentration in occipital cortex and pituitary gland. In a study of mercury in Swedish autopsy samples from 30 subjects, with an average of 13.2 amalgam surfaces, the median concentrations of methyl mercury and inorganic mercury in the occipital lobe cortex were 4 and 5 µg/kg wet weight, respectively. In one of the samples from occipital cortex the concentration of inorganic mercury (164 µg/kg) was 9 times higher than the concentration of the second highest case and fulfilled the criteria of an "extreme outlier" from a statistical point of view. The subject was found to have been employed as a dental assistant in the past (Björkman *et al.*, 2007).

Another study from Italy showed that cerebral cortex concentrations averaged about 200 µg/kg in subjects with more than 12 amalgam fillings, i.e. being over 10-fold higher than in subjects with three fillings or less (Guzzi *et al.*, 2006). Mercury levels were significantly higher in brain tissues compared with thyroid and kidney tissues in subjects with more than 12 occlusal amalgam fillings but not in subjects with 3 or less occlusal amalgams. However, no information was available on the fish consumption, therefore it was not possible to estimate the relative contribution of diet vs. dental amalgam. For comparison, adult victims who died from methyl mercury poisoning in Japan had mercury concentrations in the brain that averaged about 10 mg/kg, while much lower concentrations, about 1 mg/kg, were found in victims of foetal Minamata disease (Takeuchi and Eto, 1999). Based on these data, the total amount of mercury that must reach the brain to cause a condition commensurable with severe clinical disease or fatal poisoning would therefore be 1 mg/kg brain or more (that is 5 fold higher than the ones measured in individuals bearing more than 12 amalgam fillings). However, in a recent assessment of the neurological problems from Minamata poisoning described by Takeuchi and Eto (1999), methylmercury uptake was re-evaluated. Regarding the neurological symptoms no dose response relationship was established, limiting the interpretation of the earlier described results (Maruyama *et al.*, 2012).

In living kidney donors, the kidney mercury concentration increased by 6% for every additional amalgam surface, but was not associated with fish consumption, thus suggesting that amalgam fillings constitute a main source of inorganic mercury exposure (Barregard *et al.*, 2010). Since the major part of mercury in the kidneys has a half-life of about 2 months (Sallsten *et al.*, 1994), the kidney mercury concentrations likely reflect exposures during the most recent year or so. While some sex difference in kidney mercury retention has been reported, animal studies suggest that genetic factors may substantially affect mercury excretion in the urine and mercury accumulation in the kidneys (Ekstrand *et al.*, 2010). This notion is supported by human epidemiological evidence on differences in elimination associated with gene variants (Goodrich *et al.*, 2011), as described below.

3.3.1.4. Exposure to mercury in dental personnel

The mercury body burden of dental personnel is usually higher than in the general population. The mean urine mercury levels in dental personnel has been variously reported to range from 3 µg/L to 22 µg/L, compared to 1-5 µg/L as the normal range for non-occupational groups (Hørsted-Bindslev 2004). The increased body burden is attributed to dental personnel mixing and applying dental amalgam and removing amalgam restorations.

Ritchie *et al.*,(2004) showed that dentists had, on average, urinary mercury levels over 4 times that of control subjects. All but one dentist had urinary mercury below the UK Biological Monitoring Guidance Value of 20 µmol mercury /mol creatinine. Over 67% of the 180 surgeries visited had environmental mercury measurements in one or more areas above the Occupational Exposure Standard (OES) in UK. In the majority of these surgeries the high levels

of mercury were found at the skirting and around the base of the dental chair. In 45 surgeries (25%) the personal dosimetry measurement (i.e. in the breathing zone of dental staff) was above the OES.

Correlations have been found amongst dentists between urinary mercury levels and the number of hours worked in the surgery ($r=0.22$, $P=0.006$) and the number of amalgam restorations placed ($r=0.38$, $P<0.001$) and removed ($r=0.29$, $P<0.001$) in a week, with urine mercury levels in dentists ranging from 0.02 to 20.90 (mean 2.58) nmol mercury per nmol creatinine. A contributing and thus confounding factor in such investigations is the number of amalgam surfaces dentists have in their own mouths (Ritchie *et al.*,2002, Ritchie *et al.*,2004).

Dental personnel may now be exposed to much less mercury than in the past, in view of the increased use of encapsulated dental amalgam, improvements in amalgam capsule design, the heightened awareness and practice of appropriate dental mercury hygiene measures, and the increasing use of alternative, non-mercury-containing materials (Hørsted-Bindslev 2004). However, despite trends to reduce exposure to mercury, large, highly statistically significant differences ($P<0.0001$) may be found between dental personnel (in particular dentists) and controls, with respect of mean urinary, hair (head and pubic) and nail (finger and toe) mercury levels (Morton *et al.*, 2004). Nevertheless, according to head hair mercury data acquired over 35 years in Scottish dental practice (Duncan *et al.*, 2011) median concentrations were reduced from 8.6 µg/g in the period 1975-1979 to 0.5 µg/g in the period 2005-2009. The reduction was attributed to preparation techniques and increased awareness. In comparison, mean hair mercury concentration in the U.S. population of women in childbearing age is 0.20 µg/g (McDowell *et al.*, 2004).

High levels of exposure can also occur during preclinical training of students. A study in the Dental Simulation Laboratory in a dental school in Puerto Rico revealed substantially higher exposure levels for mercury vapour than otherwise typical for dental clinics. Thus, eight-hour averages exceeded a level of 100 µg/m^3 by several-fold. In contrast, mercury bound to particulate matter (PM10) was low (0.1 – 1.2 µg/m^3). In the Dental Clinic itself the levels were below 100 µg/m^3 (Gioda *et al.*, 2007). In a more recent study in Canada it was observed that mercury vapour exposure during dental training on amalgam removal remained below occupational exposure limits (Warwick *et al.*, 2013).

Since most dental chair-side personnel do not touch dental amalgam during mixing and placement anymore, it is considered that the main sources of mercury exposure are aerosols, created in the immediate working environment during placing and in particular the removal of restorations of dental amalgam, and the exhaust air from dental vacuum systems. In a study with three different dental clinics, one clinic with 30 dental chairs had about 1.5 times the concentration of Hg directly at the vacuum outlet than NIOSH recommendation (Stone *et al.*, 2007). Interestingly, another clinic with 100 dental chairs and a 15 times larger number of amalgam fillings placed per day was well below the NIOSH level. Immediate working environment aerosols and exhaust air from dental vacuum systems may be inhaled. The wearing of face masks provide little, if any, respiratory barrier to mercury vapour.

In a recent study in Canada it was observed that mercury vapour exposure during dental training on amalgam removal remained below occupational exposure limits (Warwick *et al.*, 2013).

3.3.1.5. Considerations on exposure

All exposure measurements are subject to imprecision and may not reflect the true mercury concentrations in the target organs. Mercury exposure is generally expressed as total mercury in body fluid or tissues, without differentiating between organic vs. inorganic forms as well as between sources (dietary vs. dental amalgam or other minor sources). As a general caveat, exposure imprecision tends to bias study findings towards the null hypothesis, i.e. the dose-related toxic effects may be underestimated (Grandjean 2008; Grandjean and Budtz-Jørgensen, 2010)

The use of chelating agents (e.g. DMPS) was found to be of no added diagnostic value (Vamnes *et al.*, 2000) and chelating substances may be associated with notable side effects (Schuurs *et al.*, 2000).

There may be differences in internal exposure since mercury excretion may differ between boys and girls 8-18 years of age, treated with dental amalgam (Woods *et al.*,2007). Mercury is eliminated as glutathione (GSH) conjugates (Custodio *et al.*, 2005). Goodrich *et al.*,(2011) suggest that polymorphisms in selenoproteins and glutathione-related genes may influence elimination of mercury in the urine and hair or mercury retention following exposures to inorganic mercury (via dental amalgams) and methyl mercury (via fish consumption). (See paragraph 3.3.2.1)

While several common mutations of the catalase gene (*CAT*) are known, their impact on the mercury toxicokinetics is unknown. Alcohol intake may inhibit this enzyme. Experimental studies in guinea pigs suggest that combined ethanol and mercury vapour exposure will lead to increased mercury retention in the brain, heart and kidney when compared to exposure only to mercury vapour (Yoshida *et al.*,1997).

Sherman *et al.*,(2013) suggested that Hg isotopes can be used to differentiate between exposure to fish-derived inorganic mercury and elemental mercury inhaled from dental amalgams. A large part of the urinary mercury was found to be derived from methyl mercury due to fish consumption. Demethylation of methyl mercury from seafood gave a major contribution to the mercuric mercury excreted in the urine in North American seafood-consumers with fewer than 10 amalgam fillings. Only for individuals with more than 10 amalgam restorations did a large percentage of the mercury derive from exposure to elemental mercury.

3.3.1.6. Conclusions on mercury exposure from dental amalgam

Exposure of individuals to mercury from dental amalgam fillings has been estimated based on assumptions regarding relative exhalation/inhalation of elemental mercuryvaporised in the oral cavity and ingestion of Hg dissolved in saliva. Exposure assessments based on such considerations have a significant variation due to differences in systemic availability of Hg after inhalation and ingestion. Moreover, individual factors influencing mercury-release from dental amalgam fillings (such as gum chewing, tooth brushing, bruxism, dietary habits, and different rates of Hg releases from different amalgam types) are difficult to consider in such assessment.

The SCENHIR therefore performed the exposure assessment based on urinary excretion of Hg in individuals with and without amalgam fillings. Data on urinary excretion of mercury are available on a large number of subjects from several surveys. Urinary excretion of mercury is considered a suitable biomarker of systemic exposures to elemental and inorganic mercury, though some of this may have been derived from organic mercury that was demethylated. In addition, attention must be paid to the fact that urinary mercury excretion is affected by several other factors other than absorption of elemental mercury from amalgams. Fish and seafood consumption has a major influence on mercury body burden in the general population and few studies have been designed to separate the contribution from the various sources. Data on total urinary excretion indicate that dental amalgam restorations are currently considered the main source of inorganic mercury exposure.

However, recently results obtained by using mercury isotopes to differentiate between exposure to fish-derived or amalgam derived-mercury in the urine indicate that a large part of the urinary inorganic mercury was found to be derived from fish consumption and only for fish-consumer-individuals with more than 10 amalgam restorations a large percentage of mercury derives from exposure to elemental mercury from amalgam. Consequently at low levels of exposure from amalgam, the urinary mercury excretion will provide an imprecise indication of that source of exposure for inorganic mercury exposure. Unfortunately no other non-invasive

biomarker is available, nor is any non-invasive way to estimate the levels possibly accumulated in different tissues.
Estimated daily absorption of inorganic mercury from dental amalgam ranges from 3 – 17 µg/day. It also has been estimated that in urinary excretion of mercury each amalgam filling will contribute to an increase of 0.1 µg Hg/L. The mean urine mercury levels in non-occupational groups range from 0.1 to 5 µg/L, while in dental personnel reported ranges are between 3 µg/L and 22 µg/L.

3.3.2. Mercury toxicology

In general, the toxicology of mercury is highly dependent on the route of administration, the exposure conditions and the speciation of mercury. Since human exposure to mercury from dental amalgams may occur by inhalation of mercury vapour released from the dental fillings into the oral cavity, by ingestion of the released inorganic mercury, or swallowing small pieces of amalgam releasing mercury in the alimentary tract, this discussion focuses on the toxicology of inorganic mercury. The ECHA website indicates the following classification for mercury (http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d872986-171c-222a-e044-00144f67d249/AGGR-995f8d07-ac73-4081-8ad0-ed8b5616e7ee_DISS-9d872986-171c-222a-e044-00144f67d249.html).

Table 2: Hazard statements

Hazard statements	Risk phrases	Safety phrases
H330: fatal if inhaled	R26: very toxic by inhalation	S45: in case of accident or if you feel unwell, seek medical advice immediately
H360: may damage fertilityor the unborn child	R61: may cause harm to unborn child	S53: avoid exposure - obtain special instructions before use
H372: causes damage to organs	R48/23: Toxic: danger of serious damage to health by prolonged exposure through inhalation	S60: this material and its container must be disposed of as hazardous waste
	R50/53: - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment	S61: avoid release to the environment

It should be noted that classification is a hazard based process, referring to the intrinsic toxicological potential, with no reference to the doses able to elicit the effects. The dose-response is a concept related to risk assessment.

3.3.2.1. Toxicokinetics

General toxicokinetics

Mercury vapour is lipophilic and can pass biological membranes, including the blood-brain barrier and placenta, thus resulting in deposition in the central nervous system, including the foetal brain. The vapour dissolved in the blood and tissues rapidly becomes oxidised due to catalase activity. Ionic Mercury becomes bound to some extent to metallothionein and accumulates in the kidneys. Excretion takes place mainly through the urine and some is eliminated through faeces and sweat (Sanfelieu, 2003).

Oral ingestion of liquid elemental mercury results only in a very limited absorption, typically <0.01 % of the dose (ATSDR, 1999; MAK, 1999; Klaassen, 2001). Dermal absorption of liquid elemental mercury is also very limited. In contrast, approximately 80% of the inhaled elemental mercury vapour is absorbed in the lungs. Due to the high lipid solubility, elemental mercury rapidly penetrates alveolar membranes and is then distributed to all tissues of the body. Elemental mercury is slowly oxidised in the blood in a saturable process to give Hg^{2+} probably by catalases. Due to the ease of saturation of the enzymatic oxidation of elemental mercury to Hg^{2+}, the proportion of inorganic mercury in blood increases with increasing dose of inorganic mercury. A small part of the elemental mercury vapour dose received is also eliminated by exhalation and a small part of the dose is delivered to the central nervous system.
Human toxicokinetic data are scant: it has been reported that after a single exposure to mercury vapour the half-time of distribution to the plasma compartment is approximately 5 hr (Sandborgh-Englund *et al.*, 1998). The amount of mercury in plasma at the time of the peak concentration was 4% of the inhaled dose (95% confidence limit, 3–5%). Approximately 7% of the initial dose is found deposited in the cranial region after a single exposure to nontoxic levels of the vapour. The kidney is the main depository.
When experimental toxicology data are considered, it appears that in squirrel monkeys, a 4-hour exposure to mercury vapour led to a brain retention of 0.27 % of the absorbed amount. In mice, a somewhat higher immediate retention of about 1.2 % was seen, with a decrease over several days to about 0.4 % (Berlin *et al.*, 1969). One can assume that up to 0.3-7% of the absorbed dose may be retained in the central nervous system. Thus, the daily inhalation of up to 10 µg from amalgam fillings may after almost complete absorption result in a brain retention of up to 0.03 – 0.7 µg per day, or an increase in the concentration up to 0.1 µg/kg per day assuming a brain of 1 kg. Although these crude estimates likely represent a worst-case scenario, they indicate an approximate order of magnitude for further consideration.

A recent review of pharmacokinetic modelling studies concluded that predictions using a long half-life of 27.4 years for mercury in the brain are consistent with autopsy findings, and that the evidence from such studies point to a half-life of inorganic mercury in human brains of several years to several decades (Rooney, 2014).

Within the brain, mercury vapour results in high concentrations in the cerebellum, especially in Purkinje cells (Sørensen *et al.*, 2000). Autoradiography studies of marmoset monkeys and mice exposed to radioactive $^{203}Hg^0$ vapour documented that the retention in the central nervous system includes specific accumulation in the anterior horn cells of the spinal cord (Roos and Dencker, 2012; Rooney, 2013).

Methyl mercury elimination in humans mainly occurs via the biliary route after conjugation with liver glutathione S-transferases (GSTs), which produce a stable glutathione–metal conjugate which is then, eliminated mainly via faeces (Ballatori and Clarkson, 1985). However, some mercury can be reabsorbed, thus contributing to the inorganic mercury circulating in the blood. Excretion of inorganic mercury takes place via both urine and faeces. Urinary mercury originates mainly from mercury in kidney tissue.

GSTs are present in all mammalian tissues. They are divided into several classes dependent on their cell location and structure.

GSTs are highly polymorphic in humans; e.g. GSTM1*∗0 (cytosolic mu (µ), subfamiliy 1, null genotype) and GSTT1*∗0 (cytosolic theta (θ, subfamily 1, null genotype) resulting in the

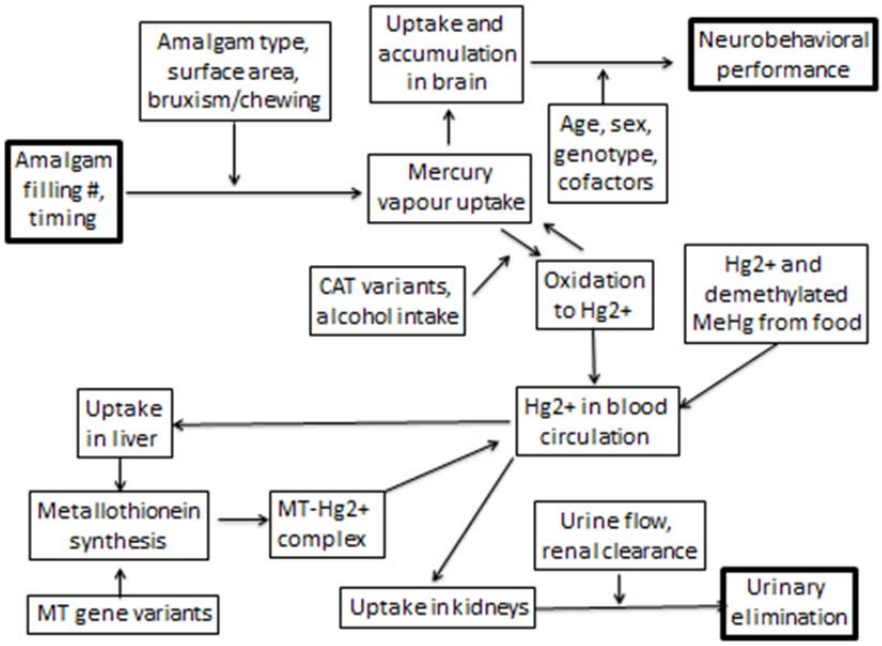
deletion of the entire gene. GST polymorphisms may be associated with methyl mercury detoxification (Mazzaron Barcelos *et al.*, 2012).

Demethylation of methyl mercury from seafood (mainly by gut microflora) may also contribute to the mercuric mercury excreted in the urine, as previously suggested by WHO (1990) by population studies (Johnsson *et al.*, 2005), and by recent studies on mercuryisotopes (Sherman *et al.*, 2013). Indeed, species involved in environmental mercury methylation are present in the human gut (Gibson *et al.*, 1993), and limited evidence supports the notion that human faecal and oral microorganisms can generate methyl mercury from inorganic mercury (Edwards and McBride, 1975; Leistevuo *et al.*, 2001). However, the extent and the rate to which this happens given rise to increased methyl mercury exposure due to dental amalgam is unclear.

Thus, the urinary mercury excretion may not solely originate from amalgam fillings and other sources of elemental and inorganic mercury have to be considered. Sherman *et al.*,(2013) reported that while hair-mercury from dental professionals reflect isotope ratios typical for seafood, the urinary mercury reflected mercury isotope content from dental amalgam. However, in urine also mercury isotope content was noted similar to ratios in seafood as well, though with a wide variability that probably reflect differences in dietary habits. The investigators calculated that, in North American seafood-consumers with fewer than 10 amalgam fillings, most of the mercury in urine comes from demethylation of methyl mercury absorbed from seafood. Accordingly, at low levels of exposure from amalgam, the urinary mercury excretion will provide an imprecise indication of the inorganic mercury exposure. At higher exposure levels, occupational exposure studies also document substantial variability in urinary excretion levels (Symanski *et al.*, 2001). Part of this variability may be related to additional factors such as sample contamination, diurnal variation in exposure and urine production, usage of spot samples, and routine laboratory variability. The authors conclude that in the use of random- and mixed-effects models that combine data across occupational groups, additional studies are warranted to evaluate whether it is reasonable to assume common variances and covariances among measurements collected on workers from different groups.

However, the extent to which this happens and results in increased methyl mercury exposure is unclear.

Figure 1: Fate of inorganic mercury and potential effects



Source: Philippe Grandjean

3.3.2.2. Toxicity of Elemental Mercury

The toxicity of elemental (mercury vapour) and inorganic mercury in animals was recently evaluated by the EFSA and by the JECFA. Both used the results of a 6-month repeated dose study performed in the 1990s as a basis to derive a tolerable weekly intake (TWI) based on effects on absolute and relative kidney weights in rats ($BMDL_{10}$ of 0.06 mg/kg b.w. per day) applying the standard safety factors.

The EFSA (2012) also evaluated some recent studies (Huang *et al.*, 2011; Lukačínová *et al.*, 2011, 2012) that reported ototoxicity and reproductive toxicity. Both studies used only a single dose level. In the Huang study, ototoxicity was observed at a dose equivalent to 0.37 mg/kg b.w. per day as mercury, which is a dose level approximately 6 fold above the $BMDL_{10}$ used as point of departure in the risk assessment. The multigeneration study by Lukačínová *et al.*,(2011) (single dose level of 0.022 – 0.029 mg/kg b.w. per day expressed as mercury) reported adverse effects on survival, lifespan and reproductive parameters at a lower daily dose of mercury exposure than that reported to induce kidney effects. The results of this study were not considered in EFSA's risk assessment due to significant limitations in study design and reporting (i.e. only one dose level tested), low number of animals/group and an unusually high survival (90 -100 %) in control rats as compared to 30 to 35 % in mercury-exposed rats. The SCENIHR supports this evaluation.

Recent toxicology studies have focused on developmental vulnerability to mercury vapour toxicity and the impact of genetic predisposition. In a study that involved postnatal exposure up to 20 days of age in mice, effects were assessed at 12 weeks (Yoshida *et al.*, 2011). Mercury concentrations in the brain were below 0.5 µg/g. Patterns of exposure-associated changes in gene expression in the brain were more extensive in metallothionein (MT)-I/II null mice, which also showed a decrease in locomotor activity in an open field test. In particular, decreases were detected in calcium-calmodulin kinase II (Camk2a) involved in learning and memory. The meaning and relevance of these changes for induction of adverse effects in humans are not clear yet.

3.3.2.3. Neurotoxicity of mercury in laboratory models

Several studies have demonstrated the *in vitro* toxicity of methyl mercury to neuronal cells. Rodent neuronal stem cells in culture showed increased cell death and inhibited differentiation at methyl mercury concentrations as low as 2.5-5 nM (Tamm *et al.*, 2006). Human neural crest cells derived from human embryonic stem cells were tested in a migration assay (Zimmer *et al.*, 2012). A 50% inhibition was seen at 50 nM but statistically significant effects were seen also at 5 nM, while effects at lower concentrations were not distinguishable from the background. In primary cultures of rat cerebellar granular cells (Hogberg *et al.*, 2010), gene expression of neuronal markers was determined from RNA assays after exposure to methyl mercury chloride. Changes in RNA expression and increased neuronal cell death were induced by 50 nM, while changes at 5 nM were equivocal. In a recent study, methyl mercury triggers pronounced effects ($p<0.05$) on proliferation of human amniotic fluid stem cells starting at concentrations as low as 30 nM (6 ng/mL). At higher concentrations, it induced apoptotic effects (Gundacker *et al.*, 2012).

Evidence from *in vivo* animal studies and human autopsies has shown that the most prominent feature after mercury exposure is neuronal loss and alteration of neuronal migration during brain development (Castoldi *et al.*, 2008; Costa and Giordano, 2012). *In vitro* studies have confirmed that mercury primarily targets neuronal cells with a greater affinity than glial cells (Gassó *et al.*, 2001, 2003; Suñol & Rodriguez-Farre, 2012; Costa and Giordano, 2012). The range of Hg concentrations that affect neuronal viability range from 0.4 to 2.9 µM (IC50) when using both primary cultures or neural cell lines, cerebellar granule cells (CGC) being the most sensitive to cytotoxicity (Costa and Giordano, 2012).

Cerebellar granule cells are targeted selectively by mercury compounds *in vivo* (Sanfeliu *et al.*, 2003). Despite the affinity of mercury for thiol groups present in all cells, the molecular determinant(s) of selective cerebellar degeneration remain to be fully elucidated, but neuronal glutamate transport is an important target to be taken into account when assessing mercury-induced neurotoxicity (Fonfria *et al.*, 2005).

These *in vitro* data need to be interpreted in light of the retained mercury concentrations in the brain following mercury vapour exposure, as the tissue distribution in squirrel monkeys exposed prenatally or postnatally to mercury vapour is quite similar to the distribution pattern after exposure to methyl mercury (Berlin *et al.*, 1969).

3.3.3. Toxicology of other metallic elements in amalgam

This has been assessed thoroughly in the former SCENIHR Opinion (2008). There does not seem to be any new information, except for the possibility of nanoparticles being formed by removal, normal wear and attrition of the dental amalgam fillings. This particular issue is discussed in the SCENIHR Opinion: Nanosilver: safety, health and environmental effects and role in antimicrobial resistance (2014). The elements other than mercury used in dental amalgam all have their own, different profiles in terms of essentiality and/or toxicology. There is no scientific evidence that any of those elements currently used in dental amalgam restorations constitute a risk of adverse health effects in individuals apart from allergic reactions to the individual elements.

3.3.4. Weight-of-evidence for a possible risk after exposure to dental amalgam

Regulatory limits for mercury exposures decreased over the years as adverse effects at lower levels of exposure have become better documented. As shown in table 3, inhalation of mercury at an occupational exposure limit results in an uptake of more than 60 µg of Hg per day, whereas inhalation of mercury from dental amalgams results in body burdens which are about

one-fourth or less than those considered acceptable from occupational exposures at present. Similarly, a biological exposure limit of 30 µg Hg/g creatinine in urine is 5-to-10-fold higher than that typically occurring in subjects with amalgam fillings. Thus, the margin between occupational and amalgam-related exposures is less than 10-fold. Tolerable limits for dietary exposures to mercury are relevant to amalgam safety considerations, as inhaled elemental mercury may add to the body burden of inorganic mercury. Recently, the EFSA reported that the tolerable weekly intake for methyl mercury might be exceeded due to fish consumption, while the TWI for inorganic mercury might be exceeded due to the additional inhalation exposure in people with a high number of amalgam fillings. However, evidence is weak as the data are mainly derived from model-based calculations. Studies on large patient collectives did not show any correlation of health effects with the number of amalgam restorations.

Table 3: Air concentrations, blood levels and urinary excretion of mercury in individuals with amalgam fillings compared to levels of mercury considered safe for occupational exposures.

Medium	Individual with dental amalgam fillings	Occupational limit
Air	3 – 17 µg Hg/day	70 µg Hg/day*
Urinary	1- 5 µg Hg/L	30 µg Hg/g creatinine
Blood	3 – 5 µg Hg/L	9 µg Hg/L

**Based on an alveolar ventilation of 9 L/min, a retention of 0.8 for elemental mercury. The EU recommended limit is 0.02 mg/m^3.*

3.3.5. Adverse effects in individuals with amalgam restorations

Mercury toxicity associated with methyl mercury, elemental (vapour) and inorganic mercury is well documented (EFSA 2012; ATSDR, 1999). The question remains whether mercury exposure from dental amalgams can cause adverse health effects, including neurological and kidney diseases, neuropsychological deficits and other less clearly defined conditions, such as chronic fatigue, memory impairment and depression.

The types of adverse effects may be local, systemic or psychological, and are discussed below.

3.3.5.1. Localized mucosal reactions

The possibility that restorative dental materials could be responsible for lesions within the mouth associated with direct contact between the material and the oral mucosa is obviously of importance. Such localised reactions are often discussed in the context of allergies and hypersensitivity.

In the dental clinic two reaction patterns are relevant: the delayed reaction (Type IV) and the immediate reaction (Type I). In the type IV reaction, the incomplete allergens (haptens) are brought in contact with tissue proteins by way of the oral mucosa to form complete allergens. Provided that previous sensitisation has taken place, specialised T-lymphocytes now produce inflammatory mediators causing tissue damage, seen as contact mucositis, i.e. intra-oral diffuse red zones, blisters, or ulceration with pain and burning sensation. The inflammation is not always limited to the exposure site. Contact dermatitis may be observed in the face or more distant locations as urticarial or eczematous reactions. An enhanced risk for atopic

patients to become sensitised against dental materials in general could not be established. However, for special materials like amalgam and composite resins (Bis-GMA; a methacrylate) there seems to be a higher risk for sensitisation for atopic patients (Rojas-Alcayaga *et al.*, 2012). A suspected Type IV reaction may be confirmed with an epidermal patch test (Roitt and Delves, 2006, Schmalz and Arenholt-Bindslev, 2009).

An immediate type (Type I) allergic reaction is based on the release of vasoactive humoral mediators from mast cells or basophilic granulocytes. These mediators are released from the cells upon contact with antigens binding to the IgE antibodies on their surface. The antigen specific IgE antibodies provide the specificity of the allergic response. The released mediators lead to increased capillary permeability and contraction of smooth muscles. The symptoms may consist of urticaria, asthmatic seizures, swelling of the mucosa of throat and eyes and even result in anaphylaxis, all seen within minutes. This immediate type of hypersensitivity is in general associated with allergic responses to protein allergens. Potential full allergens encountered in restorative dentistry are mainly limited to the accessories used, including residual proteins from natural rubber latex in gloves, rubber dam, polishing remedies or parts of anaesthetic cartridges and in seldom cases acrylates (Schmalz and Arenholt-Bindslev, 2009).

A chronic inflammatory response of the gingival tissue around restorations may be present, which appears as chronic gingivitis, recurrent necrotic gingivitis and periodontal pockets. When patients with self-diagnosed oral problems (142 women and 76 men) were examined, the mean concentration of mercury in the whole blood was 17.3 nmol/l and no value exceeded 50 nmol/l. Mental disorder was diagnosed in 93 cases (42.7%), including 41 cases of generalized anxiety disorder and 12 cases of panic disorder. A total of 82 patients (40%) did not work because of medical reasons or unemployment (Herrstrom and Hogstedt, 1993). However, no correlation could be demonstrated between the oral symptoms and a generalized toxic effect of amalgam fillings.

Amalgam tattoos, which are occasionally observed, are associated with the iatrogenic introduction of small particles of dental amalgam, inadvertently implanted into oral soft tissues during dental procedures. Tattoos are resistant to protracted conventional therapies. Most of the foreign bodies examined by light-microscopy and Energy-dispersive X-ray spectroscopy (EDS) methods contained amalgam (amalgam dusts) that appears either as fine granular or larger globular structures implanted in gingival tissues. There is no free mercury, but large globular pieces of amalgam, which induce metallothionein expression in adjacent histiocytes. There is no consequence to the presence of tattoos, except the unpleasant dark blue staining of the gingiva (Lau *et al.*, 2001) and currently there is no indication for the surgical removal of these tattoos.

Metals, including mercury, in close contact with skin and mucosa are well-recognised causes of contact dermatitis (Garner, 2004, Raap *et al.*, 2009). Oral lichen planus is associated with dental restorations and one of the causes may be contact allergy to constituents of dental amalgam (McPharland and Warnakulasuriya, 2012, Ahlgren *et al.*, 2013). Khamaysi *et al.*,(2006) examined 134 patients presenting with mucosal reactions, where the most frequent oral manifestations were cheilitis, peri-oral dermatitis, burning mouth, lichenoid reactions and orofacial granulomatosis. Patch testing showed several allergens in this group, including metals such as gold, cobalt, platinum, nickel and mercury. No specific association between any one metal and a specific clinical manifestation was found but mercury was not a significant factor contributing to the pathogenesis of oral lichenoid reactions. In another study on a patient group with Oral Lichen Planus (OLP) and on Oral Lichenoid Reactions, sensitisation towards amalgam was found to be more seldom than towards gold sodium thiosulfate, palladium chloride or nickel sulfate (Raap *et al.*, 2009).

When dental amalgam was removed in a subgroup of patients suspected of amalgam contact hypersensitivity lesions, considerable improvement was seen (Thornhill *et al.*, 2003). Seventy percent of these patients also showed a positive skin patch test for amalgam or mercury. Total or partial replacement of amalgam fillings following a positive skin patch test reaction to ammoniated mercury, liquid mercury, or amalgam is followed by significant improvement, when the lesions are confined to areas in close contact with amalgam fillings. Similar results have been reported in a more recent study (Luiz *et al.*, 2012) and in a review by McPharland

and Warnakulasuriya (2012). Even if there is no topographic relationship, improvement occurs in nearly all patch test-positive patients (Laeijendecker *et al.*, 2004) although there is no general evidence that either OLP or oral lichenoid lesions patients would routinely benefit from having *all* their amalgam restorations replaced (Baccaglini *et al.*, 2012). If mercury is the allergen, the removal of the filling should lead to complete remission after about 3 months. A total of 51 patients who had oral lichenoid lesions suspected to be related to the dental restorations were investigated. Fifty three per cent (n= 27) of the patients had positive patch test reactions, 24 of them for one or more mercury compounds. Nine months after the removal of the fillings, 42% of the patients were completely healed. Improvement was found in 47% especially when lesions were in close contact with restorations (Issa *et al.*, 2005). Contact with amalgams and positive patch testing are good but not absolute indicators of the beneficial effect of amalgam replacement (Montebugnoli *et al.*, 2012). This possible adverse effect of dental amalgam is widely recognised and reflected in contemporary contra-indications for the use of this material.

Burning Mouth Syndrome can occasionally be associated with a change in the appearance of the clinically normal oral mucosa but no significant association between the burning mouth patients and positive patch test reactions was found (Marino *et al.*, 2009). In some cases it may be associated with a strong allergy to mercury and a positive patch test supports the removal of the amalgam filling. Full recovery and complete remission of systemic dermatitis may occur after removal of a mercury-containing filling (Pigatto *et al.*, 2004). Patch-test analysis for the determination of mercury allergies was carried out by Wong and Freeman (2003) on a group of 84 patients with reticulate, lacy, plaque-like or erosive oral lichenoid lesions. Thirty-three (39%) of the patients had positive patch-test findings. The amalgam fillings were removed for thirty of them, and an improvement was seen within 3 months in 28 of them (87%).

3.3.5.2. Systemic effects

There are a number of epidemiological studies on the possible health effects of mercury released by dental amalgam fillings. The effects reported may affect the nervous and renal system, and also the immune, respiratory, cardiovascular, gastro-intestinal, haematological, and reproductive systems. A variety of study designs has been used, some of which are less than optimal, thus limiting the conclusions that can be drawn. Bates (2006) concluded that the available studies show little evidence of effects on general chronic disease incidence or mortality. On the other hand, although a number of new studies have been published after 2006, most of the studies reviewed were ecological, i.e. without individual exposure information, or based on proxy measures of exposure, such as number of amalgam fillings. Thus, because of exposure misclassification, such studies may overlook dose-response relationships, unless the linkage is strong.

In a New Zealand retrospective cohort study of 20.000 military personnel (84% males) followed up for 20 years, data on dental history was linked with national mortality, hospital discharge and cancer incidence databases. The study design was highly appropriate, but no association was found between dental amalgams and chronic fatigue syndrome or kidney diseases. Based on the ICD codes, amalgam exposure showed a significantly increased risk of mononeuritis of the upper limb and mononeuritis multiplex, while inflammatory and toxic neuropathy showed a decreased risk. The authors state that in the absence of supporting evidence, they regarded these results as hypothesis-generating. It is likely they have arisen as a result of the number of statistical tests that were carried out—the well-known 'multiple comparisons' issue. The number of cases for investigation of Alzheimer's or Parkinson's diseases was insufficient to draw any conclusion (Bates *et al.*, 2004).

Other population-based studies have focused on dentistry personnel in comparison with other occupational groups (Thygesen *et al.*, 2011). They are reviewed in 3.3.6.

Cross-sectional studies are less informative. For example, in 56 patients with perceived chronic mercury toxicity (various medical symptoms), mercury levels in blood and urine were within the

reference range (Eyeson *et al.*, 2010). However, the exposure assessment may not represent the causative exposure, thus preventing meaningful conclusions. Similar concerns can be raised in regard to several other studies of patient groups.

The available evidence for health effects due to mercury from amalgam fillings is discussed below in relation to specific organ systems.

Urinary system

Mortada *et al.*,(2002) investigated 49 healthy individuals with amalgam fillings and 51 matched controls. The mercury concentration in urine was correlated to the number of amalgam fillings. In the amalgam group, urinary excretion of NAG and albumin correlated with the number of fillings and albuminuria with blood and urine mercury levels. Other kidney biomarkers were not affected. Bellinger *et al.*,(2006) selected 534 children for a randomised clinical trial, comparing groups with amalgam restorations and alternative composite resins (New England Children's Amalgam Trial). After five years, renal data were obtained on 409 children. A significantly higher mean urinary mercury level was noted in the amalgam group, but the renal function was comparable in the two groups as measured by creatinine adjusted albumin levels. However, a follow up of the same group of children showed an increased prevalence of microalbuminuria among children with amalgam fillings (Barregard *et al.*, 2008), but no change in biomarkers for tubular function.

In the Casa Pia study, 507 children from Lisbon were randomised to amalgam or composite resin dental care groups and evaluated annually over a 7 year period. Analyses showed no significant association of amalgam with various renal biomarkers including microalbuminuria (DeRouen *et al.*, 2006, Barregard *et al.*, 2008). Later, some urinary porphyrins were reported to be increased in a subgroup of the youngest children in the amalgam group, but the levels were below those considered to be able to cause renal damage (Woods *et al.*, 2009). Other analyses of selected samples from the same study using different statistical methods (after data had been generated) suggest that Hg-associated urinary porphyrins are increased in amalgam treated children (Geier *et al.*, 2011) and that glutathione-S-transferases (GST)–α increased with time in amalgam treated children (Geier *et al.*, 2012). This study has been challenged by DeRouen *et al.*,(2015), authors of the original study, who draw the attention to the fact that Geier *et al.*,used a post-hoc evaluation with the potential of bias and that the statistical methods Geier *et al.*,used did not comply with current standards (e.g. no correction for multiple comparisons).

A cross-sectional study of 403 Chinese school children, about half of whom had amalgam fillings, showed a slight increase in urinary mercury concentration in children with amalgam fillings, but no difference in renal biomarkers was observed (Ye *et al.*, 2009).

A study from Saudi Arabia analysed a number of different renal biomarkers in 182 children. Only urinary NAG levels were significantly higher in children with dental amalgam fillings than in those without fillings (P=0.008). In contrast, both α1-MG and 8-OHdG levels were higher in the non-amalgam group than those with and P-values were 0.004 and 0, respectively. None of the biomarkers revealed a significant correlation with the number of dental amalgam fillings (Al-Saleh *et al.*, 2011, 2012). The authors state that confirmation of these data is needed.

Studies in rodents suggest that mercury elimination is compromised as a result of experimental kidney damage (Zalups, 1997). Systematic studies in humans have not been found.

Overall, the conclusion of available epidemiological studies is that only limited evidence suggests that mercury from dental amalgam fillings affect clinical kidney function, although any long-term risk of kidney disease in humans needs to be ascertained. The known accumulation of mercury in the kidneys and the observed effect on some porphyrin excretion and possible changes in special biomarkers are of some concern. However, additional data are necessary to evaluate whether such changes have long-term clinical significance.

Neurological System

Neurological diagnoses

Inorganic mercury is a neurotoxicant and it has therefore been suggested that it may play a role in the pathogenesis of neurodegenerative diseases such as Alzheimer's disease (Mutter *et al.*, 2010).

A cross-sectional study that found substantially elevated blood-mercury concentrations in Alzheimer patients, especially those with early-onset disease (Hock *et al.*, 1998), is difficult to evaluate, as the premorbid levels and sources of exposure are unknown. Also, this study found no association with the number of fillings as such. However, these findings have not been confirmed. A recent review of the literature reported some cases of increased mercury levels in brain tissue of patients with Alzheimer's disease but measurements in other tissues and body fluids were inconsistent. While retention in the brain would be considered most relevant, the data available do not allow a judgement on whether a relationship exists between dental amalgam and Alzheimer's disease (Mutter *et al.*, 2010).

A possible association between amalgam and multiple sclerosis has been suggested (Bates *et al.*, 2004), but the evidence is inconclusive. Thus, the small number of subjects, inadequate and imprecise exposure data, and inadequate control recruitment methods constitute limitations of the available studies (Aminzadeh and Etminan 2007).

In regard to amyotrophic lateral sclerosis (ALS), the evidence suffers from the same weaknesses as indicated above. It is thought that an interaction between mercury exposure and an individual's genetic makeup is required to produce epigenetic changes that may ultimately lead to the disease (Callaghan *et al.*, 2011).

Parkinson's disease is suggested to be linked to mercury exposure, but the disease has a multifactorial etiology. In workers exposed to mercury vapour, single-photon emission computed tomography examination revealed decreased dopamine innervation in the striatum, caudate and putamen, and a negative association with urinary mercury and simulated exposure levels (Lin *et al.*, 2011). Such findings reflect early changes that may be part of the Parkinson's disease pathogenesis. However, a nation-wide register-linkage study of dentists and dental assistants, as compared to professionals and secretaries in general practitioners' and lawyers' offices, did not show any increased risk of Parkinson's disease associated with dentistry employment although a small excess risk could not be excluded (Thygesen *et al.*, 2011). Thus, overall, the current evidence does not allow any judgment on whether mercury exposure from amalgam fillings is associated with the development of degenerative diseases of the nervous system.

A large American study of 452 2-to-5-year-old children with autism or autism spectrum disorders did not show any difference in current blood mercury concentrations in patients compared to controls (Hertz-Picciotto *et al.*, 2010). The blood levels of mercury depended both on the number of amalgam fillings and fish consumption, but they may not necessarily reflect premorbid or causative exposures.

A prospective blinded study on 100 patients with autism showed a correlation between the number of amalgam fillings in the mother during pregnancy and the severity of autism (Geier *et al.*, 2009). The patients were recruited at outpatient genetic consultations at the Genetic Centers of America. Patients whose mother had 6 or more amalgam fillings had 3.2 times greater risk of having a severe autism compared to patients with mild autism where the mother had 5 or less amalgam fillings. However, this paper shows serious limitations in methodology used (e.g. the estimation of the number of amalgam fillings present during pregnancy in the past, no adjustment for diet and socio-economic status).

In conclusion, the overall available data do not show a correlation between autism and blood mercury levels in small children. However, although causality was not demonstrated, one paper indicated a a possible association between the severity of autism in autistic children and the number of dental amalgam fillings in their mothers during pregnancy, thus suggesting a need for further research.

Neurological function tests

In the Casa Pia study (DeRouen *et al.*, 2006), annual neurological examinations were performed on 507 children. There were no significant differences between the amalgam and resin-based composite groups and it was concluded that exposure to mercury from dental amalgam does not adversely affect the neurological status of children (Lauterbach *et al.*, 2008, Mackert 2010). In the parallel study performed in the US (Bellinger *et al.*, 2006), a total of 534 children aged 6 to 10 years at baseline with no prior amalgam restorations and 2 or more posterior teeth with caries were randomly assigned to receive dental restoration of baseline and incident caries during a 5-year follow-up period using either amalgam (n=267) or resin composite (n =267) materials. The primary neuropsychological outcome was a 5-year change in full-scale IQ scores. Secondary outcomes included tests of memory and visuomotor ability. In this study, there were no statistically significant differences in adverse neuropsychological effects observed over the 5-year period in children whose caries were restored using dental amalgam or composite materials.

In a cross-sectional study of 403 Chinese school children, neurobehavioral and neuropsychological performance could not be shown to be associated with the presence of amalgam fillings (Ye *et al.*, 2009).

In cross-sectional studies of U.S. air force personnel, no significant associations were found between amalgam exposure and clinical neurological signs of abnormal tremor, coordination, station or gait, strength, sensation, or muscle stretch reflexes or for any level of peripheral neuropathy among the study participants. However, a statistically significant association was detected between amalgam exposure and the continuous vibrotactile sensation response in non-diabetic participants (Kingman *et al.*, 2005). No adjustment was made for multiple tests and the authors conclude "Overall, we found no association between amalgam exposure and neurological signs or clinically evident peripheral neuropathy". No follow-up studies have been published.

Auditory thresholds were measured in 39 non-smoking women aged 40-45 years. There was a significant positive correlation between the number of amalgam fillings and the decline in hearing thresholds, the strongest association was found at 14 kHz (Rothwell and Boyd 2008). No correlation was found for non-amalgam fillings. This has not been confirmed by other studies so far.

The visual system may also be vulnerable to mercury exposure, but the studies usually do not include the sensory test outcomes that would have revealed such deficits. In one study, visual contrast sensitivity was examined in relation to exposure from dental amalgam. A decline was shown at increasing urinary mercury excretion (geometric mean, 0.16 µg/24 h in connection with an average of 1.15 amalgam fillings per child) in 384 German children at age 6 years. According to the authors, this decline could not be classified as a disease (Altmann *et al.*, 1998).

In conclusion, there are some publications that indicate that exposure to mercury may be associated with some decline in the auditory and visual system.

Neurobehavioral functions

During the past decades, mercury and other metals have been claimed to be responsible for a series of mental health problems, with a variety of symptoms (Bratel *et al.*, 1997a,b), not limited to neurobehavioural ones.

A series of patients with various health complaints were referred to the Dental Biomaterials Adverse Reaction Unit in Bergen, Norway (Lygre *et al.*, 2005). The complaints were heterogeneous. Many individuals displayed multiple subjective symptoms associated with several organ systems. The most common were fatigue, muscle and joint pain, dizziness and headache. Intra-oral symptoms were related to burning sensations, taste disturbances and dry mouth. After removal of the mercury-containing fillings, a small decrease in the intensity of different symptoms was noted. Intra-oral symptoms were decreased and the decrease was statistically significant for taste disturbances (p=0.001), dry mouth (p=0.034), and stiffness/paraesthesia (p=0.05). However, the symptoms were still higher than in a reference group sampled from the general population in Norway.

Follow-up studies on the above-mentioned patient study were recently published (Sjursen *et al.*, 2011, Lygre *et al.*, 2012). Three years after removal of amalgam fillings most of the health complaints decreased, being statistically significant for taste disturbances, pain from muscles and joints, gastrointestinal complaints, complaints from ear/nose/throat and fatigue. Interestingly, serum levels of several Th1 cytokines were slightly but significantly increased in the patient group before removal of the fillings and some of them were normalised one year after (Björkman *et al.*, 2012). It is unclear if raised cytokine levels may explain some of the symptoms.

Another study from Germany compared three strategies in 90 patients with health complaints attributed to amalgam fillings. The individuals were randomly assigned to either removal of amalgams fillings, removal combined with doses of vitamins and trace elements, or participation in a health promotion program without removal of dental amalgam. In all three groups clinically relevant improvements were observed after 1 year, with no statistically significant difference between the groups (Melchart *et al.*, 2008).

Two longitudinal studies were carried out on a Swedish population including patients with amalgam related complaints. The first one evaluated cognitive functions in 342 patients and 342 matched controls (Sundström *et al.*, 2010). None of the cognitive tests showed any difference between the groups. The second study involved 337 patients with self-reported amalgam complaints and the same number of matched controls (Sundström *et al.*, 2011). Many of the patients with complaints had experienced negative life events as somatic illness, death of a very close family member or financial problems. It was concluded that adverse negative life events could play a vital role in understanding and explaining amalgam-related complaints.

A German study analysed two different databases. In the first, 90 patients attributed their health complaints to dental amalgam, and in the second 116 patients from an outpatient unit for environmental medicine attributed their symptoms to environmental sources other than amalgam. The results showed some differences in symptomatology, while general psychological distress was similar in both groups, indicating no strong evidence for an amalgam-specific syndrome (Weidenhammer *et al.*, 2009).

In conclusion, patients with self-reported symptoms attributed to amalgam fillings constitute a heterogeneous group; the study design presents possible selection bias, not having defined inclusion/exclusion criteria, thus limiting the validity of data, which are difficult to interpret. Negative life events and environmental factors may also play a role.

Neuropsychological development

The developing brain is known to be uniquely sensitive to neurotoxic damage, but exposures in early life generally result in non-specific deficits that may be difficult to document in the presence of multiple risk factors (Grandjean and Landrigan, 2014).

Two randomised, controlled clinical trials have been carried out on the neuropsychological and renal effects of dental amalgam in children (Bellinger *et al.*, 2006 and 2007, DeRouen *et al.*, 2006).

In the first study 534 children aged 6 to 10 years living in the New England area (USA), were randomly assigned to receive dental restorations using either amalgam (n=267) or resin composites (n=267). They were selected from a background population almost 10 times larger and re-examined after 5 years. No difference appeared in full-scale IQ. No difference was found in the general memory index. It was concluded that the exposure to mercury from dental amalgam at this age, on average, was not associated with any detectable adverse neuropsychological effects over a five year period and that the use of dental amalgam is not associated with an increase in children's risk of experiencing neuropsychological dysfunction. The findings suggest that the health effects of amalgam restorations in children need not be the basis of treatment decisions when choosing restorative dental materials. Another follow-up study showed no evidence that exposure to mercury from dental amalgams was associated with adverse psychosocial outcomes over the five-year period following initial placement of amalgams. All significant associations favoured the amalgam group (Bellinger *et al.*, 2008).

In the other randomised clinical trial ("The Casa Pia study"), annual follow-up for 7 years was carried out on 507 children in Lisbon, Portugal (DeRouen *et al.*, 2006). The children received either amalgam restorations (n=253) or resin composites (n=254). The creatinine-adjusted urinary mercury levels were 1.8µg/g in the amalgam group, and 1.9 µg/g in the composite group. No statistically significant difference was found in measures of memory, attention, visual function, or nerve conduction velocities over all the 7 years of follow-up. The authors also noticed that the need for additional restorative treatment was approximately 50% higher in the composite group. These data suggest that exposure to dental amalgam restorations within this age range has no important adverse effect on average psychological development, with the superior performance of the amalgams compared to alternatives being noteworthy.

However, further examination of the data, with assessment of the heterogeneity of the coproporphyrinogen oxidase gene (CPOX) gene (CPOX is an enzyme responsible for the conversion of coproporhyrinogen III to protoporphyrinogen III in the haeme biosynthetic pathway), showed decreased neurobehavioral test performance correlated with increased urinary mercury level in boys with the CPOX4 variant (Woods *et al.*, 2012). This enzyme defect causes hereditary coproporhyria (HCP), in which one third presents with neurological symptoms. The disease is latent before puberty although a few homozygous cases with onset in early childhood have been reported (Sassa, 2006). HCP can be induced by drugs, environmental stressors and diet changes.

Examination of other genetic polymorphisms in the genes of metallothionein and catechol-O-methyltransferase also showed that certain variants increased the susceptibility of boys to adverse neurobehavioral effects of mercury (Woods *et al.*, 2013, 2014). It is important to note that the three articles by Woods *et al.*,(2012, 2013, 2014) do not compare amalgam versus alternative treatment, but evaluate the association between mercury levels in urine and outcome of the neurobehavioral tests. The authors estimate that only about 17 % of the urinary mercury level variation was due to amalgam (15 % in girls), indicating considerable background mercury exposure unrelated to dental amalgam. They therefore conclude that the findings do not support an association between mercury in dental amalgam and adverse neurobehavioral outcome observed (Woods *et al.*, 2013, 2014).

A retrospective study of 587 mother-child pairs from the Seychelles evaluated the association between prenatal exposure from maternal amalgam restoration status and the results of six neurodevelopmental tests at the age of 66 months. None of the tests showed an adverse association with the number of amalgam fillings in the mothers during gestation (Watson *et al.*, 2011). This cohort also failed to show any clear evidence of adverse neurotoxic effects of methyl mercury exposure (Karagas *et al.*, 2012).

Likewise, in a cross-sectional study of 403 Chinese school children, neurobehavioral and neuropsychological performance could not be shown to be associated with the presence of amalgam fillings (Ye *et al.*, 2009).

In conclusion, there is no evidence that amalgam negatively influences the neuropsychological development of children.

Immune System

Mercury is able to induce autoimmunity in susceptible strains of rodents and so the question arises as to whether such effects are seen in humans with respect to amalgam related mercury exposure.

In 24 patients heavily exposed to amalgam and showing various adverse effects, none developed autoimmunity to glomerular basement membrane, even in patients showing allergy to mercury (Guzzi *et al.*, 2008).

The susceptibility to sensitisation to dental materials was compared in 40 atopic and 40 non-atopic patients. Among the atopic patients, 67 % were sensitised to one or more allergens, including amalgam and ammoniated mercury, while 55 % of the non-atopic patients were sensitised (Rojas-Alcayaga *et al.*, 2012). The difference is not significant ($p>0.05$) and thus suggests the need for further studies.

A subpopulation of the participants in the New England study were tested for *in vitro* manifestations of immunotoxic effects of dental amalgam. T-cell and monocyte responses were slightly diminished 5-7 days after amalgam restorative treatment, but no differences were observed at follow-up at 6, 12 or 60 months (Shenker *et al.,* 2008).

In a Norwegian study of immune markers in patients with self-reported health complaints associated with amalgam fillings, an increased level of Th1 type proinflammatory cytokines was found in the patients. Twelve months after removal of the fillings, the cytokine level was normalised for most of the cytokines (Björkman *et al.,* 2012) along with a decrease of the symptoms (Sjursen *et al.,* 2011). It is unknown if the increased level of proinflammatory cytokines might have played a role for the health complaints.

In conclusion, inorganic mercury exposure may cause adverse effects on the immune system. However, there is no evidence that autoimmune disease is provoked in humans by mercury exposure from amalgam fillings. In some patients with allergy to mercury, clinical improvement is seen after removal of amalgam fillings. There is some evidence that exposure to mercury influences proinflammatory cytokine levels, but the clinical implications are not clear.

Reproductive system

Although reproductive effects have been addressed in several of the studies discussed in this Opinion, there is very little data available on this subject. There is no evidence of any association between amalgam restorations and either male of female fertility or obstetric parameters. One study that attempted to examine the question of fertility in detail failed to show any correlation between the mercury burden from amalgam restorations and male fertility disorders (Hanf *et al.,* 1996).

The fecundability of 558 female dental surgeons was examined vs. 450 high school teachers. Occupational exposure had no clear adverse effects on fertility among female dental surgeons, except for a possible effect in the last pregnancy of multiparous dental surgeons. However it should be noted that beside mercury, dentists were occupationally exposed also to chloroform, ethanol, benzene, which could act as confounding factors (Dahl *et al.,* 1999).

Other effects

A study of 75 mother-child pairs from Slovakia showed that exposure to mercury from amalgam and the environment influences thyroid hormone status with e.g. lower thyroxine levels in the mothers. However, in this study, mercury exposure of children did not correspond with the cord or maternal blood mercury at the time of delivery. Mercury exposure status of children at age of 6 months depended more likely on other sources than prenatal exposure. (Ursinyova *et al.,* 2012). The relationship between blood mercury levels and antithyroid antibodies was reported (Gallagher & Meliker, 2012). A higher frequency of autoantibodies towards thyroglobulin was noted in women with the highest mercury levels. Although in the latter study dental amalgam presence was not considered, the findings appear meaningful even if the clinical implications are not clear.

Bergdahl *et al.,*(2007) and Naorungroj *et al.,*(2013) found that edentulism was correlated with lower cognitive status. Tooth loss and gingival bleeding were markers of poorer executive function among dentate people. The association of lower cognitive scores with edentulism suggests that past oral diseases may be a risk indicator for cognitive decline, whereas the association with gingival inflammation indicates a possible effect of cognitive decline on oral health.

The relationship between mastication and cognitive function remains unclear, but both animal and experimental human studies suggest a possible causal relationship (Hansson, 2013). They hypothesised that natural teeth are of importance for hippocampus-based cognitive processes, such as episodic long-term memory. A population-based sample of 273 participants (55-80 years of age; 145 women) was investigated in a cross-sectional study. The participants underwent health assessment, completed a battery of cognitive tests, and took part in an extensive clinical oral examination. The number of natural teeth contributed uniquely and significantly to explaining variance (3-4%) in performance on measures of episodic memory and semantic memory over and above individual differences in age, years of education,

gender, occupation, living conditions, and medical history. The number of natural teeth did not have an influence on the performance of measures of working memory, visuospatial ability, or processing speed. Within the limitations of the current study, a small, but significant, relationship between episodic memory and number of natural teeth is evident.

The influence of other, sometimes confounding, parameters in investigating possible relationships between dental amalgam exposure and biochemical or psychological alterations need to be addressed.

Occupational studies have contributed evidence that prolonged exposure (approximately 15 years) to mercury vapour can affect sensory perception in regard to the visual system, resulting in sub-clinical color vision impairment (Urban *et al.,* 2003). Thus, permanent impairment of contrast sensitivity has been documented in former workers from a lamp manufacturing facility (Costa *et al.,* 2008). Furthermore, in workers with exposure to mercury vapour at least one year ago and a current urinary mercury excretion average of 1.4 µg/g creatinine, deficits were detected in colour vision (Feitosa-Santana *et al.,* 2008). Later follow-up supported the conclusion that the deficits may be permanent (Feitosa-Santana *et al.,* 2010). In contrast, another study from Poland showed less clear differences in colour vision in currently exposed workers (Jedrejko and Skoczyńska, 2011). These data are of importance, as vision is usually not included in neurobehavioral assessment batteries, although vision could well be a particularly sensitive target for mercury vapour.

The earlier, now banned use of mercury as antimicrobial agent was reported to induce antibiotic resistance. (Hall *et al.,* 1970, Joly *et al.,* 1975 and Poiata *et al.,* 2000). For the induction of antibiotic resistance in relation to the use of dental amalgam, contradictory studies were reported (Summers *et al.,* 1993, Ready *et al.,* 2007, Roberts *et al.,* 2008). However, in the positive studies the increase in antibiotic resitance did not seem to influence the health of the individual patients.

In general, the intestinal exposure to mercury from dental amalgam seems to be extremely low; as a consequence an effect on intestinal flora is not anticipated.

General conclusion

The exposure of the general population to mercury is mainly due to fish consumption (methyl mercury plus inorganic mercury to a lower extent) and dental amalgam (elemental mercury vapour, inorganic mercury). Elemental, organic and inorganic mercury is toxic to humans and experimental animals, the mechanisms and the degree of toxicity being different depending on the mercury forms. Individual variation in response has been reported especially in determining exposure; age also plays a role in susceptibility, in that the developing brain is more prone to the toxic effects of mercury.

The EFSA (2012) reported that the tolerable weekly intake for inorganic mercury might be exceeded due to the additional inhalation exposure in people with a high number of amalgam fillings. This information is derived from mainly model-based calculations. However, in direct patient studies from Ahlqwist *et al.,*(1993, 1995) no correlation of possible health symptoms for cardiovascular disease, diabetes, cancer and early death in Swedish women with the number of existing amalgam filling was found. In a further study on a large population of 4,787 patients claiming health effects from amalgam (Melchart *et al.,* 1998) no significant correlation between the intensity of complaints or particular groups of symptoms and the number of amalgam-filled surfaces was found. Therefore, no conclusions related to restrictions of the number of amalgam fillings can be drawn.

Concerning the urinary system, several studies show that parameters of kidney function may be influenced by mercury from amalgam, but there is no convincing evidence that dental amalgam is associated with a clinically decreased kidney function in the patients in the short or long term. On the other hand, decreased kidney function (decreased renal clearance) is likely to decrease the ability to eliminate mercury and other substances via the urine.

For the neurological system, there is no clear evidence for an increased risk for Alzheimer's disease, Parkinson's disease or amyotrophic lateral sclerosis associated with amalgam fillings. The data are inconclusive for multiple sclerosis.

Likewise, a possible association between amalgam fillings and clinical signs of peripheral neuropathy (paraesthesia) has not been replicated in more recent studies.

The visual and auditory system may be influenced by mercury from amalgam fillings. There is some evidence that indicates that exposure of the mother in early pregnancy to mercury from amalgam may promote the development of autism in the child. Large studies have been carried out to evaluate the neuropsychological development in children with amalgam fillings or alternative treatments. These studies do not give convincing evidence for a negative effect on the children.

A special patient group is constituted by individuals that attribute various health complaints to amalgam restorations. Some of these patients have a psychiatric or psychological disorder and in some cases a negative life event has been experienced by them. In general, the symptoms seem to improve after removal of the amalgam fillings, but symptoms also resolve after a health promotion program without removal of dental amalgam (Melchart *et al.*, 2008).

The immune system is influenced by mercury exposure in experimental animals and humans. There is no evidence for an increased risk for autoimmune disease due to amalgam fillings, but it seems that the level of Th1 type cytokines may be increased by mercury exposure. The main adverse immune reactions in patients are local reactions near the amalgam restorations, which mainly resolve after removal of the amalgam fillings. In addition, some patients may develop an allergic response to mercury or the dental amalgam.

The local effects of dental amalgam are well established as well as the possibility for individual patients to show allergy to mercury, but they occur at low frequency. Regarding the systemic effects, several papers have suggested effects of dental amalgam exposure on the central nervous system. Since contrasting results have also been published, further studies are needed in order to confirm or negate these findings.

Unfortunately, many of the studies reviewed have imprecise exposure assessment, incomplete adjustment for covariates, and genetic polymorphism has not been considered.

3.3.6. Epidemiological and clinical evidence concerning adverse effects of dental amalgam in dental personnel

Long-term retention in brain and kidneys is impossible to measure in clinical studies (see 3.3.2.2), and mercury concentrations in blood and urine samples may not be sufficiently informative in regard to cumulated past mercury exposures from different origins. As an example, measurement of mercury in autopsy samples showed a case of brain cortex with a mercury concentration of 164 µg/kg, i.e. 9 times higher than the concentration of the second highest case; the subject was later found to have been employed as a dental assistant in the past (Björkman *et al.*, 2007). Mercury concentrations in urine and blood may therefore be misleading as they reflect more recent exposures to mercury. Thus, many studies have used occupational status as a proxy for mercury vapour exposure (Hørsted-Bindslev, 2004). When reviewing past studies of dental personnel, exposure conditions must be considered, in particular the handling of both silver and copper amalgam filling materials without protective gloves and without a proper ventilation system. However, even recent studies support the notion that dental assistants have more frequent neurological symptoms, although the association to mercury vapour exposure is uncertain, as the symptoms are generally non-specific, and other chemical risk factors may have been present (Ngim *et al.*, 1992, Moen *et al.*,2008, Hilt *et al.*, 2009).

No clear association has been detected between mercury exposure and negative health effects in dentists, although their mercury blood level is higher than in a control population. The life span of dentists was shown to be three years greater than that for a control non-dentist group. The same type of effect was seen with many other parameters, indicating that the general health of dentists is good (McComb, 1997). The data do not allow for appropriate adjustment for beneficial factors associated with the dental profession, but these

factors at least appear to exceed any perceived disadvantageous effects due to mercury exposure.

Heggland *et al.*,(2011) investigated whether women who have worked as dental personnel in Norway, a group with possible previous exposure to mercury vapour, have had an excess risk of having children with congenital malformations or other adverse pregnancy outcomes compared to the general population. A cohort of female dental personnel was identified from the archives of the public dental healthcare and the national trade unions in Norway. Data on births and pregnancy outcomes during 1967–2006 were obtained from the Medical Birth Registry of Norway (MBRN). The final cohort of dental personnel consisted of 4482 dental assistants and 1011 dentists. All other women registered in the MBRN were assigned to the control group, in total 1 124 758. Excess risks of several adverse pregnancy outcomes for dental personnel compared to the general population were estimated. Analyses were conducted for the whole time period as well as stratified by 10-year periods.

Female dental personnel had no observed increased occurrence of congenital malformations (including malformations of the central nervous system, dysplasia of the hip, clubfoot, malformations of the heart and great vessels), low birth weight, preterm birth, small for gestational age, changed gender ratio, multiple birth, stillbirth, or prenatal death. On a group level, they did not observe any excess risks of congenital malformations or other adverse pregnancy outcomes among female dental personnel in Norway during 1967–2006 compared to the general population. Svendsen and Hilt (2011) emphasised that assessment and classification of exposure is essential in epidemiological studies and questionnaires might not be the best method to estimate exposure. They found a marked difference between the pairs of employees working in the same clinic regarding the start and termination years for the different preparation methods, and this was partly independent of their occupation. Kappa values for using different preparation methods in the questionnaire and at the interview varied between 0.41 (moderate) to 0.88 (very good). The results of this study indicated that a mailed questionnaire will cause misclassification of exposure.

The observed occurrence of false positive exposure classifications from the questionnaire compared to the interview was higher than for false negative. This is important and may result in serious bias if the prevalence of exposure is low. Due to missing information, detailed questionnaires may also be inefficient if the goal is to construct exposure measures from combinations of several answers in the questionnaire.

Dentists were significantly more likely than control subjects to have suffered from disorders of the kidney (6.5 % vs. 0.6 %) but these self-reported symptoms were not significantly associated with their level of mercury exposure as measured in urine (Ritchie *et al.*, 2004). This difference between dentists and controls remained significant after correcting for multiple comparisons and after adjusting for age and sex using logistic regression (adjusted odds ratio of kidney disorders for dentists: 15.2 (95% CI = 1.8 to 126.3; p = 0.01). As exposure was assessed cross-sectionally, it is possible that the kidney disease resulted in a decreased urinary mercury excretion.

A US study of dentists and dental assistants suggested that an increased prevalence of symptoms of depression, anxiety, and memory was associated with two genetic polymorphisms thought to convey hypersusceptibility to mercury vapour toxicity (Heyer *et al.*, 2009).

More recent epidemiological studies have utilised registry information and therefore avoided problems associated with self-selection and other biases. Still, such studies assumed that all subjects with the same occupational title have the same exposure, thereby introducing possible misclassification. A Danish nation-wide registry study of hospital admissions of 122,481 workers, including 5731 dentists and 33,858 dental assistants, as compared to professionals and secretaries in general practitioners' and lawyers' offices, did not show any increased risk of Parkinson's disease, neurological disease, or kidney disease, associated with dentistry employment (Thygesen *et al.*, 2011).

A US study using pharmacy utilisation data examined a representative sample of dentists and a matched control group and found increased prescription utilization of specific illness medications for neuropsychological, neurological, respiratory, and cardiovascular disease

(Duplinsky and Cicchetti, 2012). However, the link of adverse outcomes to mercury exposure from amalgam work in either of the two latter studies is not clear.

Neurobehavioural tests in 98 dentists (mean age 32, range 24-49) and 54 unexposed controls (mean age 34, range 23-50) consisting of motor and visual function tests showed a deficient performance of the dentists compared to the controls. The performance decreased at increased dose, calculated as the product of the average air mercury concentrations and years of exposure. The dentists were exposed to an average personal air concentration of 0.014 (range 0.0007-0.042) mg/m^3 for a mean period of 5.5 (range 0.7-24) years (Ngim *et al.*, 1992).

Clinical neurological findings

Sletvold *et al.*,(2012) investigated whether dental personnel with previous exposure to metallic mercury (vapour) have later developed disturbances in cognitive function. Ninety-one female participants who had been selected from a previous health survey of dental personnel were investigated neuropsychologically within the following domains: motor function, short-term memory, working memory, executive function, mental flexibility, and visual and verbal long-term memory. The scores were mainly within normal ranges. Relationships between an exposure score, the duration of employment before 1990, and previously measured mercury in urine as independent variables and the neuropsychological findings as dependent variables, were analysed by multiple linear regression controlling for age, general ability, length of education, alcohol consumption, and previous head injuries. The only relationship that was statistically significant in the hypothesised direction was between the previously measured urine mercury values and visual long-term memory, where the urine values explained 30% of the variability. As the study had a low statistical power and also some other methodological limitations, the results have to be interpreted with caution. They concluded that neuropsychological findings indicative of subsequent cognitive injuries are difficult to find in groups of otherwise healthy dental personnel with previous occupational exposure to mercury.

Hilt *et al.*,(2009) examined if Norwegian dentists have an increased prevalence of symptoms consistent with neurological and/or cognitive malfunction. The study group consisted of 406 dentists from central Norway and 217 controls from the general population, all under the age of 70. They had responded to a standardised postal questionnaire (Euroquest) inquiring about seven symptoms in regard to neurology, psychosomatics, memory, concentration, mood, sleep disturbances, and fatigue. A score was calculated for each symptom based on 4 to 15 single questions scored on a scale from 1 (seldom or never) to 4 (very often).

The dentists and controls had a participation rate of 57.2 % and 42.9 % respectively. The dentists reported no more cognitive symptoms than the controls, with low average symptom scores from 1.16 for neurological symptoms in males to 1.73 for fatigue in females. Corresponding figures for the controls were 1.22 and 1.77. There were a total of 1.2 % of the dentists and 1.8 % of the controls who reported having three or more of the seven symptoms "often" or more frequently.

In conclusion, the Norwegian dentists did not report more cognitive and neurological symptoms than controls from the general population.

3.3.7. Genetic predisposition of individuals and subpopulations

As with many exogenous substances, genetic factors may also contribute to the individual susceptibility to mercury toxicity based on mercury toxicokinetics (Julvez and Grandjean, 2013). However, there is limited knowledge about genes that specifically influence mercury toxicokinetics and toxicity. GSH-related genes have broad substrate specificities.

Glutathione (GSH) related enzymes play a role in mercury toxicokinetics, and several studies have addressed the impact of polymorphisms in glutathione-related genes (Clarkson *et al.*, 2007). An association between GSTM1 and GSTT1 null genotypes and the GST polymorphisms may be associated with methyl mercury detoxification (Mazzaron Barcelos *et al.*, 2012). In

dental professionals from Michigan (US), the glutathione S-transferase GSTT1 deletion was associated with decreased urine mercury concentrations (Goodrich *et al.*, 2011).

The metabolism of mercury is also likely to be influenced by binding to certain ligands, such as selenoproteins and metallothioneins. In the same dental professionals, adjusted urinary mercury excretion was higher in individuals with selenoprotein 1 (SEPP1) rs7579 CT+TT genotypes compared to those with CC (Goodrich *et al.*, 2011). This is a possible protection mechanism.

In a population from Northern Sweden the glutathione transferase (GST) P1-105 and -114 genotypes influenced the retention of methylmercury in individuals that consumed fish 2-3 times a week. The erythrocyte mercury was higher, depending on the phenotype (Schlawicke Engstrom *et al.*, 2008). However, no association with clinical symptoms was demonstrated.

In Ecuadorean gold miners and gold buyers highly exposed to mercury vapour, the glutamyl-cysteine ligase GCLM-588T allele (which is associated with lower glutathione production) was associated with increased blood, plasma and urine mercury levels (Custodio *et al.*, 2005). Subjects with the GCLM-588 CC genotype had half as high a urinary mercury excretion as expected from exposure data. In regard to adverse effects linked to mercury exposure, there was no evidence that the glutathione genotypes modified the relationship between exposure and neurotoxic effects due to gold mining in Ecuador (Harari *et al.*, 2012).

For metallothionein, the small number of subjects with MT1M A or MT2A CC genotypes had lower urinary mercury levels than did those with MT1M or MT2A GG genotypes. The study gave little evidence of effect modification of the single nucleotide polymorphisms (SNPs) on the relationship between mercury biomarkers and peripheral nerve function. Their study suggested that some metallothionein genetic polymorphisms may influence the biomarker concentration at levels of exposure relevant to the general population (Wang *et al.*, 2012).

Although less certain, the data suggest that additional factors beyond glutathione metabolism affect mercury toxicokinetics. Certain mercury transporter genes may also modify the urinary excretion of mercury. In populations from Indonesia, the Philippines, Tanzania and Zimbabwe exposed to mercury vapour from gold mining, SNPs in four transporter genes appeared to affect mercury concentrations in urine, such as solute-carrier family 22 members 6 and 8 (SLCA22A6/OAT1 and SLCA22A8/OAT3), solute-carrier family 7 member 5 (SLC7A5/LAT1), and ATP-binding cassette sub-family C member 2 (ABCC2/MRP2) (Engstrom *et al.*, 2013). As this study was done in populations from Southeast Asia and Africa, confirmatory data are needed for European populations.

These data suggest that mercury toxicokinetics may depend on genetic polymorphisms including enzymes involved in glutathione metabolism, glutathione transferases, and other ligands or transporters, although no relationship was reported with these variants and Hg-induced adverse effects.

The impact of genetic variants was considered in regard to neurobehavioral outcomes or effects on moods in male dentists and female dental assistants from Washington State. Genetic polymorphisms include the brain-derived neurotropic factor (BDNF)(Echeverria *et al.*, 2005; Heyer *et al.*, 2004), coproporphyrinogen oxidase gene (CPOX) (Echeverria *et al.*, 2006), catechol O-methyltransferase (COMT) (Heyer *et al.*,2009, Woods *et al.*,2014), and the serotonin transporter gene promoter region (5-HTTLPR) (Heyer *et al.*, 2008). The biological plausibility of these association is link to the function of the gene product: CPOX is involved in the haeme biosynthesis of crucial biochemical importance. As a result, the mercury-associated porphyrin profile in urine is changed (Woods *et al.*, 2005; Heyer *et al.*, 2006). COMT is involved in the metabolism of catecholamine neurotransmitters, while 5-HTTLPR affects another key transmitter substance in the brain. However, some of these studies (Heyer *et al.*, 2006) have been challenged due to methodological problems (Björkman 2007).

Similarly, the presence of the metallothionein MT1M mutant or MT2A mutant (33 and 39% of frequency, respectively) in boys, but not the girls in the Casa Pia trial, was reported in an in an additional evaluation after the completion of the original study to be associated with significant mercury-dependent deficits in neurobehavioral function (Woods et al., 2013). By using exploratory methods additional analysis of clinical data with statistical models may indeed find some associations. However, using an explotory method for data analysis evaluates multiple associations and should be considered as hypothesis generating for further clinical research (DeRouen et al., 2015).

In the most recent of the studies related to the Casa Pia Clinical Trial, the 330 enrolled subjects were genotyped for 27 variants of 13 genes that are reported to affect neurologic functions and/or Hg disposition in adults (Woods *et al.,* 2014). Urinary mercury concentrations, reflecting mercury exposure from any source, served as the mercury exposure index. Modelling strategies were employed to evaluate potential associations between allelic status for individual genes or combinations of genes, mercury exposure, and neurobehavioral test outcomes assessed at baseline and for 7 subsequent years during the clinical trial. A significant modification of mercury effects on neurobehavioral outcomes was observed with variant genotypes for 4 genes (CPOX, MT1M, MT2A, COMT). Modification of mercury effects on a more limited number of neurobehavioral outcomes, was also observed for other variants in boys, but the modification was limited in girls (Woods *et al.,* 2014). This gender differences, although not explained by the authors, can be likely attributed to kinetic differences, affecting mercury exposure.

Julvez *et al.,*(2013) report that in a study population as a whole, no adverse effect of methylmercury exposure on neuropsychological outcomes could be identified, and indication of some effects became apparent only when the genetic variants were included in the analysis. The common BDNF polymorphism is shown to affect the neurotoxicity of methyl mercury exposure, but polymorphisms in CPOX appear unrelated to cognitive development (Julvez *et al.,* 2013) in contrast with results obtained by the Wood group.

Recently a review was published reporting the possible genotype–mercury interactions influencing health outcomes, in relation to Hg kinetics, transport, and dynamics (Basu *et al.,* 2014). Quantitative knowledge on the weight of polymorphism should help in improving the assessment factors in carrying out the risk assessment. Whenever data are available they should be used to refine the default factor. The authors highlighted that while different groups investigated the kinetic factors, a large portion of studies to date involving the interaction of polymorphisms and Hg exposure on health outcomes stem from a single research team studying a cohort of male dentists and female dental assistants with occupational elemental (inorganic) Hg exposure and the Casa Pia Clinical Trial on children.

Although the considerations given by the authors refer to data on methyl mercury, their estimation advocates for a default factor of 10. Indeed, they estimated that hair mercury predictions for frequent fish consumers (equivalent of 6 cans of tuna per week) varied 8-fold depending on genotype' (Basu *et al.,* 2014). So, irrespective of the existence of vulnerable sub-groups, the available data seem to indicate that they are covered by the default uncertainty factor of 10 generally used in the risk assessment to account for genetic heterogeneity in the human population.

Accordingly, the European Food Safety Authority argued that for methylmercury a partial uncertainty factor of 2 would be sufficient when a benchmark dose level (BMDL) had been obtained from a birth cohort that would represent the most vulnerable population (European Food Safety Authority, 2012).

The studies presented above seem to indicate that genetic variations, relatively common to the general human population, may have an influence also on responses to mercury -induced toxicity but gaps in knowledge still exist. However, no prospective clinical studies clearly showing the influence of genetic variations on the occurrence of adverse effects due to mercury from dental amalgam are available. Even in the Casa Pia group of papers, urinary mercury reflected mercury exposure from any source, therefore it could not be ascribed to dental amalgam.

There is no accepted and validated method available for identifying such risk groups.This is important as genetic variants may also play a role for alternative dental restorative materials (see below). Therefore, especially in this area further research is needed before clinical conclusions can be drawn.

3.3.8. Experience with non mercury-based fillings/amalgams

There does not seem to be any new information or new products based on non-mercury-based metallic fillings/amalgams for direct restorations, since the former Opinion (2008).

3.3.9. General Observations on Amalgam Efficacy

The efficacy, longevity and general performance of amalgam restorations has been assessed on many occasions in the past, and it is not necessary to review these studies here. Whatever the material chosen, direct restorations may fail, primarily through secondary caries, fracture of the restoration or tooth, marginal deficiencies or wear. The rates at which these failures occur are difficult to compare since they will vary with clinical technique and patient characteristics, and since there have been improvements to the quality of all materials over time.

It remains the view, however, that from mechanical functionality and longevity perspectives and resistance to secondary caries, possibly through anti-bacterial activity, amalgam will outlast alternative materials in many instances (Mitchell *et al.*, 2007, Soncini *et al.*, 2007). In a review from DIMDI (German Institute for Medical Documentation and Information) it was stated that only two out of six systemic reviews conclude that the expected survival time of composite fillings can be comparable to amalgams. However, these conclusions are based on the results of short term studies for composite resins which usually overestimate the longevity of filling materials (Antony *et al.*, 2008). From such perspectives, dental amalgam may still be the material of choice with many dental practitioners e.g. for large restorations and the replacement of large restorations. In a recent Cochrane systematic review on the comparative longevitiy of resin based composites and amalgams it is stated that the parallel group trials indicated that resin restorations had a significantly higher risk of failure than amalgam restorations and increased risk of secondary caries. The results from the split-mouth trials were consistent with those of the parallel group trials. More data with higher levels of evidence are warranted (Rasines Alcaraz *et al.*, 2014).

A main driving force for using composite materials instead of amalgam is the tooth-coloured appearance of composite restorations. One study from the Netherlands and one from Sweden showed very good long-term clinical effectiveness for posterior resin composite restorations with equal and better longevity than for amalgam (Opdam *et al.*, 2007; van Dijken, 2013; Opdam *et al.*, 2012). However, even under optimal conditions large composite restorations in caries risk patients failed more often than amalgam fillings (Opdam *et al.*, 2010). It is with respect to their aesthetics and non-adhesive character, which means that larger cavities have to be prepared, often with excessive tooth tissue removal, that amalgams may be seen to be inferior to the alternatives, and it is this, and not overall longevity, that is driving a change to these alternatives.

3.3.10. Conclusions on Dental Amalgam

It is recognised that mercury, which is the major metallic element used in dental amalgam, does constitute a toxicological risk, with reasonably well-defined characteristics for the major forms of exposure. The reduction in use of mercury in human activity would be beneficial, both for the general decrease in human exposure and from environmental considerations.

However, with respect to the debate about the possibility of causal relationships between the use of mercury containing amalgam and a wide variety of adverse systemic health effects and taking into account many studies and investigations into this putative causal link, there is no

unequivocal evidence to support this possibility. These studies have included assessments in children and in pregnant and lactating women. The existence of susceptible subpopulations due to genetic predisposition needs further research before conclusions can be drawn.

It is generally concluded that no increased risks on adverse systemic effects have been documented in the general population as a whole and it is considered that the current use of dental amalgam does not pose any risk of systemic disease. It is recognised that some local adverse effects are occasionally seen with dental amalgam fillings, but the incidence is low and normally readily managed. In addition, allergy against mercury can occur. It is also recognised that there have been reports of reactions to dental amalgam, which indicate that very occasionally an individual may have unexplained atypical physical or other reactions attributed to mercury. The reasons for such hypersusceptibility are poorly understood.

The mercury release during placement and removal will result in transient exposure to the patients and also to the dental personnel. There is no general justification for removing clinically satisfactory amalgam restorations as a precaution, except in those patients diagnosed as having allergic reactions to amalgam constituents.

The SCENIHR recognises that current evidence does not preclude the use of amalgam in dental restorative treatment in the general population. Dental restorative therapy during pregnancy, as for any other therapeutic treatment, should be limited as much as possible in order to reduce the exposure of the foetus. The choice of material should be based on patient characteristics such as primary or permanent teeth, pregnancy, the already existent number of dental amalgam fillings, presence of allergies to mercury or other components of the restorative materials, and presence of decreased renal clearance.

As far as dental personnel are concerned, it is recognised that they may be more exposed to mercury exposure than the general population, although the incidence and type of reported adverse effects are similar to what is observed in the general population. However, the same considerations for caution in regard to patient exposure also applies to dental personnel.

To reduce the use of mercury-added products in line with the intentions of the Minamata Convention (reduction of mercury in the environment) and under the above mentioned precautions, it can be recommended that for the first treatment for primary teeth in children and in pregnant patients, alternative materials to amalgam should be the first choice. This decision should be made after informed consent from the patient or the legal guardians.

3.4. Alternatives

3.4.1. Classification of alternatives according to chemical composition

Dental filling materials in general can be classified into those used for direct and those used for indirect restorations; some materials like resin-based composites can in certain cases be used for both. With the indirect filling technique, an impression from the intraoral situation of the patient (after cavity preparation) is taken and the actual restoration is constructed outside the oral cavity. Traditionally, an impression material is used and from the impression a cast is made on which the dental technician then fabricates the restoration. The latter is mainly either made from a dental alloy or from ceramics. Dental alloys can be gold-based, but contain many other metals to improve the mechanical and corrosion properties. These metals can be silver, copper, palladium, platinum and others. For crowns, nickel-based alloys are also described. Recently other metals, like titanium/titanium-alloys are used as well as cobalt-chromium alloys; e.g. for CNC milling or laser sintering.

Several thousand different alloys are on the market today. Alternatively, silicate-based and zirconium oxide ceramics can be used for partial and full crowns. In pediatric dentistry, prefabricated metal crowns are used as amalgam alternatives. With this technique, out of a

large variety of prefabricated crowns, the one with the best fit is selected and trimmed to further improve the fit. These steel crowns contain considerable amounts of nickel.
Recently, optical impression techniques have been introduced into dental practice; here, the impression is taken by a specifically designed camera and the restoration is constructed on a computer. Based on this data set, the actual restoration is then grinded from a ceramic (or metal) block in a 3-D-grinding machine.
Common to all indirect restorations is the fact that they must be luted to the tooth substance. For this purpose, different cements are being used, for ceramics mainly resin-based composites materials with low viscosity.
Due to the additional impression technique and the rather complicated manufacturing process, costs of such restorations are comparatively high. Technical properties of the dental alloys and ceramics are generally good. However, when health risks of these restorations are to be evaluated, one must consider not only the composition of the alloys/ceramics but also the composition of other materials used like impression materials or luting substances.

Due to the high costs of indirect restorations, direct techniques are often preferred. Currently, most attention is focused in this context on materials, such as resin-based composites, glass ionomer cement, compomers, giomers and sealants.

A composite is generally defined as a material composed of two or more distinct phases (O'Brien 2002). Dental resin composites consist of a polymerisable resin base containing a ceramic filler. They may be classified in a number of ways, the normal method being based on the size, distribution, and volume percentage of the ceramic particles. With respect to their size, this classification yields the so-called macrofill, midifill, minifill, microfill and nanofill composites. Macrofill composites contain ceramic particles ranging in size from 10-100 µm, midifill in the range from 1-10 µm, minifill in the range from 0.1-1 µm, microfill in the range from 0.01-0.1 µm (10-100 nm) and nanofill in the range from 0.005-0.01 µm (5-10 nm). Recently the European Commission has published a recommendation of the definition of nanomaterial which mentions for nanomaterials a size range of 1-100 nm (Commission Recommendation 2011/696/EU, EC 2011). Hybrid composites contain a mix of two particle-size fractions of fillers, e.g. midi-hybrids consist of mix of microfillers and midifillers, mini-hybrids or micro-hybrids consist of a mix of microfillers and minifillers and nanohybrids consist of a mix of nanofillers and minifillers.

Filler loading varies significantly between the different resin composite materials. For example in a macrofill and hybrid composite, the filler material occupies 50-80% of the composite by weight, while in a microfill composite the filler loading is limited to about 35-50% by weight.

Silorane monomers replaced the methacrylates (e.g. Bis-GMA, UDMA, TEGDMA) in the resin matrix of a recently marketed posterior resin composite material. The ring-opening chemistry of the monomers reduces shrinkage of the resin composite below 1% (Weinmann *et al.,* 2005). Recently, other resin formulations have been marketed claiming reduced shrinkage/shrinkage stress (Roggendorf *et al.,* 2011). Clinical experience with these materials is very limited.

Currently, almost all resin composites are supplied as a pre-packed single-paste system, the curing of the resins occurring by light activation. Different types of commercially available curing units have different light intensities and utilise different light sources. Light-curing units use halogen-based, light-emitting diode (LED), plasma-arc, or laser technology. The energy levels range from 300 to more than 3,000 milliwatts/cm^2.

Glass ionomer cements were introduced in 1972 by Wilson and Kent (1972) and may be considered as a combination of silicate and polyacrylate cement system. Glass ionomer cements bind chemically to dental hard tissues. Polyalkenoate chains enter the molecular surface of dental apatite, replacing phosphate ions, which leads to the development of an ionenriched layer of cement that is firmly attached to the tooth (Wilson *et al.,* 1983). More recently, so-called high-viscosity glass ionomer cements have been marketed with somewhat improved mechanical properties (Lohbauer *et al.,* 2011; Sidhu, 2011). In addition to the

original concept of glass ionomer cement, certain resin modified glass ionomer cements are now used in order to improve functionality.

Compomers were introduced in the 1990's and combine some of the benefits of composites and glass-ionomer cements. A Giomer resin composite was introduced in the early 21st century and featured the hybridisation of glass-ionomer and resin composite.

Sealants are flowable resins or glass ionomers that are applied to seal pits and fissures in permanent teeth in order to prevent the occurrence of caries. A non-resinous calcium aluminate based filling cement received CE marking 2000 as alternative material. The material particles are based on alumina (Al_2O_3) and calcium oxide (CaO), and small amounts of ZrO_2-, TiO_2-, Fe_2O_3- and SiO_2. Mixing the particles with water, which contain small amounts of Na, Li and Fe additives, results after a crystalline phase formation into a hardened cement. Reported poor mechanical properties and unacceptable clinical efficiency resulted in that the materials continued clinical use could not be justified (Sunnegårdh-Grönberg *et al.*, 2003; van Dijken & Sunnegårdh-Grönberg, 2003).

3.4.2. Chemical characterisation of alternative materials

3.4.2.1. Resin composites

Dental resin composites are composed of a wide variety of components with different chemical composition (O'Brien 2002, Powers and Wataha 2007, Roeters and de Kloet 1998). Chemicals described in the literature as possible constituents of resin-based composites are summarised in Annex 1. There is inadequate data on the composition and leachables of these materials, which is sometimes reflected in the Material Safety Data Sheets (MSDS) (Henriks-Eckerman and Kanerva, 1997; Fleisch *et al.*, 2010). According to information from the manufacturers, the dental business environment is highly competitive, and, therefore, data on product composition and chemical characterisation are presently treated as confidential business information and are not typically available to the public.

Filler material
The filler materials are of inorganic composition, such as silica glass (SiO_2), alumina glass (Al_2O_3), and combinations of glass and sodium fluoride. Silica glass is made of beach sand and ordinary glass, but also of crystalline quartz, pyrolytic silica and specially engineered aluminium silicates (e.g. barium, strontium or lithium aluminium silicate glass). Alumina glass is made of crystalline corundum, while sodium-calcium-aluminafluorosilicate glass is an example of a combination glass. A combination glass has to be considered as an engineered mixture of various glasses, which can serve as a source of fluoride ions. The radiopacity of resin composites is obtained by the addition of barium, strontium, lithium or ytterbium fluoride (YF_3) to the filler particles.

Matrix material
The matrix is of organic composition. A large group of different aromatic and diacrylate monomers and oligomers is used, such as bisphenol A-glycidylmethacrylate (Bis-GMA), ethoxylated bisphenol A-methacrylate (Bis-EMA), triethyleneglycoldimethacrylate (TEGDMA) and urethane dimethacrylate (UDMA). In the silorane resin composite, the monomer is a silorane derived from the chemicals siloxanes and oxiranes (Weinmann *et al.*, 2005). As was mentioned above, other resin formulations are recently marketed for which publicly available information, especially on the biological characteristics and the clinical experience, is scarce.

Ormocers
To overcome the polymerisation and biocompatibility problems of conventional methacrylate based resin composites, the first restorative material based on ormocer technology was marketed in 1998. Ormocer is an acronym for organically modified ceramic and the material was originally developed for electronic applications by the Fraunhofer Silicate Research Institute (Würzburg, Germany). Ormocers are synthesised through a solution and gelation

processes from multifunctional urethane and thioether(meth)acrylate alkoxysilanes (Moszner *et al.*, 2008). Monomers are better embedded in the matrix, reducing the release of monomers.
After incorporation of filler particles, the ormocer can be handled like a hybrid resin composite. Improved wear resistance has been observed compared to conventional hybrid resin composites (Manhart *et al.*, 2000). Shrinkage was equal to that of conventional hybrid resin composites despite having less filler content (Cattani –Lorente *et al.*, 2001). Ormocer with higher filler content showed shrinkage equal to low shrinkage resin composites (Yap and Soh, 2004). Due to problems with handling properties, conventional methacrylates had to be added as diluents to the marketed ormocer monomer matrix (Ilie and Hickel, 2009). Clinical performance of an ormocer material together with its adhesive system, however, was not satisfying: With a failure rate of 9.6% after 1 year, this material system did not fulfill ADA acceptance criteria for restorative materials (Oberländer *et al.*, 2001). A more recent preparation of an ormocer-based resin composite showed a better performance after four years (van Dijken and Pallesen, 2011). Studies with longer observation times are not available.

Filler particle incorporation
Coating of the filler particles with silane coupling agents (such as trialkoxysilane) ensures covalent coupling between filler and resin matrix. The carbon-carbon bond on silane molecules binds to the filler particles as well as resin monomer during polymerisation of the resin composite.

Curing of resin composite
Chemical agents (self or auto-cure) or, most commonly, light energy (ultraviolet or visible light) ensures polymerisation of dental resin composites. Dual curing, i.e. a combination of chemical and light curing is also possible. For most resin composite systems in current use, visible light polymerisation at 470 ± 20 nm wavelength is used. Depending on the curing method, various polymerisation initiators and accelerators are required. Initiators for chemical curing are usually benzoyl peroxide and benzene sulphinic acid which initiate polymerisation in the presence of an aromatic tertiary amine. For light curing systems, camphorquinone is normally used in conjunction with an aliphatic tertiary amine as accelerator. Due to the yellow color of camphorquinone, other initiators like trimethylbenzoyl-diphenyl-phosphine oxide (TPO) have been proposed as an alternative (Schneider *et al.*, 2012). In this context biphasic light curing units are now marketed with one peak at around 470 nm and one at around 420 nm.

Additional components
Resin composites contain a number of further additives, like stabilisers and inorganic oxides, and organic compounds are pigments that are added to create a range of various composite shades.

Bonding to enamel and dentine
Bonding of the resin composite, compomer and giomermaterials to hard tooth tissues is achieved by use of a bonding system that incorporates etchants, primers and bonding resins (van Landuyt *et al.*, 2007). Chemical etching using agents such as phosphoric acid, or acidic monomers are used to demineralise the tooth surface and increase the surface area. In etch-and-rinse systems, after rinsing and drying, a primer solution, composed of solvent and low viscosity resins such as HEMA, Phenyl-P, MDP, PENTA, is applied to obtain optimal wetting of the surface for the following bonding agent. Solvents used are water, acetone, ethanol and buthanol or a combination of these. The third step which bonds to the hydrophobic resin composite is achieved by the application of a very thin resin bonding layer. Classical bonding agents are composed of unfilled or with nano-filler filled resins of similar composition as the resin matrix of the composite material. Newer simplified etch-and-rinse bonding systems are composed of only two steps, combining in the second step the primer and bonding. In so-called self-etching adhesives (SEA), the phosphoric acid etching is replaced by etching of the tooth substance with acidic monomers which are included in the primer step. The applied acidic primer is not rinsed away as is the case for the phosphoric acid in the etch-and-rinse systems, but is included as a part of the hybrid layer. In the 2-step SEA, the primer application is

followed by a separate low viscous bonding step. In the 1-step SEA adhesives, etching, priming and bonding are all combined in one application step.

Glass ionomer cements

In the original form, the powder component of these cements is a sodium-calciumalumino-fluoro-silicate glass. The liquid component is composed of polyacrylic acid and tartaric acid. When the powder and liquid are mixed together, a three phase acid-base reaction occurs, involving calcium and aluminium ions leaching as the acid attacks the glass particles, hydrogel formation as the polyacrylic acid molecules crosslink, and polyalkenoate salt gelation as the polyalkenoate salt captures un-reacted glass. More recently, high-viscosity glass-ionomer cements or those in combination with a surface varnish have been marketed with somewhat improved mechanical properties (Lohbauer *et al.*, 2011; Sidhu, 2011). Glass ionomer cements have also been used with the ART technique. They can be used to restore single-surface cavities both in primary and in permanent posterior teeth, but their quality in restoring multiple surfaces in primary posterior teeth cavities need to be improved. Insufficient information is available regarding the quality of ART restorations in multiple surfaces in permanent anterior and posterior teeth (Frencken *et al.*, 2012). Other authors claim better clinical performance of high viscosity glass ionomer materials in primary teeth, but data are comparatively scarce (Mickenautsch *et al.*, 2010).

In the resin-modified cements, methacrylate monomers like HEMA have been added to improve functionality with respect to higher strength and water resistance. The materials have been further modified by the addition of photo initiators so that light-curing can occur, but they maintain their ability to set by an acid-base reaction. The setting of resin modified glass ionomer cement is identical to the polymerisation of composite resin. During this process, free radical species are generated.

3.4.2.2. Compomers

The main components of compomers are polymerisable dimethacrylate resins, such as urethane dimethacrylate and TCB, which is a reaction product of butane tetracarboxylic acid and hydroxyethylmethacrylate, and ion-leachable glass filler particles such as strontium fluorosilicate glass. The glass particles are partially silanised to achieve bonding with the resin matrix. The setting reaction is based on free radical polymerisation using photoinitiators. During the setting reaction, HEMA is released while fluoride release occurs after setting.

3.4.2.3. Giomers

Giomers are based on the technology of a reaction between fluoride containing glass and a liquid polyacid. The prereacted glass particles are mixed with resins such as urethane dimethacrylate and hydroxyethylmethacrylate, and a catalyst to initiate polymerisation. Bonding of the material is achieved through the use of self-etching primers including methacrylate resins like 2-HEMA, 4-AETA , UDMA, and TEGDMA and pre-reacted glass-ionomer filler. The bonding agent releases fluoride. In a recent 6-year clinical evaluation, posterior restorations of giomer showed a rather high failure rate (van Dijken, 2013).

3.4.3. Toxicology of components of alternative materials

The alternative restorative materials are chemically complex, with many different components, setting reaction mechanisms and opportunities to interact with tissues of the individuals in whom they are placed. However, characteristics of exposure are very difficult to determine, bearing in mind that volumes of the materials used are very small, the residence time within the body of chemicals that take part in setting reactions is usually very short and the chemical

and toxicological profiles of the set material are usually very different to those of the starting materials. In evaluating the possibilities for adverse effects arising from the clinical use of these materials, it is necessary to consider the evidence about the inherent toxicity of the chemicals used and the performance and behavior of the restorations over time. Of interest to most investigations here have been the monomers used in polymerisation reactions, which may remain unreacted and therefore present in the set material, the acids used in various phases of the setting and etching processes and ions released from glasses.

3.4.3.1. Release of substances from alternative materials

Unbound monomers and/or additives are eluted within the first hours of placement in the tooth cavity. The very nature of the polymerisation processes, involving the absorption of light energy by the material that will vary with depth within the restoration, and the subsequent conversion of monomer molecules into cross-linked macromolecules, inevitably means that some monomer molecules do not have the opportunity to take part because of diffusion limitations. The completeness of the polymerisation process is reflected by the degree of conversion. Between 15 and 50% of the methacrylate groups may remain un-reacted according to Ferracane (1994). However, this may be enough to contribute to major cytotoxic effects *in vitro* (Stanislawski *et al.,* 1999). Improvements in the material formulations have resulted in increasingly superior degrees of conversion in recent years. The effects may also be dependent on dentine permeability and residual dentine thickness (Bouillaguet *et al.,* 1998, Galler *et al.,* 2005) since dentine may absorb unbound monomers and therefore contributes to decrease the cytotoxicity of the material. This is not directly under the control of the dental surgeon although the formation of reactionary dentine may be stimulated by preparative steps. Dentine permeability may also be modified by calcium phosphate precipitation in the lumen of the tubules leading to sclerotic dentine formation. It has also been shown that the surface of composite resins exposed to oxygen during curing produces a non-polymerised surface layer rich in formaldehyde, which by itself is an additional factor of cell toxicity (Schmalz, 1998).

Monomers have been identified in dental resin composites eluates by gas and liquid chromatography/mass spectrometry. A considerable concentration of the co-monomer triethyleneglycoldimethacrylate and minor concentrations of the basic monomers Bis-GMA and UDMA as well as the co-monomer HDDMA have been detected with these methods (Geurtsen 1998; Spahl *et al.,* 1998). Kopperud *et al.,*(2010) found no substances to leach from Silorane resin composite in water, whereas silorane monomers and an initiator component were eluted from the material into an ethanol solution.

Formaldehyde is released from resin-based composites into an aqueous environment especially from the superficial oxygen-inhibited surface layer after curing but also over a prolonged period of time (Oysaed and Ruyter, 1988). This also applies to resin modified glass ionomer cements (Ruyter, 1995). Formaldehyde is very likely generated by an oxidation of unsaturated methacrylate groups (Oysaed and Ruyter, 1988).

BPA is released into an aqueous environment from resin composites which contain Bis-DMA, because Bis-DMA itself is eluted, and it is then hydrolytically and enzymatically cleaved into BPA and methacrylic acid. This release mainly takes place during the first 24 hours after placement (Schmalz *et al.,* 1999; Myers and Hutz, 2011; Fleisch *et al.,* 2010). BPA is released in small amounts from some brands of Bis-GMA based resin composites continuously, because it is a residue from the production process of Bis-GMA, in which BPA is used (Imai, 2000; Imai and Komabayashi, 2000). Earlier data on larger amounts of BPA released from Bis-GMA resins (Olea *et al.,* 1996) could not be confirmed (Schmalz *et al.,* 1999; Myers and Hutz, 2011; Imai, 2000; Geurtsen *et al.,* 1999; Hamid and Hume, 1997; Moon *et al.,* 2000; Wada *et al.,* 2004). A recent study from NIH showed that BPA and related compounds could be found in saliva and urine after restoration with resin composites (Kingman *et al.,* 2012). In saliva, most compounds returned to prerestoration levels within 8 hours, while concentrations of the study compounds in urine returned to prerestoration levels nine to 30 hours after restoration

placement with the exception of a 43 percent increase in BPA. In a recent study, the release of BPA after long-term storage was reported (Sevkusic *et al.*, 2014).
The SCENIHR Opinion "The safety of the use of bisphenol A in medical devices" (2015) concluded that release of BPA from some dental materials was associated with only negligible health risks.
Dental alloys continuously release metals into the oral environment depending e.g. on the metal content, the phase distribution within the alloy, thermal treatment and the corrosion conditions. Metals like Au, Cu, Ag, Pd are released and also Ni, Zn, Co, Ti, Cr and many others (Schmalz and Arenholdt-Bindslev, 2009).

Release of substances from and degradation of glass ionomer cements are generally regarded higher than for resin-based composites. These materials mainly release fluorides (Forsten, 1990) but also calcium, sodium, silicon, strontium, and aluminium. Some release silver or zinc (Guertsen, 1998; Hantsen *et al.*,1994). Ceramic releases – depending on the composition – substances like silicon, boron, sodium, potassium, and aluminium, some brands lithium in small amounts (Anusavice and Zhang, 1997).

3.4.3.2. Leachable substances generated by erosion and degradation

Leachable components are released due to degradation or erosion over time, the leaching process being determined not only by the degradation process itself but also diffusivity through the material. Chemical degradation is caused by hydrolysis or enzymatic catalysis. Non-specific esterases, human saliva derived esterase and pseudocholinesterase may catalyse the biodegradation of resin composite (Geurtsen 2000; Jaffer *et al.*,2002; Finer *et al.*,2004). Incubated *in vitro* with cholesterol esterase, the composites may release 2,2-bis [4(2,3-hydroxypropoxy)-phenyl]propane (bis-HPPP) and TEGDMA for up to 32 days, the amount depending on the matrix/filler ratio (Shajii and Santerre, 1999).

These esterases have been shown to hydrolyse Bis-GMA to bis-(2,3-dihydroxypropyl) ether (BADPE-4OH) by the loss of two molecules of methacrylic acid. The same enzyme converted TEGDMA into triethylene glycole and methacrylic acid and HEMA hydrolyses under acidic conditions into thylene glycole and methacrylic acid (Schmalz and Arenholt-Bindslev, 2009). During cell metabolism of TEGDMA and HEMA epoxy-intermediate 2,3-epoxymethacrylic acid is formed which is considered to be mutagenic (Durner *et al.*, 2010). The hydrolytic degradation of Bis-DMA to BPA has already been mentioned above.

It is also assumed that bonds in the pendant side chains of the macromolecule are attacked through the effect of thermal, mechanical and photochemical factors.

Water or other solvents may diffuse into the polymer, facilitating the release of degradation products, including oligomers and monomers. The leaching process is influenced by size and polarity and by hydrophilic and lipophilic characteristics of the released components (Geurtsen 1998). Softening of the Bis-GMA matrix allows the solvents to penetrate more easily and expand the polymer network, a process that facilitates the long-term diffusion of unbound monomers (Finer and Santerre 2004).

3.4.3.3. Release of ions

Ions are released from both metallic and non metallic alternative materials. Ions from dental alloys comprise a large variety like gold, palladium, platinum, silver, copper, zinc, tin, nickel, cobalt, chromium and others (Schmalz and Arenholt-Bindslev, 2009). But also non metallic alternative dental restorative materials release ions, such as fluoride, strontium and aluminium ions. The fluoride is expected to be beneficial and reduce the development of secondary caries. Presumably, the fluoride content of toothpastes and nutriments reload the material so that the

resins or resin modified glass ionomer cements do not become porous. Other ions are implicated in the colour of the restorative material, and these metal elements may interfere with the biocompatibility of the resin because they are implicated in the Fenton reaction producing reactive oxygen species that are cytotoxic. The concentration of fluoride and strontium is considered to be too low to produce cytotoxicity. In contrast, however, copper, aluminium and iron may be present in toxic concentrations. The cytotoxic cascade has been shown to be enhanced by metals such as aluminium and iron present in various amounts in some of these materials (Stanislawski *et al.*,1999; Stanislawski *et al.*, 2000; Stanislawski *et al.*, 2003).

3.4.3.4 Toxicity of resin composite monomers

Toxicity evaluation of resin composite materials is very complex, because a large variety of different substances are contained in these materials, which vary from one manufacturer to another. Furthermore, other substances may be produced during the polymerisation process, like formaldehyde. Also, different biological endpoints need to be critically discussed. This all would go well beyond the scope and the range of this report. Therefore, only key elements are mentioned here and more detailed information can be obtained from the literature (e.g. Schmalz and Arenholt-Bindslev, 2009).

The first ormocer that was markeded initially showed low cytotoxicity and mutagenicity, which further decreased after prolonged aging (Wataha *et al.*, 1999; Bouillaguet *et al.*, 2002, Schweikl *et al.*, 2005). On the other hand, Al-Hiyasat *et al.*,(2005) showed a higher cytotoxicity for another commercial ormocer in comparison with two other resin composites.
Its flowable material showed lower cytotoxicity than the restorative material. Furthermore, estrogenic effects have been described with an ormocer material, although the clinical relevance is yet unclear (Wataha *et al.*, 1999). Polydorou *et al.*,(2009) showed that an ormocer released significantly less monomers such as Bis-GMA, TEGDMA or UDMA compared to either a nanohybrid composite or a self-curing composite.

Monomers caused cytotoxicity in cultured cells with ED50 in the low millimolar to submillimolar concentrations (Kleinsasser *et al.*, 2006; Schweikl *et al.*, 2005; Schweikl and Schmalz, 1996a; Schweikl and Schmalz 1997; Schweikl *et al.*, 1998a; Schweikl *et al.*, 1996b; Schweikl *et al.*, 1998b; Schweikl *et al.*,2006). In an *in vitro* embryotoxicity screening study, BisGMA induced effects at low, non-cytotoxic concentrations suggesting a potential for embryotoxicity or teratogenicity (Schwengberg *et al.*, 2005). Siloranes showed reduced cytotoxicity (Brackett *et al.*, 2007). They also showed low genotoxic potential and can be suitable components for development of biomaterials (Schweikl *et al.*, 2004; Krifka *et al.*, 2012).

TEGDMA and the photostabiliser 2-hydro-4-methoxybenzophenone (HMBP) are cytotoxic and inhibit cell growth (Geurtsen and Leyhausen 2001). The intracellular glutathione level may be decreased by 85% by TEGDMA (Stanislawski *et al.*, 1999; Stanislawski *et al.*, 2000; Stanislawski *et al.*, 2003; Engelmann *et al.*, 2001; Engelmann *et al.*, 2002).

An *in vitro* evaluation of the cytotoxicity of 35 dental resin composite monomers and additives indicated moderate to severe cytotoxic effects (Geurtsen *et al.*, 1998). The effects vary according to the material tested, but also they strongly dependon the cells used for testing. For example, human periodontal ligament and pulp fibroblasts are more sensitive than 3T3 and gingival fibroblasts (Geurtsen *et al.*, 1998). With the exception of a very few reports, there is a general consensus that resin-containing restorative materials are cytotoxic (Geurtsen *et al.*, 1998; Geurtsen, 2000; Schmalz, 1998), greater effects generally been seen at early intervals after preparation.

At clinically relevant concentrations and for different cell lines, TEGDMA and HEMA have been shown to increase the intracellular concentration of reactive oxygen species (ROS) (Stanislawski *et al.*, 2003; Schweikl *et al.*, 2006). Monomer-induced oxidative stress is

associated with the depletion of the non-enzymatic antioxidant glutathione and modified expression of enzymatic antioxidants (Volk *et al.*, 2006; Schweikl *et al.*, 2006; Krifka *et al.*, 2012). The presence of these resin monomers also leads to DNA damage (genotoxic effect) in vitro probably due to oxidation processes (Schweikl *et al.*, 2007), DNA strand breaks (Kleinsasser *et al.*, 2006; Durner *et al.*, 2011), a cell cycle delay (Schweikl *et al.*, 2006; Schweikl *et al.*, 2007) and to apoptosis (Janke *et al.*, 2003; Krifka *et al.*, 2012). In p53 deficient culture systems (V79 cells), mutation can be observed after exposure to TEGDMA or HEMA (Schweikl *et al.*, 1998; Schweikl *et al.*, 2001). Furthermore, the ability of dental human pulp cells for biominerlisation (here: formation of new dentin) is blocked by TEGDMA (Galler *et al.*, 2011) as well as the bacterial defense system of macrophages (Schmalz *et al.*, 2011).

Only limited toxicity data for the monomers used in dental resin composite systems are available. Major differences in the degrees of cytotoxicity of various resin composite materials have been found (Schedle *et al.*, 1998; Franz *et al.*, 2003; Franz *et al.*, 2007). Most tested materials showed only mild cytotoxicity comparable to amalgam or less than amalgam but there were a few exceptions. Most of the available toxicity data have been generated in in-vitro systems that focus on genetic toxicity of the compounds in standard test systems such as the Ames-test, and on cytotoxicity in gingival fibroblasts. TEGDMA, UDMA and HEMA have all been shown to be positive in the COMET assay indicating induction of DNA-damage in mammalian cells. HEMA, BisGMA and TEGDMA also induced gene mutations in mammalian cells by a clastogenic mechanism.

The limited data on these monomers in experimental animals include studies on absorption, distribution, metabolism and elimination (ADME) on HEMA, TEGDMA and Bis-GMA after oral application of radiolabelled compounds. A rapid absorption of these compounds from the gastrointestinal tract and a rapid catabolism by physiological pathways to carbon dioxide, which is exhaled, has been described, although important details are still unknown (Reichl *et al.*, 2001a; Reichl *et al.*, 2002a; Reichl *et al.*, 2002b; Reichl *et al.*, 2001b; Reichl *et al.*, 2002c; Reichl *et al.*, 2008; Durner *et al.*, 2009). During this process, highly mutagenic epoxy compounds (2,3-epoxymethacrylic acid) are produced (Durner *et al.*, 2010).
No direct data on toxic effects of resin monomers in animals are available from publicly accessible sources. However, since the materials used as a basis for resin generation are derivatives of methacrylic acids and glycidyl ethers, the well-studied toxicology of methacrylate and its esters may be used as a basis for structure activity relationships to predict major toxicities.

Methylmethacrylate, as a relevant resin monomer, is rapidly absorbed after oral administration in experimental animals and is rapidly catabolised by physiological pathways to carbon dioxide. The major toxic effects of methylmethacrylate in animals are skin irritation and dermal sensitisation. In repeated dose-inhalation studies, local effects on respiratory tissue were noted after methylmethacrylate inhalation. Neurotoxicity and liver toxicity were observed as systemic effects after inhalation of methylmethacrylate in rats and in mice to concentrations above 3000 ppm for 14 weeks. For developmental toxicity of methylmethacrylate a NOAEC > 2000 ppm was observed. Methylmethacrylate is also clastogenic at toxic concentrations (EU-RAR 2002).

A detailed overview of the toxicity of glycidyl ether compounds is available (Gardiner *et al.*, 1992), although it is based mainly on unpublished study reports. Skin irritation and sensitisation were the major toxicities observed. In addition, positive effects in genetic toxicity testing were seen with many glycidyl ethers at comparatively high concentrations.

For BPA release from dental materials acute exposure was reported (Joskow *et al.*, 2006) to be in total 110 µg for six fissure sealants placed at one time with Bis-DMA containing material and 5.5 µg for sealants free of Bis-DMA. For chronic exposure, data are scarce. It is known from the elution behavior of resin-based materials that most of all eluable substances are eluted during the first 24 hours (Ferracane *et al.*, 1994; Ferracane *et al.*, 1995). No further degradation of Bis-GMA or related products to BPA was observed so far. However, recently it

was reported that BPA was released only after storage of several months (Sevkusic *et al.*, 2014).

EFSA (2015) established a temporary (t)-TDI of 4 µg/kg b.w./day for oral exposure to BPA based on kidney alterations as the critical effect. The latter dose would mean for a 25kg child a tolerable daily intake would be 100 µg, which is higher than the amount of BPA acutely released immediately after placement of a Bis-DMA-containing fissure sealant material on 6 teeth. Therefore, no acute or chronic estrogenic effect is to be expected from the use of Bis-GMA (and Bis-DMA free) resin-based composites/sealants. Even for the Bis-DMA containing resin composites/sealants the risk cannot be regarded as unacceptable under the given assumptions.

Saliva had been collected from 8 male volunteers; 4 had received 38 $\pm$ 3 mg of a Bis-DMA containing sealer and one which was Bis-DMA free. The saliva samples had been collected before and immediately after placement as well as 1 hour and 24 hours later (Arenholt-Bindslev *et al.*, 1999). The results show an estrogenic activity elicited by those saliva samples from patients with the Bis-DMA contains fissure sealant, but not from patients with a Bis-DMA free Bis-GMA based sealant (Arenholt-Bindslev *et al.*, 1999). The estrogenic activity could only be observed immediately after placement. After one or 24 hours no estrogenic effect could be observed. Other authors have reported similar results (Tarumi *et al.*, 2000; Fung *et al.*, 2000; Kingman *et al.*, 2012). Other components than BPA of composite resin eluates like a photostabiliser [HMBP], a photointiator [DMPA], an inhibitor [BHT] or a phthalate compound [BBP] were in vitro estrogenic, but the amounts of these substances released were very small and the risk possibly negligible in the clinical situation (Wada *et al.*, 2004).

In ovariectomised mice, a high dose of bis-GMA via subcutaneous route had no effect on DNA, RNA and DNA/RNA ratio compared to the control group were observed but a modest increase of uterus weight (Mariotti *et al.*, 1998). This was apparently due to an unspecific increase in collagen but not due to an increase of the cell number, and the dose in this experiment was far higher than any expected exposure in humans (Mariotti *et al.*, 1998); thus no unacceptable risk for the patient was concluded.

In conclusion, resin-based composite materials are today for many clinical situations recognised tooth-coloured materials to restore lesions; e.g. due to caries, erosion or trauma or to prevent caries (fissure sealants). According to present knowledge, for Bis-GMA-based materials with no Bis-DMA, additional exposure evaluation shows no risk for BPA-related acute or chronic effects, because no or very little BPA is released from dental materials (SCENIHR, 2015). However, BPA present as impurity/residue from the manufacturing process may be released.

For Bis-DMA containing materials, BPA release was consistently shown. The amount was so low that according to present knowledge, no adverse effect is expected (SCENIHR, 2015). However, if for personal considerations and wishes of a patient, any BPA exposure shall be minimised, products containing Bis-DMA should not be used. To better inform the user (dentist and patient), the content of dental materials should be declared.
No adverse effects were noted in reproductive toxicity studies of BisGMA (Moilanen *et al.*,2014) or TEGDMA (Moilanen *et al.*,2013) conducted in mice at doses at least 100-fold higher than estimated clinical exposure from use of composite restoratives.

3.4.3.5 Toxicity of other alternative materials

Under this heading dental alloys, glass ionomer cement including those with resin ingredients and ceramics are summarised. Metals released from dental alloys are – depending on the element and its oxidation stage – cytotoxic (Schedle *et al.*,1995; Schmalz *et al.*, 1997). Cytotoxicity of alloys depends on the corrosion rate, which with high gold alloys is generally smaller than with less noble alloys. Some Ni-containing alloys and Pd-Cu alloys but also Cu

containing gold alloys are clearly cytotoxic (Wataha and Schmalz, 2001). Some metals are mutagenic, but the clinical relevance is not yet clarified for the use in dentistry (IARC, 1996). Alloys used for ceramic metal restorations may cause inflammation of the surrounding gingiva due to the release of metals (Schmalz and Arneholdt-Bindslev, 2009). Certain metals released from dental alloys like Ni, Cr, Co and Pd are well known to elicit as haptens allergic reactions. Also, Au has been described as an allergen (Møller, 2002). Cross reaction between Ni and Pd have been reported (Garhammer *et al.*, 2001; Hindsen *et al.*, 2005). Oral lichenoid reactions could be associated with an Au or Pd allergy (Raap *et al.*, 2009). Like for amalgam, patient groups claimed systemic reactions caused by dental alloys, but these claims could not be substantiated except for allergies (Schmalz and Arneholdt-Bindslev, 2009).

Glass ionomer cements are only cytotoxic, when not fully set (Ersev *et al.*, 1999). Neither mutagenicity nor allergic reactions have been reported, but in direct contact with the dental pulp, severe tissue damage occurs (Schmalz *et al.*, 1994). Resin modified glass ionomer cements and compomers have biologic characteristics similar to resin composites. One resin modified glass ionomer cement was strongly cytotoxic and mutagenic (Heil *et al.*, 1996; Ribeiro *et al.*, 2006).

Ceramic materials are – with very few exceptions – not cytotoxic, mutagenic and do not cause allergic reactions. Radioactivity was measured, but the doses were considered low (Schmalz and Arneholdt-Bindslev, 2009). Many ceramic materials have to be luted to the dental hard tissues using resin-based materials and therefore biological problems associated with resin materials (see above) have to be considered.

3.4.4. Exposure

As noted earlier there are very limited data on exposure levels to the components of alternative dental restorative materials. Unlike the situation with amalgam, there are no obvious markers for exposure. Moreover, there are significant limitations to the determination of these exposure levels. The molecules used in any setting reaction, whether that is a polymerisation or an acid – base reaction, are by definition chemically reactive with a potential to exert toxic effects in humans. However, the reaction involves a small amount of material and usually takes place very quickly, following which many of these molecules have been irreversibly changed into far less reactive species or trapped within a solid mass with very limited capacity to diffuse and leach out. It is therefore expected that there will be a low but detectable level of exposure to many of these molecules during placement of the restoration. This is followed by a considerably reduced level, during the lifetime of the restoration.

The monomers used in dental resin-based materials are volatile and it is usually possible to smell them in dental clinics. The exposure of dental personnel to airborne methacrylates was studied during the placing of resin composite restorations in six dental clinics in Finland by Henriks-Eckermann *et al.*,(2001). Both area and personal sampling were performed, and special attention was paid to measurement of short-term emissions from the patient's mouth. The median concentration of HEMA was 0.004 mg/m^3 close to the dental nurse's work-desk and with a maximum concentration of 0.003 mg/m^3 in the breathing zone of the nurse with a maximum concentration of 0.033 mg/m^3. Above the patient's mouth the concentration of 2-HEMA was about 0.01 mg/m^3 during both working stages, i.e., during application of adhesive and resin composites and during finishing and polishing of the fillings. Maximum concentrations of 3-5 times higher than median concentrations were also measured.

TEGDMA was released into the air during the removal of old resin composite restorations (0.05 mg/m^3) but only to a minor extent during finishing and polishing procedures. The results showed that, except for short-term emissions from the patient's mouth, the exposure of dental personnel to methacrylates is very low. Measures to reduce exposure were discussed, as the airborne concentrations of methacrylates should be kept as low as possible in order to reduce the risk of hypersensitivity. In a study from Germany similar concentrations for HEMA and TEGDMA have been measured (Marquardt *et al.*, 2009). Other than those papers, there seems

to be limited information about the actual level of exposure to volatile monomers in a clinical situation.

Polymerised resin-based materials contain various amounts of residual monomers and polymerisation additives that may leach from restorations. The release may remain on a high level for some days (Polydorou *et al.*, 2007). In addition, as noted above, chemical, microbiological and wear impacts are observed over time, and occlusal or approximal degradation of resin composite restorations occurs (Groger *et al.*, 2006; Söderholm, 2003).

Most information on the release of material components is based on laboratory models with solvents such as ethanol, water, saline, artificial saliva or culture media. Gas chromatography and mass spectrometry of the solutes from resin composites, compomers and resin modified glass-ionomers have demonstrated the presence of a number of organic leachables such as monomers, co-monomers, initiators, stabilizers, decomposition products and contaminants. Some of them have been identified as the low viscosity monomers EDGMA, TEGDMA and HEMA together with initiator and co-initiators such as hydroquinone, camphorquinone, and DMABEE and an ultraviolet absorber, Tinuvin P (Lygre *et al.*, 1999; Michelsen *et al.*, 2003). Attempts at quantification have shown that elution from different materials differs significantly (Michelsen *et al.*, 2006) and the data are contradictory. Bis-GMA, Bis-EMA, UDMA and various additives have been shown to leach (Rogalewicz *et al.*, 2006), although others have failed to demonstrate BisGMA and UDMA in aqueous extracts, even though TEGDMA-based composites released high amounts of monomers (Moharamzadeh *et al.*, 2007). Under simulated in vitro chewing conditions TEGDMA release from a resin composite was analysed; with or without chewing most TEGDMA was released in the first 26 hours, then the amount declined. Around 2.6% of the included ^{14}C labeled TEGDMA was released after 86 hours (Durner *et al.*, 2010).

It is reasonable to assume that similar leaching reactions take place in patients, depending on the composition of the material, the effectiveness of the polymerisation process and the chemical impact of the oral environment, although limited information is available on the concentration of components from amalgam alternatives in patient saliva or other body fluids. There are some exceptions, such as acrylic monomers from soft liners and phthalates from denture base materials (Lygre *et al.*, 1993; Lygre 2002).

Bisphenol-A (BPA) can be released from resin-based materials (Olea *et al.*, 1996; Pulgar *et al.*, 2000) with more BPA being eluted in the polymerised state than in the unpolymerised. However, from unpolymerised samples fewer substances are released than from polymerised ones, which is in contradiction to studies reported elsewhere in the literature (Schmalz and Arenholt-Bindslev, 2009). Furthermore, a large number of other authors who studied BPA release using a large variety of test methods and materials could not detect BPA with the exception of a Bis-DMA containing sealant. Because of the contradictory results, the analytical methods used by Olea *et al.*,(1996) and Pulgar *et al.*,(2000) were heavily questioned (Imai, 2000; Imai and Komabayashi, 2000; Schmalz and Arenholt-Bindslev, 2009; Fleisch *et al.*, 2010; Myers and Hutz, 2011).

It was shown that materials containing Bis-DMA released BPA immediately after application into the patient's saliva. After 24 hours the BPA concentrations in saliva returned to pretreatment level (Schmalz *et al.*, 1999; Arenholt-Bindslev *et al.*, 1999). In the same study, a Bis-GMA-based pit and fissure sealant that contained no primary BPA contamination was not found to release BPA into saliva. BPA release from Bis-DMA containing sealants have been reported by other authors (e.g. Joskow *et al.*, 2006). BPA could not be detected in the blood samples and urine content of BPA was most elevated in patients after Bis-DMA material application one hour after placement and then decreased after 24 hours.

Bis-DMA was cleaved hydrolytically under alkaline conditions, using porcine esterases and human saliva. BPA could be detected, but this was not the case with Bis-GMA (Schmalz *et al.*, 1999). It can be concluded that Bis-DMA is initially eluted from Bis-DMA-containing pit and fissure sealants, which is then degraded to BPA in saliva. BPA degradation from Bis-GMA could not be demonstrated under the given analytical conditions (Schmalz *et al.*, 1999).

As BPA is used during the production process of Bis-GMA, residues of BPA may be present. These have been estimated by Imai (2000) to be at maximum 10µg/g unpolymerised resin. Experimental addition of 100 µg/g of BPA to a resin composite resulted in a BPA release being lower than for TEGDMA, and over ten years 12% (water) or 53% (methanol) BPA from the original BPA content of the resin was calculated to be released. From 1 g of this resin during 10 years patients may be exposed to minute amounts of 4 ng/day (water) or 16ng/day (methanol) (Imai and Komabayashi, 2000).

A study performed by the American Dental Association (2014) shows that bis-GMA-based dental restorative materials have the potential to release BPA at a detectable level. Furthermore, bis-DMA and bis-EDMA also demonstrated a high potential to release BPA. All sources of raw bis-GMA had detectable levels of BPA. However, all of the tested dental restorative composites released BPA at levels that are far below the daily exposure limits set by the U.S. Environmental Protection Agency and the European Food Safety Authority.

Summarising the data, it can be stated that patients may only be exposed to minute amounts of BPA from Bis-GMA resins due to possible impurities. From materials containing Bis-DMA, BPA exposure of patients could consistently be found, but mainly during the first 24 hours after placement. In addition the risk assessment due to BPA release from dental amalgam has been carried out and described in the recent opinion by SCENIHR (2015), showing that no concern is associated with these dental material.

Nano-particles

Recently, attention was drawn to another exposure source for patients and dental personnel with a possible toxicological relevance: the formation of nanoparticles during the placement or the removal of resin composite fillings (van Landuyt *et al.*, 2012). From a large group of contemporary resin composite materials, blocks were formed, ground as is done in a dental practice and the dust was analysed. Small respirable dust particles were found and the ratio of dust particles < 1 µm to those >1 µm ranged between 3:1 to 9:1.

This was confirmed in a recent study by Bogdan *et al.*,(2014), showing that nanoparticles were generated during shaping of materials independent of the amount and size of the filler particles.

Exposure measurements of dust in a dental clinic revealed high peak concentrations of nanoparticles in the breathing zone of both dentist and patient, especially during aesthetic treatments or treatments of worn teeth with composite build-ups (Van Landuyt *et al.*, 2014). Analysis of the particles generated by abrasive procedures confirmed that all tested composites, including both conventional and nano-composites, released airborne nanoscale particles.

3.4.5. Potential adverse effects in patients

On the basis of the above comments on the composition of the alternatives to amalgam, the possible exposure levels associated with their components and known *in vitro* data on their toxicity, a general assessment of potential adverse effects in patients may be made.

3.4.5.1. General

The components released from dental restorative materials comprise a long list of xenobiotic organic substances and metallic elements (Schmalz 2005; Wataha and Schmalz 2005). The components are subject to oral mucosal, pulpal and gastrointestinal absorption, and, for aerosols, pulmonary absorption, the passive diffusion through cell membranes being guided by factors such as the concentration gradient, molecular size, polarity, lipophilicity, and hydrophilicity.

Toxic effects after inadvertent contact with chemicals associated with restorative dentistry may appear as acute soft tissue injuries among dental patients. Local chronic reactions of irritation,

or of combined irritation and hypersensitivity, appear as lichenoid reactions of the gingiva or mucosa. It is generally accepted that the amount of potentially toxic substances absorbed from alternatives to amalgam is too small to cause systemic reactions by dose-dependent mechanisms in target organs. However, this statement does not deny that adverse reactions may occur, elicited by minute quantities of released substances, including allergies and genotoxicity. Of these, only allergy has been confirmed among dental patients.

The cytotoxicity and genotoxicity of substances leached from resin-based materials and metallic elements have been the subject of extensive studies using cell culture techniques and a bacterial mutation test (Ames test). Substances such as TEGDMA and HEMA cause gene mutations *in vitro*. Studies on the intracellular biochemical mechanisms have clarified various effects such as cell membrane damage, inhibition of enzyme activities, protein or nucleic acid synthesis etc. (Schweikl *et al.*, 2006). At present, the clinical relevance of these *in vitro* studies is uncertain.

The release of Bisphenol A from Bis-GMA based materials such as fissure sealants and composites into saliva has been of special interest because of its potential estrogenic effect (Joskow *et al.*, 2006). The concentration of released Bis-GMA from certain types of sealants has been reported to be within the range at which estrogen receptor-mediated effects were seen in rodents (Schmalz *et al.*, 1999). However, the release from resin-based restoratives is much lower. The conversion of Bis-GMA to Bis-MA is minimal in resin-based materials if pure base monomers are used (Arenholt-Bindslev and Kanerva, 2005). The minute concentration in resin-based amalgam alternatives is not considered to be a problem.

It must be noted that there are other alternatives to amalgams in addition to these resin- and cement-based materials. These primarily include a variety of different alloys and ceramics used for indirect restorations. These, however, do not represent clinically relevant options for the treatment of the vast majority of teeth and are only used when direct restorations are contra-indicated. Although idiosyncratic responses may be encountered with most materials (Ahlgren *et al.*, 2002), and there may be exposure even to gold from such restorations (Ahlgren *et al.*, 2007), there are very few indications that such materials have the potential for adverse effects with the exception of allergies towards metals like nickel, cobalt, palladium and even gold (Schmalz and Arenholt-Bindlev, 2009).

3.4.5.2. Allergy/Immune system

Potential allergens among amalgam alternatives

There is limited possibility to predict the allergenic potential for a foreign substance on the basis of chemical composition using Quantitative Structure-Activity Relationship (QSAR) analysis. However, experimental testing such as the Guinea Pig Maximisation Tests or the Murine Local Lymph Node Assay, and empirical results after years of testing substances causing allergies have given some leads: the strongest allergens are often low molecular weight, aromatic, lipid soluble substances, or otherwise chemically active substances that react with proteins. Metal and metal salts are also high ranking haptens. On this basis, monomers, cross-linking agents, chemicals associated with the polymerisation process, and degradation products, all associated with resin-based materials, are important candidates for allergic responses among users of these alternatives, including dental patients and professionals. A short list of allergens relevant to resin-based amalgam alternatives is presented in Table 4.

Although an allergic reaction may be provoked by haptens derived from dental materials, the sensitisation process may be caused by substances unrelated to dentistry. Plastics are met with in everyday life and in occupations such as construction work and printing. For anatomical reasons both the allergic sensitisation and the allergic response are more easily obtained on skin than in the oral tissues. Epidermal tests are therefore adequate also for observations of intraoral adverse effects. A positive patch test is an indication of a causal relationship between the substance and the suspected allergic reaction, but does not provide definitive evidence without other criteria of causality, which often cannot be performed for practical and ethical reasons.

Table 4: Some allergens in resin-based amalgam alternatives (primers, bonding agents, resin composites, glass ionomers, resin modified glass-ionomers, compomers etc.).

Methacrylate monomers
2-hydroxy ethyl methacrylate
Triethylene glycol dimethacrylate
Pyromelilitic acid dimethylmethacrylate
Bisphenol-A glycidyl methacrylate
Urethane dimethacrylate
Bis-phenol-A polyethylene glycol diether dimethacrylate
Ethylene glycol dimethacrylate (EGMDA)
Other substances
Benzoyl peroxide, camphorquinone (initiators)
Tertiary aromatic amine (activator)
Methylhydroquinone (inhibitor)
2-hydroxy-4-methoxy benzophenones, (UV absorber)
2-(2-hydroxy-5 methylphenyl) benzotriazole (UV absorber)

3.4.5.3. The role of bacteria

The presence of bacteria located at the interface between composite materials and dental tissues may be important (Hansel *et al.*, 1998). EGDMA and TEGDMA promote the proliferation of cariogenic microorganisms such as *Lactobacillus acidophilus* and *Streptococcus sobrinus*; TEGDMA stimulates the growth of *S mutans* and *S salivarius* in a pH-dependent manner (Khalichi *et al.*, 2004). This provides one explanation for caries that develop beneath restorations of resin-containing materials. In addition, bacterial exotoxins have harmful effects on pulp cells after diffusion throughout dentine tubules.

It is also important to note that effects on dental pulp associated with restorations may be caused by bacterial contamination rather than the materials themselves (Bergenholtz *et al.*,1982; Bergenholtz 2000). This is still a matter of controversy and a few reports still consider that the pulp reaction to adhesive systems is generally minimal (Murray *et al.*, 2002; Murray *et al.*, 2003). Improvements of resin-containing materials and bonding agents and techniques have reduced the significance of shrinkage and gaps at the interface, which may be less than 1 µm (Hashimoto *et al.*, 2004). However this is still a large gap for many microorganisms such as lactobacilli that are less than 0.1 µm in diameter, and therefore the microbial parameter cannot be ignored.

Clinical studies in high risk caries groups report more secondary caries when composites restorations are used compared to amalgam (Opdam *et al.*, 2010), and recurrent caries is the primary reason for composite replacement (Burke *et al.*, 2001). Recurrent caries is primarily located at the gingival margin of the restoration (Mjor, 1998). The vitality of the biofilm formed on composites is higher compared to amalgam (Auschill *et al.*, 2002).

Biofilm grown on dental composites in vitro have been shown to lead to chemical degradation of the composite and to increase the surface roughness of the composite material (Beyth *et al.*,2008; Gregson *et al.*, 2012). However, a 30-day old *S. mutans* biofilm did not have a negative impact on surface roughness or hardness of a composite, but surface degradation was evident. (Fucio *et al.*, 2008).

Resin composites are vulnerable to hydrolytic degradation of polymerised methacrylates (Gopferich, 1996), and the dentin-resin interface have been shown to be degraded by water

sorption, possibly by two degradation patterns, disorganisation of the collagen fibrils and loss of resin in interfibrillar spaces (Hashimoto *et al.*, 2003). In addition, degradation of resin composite materials by bacterial and salivary esterases have been shown to occur (Shokati *et al.*, 2010; Bourbia *et al.*, 2013). These findings show that bacteria may have an active role in breakdown of adhesives and composites, and that degradation at the dentin-resin interface may increase bacterial microleakage (Kermanshahi *et al.*, 2010). In addition, it has been shown that the presence of a multi-species biofilm may lead to degradation at the dentin-composite interface, and that the degree of degradation varies between different composite restorative systems (Li *et al.*, 2014).

Interestingly, both unlined and bonded amalgam restorations show reduced marginal leakage when compared to composites (Ozer *et al.*, 2002; Alptekin *et al.*, 2010).

Monomers used in dental composites have been described to promote proliferation of oral microorganisms such as *Lactobacillus acidophilus* and *Streptococcus sobrinus* by measuring an increase in absorbance during growth (Hansel *et al.*, 1998). However, the effect of monomers is controversial, as others have shown that the actual bacterial number, colony forming units, of *S. sobrinus* and *S. sanguinis* did not increase when exposed to TEGDMA or DEGDMA. The increase in absorbance was described to be caused by vesicular formation around bacteria when exposed to ethylene-glycol monomers, causing an increase in particle size and not increase in the actual number of bacteria (Takahashi *et al.*, 2004). However biodegradation products of the monomers have been shown to affect bacterial growth. The hydrolysed end products of TEGDMA, metacrylic acid and triethylene glycol, have been shown to exert opposite effects on bacterial growth. Metacrylic acid may inhibit growth of *S. mutans* and *S. salivarius*, whereas triethylene glycol accelerated the growth of *S. mutans* at low pH (Khalichi *et al.*, 2004). Triethylene glycol has also been shown to affect gene expression of glycosyltransferase B, a known virulence factor involved in production of extracellular polysaccharides of *S. mutans*. This finding shows that low concentrations of monomers and their degradation products may affect virulence gene expression of bacteria (Khalichi *et al.*, 2009).

3.4.6. Epidemiological and clinical evidence concerning adverse effects of alternatives in patients

Studies published by Maserejian *et al.*,(2012 a, 2012 b; 2014) concerning possible adverse effects related to exposure to bisGMA-based dental composite restorations have contrasting results. A post-hoc analysis of the Casa Pia Study showed that exposure to bisGMA-based dental composite restorations was associated with impaired psychosocial function in children in comparison to amalgam (Maserejian *et al.*, 2012a). The same authors published another study related to neuropsychological development, finding insignificant associations (Maserejian *et al.*, 2012b). A more recent analysis showed that use of sealants (containing BPA) or preventive resin restorations were not associated with behavioural, neuropsychological, or physical development in children (Maserejian *et al.*, 2014).

3.4.6.1. Case reports

Several cases and series of cases confirming allergic reactions caused by tooth-coloured restorative materials have been published. For example, an early case report described a female patient who developed a rash and hives on her chest, arms and legs after treatment with a composite (Nathanson and Lockhart, 1979). Patch-testing indicated that Bis-GMA was the provoking agent, whereas the sensitisation might have taken place by contact with a cross-reacting epoxy product. Patch tests also indicated Bis-GMA in a case of peri-oral erythema and crusting of cheeks following the application of a bonding agent for resin composite and glass ionomer fillings (Carmichael *et al.*, 1997). Moreover, stomatitis and peri-oral dermatitis was attributed to Bis-GMA in a filling material (Kanerva and Alanko 1998). Even

immediate type allergic reactions have been described after contact with a Bis-GMA resin composite used for fissure sealing (Hallström, 1993; Schmalz and Arenholt-Bindslev, 2009). Other relevant molecules were reported to be TEGDMA and HEMA, which are used in materials for bonding resin composites to the tooth structures (Aalto-Korte *et al.*, 2007; Drucker and Pratt, 2011; Schmalz and Arenholt-Bindslev, 2009). In general, clinical symptoms comprise intraoral, perioral and extraoral reactions (Tillberg *et al.*, 2009). Local lichenoid reactions similar to those described for amalgam, have also been attributed to composite fillings. In one case patch testing indicated EGDMA as the allergen (Auzeerie *et al.*, 2002), whereas other cases indicated formaldehyde derived from the resin (Lind, 1988). Ulcerating gingivitis localised to resin composite fillings was explained as a delayed reaction to the UV-absorber Tinuvin P (Björkner and Niklasson, 1979).

Metals and alloys are another group of materials which can be used as alternatives to amalgam. While cases of allergic reactions to nickel are well known (Schmalz and Arenholt-Bindslev, 2009), reactions towards palladium (Garhammer *et al.*, 2001) have also been reported and a cross reactivity between nickel and palladium was proposed (Garhammer *et al.*, 2001). Also, cases of contact allergy to gold and the relationship with OLL have been reported (Ahlgren *et al.*,2012).

Reactions to cobolt-chromium metal-ceramic fixed partial dentures and crowns have also been reported (Sélden *et al.*, 1995; Wang *et al.*, 1996). Alloys must be processed by dental technicians to produce crowns, partial crown or inlays. This is traditionally done after taking an impression of the patient's mouth and then making a cast.. Cases of allergic reactions towards impression materials have been described (Mittermüller *et al.*, 2012).

For deciduous teeth, steel crowns are advocated as amalgam replacement. A case of delayed hypersensitivity with perioral skin eruptions after insertion of such a crown in a 13-year-old girl was reported (Yilmaz *et al.*, 2012).

The multitude of case reports with the various alternatives used indicate a concern for adverse reactions of these alternatives. However, currently no general conclusions can be made based on the available information.

3.4.6.2. Reports from adverse reaction registry units

In the years 1999-2002 the Norwegian Dental Biomaterials Adverse Reaction Unit received an increasing number of reports of adverse reactions associated with composite materials, although these were still outnumbered by reactions to amalgam and other alloys (Lygre *et al.*, 2003; Vamnes *et al.*, 2004). Swedish data showed a similar tendency. Patch-testing of referred patients demonstrated positive reactions to methacrylates and additives relevant to resin- based materials, although the most frequent allergens were nickel, gold, cobalt, palladium, mercury and chromium. A survey by the UK registry indicated that the number of adverse reactions caused by resin-based materials, amalgam alternatives included, was about 14 % of the total number of patient reactions (Scott *et al.*, 2004). The UK Registry and the Swedish Registry have been discontinued since the former version of this Opinion was published.

The discussions concerning potential adverse reactions related to the use of dental amalgam have also focused on potential side-effects from other materials, such as polymer-based filling materials and associated products, e.g. bonding agents, and cast gold alloys. There are no harmonised criteria for what can be classified as an adverse reaction related to dental materials. Under-reporting was a recognised problem and lack of awareness and lack of clarity as to what constitutes an adverse reaction may be contributory factors.

The Dental Biomaterials Adverse Reaction Unit is a permanent activity funded by the Norwegian Government and located at the Department of Clinical Dentistry, University of Bergen.The Dental Biomaterials Adverse Reaction Unit has three main purposes:

1) Recording of adverse reactions

Dentists, dental assistants and physicians report to the Adverse Reaction Unit when any kind of side effect related to dental materials is observed. Both subjective and objective reactions can be recorded. The information is evaluated, coded and collected in a database at the Unit.

2) Clinical examination of referred patients

At the Adverse Reaction Unit, patients who exhibit reactions that are suspected to be associated with dental biomaterials can be referred from the patient's primary dentist or physician for additional examination. No dental treatment is given at the Adverse Reaction Unit. The aim is to collect clinical data on the various aspects of adverse reactions, particularly those which are not directly related to local reactions. The referral routines are designed so that a co-operation is required between the patient's primary physician and dentist.

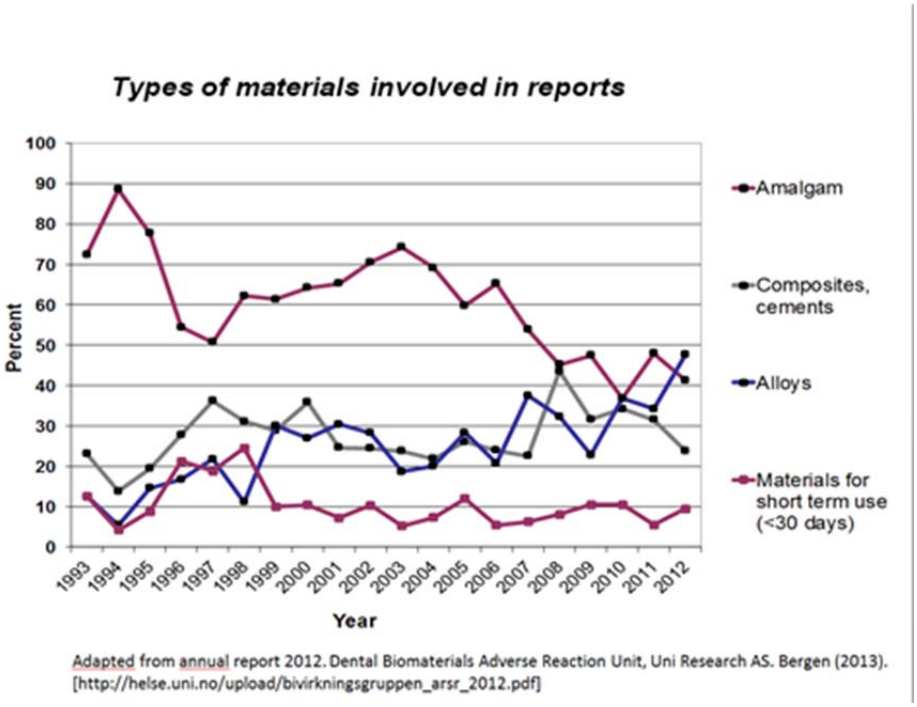
3) Information activities

The Unit gathers informational material pertaining to dental materials and their potential risks for both health personnel and the public.

Unfortunately, the Unit only publishes its Annual Report in Norwegian. However, the following graph indicates the types of materials involved in reports from 1993 to 2012.

Figure 2: Types of dental materials involved in adverse reaction reports

Adapted and translated from Annual Report Dental Biomaterials Reaction Unit 2012, courtesy of Professor Lars Björkman.



Adapted from annual report 2012. Dental Biomaterials Adverse Reaction Unit, Uni Research AS. Bergen (2013). [http://helse.uni.no/upload/bivirkningsgruppen_arsr_2012.pdf]

Since all dental materials pose a potential risk to patients and members of the dental team, the post-market monitoring of adverse reactions caused by dental materials should be considered essential.

The Directive concerning medical devices (93/42/EEC) requires the manufacturers to have postmarketing surveillance data which are reviewed by the Notified Bodies on audits. The Competent Authorities have a vigilance system for adverse events with medical devices. However, this information is not publically accessible.

The US Food and Drug Administration has active reporting systems for adverse events concerning all types of medical devices, including dental materials. Their MAUDE database houses medical device reports submitted to the FDA by mandatory reporters (manufacturers, importers and device user facilities) and voluntary reporters such as health care professionals, patients and consumers.

3.4.6.3. Reports from dermatological units

A Finnish multicentre study based on dental screening allergens on 4000 patients concluded that methacrylates, particularly HEMA, were responsible for 2.8 % of reactions, which were otherwise dominated by metal salts (Kanerva *et al.*, 2001). A Swedish investigation showed positive patch tests to methacrylate allergens in 2.3 % of the patients (Goon *et al.*, 2006). The most common of these allergens was HEMA, followed by EDGMA, TEGDMA, and MMA. Simultaneous positive reactions were frequent. Only one patient reacted to Bis-GMA, whereas reactions to HEMA alone were seen in most patients. Data from Israel after testing of patients with oral manifestations such as cheilitis, burning mouth, lichenoids, and orofacial granulomatosis also ranked HEMA as the most frequent dental allergen after the metal salts (Khamaysi *et al.*, 2006).

1632 subjects had been patch tested to either the dental patient series or dental personnel series at the department of Occupational and Environmental Dermatology, Malmö, Sweden. Positive patch tests to (meth)acrylate allergens were seen in 2.3% (30/1322) of the dental patients and 5.8% (18/310) of the dental personnel. The most common allergen for both groups was HEMA, followed by EGDMA, TEGDMA, and methyl methacrylate (Goon *et al.*, 2006). The prevalence of acrylate/methacrylate allergy was in Singapore – slightly lower compared to Malmö (Goon *et al.*, 2008).

In a series of 121 patch-tested patients suffering from several intra-, peri- and extraoral symptoms, the most common allergens detected included goldsodiumthiosulphate (14.0%), nickel sulfate (13.2%), mercury (9.9%), palladium chloride (7.4%), cobalt chloride (5.0%), and 2-hydroxyethyl methacrylate (5.8%) (Khamaysi *et al.*, 2006). Twenty-eight of 206 patients had positive patch-test reactions to metals used in dentistry. The number of positive patch-test reactions was highest for gold sodium thiosulfate, palladium chloride, and nickel sulfate (Raap *et al.*, 2009).

3.4.6.4. Questionnaire studies

A few attempts have been made to estimate the incidence of adverse effects of dental materials among dental patients. However, no studies have focused specifically on alternatives to amalgam. After about 10 000 dental treatments, one fifth of which were resin composite restorations, 22 adverse reactions were observed, none of them being related to tooth coloured restorative materials. Thirty-one dentists, representing a collective practice time of 387 years, recollected 70 cases of adverse effects, of which two were attributed to temporary resin-based and denture base materials, and 5 to copper cement, but none to alternatives to amalgam (Kallus and Mjør, 1991).

Other questionnaire studies have aimed at obtaining incidence rates of material related side effects in dental specialty practices such as paedodontics, orthodontics, and prosthodontics. Data from paedodontics indicated one reaction in 2400 patients, but only a minimal part was attributed to alternatives to amalgam (Jacobsen *et al.*, 1991). Orthodontics and prosthodontics do not regularly include the placement of restorative amalgam alternatives, but resin-based materials of similar composition are used. In orthodontics, only one of 41 000 patients showed an intra-oral reaction to an orthodontic composite, but nine others reacted to resin-based removable appliances, retention appliances, activators, and polymeric brackets (Jacobsen and Hensten-Pettersen 2003). However, some of these appliances are often made by chemically

polymerised methacrylates, containing relatively higher concentration of potentially allergenic residual monomers as compared to well-cured restorative composites. Questionnaire data from prosthodontics could be interpreted to indicate a reaction rate of one per 600 patients for resin-based prosthodontic materials (Hensten-Pettersen and Jacobsen 1991).

More recently, New Zealand dentists were asked about their experience with (non-amalgam) dental alloy allergies. As many as one in six general practising dentists have encountered allergic reactions to metal alloys in their patients (Zhou *et al.*, 2010).

3.4.6.5. General Comments

Case reports and reports from dermatological units highlight the possibility of adverse effects related to identified dental materials. Information from these sources is helpful in a field where these events are infrequent. The adverse reaction registry units in some countries contribute data on the relative frequency of the different adverse reactions, including those to amalgam alternatives. However, since participation by dental personnel is voluntary, the amount of under-reporting of patient reactions is unknown. The existing epidemiological studies offer an impression of the different material related adverse effects as perceived by dental personnel. However, none of these studies are well suited as a basis for estimation of the prevalence of reactions caused by specific allergens associated with amalgam alternatives or other materials.

In spite of these drawbacks, an attempt to rationalise the risk of material-related adverse effects in dentistry on the basis of published reports has appeared (Schedle *et al.*, 2007). Large variations were found, ranging between 1:10 000 and 1:100 for dental patients. A FDI-report also points to the fact that the vast majority of patients have encountered no adverse reactions, but dentists were advised to be aware of the possibility of reactions to resin-based materials (Fan and Meyer, 2007). The importance of satisfactory curing of these materials was specifically underlined. It is assumed that the most frequent potential allergens associated with resin-based amalgam alternatives are found in Table 5.

Furthermore, non-amalgam dental alloy-based alternatives for dental amalgam used in inlays, partial or full crowns contain metals such as nickel, palladium or gold for which allergic reactions are repeatedly being reported with partially higher frequencies than for dental amalgam (Schmalz and Arenholt-Bindslev, 2009).

3.4.7. Epidemiological and clinical evidence concerning adverse effects of alternatives in dental personnel

The potential for adverse effects due to alternative restorative materials amongst dental personnel is widely recognised (Hume and Gerzina, 1996). Most of the evidence of adverse effects takes the form of case reports, findings from surveys (Örtengren, 2000) and reports from national reporting systems (van Noort *et al.*, 2004) as well as from dermatological units (Goon *et al.*, 2006).

The study from Sweden shows a 2-3 times higher sensitisation rate for dental personnel as compared to patients. Given the extent of the use of alternative restorative materials, hundreds of millions of restorations annually, and the possibility that <7% of dental personnel may report skin symptoms when working (Örtengren, 2000), it is surprising that the reported incidence of adverse effects due to alternative restorative materials is low (van Noort *et al.*, 2004). The prevalence of verified allergic contact dermatitis amongst dental personnel (<1%) is much lower than the prevalence of self-reported skin symptoms (<7%) (Örtengren, 2000).

Most of the adverse reactions reported take the form of contact dermatitis, which in severe cases may be associated with paraesthesia of the finger tips (Kanerva *et al.*,1998). Reactions around the eyes, generalised skin itching and bronchial problems have been reported, but these are rare (Hume and Gerzina 1996).

HEMA appears to be a common sensitiser, although a small minority of dental personnel may have positive patch-tests to BisGMA and/or TEGDMA (Kanerva *et al.,* 2001). It is relevant that relatively low molecular weight resin monomers, including HEMA and TEGDMA take only a few minutes to diffuse through latex gloves of the type worn by dental personnel, while higher molecular weight monomers, such as BisGMA, take a little longer to pass through the relatively thin latex of treatment gloves (Jensen *et al.*, 1991; Munksgaard, 1992). These findings emphasise the importance of a "no-touch" technique when handling resin-based restorative materials, even when wearing gloves. This approach to the handling of resin-based restorative materials is highlighted in manufacturers' directions for use.

Regarding the lower incidence of allergic responses to resin-containing alternative restorative materials in patients relative to dental personnel, Kallus and Mjör (1991) and Hensten-Pettersen and Jacobsen (1991) suggest that this may be related to the fact that the principal exposure of dental personnel is to methacrylates as monomers during the handling of uncured materials. Adverse effects of alternative restorative materials in dental personnel may, as a consequence, be minimised by the avoidance of contact with, in particular, low molecular weight monomers during the handling and placement of uncured materials. The effects may be further reduced by the use of effective face protection, water cooling and suction, as appropriate, in all operative procedures involving both cured and uncured resin-based materials and associated systems. On the other side, it was reported that in a room where resin composites are used, monomer concentration in the air is elevated which means that a further source of exposure exists (Marquardt *et al.,* 2009). However, the concentrations were very low.

Between 1995 and 1998, 174 dental personnel were referred as patients to the Department of Occupational and Environmental Dermatology, Stockholm (Wrangsjö *et al..* 2001). After clinical examination, 131 were patch tested with the Swedish standard series and 109 with a dental screening series. Furthermore, 137 were tested for IgE-mediated allergy to natural rubber latex. Hand eczema was diagnosed in 109/174 (63%), 73 (67%) being classified as irritant contact dermatitis and 36 (33%) as allergic. Further diagnoses included other eczemas, urticaria, rosacea, psoriasis, tinea pedis, bullous pemphigoid or no skin disease. 77/131 (59%) had positive reactions to substances in the standard series and 44/109 (40%) to substances exclusive to the dental series. 24/109 (22%) patients had positive reactions to (meth)acrylates, the majority with reactions to several test preparations. Reactions to HEMA, EGDMA and MMA were most frequent. Nine of the 24 were positive only to (meth)acrylates, the remaining 15 also had reactions to allergens in the standard series. Irritant hand dermatitis was the dominant diagnosis. Contact allergy to (meth)acrylate was seen in 22% of the patch-tested patients, with reactions to three predominant test substances. In one third of these cases the (meth)acrylate allergy was seen together with atopy and/or further contact allergies.

Also, less severe allergic skin reactions among dental personnel have been diagnosed as caused by methacrylates, secondary in frequency only to chemicals related to natural rubber latex (Alanko *et al..* 2004). Hand dermatoses, together with eye-, nose-, and airway reactions are consistent findings among dental personnel, although the role played by amalgam alternatives is undecided (Sinclair and Thomson 2004; Andreasson *et al..* 2001).

The Finnish Register of Occupational Diseases diagnosed 24 cases of occupational asthma or rhinitis caused by methacrylates during the years 1990-98 .The incidence rate of occupational respiratory disease was considered greater than in the whole population (Piirilä *et al.,*2002).

Preventive actions such as change in hygiene factors, use of no-touch techniques when working with methacrylates, less use of latex and awareness of risk factors seems to keep the prevalence of skin and respiratory symptoms low among dental personnel (Schedle *et al.,* 2007).

3.4.8. Potential adverse effects of ancillary items and equipment

3.4.8.1. Photopolymerisation energy sources

Light sources are used to activate chemical photoinitiators, by absorption of photons, in order to initiate polymerisation in many restorative materials (Small, 2001). The applied light dose (radiant exposure; [J/m^2]) depends on the radiation power emitted per unit area (irradiance; [W/cm^2]) multiplied by time [in seconds]. Each photoinitiator has its unique radiation absorption spectrum, i.e. photons of specific wavelengths (energies) only are absorbed and to different degrees. The most common photoinitiator is camphorquinone which absorbs visible light between ~400-500 nm with an absorption peak at 468 nm. The main advantages of light-cured resin composites compared to chemically cured products are based on the fact that mixing of components in the clinic is not required, resulting principally in less porosity, better curing control, less curing time and ease of placement (Krämer *et al.*, 2008).

Types of light curing units

Dental curing systems use light sources such as light-emitting diodes (LEDs), quartz-tungsten-halogen lamps (QTH), xenon-plasma arcs (PAC) and lasers of which LEDs are the most widely used. A small percentage of the lamp source emission is visible light: 15%; 5%; 1% for LEDs; QTH and PAC, respectively. The remaining emission is heat (all lamps) and infrared radiation (IR) (not from visible light LEDs). LED dental curing lamps, based on solid-state semiconductor technology emit radiation in the visible and IR part of the electromagnetic spectrum within relatively narrow wavelength bands. Typical bandwidth for dental LEDs are 30-50 nm, and since bands exist that match the absorption spectra of commonly used photoinitiators, both around 400 nm and around 470 nm filters are not required. The irradiance of 13 lamp products measured in the 400 to 515 nm range varied from ~600 - 2000 mW/cm^2 (Bruzell and Wellendorf 2008). Some LEDs marketed in 2008 claim irradiance values up to 5000 mW/cm^2. The lifetime is longer and irradiance more stable for LEDs than for halogen lamps.

QTH lamps with halogen inside quartz bulbs generate light through the heating of a tungsten filament to high temperatures. A drawback of halogen bulbs is that the generation of heat causes a degradation of the components of the curing unit over time. The irradiance declines consecutively, which compromises the curing ability of the unit. The IR and some UV radiation is filtered to emit wavelengths in the violet-blue range only (~380-515 nm). The irradiance of halogen lamps tested between 2002-2007 varied from ~400 to ~3400 mW/cm^2.

Plasma-arc lights are made up of two electrodes in a gaseous, e.g. xenon-filled bulb. The plasma is heated to several thousand degrees Celsius and emits UV, visible and IR radiation which is filtered to allow mainly blue light (390-500 nm). Typical irradiance is ~3000 mW/cm^2.

Lasers can emit optical radiation at single (monochromatic) wavelengths as a result of the excitation of atoms of suitable gases/liquids/solids to specific energy levels. Argon lasers suitable for photopolymerisation emit at 488 nm and may have a power output up to 5000 mW, but the operating power is usually around 250 mW.

Dental curing lamps are classified as medical electrical equipment and should comply with a specific standard to indicate the potential risk of adverse health effects (International Electrotechnical Commission (IEC) 60601-2-57:2011). According to the rules in this standard, several dental curing lamps will be classified in the second highest group, indicating that the risk is moderate, but that the aversion response of the eye cannot be relied on completely.

Light-curing of resin composites

The dental curing lights initiate polymerisation of resin-based dental restorative materials by emission of radiation to be absorbed by photoinitiators in the material. The surface of the light delivery device should, ideally, be positioned a few mm from the material surface. Increasing the distance will normally decrease the irradiation, depending on the area of the emission relative to the area to be cured. The radiant exposure required for optimal curing, i.e. achieving adequate depth of resin composite layer without sacrificing mechanical properties while minimizing heat generation, is material dependent and is of the magnitude 10 000-50

000 mJ/cm^2. Recommended irradiances and curing times may vary from 300 mW/cm^2 to > 2000 mW/cm^2 and ~5-100 s respectively, to obtain a 1.5-4 mm thick layer of resin composite polymer, depending on the material colour, degree of opacity/translucency, particle size and -volume and chemical composition. So-called bulk-fill materials have increased translucency that increase the layer thickness (Musanje & Darvell, 2003; Bruzell and Wellendorf, 2008; Ilie *et al.*,2013).

Risk issues

Exposure of the eyes

The eyes of the lamp operators and assistants are at risk from acute and cumulative effects, mainly due to back-reflection of the blue light. Some LEDs emit shorter wavelengths (close to UV, approx. 400 nm) in addition to the blue, and this radiation is potentially damaging to anterior parts of the eye, such as the cornea and lens. Exposure to intense visible light radiation sources in a dental clinic necessitates the use of eye protective filters to avoid blue-light photochemical retinal damage. Normally, the light from a curing lamp does not reach the patient's eyes. However, if the risk is increased, eye protection should be used by patients as well. Increased risk includes for e.g. light curing of the front teeth and treating patients with ocular disease or intraocular lens implants (due to e.g. cataract surgery). Such lenses offer various degrees of UV- and blue light protection, but they offer less protection from wavelengths emitted from an LED lamp than the middle-aged eye does (Mainster, 2006). Bruzell *et al.*,(2007) measured the visible light transmittance of eye protective filters of which half the number were unsuitable for use with light curing.

Exposure of skin and oral tissues

Both materials and radiation intended for curing can be exposed to patients' oral tissue or dentists' finger skin. The two agents combined can cause photosensitisation effects, which is typical of UVA (320 -400 nm) and visible radiation (400-800 nm). UV can also induce direct effects. Although in vitro studies have shown that blue light of doses relevant for dental light curing can induce small cytotoxic effects (Bruzell Roll *et al.*,2004; Opländer *et al.*, 2011), these lamps do not appear to cause damage to healthy skin under normal use. However, thermal effects can occur with irradiances above ~100 mW/cm2 after a few minutes depending on local tissue factors such as blood circulation. There are reports of accidental oral soft tissue burns with the use of LEDs (Spranley *et al.*, 2012). Quartz-halogen lamps and a few LEDs emit some radiation in the UV-and short wavelength visible band (380-410 nm). Chadwick *et al.*,(1994) assessed the level of UVA (340- 400 nm) emitted from three previously used halogen sources and the level of protection afforded by six brands of surgical gloves. It was concluded that the risk of initiating adverse dermatological consequences such as photosensitisation as a result of exposure to relatively low irradiance of UVA, is minimal in normal usage. Furthermore, glove material absorption of UVA has been reported to be up to a third lower than reported in the Chadwick-study (Lehtinen *et al.*, 1990). However, some LED lamps on the market today emit up to 1100 times higher irradiance in the UVA, which implies that the risk for photosensitisation of skin, due to the combined effect of curing lamp emission and chemicals, has increased during the last 10 years. Nevertheless, it should be kept in mind that UV (bandwidth 100–400 nm, encompassing UVC, UVB and UVA) is classified as carcinogenic to humans (International Agency for Research on Cancer (IARC)).

Dental light curing units with emission mainly in the visible spectrum, but also with a fraction of UVA (380-580 nm; unknown irradiance) have been shown to cause the disappearance of Langerhans cells (antigen presenting cells of the skin) 3 days after exposure in a model of human skin heterotransplanted into nude mice (Bonding *et al.*, 1987). Several studies have shown that UV radiation on skin has immunosuppressive effects, in particular wavelengths shorter than about 320 nm (reviewed by Schwartz, 2008). The suppression is primarily affecting the adaptive immune response due to an impairment of antigen presenting cells and an emergence of T regulatory cells (Duthie *et al.*, 1999). The innate immune response may in contrast be enhanced, explaining why solar exposure does not favour bacterial infections in general (Liu *et al.*, 2006).

There does not seem to be any scientific studies on the possibility of adverse reactions other than the thermal mentioned above in the oral mucosa after exposure to high intensity visible blue light.

Light as a cofactor in photobiological reactions

Most manufacturers state in the instructions for use that dental curing lights should not be used in patients with light sensitivity diseases such as urticaria solaris or porphyrias – or who are currently on photosensitising medication. Examples of such drugs are found in the groups of NSAIDS, antidepressants, antipsoriatics and antibiotics (tetracyclines) (Kleinman *et al.*, 2010; deLeo 2000). Some photosensitising drugs can accumulate in skin, nails, teeth and ocular tissue. Photosensitising reactions, i.e. phototoxic and photoallergic reactions due to the absorption of UV or light by absorbing molecules, chromophores, with subsequent production of reactive oxygen species (ROS), radicals and other toxic photoproducts constitute a potential risk with the use of light sources in dentistry. Exogenous chromophores are, for example, the above-mentioned drugs, edibles and dental material components. Endogenous chromophores are for example DNA, porphyrins, flavins, haemoglobin and bilirubin. An example of combined chemical substance and light effect (no phototsensitisation) was shown *in vitro*: the depletion of glutathione (GSH) by methacrylates led to increased cytotoxicity following UVA/blue light irradiation with the formation of ROS (Christensen and Bruzell, 2010). Although the dose from the high intensity lamps are in the same range of what is used for dermatological skin testing of photobiological reactions, phototoxic or photoallergic reactions have not been documented in the context of oral medicine. This may partly be explained by the fact that the diagnoses of photoallergic/-toxic reactions are difficult to distinguish from other allergic reactions as the manifestations are similar. Furthermore, tissue reactions experienced by a patient after a dental treatment will easily be associated with any material used. The EU-directive (2006) on safety regarding occupational exposure to artificial optical sources includes photosensitising reactions as a risk factor, and the dental curing lamp is encompassed by this directive. The possibility of photo-related reactions should be taken into account in the evaluation of dermatological conditions in dental personnel.

Exposure of teeth

The curing lamps with high irradiance may cause local heating. Laboratory studies show temperature rises, at 3 mm distance from the light source, from 4.1°C to 12.9°C (~300 mW/cm^2), and from 17.4°C to 46.4°C (~11000 mW/cm^2) for LED and halogen lamps, respectively (Yap and Soh, 2003). Furthermore, a LED with irradiance of 1100 mW/cm^2 caused a pulpal temperature increase of 6 °C after 10 s (Durey *et al.*, 2008). In vitro studies with thermocouples placed in pulp chambers of extracted teeth showed a moderate rise in pulpal temperature. In a vital tooth this does not seem to be a problem, possibly due to the heat convection effect of the blood circulation. In subjects with impaired blood circulation and with many restorations or carious teeth, temperature increases may be higher. The recent introduction of LEDs with irradiance of more than ca. 1500 mW/cm^2 might increase the risk of thermal damage to the pulp.

Temperature rise

For high irradiance light curing units (e.g. > 3000 mW/cm^2 as presented in Rueggeberg, 2010) temperature raise in the pulp chamber with 0.75 to 1 mm residual dentin thickness was over the critical value of 5 to 6 °C (Rueggeberg, 2010). As dentin is known to be a good thermal isolator, generally heat damage to the pulp in shallow and medium depth cavities is not expected. However, heat damage on the pulp in cavities closer to the pulp or with pulp exposure is to be expected. In addition, this may also occur with lower irradiance but prolonged curing times.

Furthermore, if the treatment is performed under local anaesthesia with vasoconstrictors, blood circulation is reduced and heat removal from the pulp is impaired (Jandt and Mills, 2013). If inadvertently, the light source is directed to the soft tissues, like the lips, severe burning has been described with rubber dam offering no protection (Spranley *et al.*, 2012). On

the other side, insufficient curing, which is observed in daily practice (Price, 2013), may increase the release of substances and increase its toxicity (Sigusch *et al.*, 2009).

Electromagnetic compatibility

Although a report exists of headache associated with curing light exposure in a Parkinson's patient with implanted brain stimulator electrodes (Vangstein, 2003), two studies of possible electrical or electromagnetical interference of implants with dental curing lamps concluded that no significant effects on the equipment were found (Miller *et al.*, 1998; Roberts, 2002). However, a battery-operated LED curing lamp was found to interfere with the sensing and pacing activity of pacemakers and implantable cardioverter-defibrillator devices (Roedig *et al.*, 2010).

Ineffective treatment/inferior quality of restoration

Inferior curing caused by e.g. cracks or material build-up on the light guide will increase the amount of monomers and may lead to increased risk of toxicity. Incorrect positioning of the lamp, such as too large a distance between the light and the material to be cured, may cause less than optimal curing and overexposure of oral tissues (Price *et al.*, 2014). Many dental curing lights have an integrated photometer to check that the irradiance is sufficient for the intended use. Alternatively, a separate photometer or a more advanced spectrophotometer or radiometer can be used. When performing irradiation measurements it is important that the equipment used is intended to measure the wavelength range and the irradiance emitted from the lamp in question. Equipment used to measure halogen lamps 15 years ago is not necessarily intended for today's LEDs. It is also recommended to check that the depth of cure for the various composites is sufficient. The latter method checks both the quality of the light source and the quality of the composite material. This is an important aspect, since the resin-based materials have a limited shelf life. Some polymer composite materials contain photoinitiators with absorption peaks in the range 390-410 nm, and thus require radiation of lower wavelengths than does camphorquinone for polymerisation to take place.

Overall risk assessment of light curing units

There are inherent problems in the assessment of adverse effects of light exposure from dental curing lamps. Spectral characteristics vary among the different products, tissues treat radiation differently and the repair mechanisms for photo-induced damage may be insufficiently developed in oral mucosa.

The dental curing lights, when used according to the manufacturer's instructions and with proper eye protection, seem to be safe for use in most patients and users. However, the potential for adverse reactions to occur are definitely present and the manufacturer's cautionary statements about not using them in specific situations should be heeded (Bruzell Roll *et al.*,2004).

3.4.8.2. Glove use

The wearing of gloves, often of latex, but increasingly of non-latex alternatives, has become routine in the everyday dental practice. Although not advised, should alternative resin-based filling materials be handled during use, low molecular weight components may quickly pass through the glove (Jensen *et al.*, 1991; Munksgaard, 1992) and will remain in contact with the moist skin of the clinician until the gloves are removed and the hands washed at the end of the treatment. With practitioners who are sensitive to such constituents, or in the presence of skin conditions, cuts or abrasions, an adverse reaction may occur. Such reactions may be avoided by strict adherence to the no-touch techniques recommended by manufacturers of alternative restorative materials.

3.4.9. General Observations on Efficacy of Alternatives

The general observations on the efficacy of amalgam restorations (Sections 3.3.9 and 3.3.10) may be reinforced here. Alternatives to amalgam have been in clinical use for well over 30 years. They have not only addressed the issues on the aesthetics of amalgams but have facilitated a radical change in the concepts of restorative dentistry through the introduction of more minimally invasive techniques and the associated retention of more tooth substance when treating caries. This has been achieved through the use of tooth coloured materials that are themselves adhesive to tooth substances or that can achieve adhesion through the use of intermediary agents. It is recognised that their use is technique sensitive and that the procedures for their placement take longer and therefore be more expensive. It is also true that they may be more susceptible to secondary caries and, in some situations, have less longevity than amalgams (for references see sections 3.3.9 and 3.3.10). In general therefore, these tooth-coloured alternatives offer an effective modality for the treatment of dental caries in many situations.

Non-amalgam alloys and – more recently – ceramics have also been used as amalgam alternatives, although the costs involved are considerably higher because the restoration must be separately fabricated and then luted to the tooth (indirect restoration). Survival rates of such restorations are high (Felden *et al.*, 1998; Krämer *et al.*, 2008; Federlin *et al.*, 2010); however, due to the specific requirements of the technique, more sound tooth tissue has to be removed to fit such a restoration than is the case with a direct restoration using amalgam or resin-based composites.

Used as inlay/onlay more tooth substance is replaced but in the case of overlays of partial crowns the preparation should be minimal and the longevity is rather good with AFR of 2% (van Dijken and Hasselrot, 2010).

3.4.10. Conclusions on Alternatives

Alternatives to amalgam comprise a large variety of materials based on mainly acrylic resin technology, cements, ceramics or dental alloys. The materials used as alternatives to dental amalgam for direct restorations (so-called resin-based composites or resin composites) are usually chemically very complex, with certain clinical limitations or may present some toxicological risks. They frequently contain a variety of organic substances, for which toxicological data are scarce or even missing and they may undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement releasing newly formed substances like formaldehyde. Therefore, it should not be assumed that non-mercury containing alternatives are free from any concerns about adverse effects (Goldberg, 2007).

The amount of the released substances from resin composites and related materials depend on the degree of conversion. During application, the low viscous dental adhesives in non-polymerised state will in many cases be in direct contact with the oral tissues which makes penetration of the tissues possible and has potential biological risks.

With respect to those materials that incorporate polymerisable resins, it is known that some of the monomers involved in their intra-oral placement and polymerisation are highly cytotoxic to pulp and gingival cells *in vitro* and there is also evidence that some of them are mutagenic, although it is far from clear whether this has any clinical significance. Some of these substances are irritants when used by themselves in various situations and the occupational risks associated with their use are similar to those found in the printing and automotive industries. Allergies to these substances have been reported, both in patients and in dental personnel. We note that the full chemical specification of these alternative restorative materials is not always divulged and it may be difficult to ascertain exactly what they contain. In the absence of data, it may not be possible to provide a scientifically sound statement on the safety of individual products. It is also noted, however, that there are very limited scientific data available concerning exposure of patients and dental personnel to these substances.

Nevertheless, these alternative materials have now been in clinical use for well over thirty years, and this use has revealed little evidence of clinically significant adverse events. The commercially available materials have either changed substantially or been improved considerably during this time, with reduced bioavailability of harmful components through improved polymerisation processes. It is recognised that many of the new forms of these alternative materials lack long-term clinical data and as such, need to be monitored for possible risks to patients and dental personnel.

As a separate issue, it should be borne in mind that these photo-polymerisable systems require activation and that the powerful light sources now used for this purpose may constitute an additional risk for adverse effects, both to patients and dental personnel. Eye protection is extremely important.

As for amalgam, genetic predisposition may play a role for the occurrence of adverse reactions towards alternative materials. It is known that the catalase system is necessary for compensating the increase of cellular reactive oxygen species, which takes place after dental methacrylate monomer exposure (Krifka *et al.,* 2013 and 2012). Several common mutations of the catalase gene (CAT) are known (see above); however, as for amalgam, the clinical impact for alternative materials is unclear. Furthermore, it was reported that glutathione (GSH) plays an important role in the detoxification of dental methacrylate monomers: toxicity of these monomers can be increased by GSH inhibition and decreased by the addition of N-acetyl-cysteine (NAC), a precursor of GSH (Krifka *et al.,* 2012; Stanislawski *et al.,* 2003). Vulnerable individuals and subpopulations with a genetic predisposition, e.g. of a glutamyl-cysteine ligase GCLM-588T allele with a reduced glutathione production (Goodrich *et al.,* 2011; Custodio *et al.,* 2005), may also exist for dental methacrylate monomers. The influence of different variants of glutathione transferase on the cellular reactions towards resin monomers was shown (Lefeuvre *et al.,* 2004). However, clinical data are missing and more research is warranted.

Indirect restorations used as amalgam alternatives have a good survival rate, but the involved costs are considerably higher than with direct restorations and more sound tooth tissue has to be removed in order to place such a restoration in a tooth. Furthermore, metals used in these alloys are not without biological risk and ceramic restorations have to be luted in many cases with resin-based composite materials and thus the same biological problems occur as with such direct fillings.

In a recent Cochrane systematic review on the comparative longevitiy of resin-based composites and amalgams it is stated that the parallel group trials indicated that resin restorations had a significantly higher risk of failure than amalgam restorations and increased risk of secondary caries. The results from the split-mouth trials were consistent with those of the parallel group trials. More data with higher levels of evidence are warranted.

3.4.11. Comments on costs

Generally, costs for restorative treatment are based on the costs of the materials and the time needed to perform the work within the given environment. Furthermore, the longevity of a restoration influences the costs by higher replacement rates. There is general agreement in the literature that the treatment costs for amalgam fillings are lower than for resin composite restorations. The latter were rated 1.7 to 3.5 times more expensive than amalgam for a one tooth year restoration (Chadwick *et al.,* 1999). Other estimates amounted to initial costs for resin composite fillings to be 25% higher, cost per year of function to be 2.5 times higher than for amalgam (Sjögren & Halling, 2002). In a recently published report from Norway (Skjelvik and Schou Grytli, 2012) a price increase for a resin composite filling compared to an amalgam filling in the range of € 48 to 72€ was reported, which means an increase of 33 and 50 percent. However, for amalgam fillings additional costs should be considered; e.g. for amalgam waste/separator management and for cremation. In the above-mentioned Norwegian report, such costs have been estimated to be about 1 to 2 € per amalgam filling for waste/separator costs. However, such costs are varying, e.g. according to the price of the

recycled metals; presently, e.g. in Germany, recycling companies even pay (a small amount) for amalgam waste. Another problem is related to cremation, by which mercury from amalgam fillings is released into the environment. Installation of additional filters for mercury and maintaining them may add up to 18€ per cremation with an assumed 5 fillings per cremation (Skjelvik and Schou Grytli, 2012). It can be concluded that even taking the more indirect costs for amalgam into consideration, the costs for treatment of cavities with resin composites will increase the costs compared to amalgam fillings.

4. OPINION

The cited scientific evidence constitutes an update of the 2008 scientific Opinion concerning the safety of dental amalgam and alternative dental restorative materials. It evaluates new information and also some scientific articles that were not included in that version. The Opinion provides answers to the questions posed in the mandate.

4.1. The scientific and clinical evidence

The SCENIHR recognises that dental amalgam, for the general population, is an effective restorative material. From the perspectives of longevity, the mechanical performance and economics, it has long been considered and still is a material of choice, especially for certain types of restorations in posterior teeth, including replacement therapy for existing amalgam fillings. However, because dental amalgam is neither tooth-coloured nor adhesive to remaining tooth tissues, its use has been decreasing in recent years and the alternative tooth-coloured filling materials have become increasingly more popular. This is consistent with the trend towards minimal interventional, adhesive, techniques in dentistry. At the same time the quality and durability of these materials have improved. This trend towards non-amalgam restorations is emphasised by the significant reduction of training in the placement of dental amalgam restorations, and the corresponding increase in training in the use of amalgam alternatives in many dental schools in European countries.

Mercury is the metallic element of concern used in dental amalgam. Mercury is a well-recognised toxicological risk, with reasonably well-defined characteristics for the major forms of exposure such as ingestion of organic and inorganic mercury compounds and inhalation, of elemental mercury vapour. Respiratory air concentrations, blood levels and urinary excretion of mercury in individuals with amalgam fillings indicate that the levels of exposure encountered are 5 to 30 times lower than those permitted for occupational exposure. Tolerable limits for dietary exposures to mercury are relevant to amalgam safety considerations, as inhaled elemental mercury may add to the body burden of inorganic mercury. Dietary mercury exposure in the general population in Europe does not exceed the TWI for methyl mercury and inorganic mercury, except in heavy fish-consumers. EFSA (2012) reported that the tolerable weekly intake for inorganic mercury might be exceeded due to the additional inhalation exposure in people with a high number of amalgam fillings. However, evidence is weak as the data are mainly derived from model-based calculations. Studies on large patient collectives did not show any correlation of health effects with the number of amalgam restorations.

Local adverse effects in the oral cavity are occasionally seen with dental amalgam fillings, including allergic reactions and an association with clinical features characteristic of lichen planus, but the incidence is low (<0.3% for dental materials in general) and usually readily managed. Regarding systemic effects, elemental mercury is a well-documented neurotoxicant, especially during early brain development, and inorganic mercury also constitutes a hazard to kidney function. The presence of dental amalgam has been suggested to be associated with a variety of systemic conditions, particularly neurological and psychological/psychiatric diagnoses, including Alzheimer's disease, Parkinson's disease, and multiple sclerosis as well as kidney disease. These possible risks are not substantiated. However, recent studies suggest that the genetic make-up may be the cause of a higher mercury internal dose for some individuals, possibly making them more vulnerable to mercury toxicity than the average.

Mercury concentration in the adult brain is associated with the number of amalgam fillings. In the foetus mercury concentration in the foetal kidney but not the brain showed a trend associated with the mothers'number of amalgam fillings. Because the elimination half-life for inorganic mercury in the brain estimated by means of a PB-PK model exceeds 10 years, mercury is likely to accumulate in the central nervous system.

The accumulated concentrations in brain tissue may reach values that are similar to those inducing neurochemical changes in *in vitro* experimental models. Such effects have not been

convincingly demonstrated in humans and so far, studies in children of school age did not convincly demonstrate amalgam-associated neuropsychological deficits. However, recent studies suggest that genetic polymorphisms concerning mercury kinetics may influence the degree of individual susceptibility with regard to mercury internal exposure and consequently toxicity. This may raise some concern for possible effects on the brain of mercury originating from dental amalgam. However, so far such effects have not been documented in humans, although some evidence on alteration of mercury dynamics have been reported. The transient mercury release during placement and removal will result in transient exposure to the patients (resulting in a transient increase in plasma mercury levels) and also to the dental personnel. Therefore there is no general justification for removing clinically satisfactory amalgam restorations, except in those patients diagnosed of having allergic reactions to one of the amalgam constituents. Recent studies do not indicate that dental personnel in general, despite somewhat higher exposures than patients, suffer from adverse effects that could be attributed to mercury exposure due to dental amalgam. Exposure of both patients and dental personnel can be minimised by the use of appropriate clinical techniques.

The alternative materials also have certain clinical limitations and toxicological risks. They contain a variety of organic substances and may undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement. Therefore, it should not be assumed that non-mercury containing alternatives are free from any concerns about adverse effects. With respect to dental composite restorative materials and hybrid systems that incorporate polymerisable resins, it is known that some of the monomers used are highly cytotoxic to pulp and gingival cells in vitro. There is also evidence that some of these are mutagenic *in vitro* although it is far from clear whether this has any clinical significance. Allergies to some of these substances have been reported, both in patients and in dental personnel.

It is noted that there are very limited scientific data available concerning exposure of patients and dental personnel to the substances that are used in alternative restorative materials. It is recognised that such data are very difficult to obtain. Further toxicological research on the various components of these alternative dental materials is warranted.

Alternative materials have now been in clinical use for more than thirty years, initially in anterior teeth and later also for restorations in posterior teeth. This clinical use has revealed little evidence of clinically significant adverse events. However, there is an increase in patients' claims with increasing use of these materials. It is also important to note that the commercially available materials have changed substantially and improved considerably over this time, especially concerning their physical and mechanical properties and their adhesion to dental hard tissues.

Resin-based composites contain a large variety of organic substances, for which toxicological data are scarce or missing and available information on the composition and on leachables of these materials is inadequate. Leaching occurs directly after curing from remaining un-reacted groups in the body of the restoration and in the non-polymerised surface layer of the restoration exposed to oxygen during curing. Leachable components may also be released due to degradation or erosion over time, the leaching process being determined not only by the degradation process itself but also by diffusivity through the material. Chemical degradation is caused by hydrolysis or enzymatic catalysis. Other degradation factors are thermal, mechanical and photochemical. Unreacted monomers, catalysts, formaldehyde and – in some cases – bisphenol A are released. Dental alloys continuously release metals into the oral environment depending e.g. on the metal content, the phase distribution within the alloy and the corrosion conditions. Metals like gold, copper, silver and palladium are released but also nickel, zinc, cobalt and chromium and many others. Glass ionomer cements release fluorides and calcium, sodium, silicon, strontium, and aluminium. Ceramics release substances like silicon, boron, sodium, potassium, and aluminium, some brands also release lithium in small amounts.

The cytotoxicity and genotoxicity of substances leached from resin-based materials, of metallic elements from alloys and of glass ionomer cements have been the subject of extensive studies using cell culture techniques and bacterial mutation tests. Some of the released substances, especially from resin-based composites and from alloys, are highly cytotoxic to pulp and gingival cells *in vitro* and there is also evidence that some of the released monomers are

mutagenic, although it is unclear whether this has clinical significance. Studies on the intracellular biochemical mechanisms have clarified various effects such as cell membrane damage, inhibition of enzyme activities, protein or nucleic acid synthesis, increase of radical oxygen species concentration, etc. The risk associated with the release of Bisphenol A from resin dental materials was recently evaluated and considered to be negligible. (SCENIHR 2015). Substances from resin materials such as TEGDMA and HEMA, but also metals from alloys like nickel, cobalt and palladium, cause allergies in patients and dental personnel. Recently, increased attention has been directed to the possibility of photo-related reactions and to the effect of high energy light curing units. Specific safety precautions are necessary to prevent eye damage of patients and dental personnel (by proper eye protection) and heat related effects (burning of the gingiva or the dental pulp). Photo-related reactions should be taken into account in evaluation of dermatological conditions in patients and dental personnel.

The SCENIHR notes that the full chemical specification of these alternative restorative materials is not always divulged, and it may be difficult to know exactly what they contain. As a result, there is limited toxicological data publicly available for these materials. Dental restorative materials are defined as medical devices according to EU-Directive 93/42/EEC and belong to class IIa. Consequently, the certification process does not include review of the design dossier and, therefore, the chemical specification does not have to be revealed to the third party. Although manufacturers are obliged to assess biocompatibility and the risk from unintended side effects, accessible information on the toxicity of the constituents of the materials as well as relevant exposure data is lacking. Therefore, the SCENIHR notes that it is not possible to provide a scientifically sound statement on the generic safety of these materials.

It is noted that there are very limited scientific data available concerning exposure of patients and dental personnel to substances that are used in alternative restorative materials. Many of the monomers and other organic solvents used in them are volatile and need to be better identified and quantified.

More publically available research data are also needed to have a broader basis for risk evaluation. In view of the controversial nature of this subject, it would also be beneficial for the community in general to be better informed of the recognised benefits and risks.

In light of the above comments we conclude that dental amalgam already in place is not considered a health risk for the general population. Thus, pre-existing amalgam restorations should not be removed, as this intervention would result in a greater exposure to mercury. As with any other medical or pharmaceutical intervention, caution should be exercised when considering the (re-)placement of any dental restorative material in pregnant women. There is no evidence that infants or children are at risk of adverse effects arising from the use of alternatives to dental amalgam. As far as dental personnel are concerned, it is recognised that they may be at greater risk with respect to mercury exposure than the general population, although the incidence of reported adverse effects is very low.

Far less information is available concerning exposure, toxicity and clinical outcomes for alternative materials. There is some evidence that certain low molecular weight substances used in their preparation are associated with local allergic reactions, although the incidence is very low. There is no evidence that there is any association between these materials, as used clinically, and any neurological disorders or any other health disorders. We do emphasise, however, that data is sparse and the continuing evolution of these materials suggests that caution should be exercised before new variations are introduced into the market. As far as dental personnel are concerned, again there is evidence of limited numbers of cases of allergies to these materials. The pervasiveness of some of the volatile low molecular weight species throughout dental clinics should be noted.

The SCENIHR concludes that dental health can be adequately ensured by alternative types of restorative material. Furthermore, the use of resin-based alternatives allows the use of minimally interventional adhesive techniques. The longevity of restorations of resin-based alternative materials in posterior teeth has improved with the continuing development of these materials and the practitioner's familiarity with effective replacement techniques. However, in certain clinical situations (e.g. large cavities and high caries rates), the alternative materials

are still inferior to amalgam. The clinical trend towards the use of adhesive alternatives implies that a sustained reduction in the use of dental amalgams in clinical practice will continue across the European Union.

As a separate issue, it should be borne in mind that these photo-polymerisable systems require activation and that the powerful light sources now used for this purpose may constitute an additional risk for adverse effects, both to patients and dental personnel. Eye protection is extremely important.

The SCENIHR noted that indirect restorative techniques, involving the use of variety of different alloys and ceramics may also be used when direct restorations are contra-indicated. Their use, which is both time-consuming and expensive, has remained at a comparatively low level in recent years. This use is not seen as a health concern with the exeption of allergies to some metals. As a general principle, the relative risks and benefits of using dental amalgam or the various alternatives should be explained to patients to assist them to make informed decisions. This has implications concerning the provision of improved product information from the manufacturers.

The SCENIHR concludes that dental restorative treatment can be adequately ensured by amalgam and alternative types of restorative material. The longevity of restorations of alternative materials in posterior teeth has improved with the continuing development of these materials and the practitioner's familiarity with effective placement techniques, but is in certain clinical situations (e.g. large cavities and high caries rates) still inferior to amalgam.

The choice of material should be based on patient characteristics such as primary or permanent teeth, pregnancy, presence of allergies to mercury or other components of the restorative materials, and presence of decreased renal clearance. The clinical trend towards the use of adhesive alternatives is considered advantageous as it implies that a sustained reduction in the use of dental amalgam in clinical practice will continue across the European Union.

The SCENIHR recognises a lack of knowledge and a need for further research, in particular in regard to genetic susceptibility related to mercury effects and to the constituents of alternative restorative materials. Furthermore, there is a need for the development of new alternative materials with a high degree of biocompatibility.

4.2. Answers to Terms of reference

In particular, the SCENIHR is asked the following questions.

4.2.1. Question 1

Is there any new scientific evidence that justify reasons for concern from the health point of view in the use of dental amalgam as dental restoration material?

A variety of systemic adverse effects, particularly developmental neurotoxicity as well as neurological and psychological or psychiatric diseases, have been suggested to be associated with the presence of dental amalgam. The causality evidence for such effects due to dental amalgam is weak, also considering other source of mercury exposure. A recent study (Sherman *et al.*,2013) indicates that demethylation of methyl mercury from seafood gave a major contribution to the mercuric mercury in the urine with fewer than 10 amalgam fillings.

The most recent *in vitro* evidence provides new insight into the effects of mercury on developing neural brain cells at concentrations similar to those found accumulated in human brain in post-mortem specimen.

Neurological effects associated to dental amalgam have not been convincingly demonstrated in humans as caused by dental amalgam. The effects of genetic polymorphism concerning mercury kinetics may influence the degree of individual susceptibility in regard to mercury internal exposure and consequently toxicity. Some evidence on alteration of Hg dynamics have been also reported. They may raise some concern, although so far such effects have not been clearly demonstrated in humans.

4.2.2. Question 2

In view of the above, is the use of dental amalgam safe for patients and users, i.e. dental health professionals? Are certain populations particularly at risk, e.g. pregnant women or children? Is it possible to recommend certain practices to minimize patient's and user's exposure to dental amalgam?

The current evidence does not preclude the use of dental amalgam in restorative treatment in the general population. The SCENIHR recognises that dental amalgam is an effective restorative material for the general population, with low risk of adverse health effects.

The choice of material should be based on patient characteristics. The use of amalgam restorations is not indicated in primary teeth, in patients with mercury allergies, and persons with chronic kidney diseases with decreased renal clearance. As with any other medical or pharmaceutical intervention, caution should be taken when considering the placement of any dental restorative material in pregnant women. A decision to perform dental treatment during pregnancy should take into account the dental therapeutic needs of the patient and balance any potential risks (including the use of anaesthetics, along with all dental materials) against therapeutic benefits to the patient. Generally, extensive dental treatment during pregnancy is discouraged.

Placement and removal results in short-time exposure to the patients compared to leaving the amalgam intact. Therefore there is no general justification for unnecessarily removing clinically satisfactory amalgam restorations, except in those patients diagnosed as having allergic reactions to one of the amalgam constituents.

Recent studies do not indicate that dental personnel, despite somewhat higher exposures than general population as mercury in the urine, suffer from adverse effects that could be attributed to mercury exposure due to dental amalgam. In a recent study in Canada, it was observed that mercury vapour exposure during dental training on amalgam removal remained below occupational exposure limits (Warwick *et al.*, 2013).

The mercury release during placement and removal results in exposure of dental personnel. Exposure of both patients and dental personnel could be minimised by the use of appropriate clinical techniques.

Genetic polymorphisms involved in alteration of mercury kinetics and dynamics may raise some concern for vulnerable groups, although so far such effects have not been clearly demonstrated in humans.

To reduce the use of mercury-added products in line with the intentions of the Minamata Convention (reduction of mercury in the environment) and under the above mentioned precautions, it can be recommended that for the first treatment of primary teeth in children and for pregnant patients, alternative materials to amalgam should be the first choice. This decision should be made after informed consent from the patient or the legal guardians.

4.2.3. Question 3

Is there new scientific evidence on the safety and performance of alternative materials?

Alternatives to amalgam comprise a large variety of materials based mainly on acrylic resin technology, cements, ceramics or dental alloys. Except for certain metals such as gold, there are no relevant markers for assessing patient- or user exposure to the alternative materials.

Ceramics have to be luted to the dental hard tissues usually using acrylic technology products. Resin materials have to be cured mainly using light curing units. Resin-based materials achieve adhesion to tooth substances through the use of intermediary agents containing highly reactive chemicals. Their use is still technique sensitive and the procedures for their placement takes more time than for amalgam.

The data base required for safety evaluation of alternative materials is still inadequate and less complete than for amalgam. Many of the new alternative materials lack long-term clinical data. There are very limited scientific data available concerning identification and quantification of the exposure of patients and dental personnel to released substances from these materials. Further toxicological research on the various components of these alternative dental materials is warranted.

The SCENIHR notes that alternative materials are chemically very complex and also have clinical limitations and represent toxicological risks. They contain a variety of substances including organic solvents and undergo chemical reactions within the tooth cavity and adjacent soft tissues during placement. . The SCENIHR Opinion "The safety of the use of bisphenol A in medical devices" (2015) concluded that release of BPA from some dental materials was associated with negligible health risks. Non-mercury containing alternatives are not free from concerns about adverse effects. With respect to resin composite restorative materials and hybrid systems that incorporate polymerisable resins, there is *in vitro* evidence that some of the monomers used are highly cytotoxic to pulp and gingival cells. There is also *in vitro* evidence that some monomers are mutagenic although it not known whether this has any clinical significance. Allergic reactions to some of these substances have been reported, both in patients and in dental personnel. Similar to treatment with dental amalgam, the use of these materials in pregnant women is discouraged.

Studies comparing amalgam with resin-based materials showed generally better longevity for amalgam. Alternative restorations fail, primarily through secondary caries and fracture of the restoration and tooth. However, some recent studies from the Netherlands, Sweden and Denmark showed very good long-term clinical effectiveness for posterior resin composite restorations with equal and better longevity than for amalgam. But even under optimal conditions, large composite restorations in caries risk patients failed more often than amalgam fillings.

In one study, exposure to bisGMA-based dental composite restorations was associated with impaired psychosocial function in children, whereas no adverse psychosocial outcomes were observed with either urethane dimethacrylate–based compomer or amalgam treatment levels.

The indirect restorations have a good survival rate, but require removal of some additional healthy tooth tissue. The involved costs are considerably higher than with direct restorations.

Due to reported mediocre mechanical properties and clinical failures, glass ionomer cements can only be used in small, one-surface cavities. Recently, resin-based materials with reduced cytotoxicity, e.g. the methacrylate-free siloranes, have been introduced, showing good short term clinical performance. They also show low genotoxic potential and may be suitable components for development of new biomaterials.

In conclusion, amalgam alternatives have certain clinical limitations and toxicological risks. More experimental, clinical and epidemiological research is required to ensure patient safety in the future. The development of better amalgam alternatives is still the prime aim.

4.2.4. Question 4

Is it possible to recommend alternative materials and certain practices related to these materials to reduce potential risks for patients and users?

The current evidence does not preclude the use of alternative materials in dental restorative treatment in the general population.

The choice of the restorative material for treating dental cavities depends on a large number of variables, e.g. the size of the defect, the technical circumstances for restoration placement, and individual health problems like allergies, material properties, or the available funds. Therefore, the final decision on which material should be used in the individual case can only be made in the single situation between the dentist and the patient, based on informed consent. Based on current information, dental composites do not pose unacceptable risks to pregnant patients. However, the data base is scarce. A decision to perform dental treatment during pregnancy should take into account the dental therapeutic needs of the patient and balance any potential risks (including the use of anesthetics, along with all dental materials) against therapeutic benefits to the patient. Generally, extensive dental treatment during pregnancy is discouraged.

Alternative materials may also represent some health risks, so no general recommendations on the use of alternative materials can be given. One exception is for patients with a proven allergy to one of their components, which requires more information about their constituents.

4.2.5. Question 5

In case there is not enough scientific data to answer these questions, the SCENIHR is asked to formulate recommendations for research that could help to provide the necessary data.

The SCENIHR recognises a lack of knowledge and a need of further research, in particular in regard to genetic polymorphism related both to mercury and to the constituents of alternative restorative materials. Furthermore, there is a need for the development of new alternative materials with a high degree of biocompatibility.

The ideal new material meant as a true amalgam alternative should have a similar gradient in properties from cavity floor to surface, as in a natural tooth, and be cost effective and non-toxic to human health and the environment (safe and efficacious). It would seal the interface between the tooth and the restoration against the penetration of bacteria and common ions from saliva and food, be adhesive to the tooth with little to no shrinkage, interact favourably with carious dentin and enamel (preferably with healing/demineralising properties), be clinically easy to use in a variety of settings, and be fracture- and wear-resistant and repairable.

The present report has clearly identified that in some areas there are not enough scientific data to provide firm answers to the questions formulated by the EU Commission. Therefore, the future research agenda should first of all address improvement of knowledge on toxicological profile of alternative material and the development of new materials, both organic and inorganic. Improved tools for their evaluation are also needed and both points are specified below. In addition further research on the individual susceptibility of the mercury from amalgam and on the constituents of alternatives currently in use is necessary.

However, equal or more research emphasis should be placed on the further development and implementation of new caries management concepts like early intervention and of new tools for caries prevention in risk groups. It is generally accepted that restorations do not only fail due to insufficient mechanical and biological properties, but also due to a high caries activity in some patients.

<u>Improving information for materials in use.</u>

- Studies in clinical and community practice settings for materials in use should be further supported with study designs and study reports that follow internationally recognised guidelines.
- More human and environmental safety studies including mechanistic approaches, especially for chemicals from alternative materials or for nanoparticles from restorative materials, are needed.
- Risk groups for the exposure to chemicals including genetic approaches are to be identified.

Developing new materials

- While advances in polymer sciences are being made, there is a concern that we may need to move away from Bis-GMA polymer based materials for human safety and environmental reasons.
- New organic non-acrylic materials (like the siloranes) should be refined or new materials, both organic and inorganic, should be developed.
- Biomimetic material approaches should be followed to develop materials with the ability to remineralise dental hard tissues with the aim to further increase and support the minimal invasive approach to treat carious lesions.
- New materials – as true amalgam alternatives – must aim to be easily used in a variety of clinical and community settings on primary and permanent teeth and on low and high caries risk patients.
- New materials must be tested in randomized clinical trials. In addition to patient and user safety aspects, environmental safety has to be addressed.

Developing new research tools to improve knowledge for existing and for new materials

- Laboratory tests must be developed which reliably predict clinical material performance over the lifetime of the materials and, ultimately integrated into specifications for acceptance of new materials/products.
- New clinical testing schemes should be developed, by which the long term clinical behaviour of new materials can be predicted from short-term testing.
- International networks for Centres advising patients who claim health problems from dental materials should be established.
- Close collaboration with medical disciplines (e.g. allergology) and human genetics should be further developed.
- Tools should be developed, by which the process of pre-market certification can be accelerated.

5. CALL FOR INFORMATION

A call for information was issued by the Commission on 8 August 2012 with a deadline of 10 October 2012.

In total, 68 responses were received of which 35 were from organisations, 20 from individuals and 13 concerning 1 case report. Of the organisations, 15 were non-governmental, 7 public authorities and 13 other institutions, including dental associations.

In evaluating the responses from the call, submitted material has only been considered for the update of the Opinion if

1. it is directly referring to the content of the report and relating to the issues that the report addresses,
2. it contains specific comments and suggestions on the scientific basis of the Opinion,
3. it refers to peer-reviewed literature published in English, the working language of the SCENIHR and the working group,
4. it has the potential to add to the preliminary Opinion of the SCENIHR.

Each submission which met these criteria has been carefully considered by the Working Group. Overall, many of the comments were of good quality. The scientific rationale of the report has been revised to take account of relevant comments. The literature has been updated with relevant publications.

As indicated in the Opinion, the information on adverse effects of alternatives is limited. During the call for information, some additional information became available regarding the alternative restorative materials, especially concerning the release of BPA from dental resin-based materials.

6. CONSIDERATION OF THE RESPONSES RECEIVED DURING THE CONSULTATION PROCESS

A public consultation on this Opinion was opened on the website of the Scientific Committees from 09 September to 16 November 2014. Information about the public consultation was broadly communicated to national authorities, international organisations and other stakeholders.

25 organisations and individuals participated in the public consultation providing 102 comments to different chapters and sections of the Opinion. Each submission was carefully considered by the SCENIHR and the scientific Opinion has been revised to take account of relevant comments. The literature has been accordingly updated with relevant publications. The scientific rationale and the Opinion section were clarified and strengthened.

The text of the comments received and the response provided by the SCENIHR is available here:
http://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scenihr_consultation_24_en.htm

7. MINORITY OPINION

None

8. LIST OF ABBREVIATIONS

4-AETA	4-Methacryloxyethyl trimellitic anhydride
ADA	American Dental Association
ADME	Absorption, distribution, metabolism and elimination
Al2O3	Alumina glass
ALS	Amyotrophic Lateral Sclerosis
ATSDR	Agency for Toxic Substances Disease Registry
BAT	Biologischer Arbeitsplatz Toleranzwert (biological tolerance value at the workplace)
BBP	n-butyl benzyl phthalate
BHT	Butylhydroxytoluene
BDNF	Brain derived neurotrophic factor
Bis-EMA	Ethoxylated bisphenol A-methacrylate
Bis-GMA	Bisphenol A – glycidylmethacrylate
Bis-HPPP	2,2-bis[4(2,3-hydroxypropoxy)-phenyl]propane
BPA	Bisphenol A
CAT	Catalase gene
CPOX	Coproporphyrinogen oxidase
COMT	Catechol O-methyltransferase
COMET	The Single Cell Gel Electrophoresis assay
DMABEE	4-N,N-Dimethyl amino benzoic acid ethylester
DPMS	Dimercaptopropane sulfonate
EDS	Energy-dispersive X-rays spectroscopy
EFSA	European Food Safety Authority
EGDMA	Ethyleneglycoldimethacrylate
EPA	Environmental Protection Agency
DIMDI	German Institute for Medical Documentation and Information
GCLM-588T	Glutamyl-cysteine ligase allele
GSTs	Glutathione S-transferases
GSH	Glutathione
HDDMA	Hexanediol dimethacrylate
HEMA	Hydroxyethylmethacrylate
Hg	Mercury
HMBP	2-Hydroxy-4-methoxybenzophenone
IARC	International Agency for Research on Cancer
ICD	International Classification of Diseases
IEC	International Electrotechnical Commission

IRIS	Integrated Risk Information System
IR	Infrared
ISO	International Standards Organisation
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
LED	Light-emitting diode
MAK	Maximale Arbeitsplatz Konzentration (maximum concentration at the workplace)
MAF	Minor allele frequency
MBRN	Medical Birth Registry of Norway
MeHg	Methylmercury
MSDS	Material safety data sheets
MT	Metallothioneins
MT1M	Metallothionein mutant
α1-MG	Alpha 1 microglobulin
MMA	Methylmethacrylate
MRL	Minimal Risk Level
MS	Multiple Sclerosis
NAC	N-acetylcysteine
NAG	N-acetyl-β-D-glucosaminidase
NIOSH	National Institute for Occupational Safety and Health
NOAEL	No Observable Adverse Effect Level
NOAEC	No Observed Adverse Effect Concentration
NSAIDS	Nonsteroidal anti-inflammatory drugs
OES	Occupational Exposure Standard
8-OHdG	8-hydroxy-2-deoxyguanosine
OLP	Oral Lichen Planus
PAC	Xenon-plasma arcs
PBPK	Physiologically based pharmacokinetic modeling
PTWI	Provisional Tolerable Weekly Intake
RNA	Ribonucleic acid
ROS	Reactive oxygen species
QTH	Quartz – tungsten – halogen
QSAR	Quantitative Structure-Activity Relationship
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SCHER	Scientific Committee on Health and Environmental Risks
SEA	Self-etching adhesives
SiO_2	Silica glass
SNPs	Single nucleotide polymorphisms
5-HTTLPR	Serotonin transporter gene promoter region

TCB	Reaction product of butane tetracarboxylic acid and hydroxyethylmethacrylate,
TEGDMA	Triethyleneglycoldimethacrylate
TPO	Trimethylbenzoyl-diphenyl-phosphine oxide
TWI	Tolerable weekly intake
UBA	Umweltbundesamt (German Federal Environment Agency)
UDMA	Urethane dimethacrylate
UNEP	United Nations Environment Programme
UV	Ultraviolet
WHO	World Health Organisation
YF_3	Ytterbium fluoride

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Annex I. Organic chemicals in resin-based restorative materials

The following list is based on a compilation by Schmalz and Arenholt-Bindslev (2009).

Bisphenol A dimethacrylate,
CAS number: 3253-39-2

bisphenol A diglycidyl methacrylate (Bis- GMA),
CAS number: 1565-94-2

ethoxylated Bisphenol-A (Bis-EMA).
BisphenolA ethoxylate dimethacrylate
CAS number 24448-20-2
(also: CAS Number 41637-38-1 for higher molecular substance)

Urethane dimethacrylate, UDMA
CAS number: 72869-86-4

urethane bisphenol-A-dimethacrylate UPGMA
nothing found!

Triethylene glycol dimethacrylate
CAS number: 109-16-0

triethylene glycol monomethacrylate (TEGMA)
CAS number: 39670-09-2
Mol wt. 246

Tetraethylene glycol dimethacrylate
CAS number: 109-17-1

Di(ethylene glycol) dimethacrylate (DEGDMA)
CAS number: 2358-84-1

Ethylene glycol dimethacrylate (EGDMA)
CAS number: 97-90-5

1,10-Decanediol dimethacrylate
CAS number 6701-13-9

1.6 Hexanediol Dimethacrylate
CAS number 6606-59-3

2-hydroxyethyl methacrylate
CAS Number 868-77-9
1,5-pentanediol dimethacrylate
CAS number: 13675-34-8

1,4-Butanediol dimethacrylate
CAS number 2082-81-7

BDDMA-methanol-adduct ½
Nothing found

BDDMA-auto-adduct ½
Nothing found

1,2-propanediol dimethacrylate
CAS number 7559-82-2)

bis(oxymethyl)tricyclo[5.2.1.02,6]decane
nothing found

Benzyl methacrylate
CAS number 2495-37-6

3-(trimethoxysilyl)propyl methacrylate
CAS number 2530-85-0

Trimethylolpropane trimethacrylate
CAS number 3290-92-4

Methyl methacrylate
CAS number 80-62-6

Methacrylic acid
CAS number 79-41-4

Additional substances analysed for in extracts from dental composite resins by Landuyt *et al.*, 2011.

Trivial name	**Chemical name Molecular**	**mass**
BADGE	Bisphenol A diglycidyl ether	340.45

BADGE, 2,2-bis(4-hydroxyphenyl)propane, *bisphenol A* diglycidyl ether (*BADGE*)

CAS No. 1675-54-3

BHT	Butylatedhydroxytoluene	220

2,6-Di-tert-butyl-4-methylphenol

CAS Number 128-37-0

BPA	Bisphenol A	228.29

2,2-Bis(4-hydroxyphenyl)propane,

CAS Number 80-05-7

CQ	Camphorquinone	166

2,3-Bornanedione

CAS Number: 10373-78-1

DMABEE	Ethyl4-(dimethylamino)benzoate	193

CAS Number: 10287-54-4

EBPA	Bisphenol A ethoxylate	316

CAS Number: 32492-61-8

HMBP	2-hydroxy-4-methoxybenzophenone	228.25

CAS Number: 131-57-7

HQ	Hydroquinone	110.1
CAS Number: 123-31-9		
Irgacure	1,2-Diphenyl-2,2-dimethoxyethanone	256.3
CAS Number:		
MEHQ	4-Methoxyphenol	124.14
CAS Number: 24650-42-8		
PBPA	Bisphenol A propoxylate	344
(propoxylated Bisphenol A)		
CAS Number: 37353-75-6		
Quantacure BEA		
2-n-butoxyethyl-4-dimethyl-aminobenzoat		
CAS Number: 67362-76-9		
TMA	3-(Trimethoxysilyl)-propylmethacrylate	248.35
CAS Number: 2530-85-0		
TIN P (drometrizole)	2-(2-Hydroxy-5-methylphenyl)benzotriazole	225.1
CAS Number: 2440-22-4		
TMPTMA	Trimethylolpropanetrimethacrylate	338.2
CAS Number: 3290-92-4		

EUROPEAN COMMISSION

Directorate-General for Health & Consumers

Scientific Committee on Emerging and Newly Identified Health Risks

SCENIHR

Mercury Sphygmomanometers in Healthcare and the Feasibility of Alternatives

Scientific Committees
- on consumer safety
- on emerging and newly identified health risks
- on health and environmental risks

SCENIHR adopted this opinion at its 4th plenary of 23 September 2009

About the Scientific Committees

Three independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.

They are: the Scientific Committee on Consumer Safety (SCCS), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), and are made up of external experts.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Evaluation Agency (EMEA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCENIHR

This Committee deals with questions related to emerging or newly identified health and environmental risks and on broad, complex or multidisciplinary issues requiring a comprehensive assessment of risks to consumer safety or public health and related issues not covered by other Community risk assessment bodies. Examples of potential areas of activity include potential risks associated with interaction of risk factors, synergic effects, cumulative effects, antimicrobial resistance, new technologies such as nanotechnologies, medical devices including those incorporating substances of animal and/or human origin, tissue engineering, blood products, fertility reduction, cancer of endocrine organs, physical hazards such as noise and electromagnetic fields (from mobile phones, transmitters and electronically controlled home environments), and methodologies for assessing new risks. It may also be invited to address risks related to public health determinants and non-transmissible diseases.

Scientific Committee members

Anssi Auvinen, James Bridges, Kenneth Dawson, Wim De Jong, Philippe Hartemann, Peter Hoet, Thomas Jung, Mats-Olof Mattsson, Hannu Norppa, Jean-Marie Pagès, Ana Proykova, Eduardo Rodríguez-Farré, Klaus Schulze-Osthoff, Joachim Schüz, Dorothea Stahl, Mogens Thomsen, Theodorus Vermeire

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All Declarations of working group members are available at the following webpage:

http://ec.europa.eu/health/ph_risk/committees/04_scenihr/scenihr_memberswg_en.htm

ABSTRACT

This Opinion addresses the issue of whether the replacement of mercury-containing, blood-pressure measuring devices (sphygmomanometers) would (i) endanger proper health care including specific groups of patients, and/or (ii) compromise long-term translational epidemiological studies for public health. In addition, the availability and quality of alternative devices for blood pressure measurements have been considered. Blood pressure measurement is vital for the prevention and treatment of blood pressure related diseases, and for monitoring of cardiovascular homeostasis. Based on long-term experience, blood pressure measurement using the mercury sphygmomanometer is currently regarded as the gold standard method for indirect measurement of blood pressure.

Alternative devices are gradually replacing the mercury sphygmomanometer. Mercury-free sphygmomanometers which use auscultation for the determination of blood pressure have the same limitations as mercury sphygmomanometers. These limitations result from poor observer technique and/or bias and may be avoided by using automated oscillometric devices which operate under a different principle from auscultation. Although they all employ the same oscillometric principle, each oscillometric device follows a manufacturer-specific algorithm which requires individual assessment for technical accuracy and clinical validation. Accurate blood pressure measurements with automated oscillometric sphygmomanometers are possible, although they have limitations in certain patient groups. Clinical validation in these specific groups of patients is required before oscillometric devices can be used safely. For certain patient groups, blood pressure measurement by a trained observer, using mercury sphygmomanometers or a validated auscultatory alternative, remains the most accurate and reliable form of indirect blood pressure measurement. It is emphasised that all alternative devices require metrological verification and clinical validation.

For all blood pressure measurement devices, including mercury sphygmomanometers, regular maintenance is of utmost importance. For the alternative blood-pressure measuring devices, a regular metrological verification is needed to ensure the accuracy of the measurements. The metrological verification does not necessarily require the use of mercury sphygmomanometers. However, it is recommended that mercury sphygmomanometers remain available as a reference standard for clinical validation of existing and future mercury-free blood-pressure measurement devices. Therefore, the mercury sphygmomanometer should remain available as a reference standard until an alternative device is developed and recognised as such.

Keywords:

SCENIHR, Scientific Committee on Emerging and Newly Identified Health Risks, Mercury, Cardiology, Epidemiology, Public health, Blood pressure, Hypertension, Arrhythmia, Diabetes, Pre-eclampsia, Mercury sphygmomanometers, Aneroid sphygmomanometers, Oscillometric sphygmomanometers, Electronic sphygmomanometers, Mercury-free sphygmomanometers.

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EXECUTIVE SUMMARY

Mercury and its compounds are highly toxic to humans, ecosystems and wildlife. Mercury can exist in several chemical forms (Hg^{o}, Hg^{1+}, Hg^{2+}), each with its own toxicological profile. In general terms, the toxicity of these chemical forms is highest for the organic mercury compounds, followed by elemental mercury and inorganic mercury compounds. A Community Strategy Concerning Mercury was adopted in January 2005 with the key aim of reducing mercury levels in the environment and reducing human exposure. The replacement of mercury-containing blood-pressure measuring devices (sphygmomanometers) by alternative mercury-free devices raises the issue whether this would

(i) endanger proper health care including specific groups of patients, and/or

(ii) compromise long-term translational epidemiological studies for public health.

In addition, the availability and quality of alternative devices for blood pressure measurements needs to be considered.

The blood pressure measurement is vital for the prevention and treatment of blood pressure related diseases, and for monitoring cardiovascular homeostasis. The indirect measurement of blood pressure with mercury sphygmomanometers has identified arterial hypertension as a major risk factor for cardiovascular diseases. In addition to the use in clinical settings, the mercury sphygmomanometer is also used in long-term epidemiological/observational studies on cardiovascular disease development. A change in population blood pressure has a direct effect on the morbidity and mortality of cardiovascular diseases. Based on long-term experience, blood pressure measurement using the mercury sphygmomanometer is regarded as the gold standard method for indirect measurement of blood pressure. The use of the mercury sphygmomanometer has practical and technical limitations, and requires specific training. In addition, there should be a special emphasis on regular maintenance of the mercury sphygmomanometer in order to maintain its accuracy. When blood pressure is measured by a trained observer using the auscultatory technique, the mercury sphygmomanometer currently remains the most accurate device for indirect blood pressure measurement.

The mercury column functions as a pressure sensing and displaying component, so it seems likely that this can be replaced by a mercury-free manometer. Indeed, mercury-free alternatives for pressure measurement are commercially available such as the aneroid manometer and the electronic pressure transducer. These alternative sphygmomanometers use auscultation for determination of the blood pressure, and therefore, have the advantages and limitations (such as the observer performance) which also apply to the mercury sphygmomanometer, and are characteristic of the auscultatory technique. The auscultation method is based on the observation of the recurrence of the blood flow in the occluded artery (using a cuff) of the upper arm by listening to the sounds generated by the recurrent blood flow and disappearance of the sounds when the occlusion is completely removed (by dilation of the cuff), and normal blood flow is restored. In addition, there are non-auscultatory, mercury-free devices available which use the oscillometric technique to measure blood pressure based on changes in arterial pulsation during cuff inflation/deflation. Oscillometric instruments operate under a completely different principle and are thus not considered as true "alternatives" to Hg sphygmomanometers.

The various alternatives have widely varying levels of accuracy, emphasising the importance of clinical validation. Regular maintenance is of the utmost importance for proper functioning of all measurement instruments. Even validated oscillometric devices may have accuracy limitations in special patient groups, including patients with arrhythmias, diabetes, pre-eclampsia, and the elderly. These limitations do not apply to devices using the auscultatory technique. Therefore, validated non-mercury auscultatory alternatives are appropriate for these patients. For alternative blood pressure measurement devices, a metrological verification is needed to ensure the accuracy of the

measurements. Mercury sphygmomanometers are not essential as reference devices for this metrological verification (calibration). In addition, an independent device accuracy assessment is recommended to evaluate the clinical performance. Various clinical validation protocols are available to assess the accuracy of automated alternative devices against mercury sphygmomanometers.

The mercury sphygmomanometer is gradually disappearing from clinical use. Mercury-free blood pressure measuring devices (when clinically validated) are generally reliable substitutes for mercury-containing sphygmomanometers in routine clinical practice. These alternative devices include both auscultatory devices requiring a trained observer and automated oscillometric devices for which some instruction is needed. Clinically validated, auscultatory mercury-free devices are equivalent to mercury sphygmomanometers, and are thus suitable for specific groups of patients, including patients with arrhythmias, diabetes, pre-eclampsia and the elderly. The alternative devices using auscultation have similar limitations as the mercury sphygmomanometers regarding the observer technique and bias associated with auscultation itself. These may be avoided by using automated oscillometric devices, which, when properly validated, allow accurate blood pressure measurements. The oscillometric technique has mainly been clinically validated in adult populations including a wide range of blood pressures but not in a wide range of ages and clinical conditions, and should not be used in some specific clinical conditions including pre-eclampsia. There is no evidence of adverse effects on patients' health in clinical settings due to the replacement of mercury-containing sphygmomanometers by validated mercury-free alternatives. There are adequate alternatives in most clinical conditions/settings. In special conditions, such as pre-eclampsia, mercury-free auscultatory devices should be preferred until further validation of oscillometric devices.

In conclusion, when blood pressure is measured by a trained observer using the auscultatory technique, the mercury sphygmomanometer or a validated auscultatory alternative currently remains the most accurate instrument for indirect blood pressure measurement, especially for certain patient groups. For all blood-pressure measuring devices, regular maintenance is of primary importance. In order to maintain a high-level quality of blood pressure measurements it is recommended that mercury sphygmomanometers remain available as reference standards for clinical validation studies of existing and future non-mercury-containing blood-pressure measurement devices. For on-going, long-term, epidemiological studies currently using mercury sphygmomanometers it is advisable not to change the method of measurement. Therefore, it will be necessary to keep mercury sphygmomanometers available in order to compare them with the alternatives in these studies. It is emphasised that mercury devices should remain available as reference standards until an alternative standard is developed and recognised.

TABLE OF CONTENTS

1. BACKGROUND

Directive 2007/51/EC[1] (point 3 of entry 19a on mercury) requires that, "the Commission shall carry out a review of the availability of reliable safer alternatives that are technically and economically feasible for mercury containing sphygmomanometers and other measuring devices in healthcare and in other professional and industrial uses".

The sale of all mercury containing measuring devices to the general public has been banned under Directive 2007/51/EC with effect from 3 April 2009 due to concerns about the risks posed to human health from discharges of mercury to the environment from broken or discarded measuring devices. However, sphygmomanometers in healthcare were exempted as these devices were regarded by many Member States as essential for the diagnosis of certain life-threatening diseases such as arrhythmia, accelerated hypertension, as well as in gynaecology and obstetrics. The exemption also applies to other measuring devices in healthcare. That position was also in line with the consensus of opinion among the Member State experts of the Commission's Working Group on Medical Devices.

Nevertheless, the European Parliament and the Council decided during the co-decision procedure that the Commission should review the issue by 3 October 2009.

Since March 2008, The Directorate-General (DG) for Enterprise and Industry of the European Commission has been preparing for the review by addressing questionnaires to various stakeholders (Member States, non-governmental organizations, scientific organisations, and industry) in order to collect relevant information. In addition, the positions of stakeholders on mercury-containing sphygmomanometers (and the existence of alternatives) have been recorded in discussions which have taken place during the meetings of the Limitation Working Group which is responsible for the implementation of Directive 76/769/EEC.

Considering the critical importance of the health and safety of patients, DG Enterprise would like to request an opinion of SCENIHR as crucial input for the Commission's review. The Commission needs to ensure a careful examination of the available scientific and clinical evidence, so that any future action, if required, would achieve a good balance between protection of human health from adverse effects of mercury through the environment for the population in general, and protection of the health of patients requiring accurate blood pressure measurement.

[1] Available at: http://ec.europa.eu/enterprise/chemicals/legislation/markrestr/amendments_en.htm

2. TERMS OF REFERENCE

SCENIHR is requested to review the provided material and any further documentation available, and to specifically answer the following questions:

(1) Is there sufficient evidence to demonstrate that mercury-free blood pressure measuring devices such as aneroid or electronic instruments are *generally reliable* substitutes for mercury-containing sphygmomanometers?[2]

(2) Have mercury-free sphygmomanometers been adequately validated over a *wide range* of blood pressures, ages, and clinical conditions to allow for routine use in hospitals and outpatient settings?

(3) Have mercury-free sphygmomanometers been adequately validated for the diagnosis of hypertension in *specific clinical conditions* such as arrhythmia, pre-eclampsia in obstetrics and certain vascular diseases?

(4) Are mercury-based sphygmomanometers essential as reference devices for *validation* of long-term clinical epidemiological studies enrolling patients with hypertension?

(5) Are mercury-based sphygmomanometers essential as reference devices for *calibration* of the mercury-free sphygmomanometers when the latter are used for routine diagnostic purposes?

(6) Is SCENIHR aware of any *adverse effects* for patients' health due to the replacement of mercury-containing sphygmomanometers by mercury-free alternatives?

[2] Substitutes cover both liquids to replace mercury in manometers and other measurement techniques based on different technologies, such as electronic devices. The term "*reliable* substitutes" denotes devices that perform (in comparison with the mercury-based sphygmomanometers) to equal or greater accuracy when maintained and used correctly, also taking into account error statistics where known (such as error rates and the magnitude of errors) and the intervals between maintenance and recalibration.

3. SCIENTIFIC RATIONALE

3.1. Introduction

Mercury and its compounds are highly toxic to humans, ecosystems and wildlife. Therefore, the Community Strategy Concerning Mercury was adopted in January 2005 with the key aim of reducing mercury levels in the environment and to reducing human exposure.

This Opinion addresses the issue of whether the replacement of mercury-containing, blood-pressure measuring devices (sphygmomanometers) would (i) endanger proper health care including health care for specific groups of patients, and/or (ii) compromise long-term translational epidemiological studies for public health. For this purpose the availability and quality of alternative methods for blood pressure measurements have been evaluated.

3.2. Methodology

For this Opinion, evidence from a wide variety of sources, including peer-reviewed scientific and medical literature and published reports of institutional, professional, governmental and non-governmental organisations has been considered. In accordance with the practice of SCENIHR and its Working Groups, no reliance has been placed on unpublished work or publicly available opinions that are not scientifically based. Single case or anecdotal reports were generally not considered in establishing this Opinion. To review as much evidence as possible, especially where the available data are limited, attention has been given to some less rigorous studies where no other information was available. During the course of the deliberations and drafting the document, a Call for Information was issued by the Commission and the submissions have all been considered.

3.3. Mercury Toxicity

As previously described in the Opinion of SCENIHR on the use of dental amalgam (SCENIHR 2008), mercury is a metallic element that occurs naturally and also in the form of several types of ore, the mercury burden of the environment being derived predominantly from natural sources. Input into the earth's atmosphere occurs regularly through emissions from volcanoes, soil erosion and the combustion of fossil fuels. Widespread utilisation of mercury and its compounds in a number of industries over the last several centuries has resulted in the release of large amounts of mercury into the atmosphere, increasing the total amount in the ecosphere. Of special importance has been the accumulation of some mercury compounds in the aquatic food chain and the use of mercury compounds in a variety of medical and cosmetic products including dental amalgam (SCENIHR 2008).

It is also important to note that there are several different forms of mercury. First, there is elemental mercury itself, a volatile form of the liquid metal, referred to as Hg^0. Second, mercury is stable in two other oxidation states (Hg^{1+} and Hg^{2+}) and is able to form inorganic compounds, of either monovalent or divalent form, including mercuric chloride ($HgCl_2$), mercurous chloride (Hg_2Cl_2), mercuric sulphide (HgS), and mercuric selenide (HgSe). Third, mercury is able to form a variety of organic compounds, including methylmercury. There is a clear connection between all these forms with respect to the global cycle of mercury (Nielsen et al. 2006). Elemental mercury may be converted to soluble inorganic forms, which may be methylated in water, especially by microorganisms, and which enter the food-chain and accumulate in the tissues of large

predatory fish. The ratio of methylmercury in these fish to the mercury concentration in the water can be as high as 105.

Due to the widespread use of mercury in industrial settings, a large and detailed database on human effects of elemental mercury inhalation is available. A number of reviews addressing the toxicity of elemental mercury have been published (ATSDR 1999, BAT 1997, IRIS 2002, MAK 1999, UNEP 2002). Each form of mercury has its own toxicological profile, although, in general terms, the organic mercury compounds have the highest toxicity, followed by elemental mercury and inorganic mercury compounds. This is important when considering different exposure routes to these forms. Elemental liquid mercury is used in measuring devices such as sphygmomanometers, and previously thermometers.

The assessment of elemental mercury toxicity is mainly based on observations in occupationally exposed humans. Inhalation of extremely high concentrations of elemental mercury, in excess of 10 mg/m^3, may produce bronchitis and pneumonia, in addition to symptoms of the central nervous system. After long-term elemental mercury exposure in occupational settings and under occupational hygiene conditions considered as poor by present standards, the major effects of elemental mercury reported are on the central nervous system. The major manifestations of mercury poisoning from inhalation of elemental mercury are increased excitability and tremors. Characteristic symptoms after long-term high dose exposures (the inhalation of concentrations above 0.5 mg/m^3 for many years) are muscle tremors in fingers, eye lids and lips, which may progress to chronic spasms of the extremities. After chronic occupational exposure to mercury vapour, proteinuria and even a nephritic syndrome have been described in humans. The glomerular damage may progress to interstitial immune-complex nephritis. Gingivitis and hypersalivation with a strong metallic taste are considered to be further symptoms of chronic inhalation exposure to elemental mercury.

Occupational allergies to mercury were rare, even with widespread exposures to elemental mercury at the workplace and the use of mercury in medicinal preparations (including the use of Hg^{2+} due to its bactericidal activity) and consumer products (Kanerva et al. 1993).

Mercury is a serious non-degradable environmental pollutant, which eventually accumulates on the sea bed and contaminates marine life (Langford and Ferner 1999). After discharge in the environment, natural transformations and environmental pathways of mercury are very complex and greatly affected by local conditions. There are two main types of reactions in the mercury cycle that convert this metal into its various forms: oxidation-reduction and methylation-demethylation. In oxidation-reduction reactions, mercury is changed from the relatively inert Hg^0 to the more reactive Hg^{2+}. The oxidation of elemental mercury Hg^0 in the atmosphere is an important mechanism involved in the deposition of mercury on land and water. Hg^0 can volatilize relatively easily and be transported in the atmosphere. In contrast Hg^{2+} has a short atmospheric residence time due to its solubility in water, low volatility and reactive properties. Hence after this conversion, mercury can be rapidly taken up in rain water or adsorbed onto small particles and be subsequently deposited in the environment (Nielsen et al. 2006).

In the environment mercury is transformed into methyl mercury when the oxidized, or mercuric species (Hg^{2+}) gains a methyl group ($-CH_3$).This methylation is primarily a natural, biological process resulting in the production of highly toxic and bioaccumulative methylmercury compounds ($MeHg^+$) that build up in living tissues and increase in concentration in the food chain from microorganisms like plankton to fish and humans. Rates of biomethylation are a function of environmental variables affecting ion availability as well as the population sizes of methylating microbes and pH (acidic conditions are more favourable).

Humans are exposed to methylmercury almost entirely by eating contaminated fish, seafood and wildlife that are at the top of the aquatic food chain.

3.4. Blood Pressure Measurements

3.4.1. General information

Raised blood pressure throughout its range is the most significant cause of death and disability in the world (Lopez et al. 2006). Accurate blood pressure measurement is therefore vital in the prevention and treatment of blood-pressure–related diseases. Additionally, in very ill patients, accurate measurement of blood pressure is essential for monitoring cardiovascular homeostasis.

For more than a century, blood pressure has been measured worldwide both in clinical practice and medical research by auscultation using the mercury sphygmomanometer. Riva–Rocci described this indirect measurement of the blood pressure as the outside pressure needed to occlude the brachial artery (Riva-Rocci 1896). This was achieved by wrapping an inflatable bladder encased in a non distensible cuff, around the arm or leg and inflating it until the pressure on the cuff is greater than the blood pressure in the artery, and the artery is occluded. The cuff is then slowly deflated until the palpable pressure reappears through the partially compressed artery. The level of pressure on the bladder which is reflected on the manometer at the time the first repetitive sound is heard, is the maximum pressure generated during each cardiac cycle. This is defined as systolic blood pressure. The diastolic blood pressure is the level of pressure at which sounds disappear completely when the artery is not compressed and blood flow is restored. In 1905 Korotkov described the auscultatory method; this is the observation of the repetitive sounds generated by the blood flow (Korotkov 1905). As the cuff pressure reduces gradually during the deflation the Korotkov sound changes in intensity and quality, and five different stages can be distinguished (Korotkov 1905).

The indirect blood pressure measurement with mercury sphygmomanometers has been shown to be valuable in several clinical circumstances. Their extensive use has allowed the collection of the necessary evidence to identify arterial hypertension as a major risk factor for cardiovascular diseases. Most epidemiological and clinical data on hypertension as a cardio-vascular risk factor have been obtained by this blood pressure measuring device. Based on this relation to clinical disease and long-lasting experience, blood pressure measurement using the mercury sphygmomanometer currently is regarded as the gold standard method for indirect measurement of blood pressure.

3.4.2. Factors affecting blood pressure measurement

It is important to be aware of the factors that affect blood pressure measurement (Rose 1965):

(1) The technical skills of the observer;

(2) The inherent variability of blood pressure;

(3) The accuracy of the device, including its limitations and applications;

(4) The difficulty in measuring blood pressure in some special groups, e.g. the elderly, patients with arrhythmias, patients with a large arm, children, pregnant women.

The most important element in using auscultatory methods is the observer. All observers need adequate training in listening and recognising the correct sounds. Most common sources of error in many reports are mostly due to the observer, including poor hearing, difficulty/failure in interpreting the Korotkov sounds and lack of concentration. Most serious errors involve the interpretation of the Korotkov sounds and recognising diastolic pressure. Observers may be influenced by the subjects. For example, observers tend to be reluctant in diagnosing young healthy subjects as hypertensive or obese older persons as normotensive when the blood pressure is around 140/90 mmHg (systolic/diastolic blood pressure) resulting in a tendency to under read in the first case and over estimate in the latter. Observer-related issues include: prejudice and bias such as threshold avoidance; terminal digit preference; fast deflation, etc. (Beevers et al. 2001).

To accurately measure blood pressure, the following important criteria have to be applied, irrespective of what type of device is being used.

- Posture of the patient supine, sitting or standing.
- Cuff at heart level and arm supported; if not supported, isometric exercise is performed and will result in recording a higher blood pressure.
- The use of correct cuff and bladder size for the appropriate arm/leg size. Over cuffing (use of a bladder that is too large) will lead to under estimation of blood pressure, and under cuffing (use of a bladder that is too small) will over estimate the blood pressure.
- Measurement of the blood pressure on both arms at first visit to help identify consistent difference in blood pressure between the arms.
- Accuracy of the device; the device should be well maintained, in pristine condition, calibrated as per the manufacturer's instructions and validated according to accepted standards using appropriate protocols.

3.4.3. Blood pressure measurements in routine clinical practice

Repeated office blood pressure measurements are mandatory in clinical practice to characterise precisely the blood-pressure-related cardiovascular risk of individual subjects. Precise recommendations are available to ensure standardised accurate measurements (O'Brien et al. 2003, Parati et al. 2008a), which until now have been obtained in most cases through the auscultatory technique making use of mercury or aneroid sphygmomanometers. Given the fact that aneroid manometers easily lose calibration, mercury manometers have been, until now, the recommended tools for auscultatory blood pressure readings, on which the conventional management of hypertensive patients has been based over the last 60-70 years. In more recent years an increasing use of home blood pressure monitoring and 24-hour ambulatory blood pressure monitoring has been observed (both based on oscillometric blood pressure measurements), aimed at complementing the information provided by office blood pressure measurements. This is based on the evidence of a stronger prognostic value of 24-hour ambulatory and home blood pressure monitoring as compared to isolated office readings (Parati et al. 2008b, Parati et al. 2009b, Verdecchia et al. 2009). A slow progressive increase in the use of oscillometric blood pressure measuring devices at the time of the office visit has been recently observed, although auscultatory readings are still preferred by physicians in most countries.

There are a number of physiological and pathological states that may influence the ability of an oscillometric device to obtain an equivalent reading to a mercury sphygmomanometer. Oscillometric measurements are dependant on movement, and changes in the amplitude of this movement, in the artery, and therefore maybe altered. Oscillometric measurements cannot be relied on in patients with arrhythmias, or some valvular heart disease such as aortic incompetence. Other patients with altered vascular compliance, such as diabetics, or the elderly, could have less accurate blood pressure readings using oscillometric measurement. Changes in vascular compliance may also be confounded by oedema, intravascular volume, hyperdynamic circulation and by changes in cardiac output such as pre-eclampsia, in which oscillometric readings frequently underestimate the blood pressure (Shennan and De Greeff 2007). Although the accuracy and reproducibility of Korotokov sounds in these disease states are not known, listening to the Korotkov sounds remains the technique in which current knowledge of indirect blood pressure is determined, and therefore, the auscultatory method of blood pressure is recommended in such populations.

3.4.4. Blood pressure measurements in epidemiological / observational studies

Very comprehensive research on population blood pressure exists throughout the world. These studies are essential for defining hypertension prevalence, awareness and treatment in any geographical region/country. A change in population blood pressure of 2 mmHg in systolic blood pressure translates to a change in stroke mortality of ten percent and coronary heart disease mortality of seven percent (Lewington et al. 2002). Therefore, data on progression from normotension to prehypertension and hypertension are very important in epidemiological research. The data have documented that prehypertension carries an increased risk for cardiovascular morbidity and mortality, and a high risk for progression to sustained hypertension (Hansen et al. 2007a, Julius et al. 2006). In this respect, changes from normotension to prehypertension are as important as the observation of hypertension itself. Reliable data are heavily dependent on blood pressure measurements carried out meticulously by properly trained personnel and with precise equipment. For this, adherence to a standardised technique over time is crucial. Findings of changes in population blood pressure are only meaningful if they are ascertained to be true differences and not related to a change in methods applied.

Nearly all results on population blood pressure have been obtained by the use of a standard mercury sphygmomanometer by well-trained health personnel (Cutler et al. 2008). Despite this, the readings are not without observer bias and end-digit preference. In an attempt to minimise observer bias and end-digit preference, a number of highly recognized epidemiological research institutions have used the Random Zero Mercury Sphygmomanometer, where the reader has to subtract a random chosen magnitude of mmHg (from 0 to 20 mmHg) at the very end of the measurement. Despite minimising observer bias, the equipment has been shown to slightly underestimate the "true" blood pressure level as obtained by the use of a standard mercury manometer (Yang et al. 2008). Another approach that has been employed is the "London School of Hygiene Sphygmomanometer" (Andersen and Jensen 2007) where the reader is blinded to the mercury column but has to tap a button when they hear the first and the fourth Korotkov sounds (phase 1 and phase 5).

In recent years, 24-hour ambulatory blood pressure measurements have been introduced in population studies and comprehensive databases have been constructed, e.g. the Idaco Database on population studies with contributions from many parts of the world (Hansen et al. 2007b). All these studies have convincingly shown that 24-hour ambulatory blood pressure measurements determined with oscillometric devices (at approximately 80 readings over 24 hours), are superior for prediction of cardiovascular morbidity and mortality as compared to a few measurements of blood pressure performed in clinical conditions with a standard mercury sphygmomanometer. In almost all these studies, although not exclusively, the comparator has been the standard mercury sphygmomanometer (Hansen et al. 2007b).

Research into normal values for home blood pressure and the prognostic implication is less comprehensive. This research has been almost exclusively carried out with automatic oscillometric devices, with measurements being compared to the mercury sphygmomanometer. Data are accumulating showing that the predictive prognostic value of a certain number of home blood pressure readings is superior to a single or a few blood pressure readings performed in a clinic using a mercury sphygmomanometer (Sega et al. 2005). The home readings are a reflection of more precise estimation of the actual blood pressure levels over many readings as compared to few readings in the clinical setting. So far, comparisons of measurements obtained with mercury sphygmomanometer versus oscillometric automatic devices, obtained in the same clinical setting for determination of population blood pressure and prognostic implications, are missing. However, in the Pamela Study, three clinic readings with a mercury sphygmomanometer were compared to two home blood pressure oscillometric readings (Sega et al. 2005). As expected, the clinical readings were somewhat higher, but the prognostic implication was not that much different.

In long-term outcome clinical trials, usually running for three to five years, mercury sphygmomanometers have been used as the gold standard for office blood pressure measurement. In some recent trials (the HOT Study, the ASCOT Study and the OnTarget Study) automatic oscillometric devices were used (Dahlöf et al. 2005, Hansson et al. 1998, Yusuf et al. 2008). In some of these studies it was shown that small differences in measured blood pressure already can have an impact on cardiovascular diseases.

There is rapidly growing information on normal values and the prognostic implications of 24 hour ambulatory blood pressure measurements with oscillometric devices, while knowledge on self/home blood pressure measurements with oscillometric devices is less substantial. So far, a direct comparison between clinic blood pressure and prognostic implication based on measurements carried out with mercury sphygmomanometer and those with automatic oscillometric devices is lacking.

In conclusion, the vast majority of information on population blood pressure (secular trends, progression to hypertension and prognostic implications, and also the benefits from treatment-induced blood pressure reduction in terms of cardiovascular events prevention) has so far been obtained with the use of mercury sphygmomanometers. Reliable data on changes in population blood pressure level, incidence and prevalence of hypertension, awareness and treatment, derived from follow-up studies are dependent on the use of consistent and trustworthy methods. It can be expected that epidemiological/observational studies in the future will comprise repetitive blood pressure measurements at home carried out with well-calibrated, well-validated automatic oscillometric equipment. For the moment, mercury sphygmomanometers are essential for such validation of newly developed blood pressure measurement devices. Otherwise, the conclusions based on the results of long–term epidemiological studies on changes in population blood pressure may be seriously jeopardised.

3.5. Mercury sphygmomanometers

The mercury-containing sphygmomanometer should not be viewed as an absolute standard. It is however, with all its faults as an indirect blood pressure determination, the method used to establish our current knowledge. Since Riva-Rocci's times mercury sphygmomanometers associated with the occlusion-auscultatory technique have been used in clinical and epidemiological studies on hypertension. They represent the cornerstone for cardiovascular disease prognosis and prevention, as well as in the daily clinical management of patients with high blood pressure. As a result of this time-honoured use, blood pressure values are still quantified in mmHg both in current practice and in research, and doctors keep watching the mercury column as the most faithful indicator of the blood pressure levels in their patients. A commonly perceived advantage of mercury manometers lies in the fact that, when they are well maintained (see below), they offer "absolute" measurements of blood pressure, and represent a "gold standard" reference technique used to validate all other methods which provide information on blood pressure levels in mmHg without using a mercury column. The blood pressure measurement based on the mercury sphygmomanometer is an indirect blood pressure determination, and is difficult to perfectly mimic with other techniques unrelated to auscultation of Korotkov sounds.

3.5.1. Characteristics

The high-density of liquid mercury metal provides an acceptable short length of the rising column for visualization of the pressure in the cuff. Therefore, the mercury column in a sphygmomanometer is used as a simple, gravity-based unit. When properly maintained and serviced and when used by knowledgeable trained health professionals, it can give accurate indirect measurements of both systolic and diastolic pressure. Currently it is considered to be the most accurate technique (O'Brien et al. 2003).

A complete mercury sphygmomanometer requires a cuff, bladder, tubing and a rubber bulb, and should be maintained in good condition and serviced regularly according to the manufacturers' instructions. Mercury sphygmomanometers are easily checked and maintained, but great care should be taken when handling mercury. The revised European Standard (EN 1060 series) recommends that mercury sphygmomanometers display a warning to this effect (CEN 1995a).

3.5.2. Limitations

Despite its widespread availability for almost a century, there can be major problems with the use of mercury sphygmomanometers in clinical practice. Reports from hospitals and family practices have suggested that many mercury sphygmomanometers are defective because of poor maintenance (Beevers and Morgan 1993, Burke et al. 1982, Feher et al. 1992, Gillespie and Curzio 1998, Hutchinson et al. 1994, Markandu et al. 2000, Wingfield et al. 1996).

Moreover, several studies have shown that there is a lack of knowledge of the technical aspects of the actual blood pressure measurement in both doctors and nurses and other health care professionals who use the mercury sphygmomanometers. The reports also suggest that the technique of blood pressure measurement is not applied very well. Additionally, there is a lack of knowledge of the appropriate blood pressure equipment and how to maintain the devices so that they are calibrated and in pristine condition. One should be aware of the fact that issues of maintenance are a factor for every blood pressure measurement device.

There are several other limitations of using the auscultatory method which affect both mercury and aneroid manometers:

- Terminal digit preference: Tendency of the observer to round off the number to their choosing e.g. 144/96 mmHg as 140/100 mmHg or 150/90 mmHg (systolic/diastolic blood pressure). This is the zero preference. The observer finds it easier to read the prominent larger 10 mmHg markings instead of the smaller, 2 mmHg markings.
- Errors may occur when the manometer is not kept vertical (see fig. 1), and the device is rested on the side of the bed or, having it tilted against the pillow. This is an issue when the device is being used at the patient's bedside, not when used for public-health monitoring.

Positioning of the Hg manometer

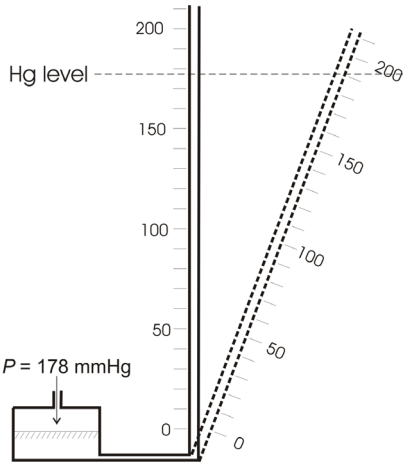

Figure 1: Measurement error due to incorrect positioning of the Hg manometer. In this diagram the incorrect positioning of the tube results in a measurement error of ca. 12 mmHg.

- Inflation/deflation system:

Another important limitation to consider is the performance of the inflation/deflation system and of the occluding bladder encased in a cuff, and proper application of auscultation with a stethoscope. Those issues apply to all blood pressure measuring devices using the auscultatory method.

The inflation/deflation system consists of an inflating and deflating mechanism connected by rubber tubing to an occluding bladder. The standard mercury sphygmomanometers used in clinical practice are operated manually, with inflation being effected by means of a bulb compressed by hand and deflation by means of a release valve, which is also controlled by hand. The pump and control valve are connected to the inflatable bladder and thence to the sphygmomanometer by rubber tubing. Leaks from cracked or perished rubber make accurate measurement of blood pressure difficult because the fall of the mercury cannot be controlled. The length of tubing between the cuff and the manometer should be at least 70 cm and that between the inflation source and the cuff should be at least 30 cm. Connections should be airtight and easily disconnected.

In addition, technical (maintenance) problems may exist such as:

(i) Oxidisation of the mercury is another very common occurrence, which can increase with time and make the columns difficult to read.

(ii) The markings on the column also fade with time, again making it impossible to read accurately.

(iii) Dynamic response, see 3.5.3.

3.5.3. Technical accuracy of Hg sphygmomanometers

The mercury manometers incorporate the (non SI unit) mmHg as a read-out system. The use of this manometer does not automatically guarantee that the cuff pressure measurement is always correct. In 1952, the Physikalisch-Technische Bundesanstalt in Germany issued requirements for these sphygmomanometers on a voluntary basis. The International Organisation of Legal Metrology published its first International Recommendation (IR 16) in 1973 and at approximately the same time national standards and similar documents were published in several countries such as the USA and Switzerland. Since then, these documents have been updated several times. To support the "Council Directive 93/42/EEC concerning medical devices" the European standards organisation CEN developed a standard (EN 1060, part 1-4) between 1995 and 2004 (CEN 1995a, 1995b, 1997, 2004), which became a harmonized standard in that framework. Recently the international standard organisations ISO and IEC jointly developed standards to test sphygmomanometers; they were published between 2007 and 2009 (IEC 2009, ISO 2007). These standards are expected to replace the CEN standards in the near future.

Regarding the accuracy of Hg manometer there are three main aspects to be considered:

- positioning of the Hg manometer (see above)
- dynamic response of the Hg column (see below)
- clearness of the display (see above)

Since the technical accuracy of the Hg manometer is affected by the inclination relative to gravity, means need to be provided to ensure the correct positioning of the reservoir and the tube, e.g. a water-level. Figure 1 illustrates the effect of incorrect positioning on the accuracy. According to ISO 81060-1 (ISO, 2007) a portable Hg manometer "shall be provided with an adjusting or locking mechanism to secure it in the position for use as indicated in the accompanying documents".

Dynamic response of the Hg column

To prevent the spillage of Hg the ISO 81060-1 standard requires the following:

The Hg manometer shall incorporate a stopping device at the top of the tube that

- permits both the inward and outward flow of air, and
- prevents the passage of liquid mercury.

The reservoir shall also be fitted with a stopping device to prevent the Hg from flowing out of the reservoir neck and into the attached tubing and permits the inward and outward flow of air.

When the passage of air is limited owing to contamination or deterioration of the stopping devices, the falling pressure is displayed with some delay by the mercury column in the tube. This delay prevents the user from reading the correct pressure value; when measuring during cuff pressure deflation, there will be a systematic error resulting in too high blood pressure values.

Consequently the metrological test of a Hg manometer has to include

- the accuracy of the static pressure display, checked in pressure steps not greater than 50 mmHg;
- the dynamic response by a rapid pressure change; and
- the clearness of the tube by visual inspection.

The following list summarises the technical features determining the accuracy of mercury sphygmomanometers (O'Brien et al. 2003).

Features affecting accuracy of the mercury sphygmomanometer:

- The top of the mercury meniscus should rest at exactly zero without pressure applied; if it is below, add mercury.
- The scale should be clearly calibrated in 2 mm divisions from 0 to 300 mmHg and should indicate accurately the differences between the levels of mercury in the tube and in the reservoir.
- The diameter of the reservoir must be at least ten times that of the vertical tube, or the vertical scale must correct for the drop in the mercury level in the reservoir as the column rises.
- Substantial errors may occur if the manometer is not kept vertical during measurement. Calibrations on floor models are especially adjusted to compensate for the tilt in the face of the gauge. Stand-mounted manometers are recommended for hospital use. This allows the observer to adjust the level of the sphygmomanometer and to perform measurement without having to balance the sphygmomanometer precariously on the side of the bed.
- The air vent at the top of the manometer must be kept patent, as clogging will cause the mercury column to respond sluggishly and to overestimate pressure.
- The control valve is one of the most common causes of error in sphygmomanometers and when it becomes defective it should be replaced. Spare control valves should be available in hospitals and a spare control valve should be supplied with sphygmomanometers.

3.6. Technical aspects of the alternatives to Hg sphygmomanometers

The Korotkov sounds in the artery may be detected by auscultation which may be performed either manually (by the observer) or automatically (by electronic equipment). Since the Hg manometer is only the pressure sensing and displaying component in the occluding cuff technique, other manometers can be used instead. Although a lot of different pressure measuring techniques are conceivable, the following two are applied in sphygmomanometers:

- An aneroid manometer with an analogue display (circular scale with a pointer) and
- An electrical pressure transducer with analogue look, but digital display.

In addition to the alternative devices using auscultation, there also exists the oscillometric technique which does not use auscultation, but instead uses the oscillation in the cuff pressure due to the pulsation in the artery.

3.6.1. Auscultatory mercury-free sphygmomanometers

3.6.1.1 Non-automated auscultatory devices

Sphygmomanometers using aneroid (or mechanical) gauges (based on an elastic pressure sensing element) are common alternatives to Hg sphygmomanometers. The aneroid machines do not use liquid to display the information about the estimated values for the blood pressure levels.

ANEROID sphygmomanometers have been available for probably as long as the mercury manometer. They are commonly used for handheld sphygmomanometers, but are also available for portable or wall-mounted sphygmomanometers. The reliability of the aneroid manometer is affected by the technical design of the device and the quality of its production to a much greater extent than the mercury manometer. As one example, the long-time stability (reproducibility) of the aneroid manometer requires a pre-aging of the elastic pressure sensing element.

Another important issue is the sensitivity to mechanical shock. A simple standard aneroid manometer will not usually withstand drops from the table or heavy strokes. Since this is not acceptable in daily life the ISO/IEC Joint Working Group was the first to introduce requirements on mechanical strength for portable and handheld aneroid manometers. With the exception of stationary non-automated sphygmomanometers, including the aneroid type, all devices must function normally following a free fall from 25 cm. Additional requirements exist for all non-automated sphygmomanometers, including the aneroid type when they are labelled "Shock Resistant"; these must withstand drops from 1 m without the loss of performance. Devices following the requirements of ISO 81060-1, especially those labelled "Shock Resistant", will be robust enough for normal handling.

However, there are some reservations about the maintenance of the mechanical parts of the aneroid machine (Coleman et al. 2005). Other limitations with auscultation are similar to those with mercury manometer.

ELECTRONIC devices translate the pressure in the cuff into analogue-like or numerical display. The Hg column is simulated by a LCD (or LED), or there is a numerical display, or the pointer of the aneroid gauge is simulated by LEDs (Graves et al. 2004, Stergiou et al. 2008a).

These devices measure the pressure of the cuff with an electrical transducer similar to an automated sphygmomanometer. Regarding the pressure measurement, these devices follow the requirements for automated sphygmomanometers. A disadvantage of these devices is that electrical power is required.

3.6.1.2 Automated auscultatory devices

The first automated sphygmomanometers became available in the 1970s. These devices were designed to replace the observer and their stethoscope with a microphone and some analogue electronics. The microphone is placed in a small pocket in the cuff. The analogue electronics amplifies and filters the Korotkov sound detected by the microphone, and each detected Korotkov sound is displayed by a flashing light (LED). The user of the device has to place the cuff on the upper arm, place the microphone over the brachial artery on the upper arm, and inflate and deflate the cuff manually. They also have to read the displayed cuff pressure at the moment the LED starts to flash for systolic and at the moment it ceases to flash for diastolic blood pressure. There are still some of these devices available on the market (see Figure 2). The main applications for these devices are blood pressure measurements in subjects with an irregular heart beat, as oscillometric sphygmomanometers cannot give reliable readings in these situations.

Figure 2 Example of an auscultatory sphygmomanometer, which indicates Korotkov sounds by a flashing LED (red LED on the left). The cuff with the microphone is not shown[3].

[Source: http://www.boso.de/Produktdetails.21.0.html?&tx_produkte_pi1[showUid]=34]

Another area of application of automated auscultatory sphygmomanometer is non-invasive blood pressure measurement during ergometric stress testing, because the oscillometric technique cannot be used here due to its sensitivity on arm movement. These devices are fully automated, i.e. they pressurise the cuff automatically and display numerical values of the blood pressure.

Figure 3 Ergometer with automated auscultatory sphygmomanometer[3]. [Source: http://testserver.vollewanne.de/de/sana-bike_250f/sana-bike_250f.php]

[3] Disclaimer: The devices shown on figures 2 and 3 are only for illustration as examples of the various existing applications irrespective of their validation status. The European Commission does not endorse their use or their manufacturers.)

The reliability of the blood pressure measurement of the automated auscultatory sphygmomanometer described above is highly dependent on the correct placement of the microphone over the brachial artery. Too much noise is another limitation of the application of such devices.

In recent years automated devices have been developed which measure the blood pressure using both the oscillometric and the auscultatory technique. These devices usually place the microphone not in the cuff but in the housing of the device. The Korotkov sound is transferred through the bladder and the hose to the microphone. Some devices give priority to the results determined by the oscillometric method, using the auscultatory signal for identifying artefacts due to arm movement or beats on the cuff. Other devices give priority to results determined by the auscultatory method and use the oscillometric measurement as a backup.

3.6.2. Non-auscultatory mercury-free sphygmomanometers

The non-auscultatory mercury-free sphygmomanometers use the oscillometric technique to measure the blood pressure based on changes in the artery pulsation during cuff inflation/deflation. These alternatives to the mercury sphygmomanometer are easy and uncomplicated to use. They do not use the auscultation technique, and it is easier to train users. Increasingly, they are used by patients for home blood pressure monitoring and also almost exclusively for 24-hour ambulatory blood pressure monitoring. They need very little maintenance, costs vary according to the additional capabilities of the machine, and calibration testing is needed regularly as per the manufacturer's instructions, usually within two years. The inflation of the cuff may be performed manually (semi-automated) or automatically; however, the deflation is controlled by the device.

3.7. Clinical aspects of the alternatives to Hg sphygmomanometers

A wide variety of devices can be used to measure blood pressure and apart from the intensive care setting, the majority remain non-invasive and include non-automated auscultatory devices (aneroid, non-mercury auscultatory), semi-automated and automated devices (that can be used either at the upper arm, wrist or finger). The alternatives to Hg sphygmomanometers have hugely different levels of reliability.

3.7.1. Auscultatory devices

ANEROID devices – These devices are mercury free, commonly used in clinical practice, and require auscultation to determine blood pressure. They consist of a system of bellows and gears that expand to display pressure using a gauge needle and a pressure display. These devices are easily susceptible to damage and drift of the cuff pressure measurement (Waugh et al. 2002) particularly if they are portable (Bailey et al. 1991) and this leads to inaccurate measurements. A recent study in a primary care setting (in the United Kingdom) has shown that more than 50 percent of aneroid devices had a cuff pressure measurement error >3mmHg compared to only 8 percent of mercury and automated devices combined (Coleman et al. 2005). This is consistent with previous literature. It is therefore recommended that these devices undergo a metrological check at least annually, although the implementation of this recommendation appears unlikely especially in primary care (Rouse and Marshall 2001). The number of erroneous readings obtained with aneroid devices is likely to be significant. Improvements in the technology to prevent measurement error may lead to a suitable and accurate alternative to the mercury sphygmomanometer. The use of harmonized ISO/CEN standards will promote further improvement of these devices.

ELECTRONIC non-mercury auscultatory devices: As an auscultatory alternative, electronic devices use a pressure sensor and a digital display (numerical, circular/linear

bar graph). Models such as the Accoson Greenlight 300 (Graves et al. 2004), PMS Mandhaus (Wilton et al. 2006) and Nissei DM-3000 (British Hypertension Society, 2006) have been introduced, all of which have received clinical recommendation following an independent accuracy assessment. As the pressure transducers used within these systems are less prone to measurement error than the bellows in aneroid devices, these auscultatory devices can be assumed to be more reliable if used by a trained observer.

The cuff pressure is displayed as a simulated mercury column using an array of LCDs, and also as a digital LCD readout. The cuff is deflated in the normal way and, when the first and fifth Korotkov sounds indicating systolic and diastolic pressure are heard, a button next to the deflation knob is pressed, which freezes the digital display to show systolic and diastolic pressures, thus offering the potential of eliminating terminal digit preference, which is a major problem with the clinical use of any auscultatory monitor. With such devices, the physician is still able to measure blood pressure using the traditional auscultatory technique, without having necessarily to rely on automated readings, and this is achieved without the problems associated with mercury columns or aneroid devices.

These devices are suitable for patients where clinical conditions such as arrhythmia and pre-eclampsia may preclude the use of automated oscillometric devices. However the reading of such devices cannot be assumed to be equivalent to the reading of a mercury column, where the interpretation of a falling column of mercury with its own inherent dynamics, with an intermittent signal of Korotkov sounds, may not be the same as an electronic alternative. For this reason formal validation is required for any new device being introduced on the market. In addition features that are added to assist with the blood pressure determination, e.g. a hold button, may introduce an error as it does not control for the recognition, and reaction time and may result in a device not reaching an acceptable standard (Stergiou et al. 2008a). However, studies on the physician's reaction time and decision time during blood pressure measurements with this method are in progress to improve the reliability of this approach.

Some non-mercury professional devices allow for both automated electronic (oscillometric) as well as auscultatory blood pressure measurement by an observer using a digital manometer (El Assaad et al. 2002, Omboni et al. 2007, Stergiou et al. 2008b, Stergiou et al. 2008c).

3.7.2. Automated non-auscultatory (oscillometric) devices

There is an ever-increasing market for oscillometric blood pressure devices that have also increased home surveillance such as self-measurement and ambulatory/24hr monitoring. Home blood pressure measurement has been shown to be more reproducible than office blood pressure measurement (Stergiou et al. 2002) more predictive of cardiovascular events (Bobrie et al. 2004, Ohkubo et al. 2004) and reliable when used by non-clinicians (Nordmann et al. 1999). The out-of-office measurements are effective at removing the white-coat effect (Parati et al. 2003) particularly when using an averaging mode (Wilton et al. 2007). Telemonitoring enables the patient to transmit home measurements directly to the clinician's computer for further analysis, potentially enhancing early identification, reducing hospital visits (Pare et al. 2007) and improving the degree of blood pressure control also in general practice (Parati et al. 2009a).

Automated devices are generally intended for use on the upper arm, but finger and wrist devices are also available. Few of these latter devices have been shown to be accurate according to independent accuracy assessments; only a small minority of wrist devices assessed achieved an acceptable accuracy (five in total) (O'Brien and Atkins 2007). Wrist devices are sensitive to errors related to positioning of the wrist at heart level, and some devices have position sensors. Very few of the wrist devices have passed clinical validation after independent assessment (Altunkan et al. 2006, Nolly et al. 2004). However, even the validated wrist devices with position sensors appear to give

significantly different blood pressure values than arm devices in a large proportion of hypertensive patients (Stergiou et al. 2008d), while in an earlier study no such differences were observed (Cuckson et al. 2004). The European Society of Hypertension Guidelines state the preference of arm over wrist oscillometric devices (O'Brien et al. 2003, Parati et al. 2008b). No finger device has yet achieved the established validation standards (Elvan-Taspinar et al. 2003, Schutte et al. 2004).

The oscillometric technique is usually used by automated devices to determine blood pressure by analysing the pressures transmitted through arterial oscillations/vibrations that occur during cuff inflation and/or deflation. The point of maximum oscillation equates to the mean arterial pressure. The recording of pressure waves is dependent on the anatomical position, elasticity and size of the artery, as well as the distribution of the surrounding tissue which is particularly difficult in the wrist. A device specific algorithm equates these signals to the pressure obtained by the pressure transducer. The technique is not generic in any way, and each device must have its algorithm validated.

Automated blood pressure measurement will eliminate the observer errors associated with the use of the manual auscultatory technique such as terminal digit preference, threshold avoidance, observer prejudice, rapid deflation etc. (Beevers et al. 2001). However, clinically significant differences exist between measurements obtained through automation compared to auscultation in many devices. Automated device accuracy is not only device dependent, but also user dependent. As these devices are more likely to be used by untrained individuals, errors related to selecting correct cuff size and taking the recommended arm position, ensuring no movement or talking during device measurement, or allowing for sufficient rest before measurements may be more pronounced than mercury sphygmomanometers. Various guidelines have been published for the correct use of automated devices with specific methodologies advocated (Chobanian et al. 2003, O'Brien et al. 2003, Parati et al. 2008a), but are not as established as training for auscultatory blood pressure measurement.

Automated devices have accuracy limitations in special groups such as those with vascular damage that influences the oscillometric signal: these include patients with diabetes, arrhythmias or pre-eclampsia, and the elderly. This is related to arterial/vascular changes in these patients, which are likely to influence the recording of pressure waves by the device. The British Hypertension Society and some websites list devices that have achieved clinical recommendation under these conditions. Arrhythmias maybe detected by devices fitted with an 'irregular pulse detection' indicator; however, clinical validation for measuring blood pressure during arrhythmias has not yet been performed. This is confounded by not having a reliable reference value as the "gold standard" as mercury sphygmomanometer is itself an indirect measure of blood pressure and how blood pressure relates to this measure is unknown in arrhythmias. A limited number of devices have been validated and found accurate for use in pregnancy (Shennan and de Greeff 2007, Chung et al. 2009) and most of these are inaccurate in pre-eclampsia. There is one anecdotal report of a maternal death in pre-eclampsia when an oscillometric device (not validated for this condition) was used and underestimated the blood pressure level (Lewis and Drife 2001).

There are some "preliminary positive" data regarding the accuracy of oscillometric devices in "difficult" populations, such as in patients with end-stage renal disease (Thompson et al. 2007), atrial fibrillation (Watson and Lip 2006), the elderly (Omboni et al. 2007) and children (Stergiou et al. 2006). However, it should be realised that there are always some patients in which the oscillometric blood pressure measurement might differ significantly from that taken by a mercury sphygmomanometer without apparent reason, probably influenced by arterial wall properties and pulse pressure (Stergiou et al. 2009, Van Popele et al. 2000,).

An accurate automated sphygmomanometer capable of providing printouts of systolic, diastolic and mean blood pressure, together with heart rate and the time and date of measurement, should eliminate errors of interpretation and abolish observer bias and terminal digit preference. Moreover, the need for elaborate training of observers would

no longer be necessary, although a period of instruction and assessment of proficiency in using the automated device will always be necessary. Another advantage of automated measurement is the ability of such devices to store data for later analysis (Parati G et al. 2008b). This development is in fact taking place, and a number of long-term outcome studies are using automated technology to measure blood pressure instead of the traditional mercury 'gold standard'. For example, in the large Anglo–Scandinavian Cardiac Outcome Trial, the validated Omron HEM-705CP automated monitor was used including thousands of patients followed for about five years (Dahlöf et al. 2005, Hansson et al. 1998, Yusuf et al. 2008).

3.7.3. Conclusions/Discussion

The mercury sphygmomanometer is disappearing from use and there are many alternative devices available to replace it. Blood pressure measurement with the auscultatory technique by a trained observer, using the mercury sphygmomanometer remains the most accurate and reliable form of indirect blood pressure measurement and is currently regarded as the gold standard.

The alternative devices using auscultation have similar limitations as the mercury sphygmomanometers regarding the observer bias associated with auscultation itself. Even though oscillometric instruments are not considered as true "alternatives" to Hg sphygmomanometers because they operate under a completely different principle, those instruments are currently replacing the Hg sphygmomanometers. The advent of accurate oscillometric devices, however welcome, is not without problems. First, oscillometric devices have been notorious for their inaccuracy in the past, although more accurate devices are now appearing on the market. Secondly, most of the available oscillometric devices were designed for self-measurement of blood pressure by patients, and it should not be assumed that they will be suitable for clinical use, or that they will remain accurate with use, although some are being used successfully in hospital practice. Thirdly, oscillometric techniques cannot measure blood pressure accurately in all situations, particularly in patients with pre-eclampsia, arrhythmias such as atrial fibrillation, and there are also individuals in whom these devices cannot measure blood pressure, for reasons that are not always apparent (Stergiou et al. 2009a, Van Popele et al. 2000).

All alternative blood pressure measurement devices need to be clinically validated in clinical protocols against the current gold standard of the mercury sphygmomanometer, until an alternative device is developed and recognised as such. Several international protocols, such as the ISO protocol (in preparation), the British Hypertension Society (BHS) and the European Society of Hypertension (ESH) International Protocol are available for such a clinical validation. A list of validated oscillometric devices is available on dedicated websites, such as the British Hypertension Society as well as other national learned societies.

3.8. Quality requirements for the alternatives to the Hg manometers

3.8.1. General (ISO standards)

In December 2007 the standard ISO 81060-1 "Non-invasive sphygmomanometers – Part 1: Requirements and test methods for non-automated measurement type" was published. This standard addresses all kinds of sphygmomanometers, "which, by means of inflatable cuffs, are used for the non-invasive blood pressure measurement by operator observation" (ISO 2007). Automated sphygmomanometers are addressed in a different standard issued in 2009: IEC 80601-2-30 "Medical Electrical Equipment – Part 2-30: Particular requirements for the basic safety and essential performance of automated non-invasive sphygmomanometers" (ISO 2009). The standard ISO 81060-2 "Non-invasive sphygmomanometers – Part 2: Clinical validation of the automated

measurement type (ISO in preparation). All three standards are expected to become European harmonized standards in the near future.

The ISO 81060-1 addresses requirements for the alternative non-automated sphygmomanometers. Because these requirements are identical for all possible manometers, they include requirements for accuracy of the cuff pressure measurement and for the resistance to vibration and shock. Some requirements are related to the specific needs of aneroid manometers. The ISO/CEN standards are non-mandatory but may be used as tools for checking the reliability of the alternatives to Hg sphygmomanometers and comply with the essential requirements of the medical device directive (93/42/EEC).

3.8.2. Technical Verification

Regular metrological testing is needed to ensure the accuracy of the blood pressure devices. Periodic maintenance and accuracy testing may be initiated by the manufacturers instructions or by legal measures (Germany, Austria, Czech Republic, and Slovakia). Statistical data on the percentage of failure of such verification exist only from ten and more years ago, at that time the number was between eight and ten percent per year (PTB-Mitteilungen, 1990). There is no indication that this number has dramatically changed.

The key element of the verification is the testing of the accuracy of the static pressure measurement by the manometer of the sphygmomanometer. In pressure steps of not more than 50 mmHg over the whole measuring range the error of the pressure measurement has to be determined. For this test a periodically calibrated reference manometer has to be used, usually a digital manometer utilising a piezo-resistant transducer. Mercury manometers are not appropriate for use as reference manometers because their resolution is not good enough and it is not easy to identify the meniscus of the mercury column in order to read exact values (less than 1.0 mmHg).

3.8.3. Clinical validation

Independent device accuracy assessment within a clinical setting is recommended before introduction and routine clinical use. Various protocols have been published to assess automated devices against a mercury sphygmomanometer during clinical use and these are referred to as clinical validation protocols. The International Protocol of the European Society of Hypertension (O'Brien et al. 2002) and the protocol of the British Hypertension Society (O'Brien et al. 1993) are widely accepted, and most commonly used in publications (see Figure 4), although similar protocols exist in Germany and USA SP10 (AAMI 2007). In addition, CEN standards including clinical validation protocols are available for the manufacturers to use (EN 1060-1, 2 and 3, CEN 1995a, 1995b, 1997). In the recent years there has been a steady increase in the clinical validation of blood pressure measurement devices (see Figure 4). All clinical validation protocols require the use of Hg sphygmomanometers as reference but the CEN standards also allow the use of alternative measurement devices.

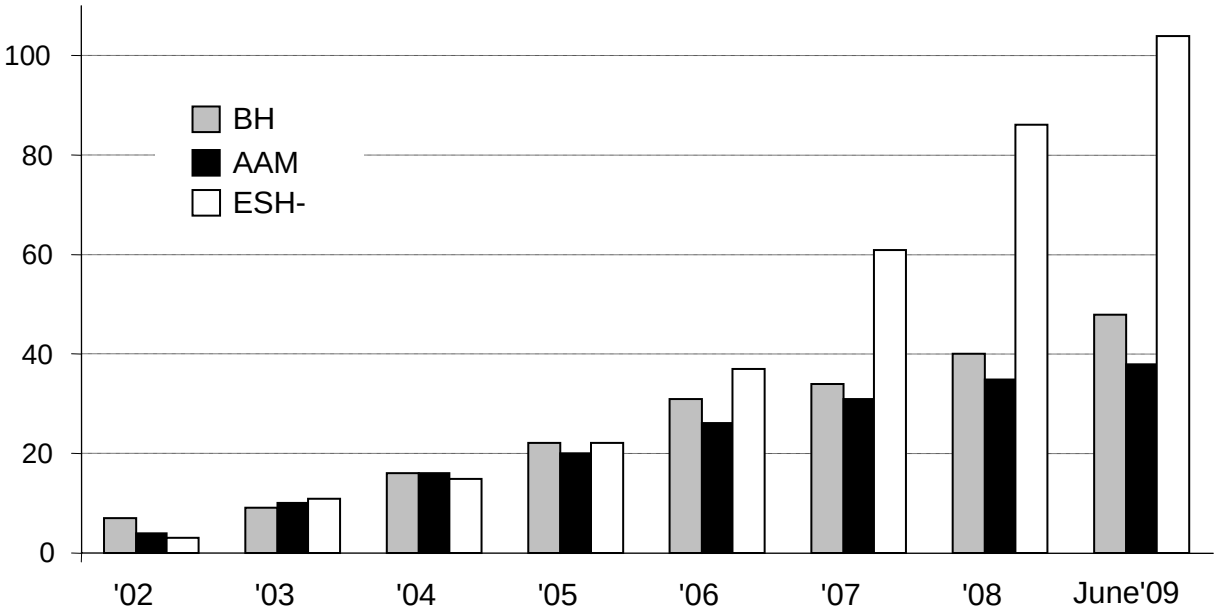

Figure 4 Cumulative graph of validation studies performed according to the European Society of Hypertension International Protocol (ESH-IP) compared to the British Society of Hypertension (BHS) and the US Association for the Advancement of Medical Instrumentation (AAMI) protocols from 2002 until June 2009 (Modified from Stergiou et al. 2009b).

The clinical validation protocols presented on Figure 4 require a series of consecutive blood pressure measurements taken over a wide range of blood pressures using the test device in comparison to the mercury sphygmomanometer as a reference. The accuracy of the test device is graded (A-D – where A or B is a pass) or given a pass/fail for systolic and diastolic pressure accuracy according to each protocol. This is usually based on the number/percentage of differences between observer and device in three categories: differences ≤5mmHg, ≤10mmHg and ≤15mmHg. In addition the mean difference and standard deviation (SD) of the difference is calculated and measured against the ANSI/AAMI SP10-1992 standard (AAMI 2007), which requires a mean difference (SD) ≤5 (8) mmHg for clinical recommendation. Devices that have been assessed according to these standards are subsequently listed on the British Hypertension Society and other websites after independent review by the respective committee members of these organisations who give a final verdict as to whether the device should be recommended for clinical use or not, based on whether the protocol guidelines were adequately followed.

Despite the concern that the majority of devices have not yet been validated, it is encouraging to note that the number of validation studies has steadily risen from only 10 in 1990 to 104 studies in 2009 [Stergiou et al 2009b). The British Hypertension Society and other websites are valuable resources for both clinicians and patients.

3.9. Discussion

Mercury is toxic, and there exists the Community Strategy Concerning Mercury with the aim of restricting the use of mercury. Mercury sphygmomanometers have been instrumental in developing the present knowledge on hypertension as a risk factor for cardiovascular diseases and its control by treatment. Therefore, they are considered the gold standard for blood pressure measurement. The need for accurate clinical measurement will always be present, and the fact that important clinical decisions will

continue to be made on very small numbers of readings (often one, and rarely more than three) emphasizes the need for maximum accuracy.

Several aneroid and automated alternative blood pressure devices have been validated against the mercury sphygmomanometer. Currently there are no reports published on any electronic device that has been validated using aneroid machines. It can be envisioned that in the future one of the alternative blood measurement devices might also be suitable as a reference for clinical validation of newly developed devices. Until a suitable mercury-free device is developed and recognised as a reference for blood pressure measurement, mercury sphygmomanometers will be needed for clinical validation studies of aneroid and automated blood pressure measurement devices.

3.10. Recommendations

It is recommended that for clinical validation studies mercury sphygmomanometers should remain available as reference for alternative mercury-free blood pressure measurement devices.

4. OPINION

Mercury and its compounds are highly toxic to humans, ecosystems and wildlife. Mercury can exist in several chemical forms (Hg^{o}, Hg^{1+}, Hg^{2+}), each with its own toxicological profile. In general terms, the toxicity of these chemical forms is highest for the organic mercury compounds, followed by elemental mercury and inorganic mercury compounds. In measuring devices like sphygmomanometers and previously thermometers, elemental liquid mercury is used. A Community Strategy Concerning Mercury was adopted in January 2005 with the key aim of reducing mercury levels in the environment and reducing human exposure. This Opinion addresses the issue of whether the replacement of mercury-containing blood-pressure measuring devices (sphygmomanometers) would (i) endanger proper health care including specific groups of patients, and/or (ii) compromise long term translational epidemiological studies for public health. In addition, the availability and quality of alternative devices for blood pressure measurements have been considered.

Blood pressure measurement is vital for the prevention and treatment of blood pressure related diseases, and for monitoring cardiovascular homeostasis. The indirect measurement of blood pressure with mercury sphygmomanometers (applying the auscultatory technique) has identified arterial hypertension as a major risk factor for cardiovascular diseases. The auscultation method is based on the observation of the recurrence of the blood flow in the occluded artery (using a cuff) of the upper arm by listening to the sounds generated by the recurrent blood flow and disappearance of the sounds when the occlusion is completely removed (by dilation of the cuff), and normal blood flow is restored. In addition to use in clinical settings the mercury sphygmomanometer is also used in long-term epidemiological/observational studies on cardiovascular disease development. A change in population blood pressure has a direct effect on the morbidity and mortality of cardiovascular diseases. Based on long-term experience, blood pressure measurement using the mercury sphygmomanometer is regarded as the gold standard method for indirect measurement of blood pressure. Several factors, however, affect the measurement of blood pressure including the technical skills of the observer, the inherent variability of blood pressure, the accuracy of the device, and the difficulty in measuring blood pressure in some special groups (e.g. the elderly, patients with arrhythmias, patients with a large arm, children, and pregnant women). The use of the mercury sphygmomanometer has practical and technical limitations, and requires specific training. In addition, there should be a special emphasis on regular maintenance of the mercury sphygmomanometer in order to maintain its accuracy. When blood pressure is measured by a trained observer using the auscultatory technique, the mercury sphygmomanometer currently remains the most accurate device for indirect blood pressure measurement.

The mercury column functions as a pressure sensing and displaying component, so it seems likely that this can be replaced by a mercury-free manometer. Indeed, mercury-free alternatives for pressure measurement are commercially available such as the aneroid manometer and the electronic pressure transducer. These alternative sphygmomanometers use auscultation for determination of the blood pressure, and therefore, have the advantages and limitations (such as the observer performance) which also apply to the mercury sphygmomanometer, and are characteristic of the auscultatory technique. In addition, there are non-auscultatory, non-mercury devices available which use the oscillometric technique to measure blood pressure based on changes in arterial pulsation during cuff inflation/deflation. Oscillometric instruments operate under a completely different principle and are thus not considered as true "alternatives" to Hg sphygmomanometers. The various alternatives have widely varying levels of accuracy, emphasising the importance of clinical validation. Regular maintenance is of the utmost importance for proper functioning of all measurement instruments. Even validated oscillometric devices may have accuracy limitations in special patient groups, including patients with arrhythmias, diabetes, the elderly and pre-eclampsia. This is related to the arterial/vascular changes in these patients affecting the oscillometric signal. These

limitations do not apply to devices using the auscultatory technique. Therefore, validated non-mercury auscultatory alternatives are appropriate for these patients.

For alternative blood pressure measurement devices a metrological verification is needed to ensure the accuracy of the measurements. In addition, an independent device accuracy assessment is recommended to evaluate the clinical performance. Various clinical validation protocols are available to assess the accuracy of automated alternative devices against mercury sphygmomanometers.

In conclusion, the mercury sphygmomanometer is gradually disappearing from clinical use and there are several appropriate alternatives available. When blood pressure is measured by a trained observer using the auscultatory technique, the mercury sphygmomanometer or a validated auscultatory alternative currently remains the most accurate instrument for indirect blood pressure measurement, especially for certain patient groups. The alternative devices using auscultation have similar limitations as the mercury sphygmomanometers regarding the observer technique and bias associated with auscultation itself. These may be avoided by using automated oscillometric devices, which, when properly validated, allow accurate blood pressure measurements. For all blood-pressure measuring devices, regular maintenance is of primary importance.

In order to maintain a high-level quality of blood pressure measurements it is recommended that mercury sphygmomanometers remain available as reference standards for clinical validation studies of existing and future non-mercury-containing blood-pressure measurement devices. It is emphasised that mercury devices should remain available as standards until an alternative standard is developed and recognised.

4.1. Specific answers to questions raised in the Terms of Reference

Question 1

Is there sufficient evidence to demonstrate that mercury-free blood pressure measuring devices such as aneroid or electronic instruments are *generally reliable* substitutes for mercury-containing sphygmomanometers?

Yes. There is sufficient scientific evidence that mercury-free blood pressure measuring devices (when clinically validated) are generally reliable substitutes for mercury-containing sphygmomanometers in routine clinical practice. These alternative devices include both auscultatory devices requiring a trained observer, and also automated oscillometric devices for which some instruction is needed.

Question 2

Have mercury-free sphygmomanometers been adequately validated over a *wide range* of blood pressures, ages, and clinical conditions to allow for routine use in hospitals and outpatient settings?

Yes. Clinically validated, auscultatory mercury-free devices are equivalent to mercury sphygmomanometers. For the oscillometric devices the situation is different as these devices have mainly been clinically validated in adult populations including a wide range of blood pressures but not in a wide range of ages and clinical conditions.

Question 3

Have mercury-free sphygmomanometers been adequately validated for the diagnosis of hypertension in *specific clinical conditions* such as arrhythmia, pre-eclampsia in obstetrics and certain vascular diseases?

Yes. Clinically validated, auscultatory mercury-free devices are equivalent to mercury sphygmomanometers, and are thus suitable for these specific groups of patients. In addition, some oscillometric devices have achieved accuracy in certain conditions although in others, like arrhythmias, the auscultation technique is necessary. Moreover,

there is a need for more clinical validations of oscillometric devices to make them usable in specific groups of patients, including elderly patients, children, and pre-eclamptic women.

Question 4

Are mercury-based sphygmomanometers essential as reference devices for *validation* of long-term clinical epidemiological studies enrolling patients with hypertension?

Yes. Mercury-containing sphygmomanometers are considered essential as reference devices for the clinical validation of the alternatives. For on-going, long-term epidemiological studies currently using mercury sphygmomanometers it is advisable not to change the method of measurement. Therefore, it will be necessary to keep mercury sphygmomanometers available in order to compare them with the alternatives in these studies.

Question 5

Are mercury-based sphygmomanometers essential as reference devices for *calibration* of the mercury-free sphygmomanometers when the latter are used for routine diagnostic purposes?

No, they are not essential as reference devices for the metrological verification (calibration) needed to ensure the accuracy of the measurement of the blood pressure devices. In general, more accurate manometers are available for metrological verification.

Question 6

Is SCENIHR aware of any *adverse effects* for patients' health due to the replacement of mercury-containing sphygmomanometers by mercury-free alternatives?

No evidence was found for adverse effects for patients' health in clinical settings due to the replacement of mercury-containing sphygmomanometers by validated mercury-free alternatives. There are adequate alternatives in most clinical condition/setting. In special conditions, such as pre-eclampsia, non-mercury auscultatory devices should be preferred until further validation of oscillometric devices.

5. MINORITY OPINION

None

6. LIST OF ABBREVIATIONS

AAMI	Association for the Advancement of Medical Instrumentation
ABPM	Ambulatory Blood Pressure Measurements
ANSI	American National standard Institute
BHS	British Hypertension Society
CEN	European Organisation for Standardisation
EEC	European Economic Community
ESH	European Society of Hypertension
ESH-IP	European Society of Hypertension International Protocol
Hg	Mercury
IEC	International Electrotechnical Commission
ISO	International Organisation for Standardisation
LCD	Liquid Crystal Display
LED	Light-Emitting Diode
OIML	Organisation Internationale de Métrologie Légale (International Organization of Legal Metrology)
PTB	Physikalisch-Technische Bundesanstalt
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SI	Système international d'unités (International System of Units)

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Scientific Committee on Health and Environmental Risks

SCHER

Opinion on Mercury in Certain Energy-saving Light Bulbs

The SCHER adopted this opinion at its 7th plenary on 18 May 2010

About the Scientific Committees

Three independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.

They are: the Scientific Committee on Consumer Safety (SCCS), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and are made up of external experts.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Evaluation Agency (EMEA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCHER

Opinions on risks related to pollutants in the environmental media and other biological and physical factors or changing physical conditions which may have a negative impact on health and the environment, for example in relation to air quality, waters, waste and soils, as well as on life cycle environmental assessment. It shall also address health and safety issues related to the toxicity and eco-toxicity of biocides.

It may also address questions relating to examination of the toxicity and eco-toxicity of chemical, biochemical and biological compounds whose use may have harmful consequences for human health and the environment. In addition, the Committee will address questions relating to methodological aspect of the assessment of health and environmental risks of chemicals, including mixtures of chemicals, as necessary for providing sound and consistent advice in its own areas of competence as well as in order to contribute to the relevant issues in close cooperation with other European agencies.

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All Declarations of working group members are available at the following webpage: http://ec.europa.eu/health/scientific_committees/environmental_risks/members_wg/index_en.htm

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1. BACKGROUND

Certain energy-saving light bulbs, namely compact fluorescent lamps (CFLs), are widely available on the market and are offered for saving electricity. They also eventually reduce carbon dioxide emissions particularly from coal-fired power plants. They fulfil the requirements of Commission Regulation (EC) No 244/2009 on ecodesign requirements for non-directional household lamps[1] (Ecodesign Regulation), in contrast to traditional incandescent light bulbs which will be phased out progressively in accordance with the Regulation.

According to Directive 2002/95/EC on the restriction of hazardous substances in electrical and electronic equipment (RoHS Directive)[2], a mercury content in CFLs not exceeding 5 mg per lamp is allowed (the mercury exemption for CFLs is listed as n° 1 in the Annex to the RoHS Directive). An indicative benchmark (best available technology) of 1.23 mg of mercury in energy efficient CFLs is provided in the above-mentioned Ecodesign Regulation (Annex IV, n° 3 of the Ecodesign Regulation).

The above-mentioned 5 mg mercury tolerance for CFLs is being reviewed on a regular basis, in line with the four-year-review period prescribed by the RoHS Directive. Such reviews aim at assessing whether the elimination or substitution of mercury is technically possible through specific design changes or through the use of other materials, provided that the negative impacts for the environment, health and/or consumer safety generated by the substitution do not outweigh the possible benefits thereof. This is indicated in Article 5 (1.c) of the RoHS Directive.

At the end of 2007, DG Environment commissioned a technical and scientific assessment of this exemption including, among others, consultation of interested stakeholders (e.g. producers of electrical and electronic equipment, environmental organisations and consumer associations). According to this assessment (Öko-Institut and Fraunhofer IZM 2009), finalised in March 2009, the elimination of mercury in CFLs is still technically and scientifically impracticable.

On the basis of this assessment, the Commission will take a decision for the review of this mercury exemption before July 2010, after consultation with the RoHS Technical Adaptation Committee (RoHS Directive, Article 7). In support of any future review, it may further be appropriate to consider the potential risks associated with the release of mercury from a CFL when it accidentally breaks in the hands of a consumer, for example while replacing a CFL. In such a case, long-term toxicological limit values may be exceeded up to 6,000 times, and the consumer's exposure to mercury may only be 10-fold below acute intoxication. Further information can be found in annex 2. Further considerations on the risk from mercury have been published elsewhere (Groth 2008), including in the event of a CFL breakage in a consumer home.

Clean-up of the debris of a broken CFL has been described as complicated, requiring, for example, the removal of the mercury droplets with adhesive tape and their disposal as special waste. This again points to the relevance of the risk caused by the breakage of a CFL in a consumer's home.

As regards the impacts of mercury emissions related to CFLs, the life-cycle of CFLs should be considered so as to weigh the risks of a mercury escape from CFLs, be it by accidental breakage or disposal as waste (instead of an appropriate recycling) against the reduction of mercury emissions from coal-based power plants due to the lower electricity consumption of CFLs (Aucott et al. 2004). Available information indicates that the reduced electricity consumption of CFLs reduces the need for

[1] OJ L 76, 24.3.2009, p. 3

[2] OJ L 17, 13.2.2003, p. 19

electricity, thus the electricity production would release less mercury, and such a decrease could, on balance, save about 10% of the mercury emissions into the environment.

Concerning disposal, Directive 2002/96/EC on waste from electrical and electronic equipment[3] (WEEE Directive) requires Member States to adopt appropriate measures in order to minimise the disposal of WEEE, including CFLs, as unsorted municipal waste and to remove mercury from the collected CFLs [see article 5 and Annex II (2) of the WEEE Directive]. A proposal to recast the Directive, made by the Commission in December 2008, strengthens the requirements for separate collection, and specifies that transport of WEEE is to be carried out in a way which optimises the confinement of hazardous substances[4].

2. TERMS OF REFERENCE

Against the above background, taking into account all available scientific assessments on mercury, including the Risk Assessment under 793/93/EEC and the previous opinions of SCHER, CSTEE, SCENIHR and the EFSA Scientific Panel on Contaminants in the Food Chain, the SCHER is requested to:

A) Assess the possible health risks to consumers, from the mercury released from accidental breakage of CFLs. In doing so, the SCHER is asked to consider risks to certain vulnerable groups of population such as children or pregnant women;

B) Taking into account the technical and scientific assessment from Öko-Institut and Fraunhofer IZM (2009), assess the potential risks to human health and environment of the alternatives available to reduce, eliminate or substitute the mercury in CFLs;

C) Assess the risk to the environment from the mercury liberated upon disposal of CFLs, taking into account the above-mentioned limit of 5 mg mercury per CFL, the requirements for separate collection of the CFLs and for removal of the mercury from the collected CFLs. Would the risk be significantly reduced by strengthening these requirements?

D) Weigh the risks identified in A), B) and C) against the reduction of mercury emissions from coal-based power plants due to the lower electricity consumption of CFLs compared to conventional household lamps. Incorporate and consider the potential health risks from mercury when CFLs are broken, accidentally in the household or after disposal, into the life cycle analysis of CFLs, taking into account the reduction of human health and environment risks resulting from the potential reduction in mercury emissions from coal-based power plants and the reduction of the emission of other pollutants due to the lower electricity consumption of CFLs compared to conventional household lamps.

[3] OJ L 17, 13.2.2003, p.24.
[4] Articles 5 and 6 of the WEEE proposal: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0810:FIN:EN:PDF

3. OPINION

3.1 Question A

Assess the possible health risks to consumers, from the mercury released from accidental breakage of CFLs. In doing so, the SCHER is asked to consider risks to certain vulnerable groups of the population such as children or pregnant women

Toxicology of elemental Hg

Effects of Hg^0 inhalation in humans have mainly been characterised after accidental short-term and high-concentration exposures, and after long-term occupational exposures. After inhalation of very high concentrations, orders of magnitude above currently valid occupational exposure limits (e.g., the German MAK-value is 84 $\mu g/m^3$) symptoms of acute toxicity characterised by restlessness, inflammatory responses in the lung, gastroenteritis and renal damage have been reported. In addition, neurotoxic symptoms such as tremor and increased sensitivity to stimuli are also reported.

After long-term Hg^0 inhalation exposures, effects on the central nervous system and kidney apparently are the most sensitive end-points of toxicity. These include effects on a wide variety of cognitive, sensory, personality and motor functions. In general, symptoms subside after removal from exposure. However, persistent effects (tremor, cognitive deficits) have been observed in occupationally exposed subjects 10-30 years after cessation of exposure.

Persons in rooms after breakage of a CFL may be exposed to mercury by inhalation and by oral intake. After inhalation, more than 80% of inhaled Hg^0 vapour is absorbed by the lungs. Ingested Hg^0 is poorly absorbed in the gastrointestinal tract (less than 0.01%). Skin absorption is insignificant in relation to human exposure to mercury vapour. The elimination of Hg^0 after inhalation is slow (half-life of inhaled Hg^0 is 60 days) with most being eliminated through urine (as mercury ions) and faeces (as Hg^0). A small amount of absorbed Hg^0 is also eliminated via exhalation and sweat (ATSDR 1992; Goldman and Shannon 2001; Halbach and Clarkson 1978; Houeto et al. 1994).

Studies on workers exposed to Hg vapour have reported a clear increase in symptoms of dysfunction of the central nervous system at exposure levels greater than 0.1 mg/m^3. Some studies also reported subtle neurotoxicity at lower concentrations. Self-reported memory disturbances, sleep disorders, anger, fatigue, and/or hand tremors were increased in workers chronically exposed to an estimated air concentration of 0.025 mg/m^3. In a recent assessment of all studies on the exposure-response relationship between inhaled Hg vapour and adverse health effects, IPCS concluded that several studies consistently demonstrate subtle effects on the central nervous system in long-term occupational exposures to mercury vapour at exposure levels of approximately 20 $\mu g/m^3$ or higher (WHO/IPCS, 2002 Hg).

The kidney is, together with the central nervous system, a critical organ for exposure to mercury vapour. Elemental mercury can be oxidized to Hg^{2+}. The kidney accumulates inorganic mercury to a larger extent than most other tissue. High-dose exposure to Hg^{2+} may cause (immune-complex mediated) glomerulonephritis with proteinuria and nephritic syndrome. Effects on the renal tubules, as demonstrated by increased excretion of low molecular proteins, have been shown at low-level exposure, and may constitute the earliest biological effect occurring after long-term exposure to air concentrations of 25-30 $\mu g\ Hg^0/m^3$.

A large number of serious and even fatal intoxications have been described after ingestion of inorganic mercury compounds, but data from humans do not allow identification of no-adverse exposure levels, especially in long-term exposure. From

studies on experimental animals, a No-Observed-Adverse-Effect Level (NOAEL) of 0.23 mg/kg per day was identified (US ATSDR, 1999; WHO/IPCS, 2002)

Children exposed to Hg^0 vapours may exhibit symptoms like breathing difficulty, swelling and erythema of the hands and feet, and pealing pink skin at the tips of the fingers and toes. These symptoms are collectively called acrodynia (Albers et al. 1982; ATSDR, 1992, 1999; CDC 1991; Clarkson 2002; Isselbacher et al. 1994; Satoh 2000).

Children and the foetus during various stages of their development are more vulnerable than adults. Fast cell proliferation and migration occur during the second and third trimester of gestation and continues to occur in the first 2-3 years of age. Neural development extends from the embryonic period through adolescence (Rice and Barone, 2000). Since mercury inhibits cell division and migration during development, the foetus and young children are particularly at risk when exposed.

Exposure assessment

A fluorescent light bulb contains 5 mg of Hg. Assuming release of the total Hg-content of a lamp after breakage into an average room, Hg concentrations in the range of or above occupational exposure limits (100 $\mu g/m^3$) can be derived. These concentrations are also well above regulatory limits for Hg in a general environment. Regarding environmental exposures, the US EPA has defined a reference concentration (RfC) of 300 ng/m^3, and the US CDC derived a maximum residue limit (MRL) of 200 ng/m^3. However, it needs to be recognized that these concentrations are applied to life-long inhalation exposures, are based on conservative extrapolations, and are considered protective for all groups of the population, including potentially sensitive subgroups. . The US EPA also has defined an acute RfC of 1.8 $\mu g/m^3$ for Hg. The acute RfC is an estimate (with uncertainty spanning an order of magnitude) of an acute continuous inhalation exposure (time weighted average with a duration up to 24 hours) without appreciable risks of deleterious effects during a life time for the human population also including sensitive subgroups.

The simple assumption of a complete evaporation of the Hg content from a broken light bulb apparently results in a wide overestimation of air concentrations of Hg over time. Indeed, most of the released Hg may re-condense, due to the low volatility of Hg. Measured data suggest that a broken CFL may produce Hg concentrations of 8 to 20 $\mu g\ Hg/m^3$ for a short time after the breakage. Air concentrations rapidly decline: concentrations $\leq 2\ \mu g\ Hg/m^3$ have been measured in a house two days after an Hg spill from a CFL. An experimental study indicates even lower concentrations, between 0.8 and 0.1 $\mu g/m^3$ Hg^0, depending on CFL lamp type, in a room after CFL-breakage (Fig. 1).

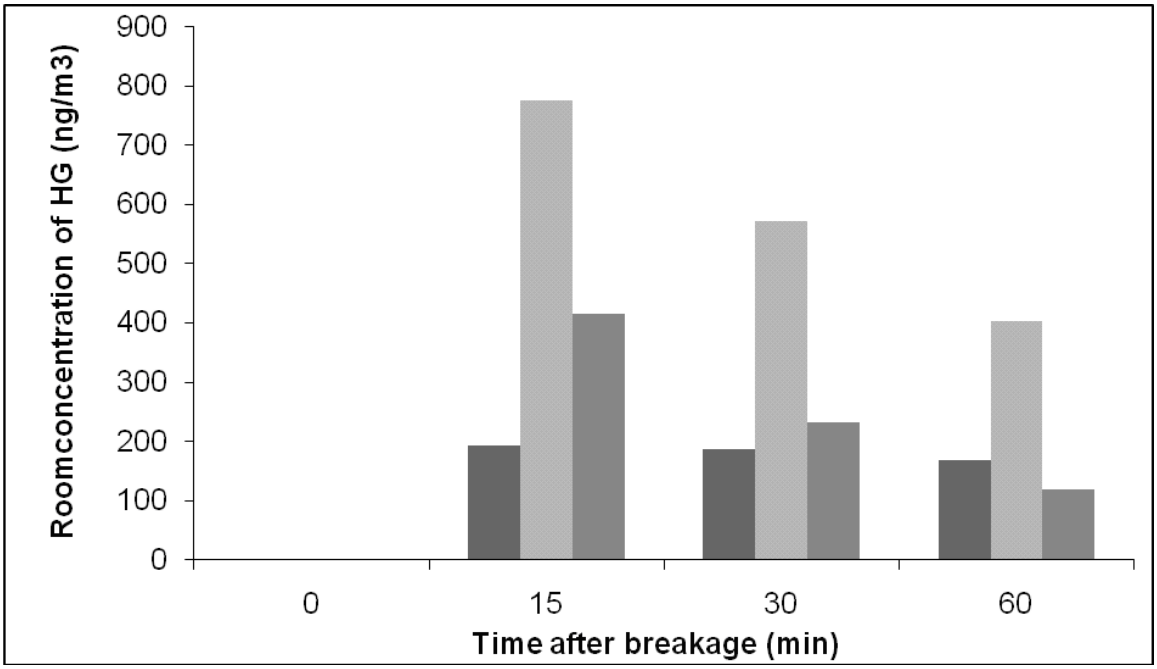

Figure 1: Time course of average air concentrations of Hg (ng/m^3) in a standard room after breakage of different types (different bar colours) of CFLs (data extracted from: Maine compact fluorescent lamp study, 2008).

However, the measured indoor air concentrations may not be indicative of the total Hg intake after a CFL breakage, since most of the Hg released may condense on surfaces, where it can persist if inadequate ventilation is present or in the absence of specific cleanup procedures. Equilibrium between Hg in air and condensed Hg will be reached and then Hg will be slowly oxidized to Hg ions. As a consequence, in addition to inhalation exposure, oral exposure to both elemental Hg and Hg ions may occur in children, due to ingestion of dust and hand-to-mouth contact. There are no data available on the potential contribution of such an exposure to total Hg-intake.

Compared to adults, children have higher exposure via various routes and internal doses of Hg due to several reasons. Children breathe more air per kg of body weight than adults at rest and tend to be more physically active than adults. Therefore, mercury vapours, if present in indoor air, may be delivered to children at higher internal doses than to adults (Miller et al. 2002). The foetus is also exposed during gestation as certain mercury species ($HgCH_3^+$) cross the placenta. A comprehensive review on mercury exposure in children is available in Counter and Buchanan (2004).

Since no data on the potential contribution of oral exposure to total Hg-intake are available for children, the SCHER recommends assessing potential Hg exposures from broken CFL lamps in an experimental setting specifically considering child behaviour. SCHER also recommends providing to customers specific instructions for Hg removal after breakage of a CFL and info for protecting children.

Based on the room air concentrations determined after breaking a CFL, a health risk for adults is not expected, since the exposure is in the range of occupational exposure limits for only a very short time. The occupational exposure limits are intended to protect adults for a 40-year work life. Due to the very low exposures and their very short duration, even sensitive subgroups in the adult population should be protected.

Given the measured Hg air concentrations after CFL breakage, the rapid decrease of these concentrations and the above-stated considerations on the RfC of Hg, the SCHER is of the opinion that a human health risk for adults due to CFL breakage is

unlikely. Regarding risk for children, possible exposures from oral intake of dust and hand-to-mouth contact cannot be evaluated due to lack of scientific data; therefore, no conclusions on potential risk are possible. The external peak exposure to Hg^0 by inhalation in adults after a CFL breakage is not translated into a sharp peak exposure of the foetus. Transfer of Hg^0 from the maternal circulation to the foetus is limited. Therefore, foetal exposure is expected to be negligible.

3.2 Question B

Taking into account the technical and scientific assessment from Öko-Institut and Fraunhofer IZM (2009), assess the potential risks to human health and the environment of the alternatives available to reduce, eliminate or substitute the mercury in CFLs.

In the context of the RoHS directive (2002/95/EC) on hazardous substances in electrical and electronic equipment, the report prepared by the Öko-Institut and Fraunhofer IZM (2009) has reviewed the Hg content in various types of lamps: compact lamps, straight fluorescent lamps for general purposes, straight fluorescent lamps for special purposes and 'other lamps' such as high-pressure sodium lamps. However, due to the absence of detailed information on the number of lamps/types used in the EU, on the disposal practices and the life time of the lamps used, the risks to the environment cannot be assessed with the information presented in this report.

The study commissioned by DG TREN and performed by the Flemish institute for technological research (or VITO), has assessed the environmental impact and life cycle of 6 types of lamps, i.e. the so-called base cases (VITO 2009). The information contained in this report allows, be it indirectly, to make an initial risk assessment of Hg contained in these types of lamps. The base cases discussed in this report and used for this opinion are:

1. Incandescent lamp, clear (CLS-C): 54 W
2. Incandescent lamp, frosted (CLS-F): 54 W
3. Halogen lamp, low voltage (HL-LV): 30 W
4. Halogen lamp, mains voltage, low wattage (HL-MV-LW): 40W
5. Halogen lamp, mains voltage, high wattage (HL-MV-HW): 300W
6. Compact fluorescent lamp, with integrated ballast (CFLi): 13W

Exposure assessment based on number of lamps sold in 2007:

The EU-27 electricity consumption in 2007 of non-directional light sources in all sectors is about 112.5 TWh (VITO 2009). This is approximately 4 % of the EU-27 total electricity consumption with 2.95% being used by the domestic sector and 1.05% in the non-domestic sector. The share of each lamp type in the energy consumption for all sectors is given in Table 1.

Table 1: Comparison of unit sales per base case in the EU 27 area (VITO et al., 2008)

	CLS-C	CLS-F	HL-MV-LW	HL-MV-HW	HL-LV	CFLi	Total
Lumen output per (lm)	594.0	572.4	480.0	5177.3	435.0	559.0	
EU 27 sales	297	767	97	84	147	353	1746

(min unit)							
Share of the EU 27 sales	17.0%	44.0%	5.6%	4.8%	8.4%	20.2%	100.0%

According to the VITO (2009) report, the production of 1 KWh releases 16 ng of Hg into the air; the production of 112.5 TWh in the EU-27 area thus emits 16 x 112.5x109 ng = 1800 kg Hg to the EU-27 air compartment.

An overview of the Hg emission of each lamp type during its use and end-of-life phase is given in Table 2. For example, the 767 million CLS-F lamps which were sold in 2007, released 659.6 kg Hg in the EU-27. This calculation is based on each lamp's emission of 0.86 mg Hg during its use and end-of-life phases. Similarly, 353 million CFLi units with an emission of 4.51 mg Hg/lamp were sold resulting in a total release of 1592 kg Hg. The higher emission per CFLi unit (4.51 mg/unit) is mainly due to the end-of-life phase (3.2 mg/unit) in which it is assumed that only 20% are recycled. The total Hg release for all lamp types in 2007 was 5264 kg Hg.

Table 2: Hg emissions and sales per lamp type in the EU 27 area (data taken from VITO, 2009).

	CLS-C	CLS-F	HL-MV-LW	HL-MV-HW	HL-LV	CFLi	Total
EU 27 sales (min unit)	297	767	97	84	147	353	1746
Hg emission during use phase (mg)	0.86	0.86	0.96	7.20	1.60	1.31	
Hg emission during the end of life phase (mg)	0	0	0	0	0	3.2	
Hg emission all lamps in the EU-27 (kg)	255.4	659.6	93.1	604.8	235.2	1592	5264
Product life time (hours)	1000	1000	1500	1500	3000	6000	
Lumen output per lamp (lm)	594.0	572.4	480.0	5177.3	435.0	559.0	
Hg emitted over life time per lumen per hour (ng)	1.45	1.51	1.33	0.93	1.22	1.34	

The VITO (2009) report is unclear about the inclusion of possible Hg release during the production phase of the lamps in the assessment. Considering the industrial and local nature of lamp production, the SCHER assumes that these potential Hg emissions will be strictly controlled and managed.

Comparison of Hg release of lamps and some other Hg sources/emissions – comparative risks assessment:

Mercury emissions from both natural sources and anthropogenic activities have been assessed in detail by UNEP (2002). Worldwide release of mercury to the atmosphere is estimated to be between 2,000 and 3,000 metric tons from anthropogenic sources and 1,400 to 2,300, due to natural sources. An assessment covering most likely uses of mercury in the US (based on data from 1995) concluded that mercury emissions into the air from anthropogenic sources amount to 145 metric tons with dental preparations contributing 0.6 tons (UNEP, 2002). An updated assessment for the year 2000 estimated a total anthropogenic release of mercury to the atmosphere of 126 tons and a contribution of 4.5 tons due to the use of dental amalgams. This updated assessment also estimated mercury releases to water from anthropogenic activities (a total of 46 tons, with 0.8 tons from intentional uses including 0.4 tons due to dental amalgams) and to soil (total of 2700 tons, with 106 tons from intentional uses including 28 tons due to dental amalgams) mostly from mining activities (Cain et al. 2007).

The European Environmental Bureau has published a detailed mass balance analysis of mercury used in dental applications (EEB 2007). This report has examined – in a quantitative manner and across the EU-27 - all sources of amalgam Hg and the pathways by which it can enter the environment. This report states that the EU-27 discharges 109 tonnes/y of mercury from dental practices and that mercury in the teeth of deceased persons contributes 14 tons Hg/y to the EU waste stream. The authors state that of this total of 123 tons, 77 tons will 'likely' end up in various environmental media: i.e. 30 tonnes in soil, 23 tonnes in the atmosphere, 14 tonnes in surface water and 10 tonnes in groundwater.

The Risk Policy Analysis report estimates that approximately 70 tons Hg/year is released (into the environment) by the EU-15 (Floyd et al. 2002). The value given for Denmark is 1 ton/y which is comparable to the values reported in the above-mentioned report (Danish EPA 2004). No further comparisons of the use quantities, release patterns and possible (predicted) environmental concentrations could be made as the type of information and calculations provided in the various reports is too diverse in nature.

From the literature available to the SCHER it may be concluded that, while dental amalgams may represent one of the major intentional uses of Hg today, the contribution of dental amalgams to Hg emission into the air is only a small fraction of the total release of Hg into the atmosphere. Releases from dental amalgams to water may be more significant, but the relative contributions of the various sources vary considerably depending on the literature source used. Information on the Hg releases of dental amalgams to the soil compartment is too scarce to assess it's relative importance and potential risks.

Finally, it should be noted that Hg releases associated with the present use of amalgams represent a small fraction of the total Hg emissions into the atmosphere and the global Hg pool due to the much larger emissions from other sources (UNEP 2002).

Compared to the above-stated 109 tons/y Hg released from dental practices, the Hg emissions originating from electricity production, lamp use and disposal is much lower (approximately 5.3 tons/y, i.e. 4.9 % of Hg originating from dental practices). For elemental Hg and Me-Hg emitted from dental practice amalgams, it was concluded that, except for point sources, no to very low environmental risks are expected. Considering that the Hg emissions from all six types of lamps discussed here is about 20 times lower than that from dental practices emissions, SCHER is of the opinion that environmental risks occurring from Hg released from all lamps, and CLFs in particular, is unlikely. However, the SCHER would like to point out that for local situations, such as lamp collection and disposal facilities which do not manage potential Hg releases properly, site-specific risks to the environment cannot be excluded. These need to be evaluated taking the site-specific characteristics of the facility and environment into account.

As stated in the answer to question A, the Hg room air concentration after breakage of a CFL is not expected to lead to a health risk for adults. For children, conclusions on the potential risk cannot be provided as the potential contribution of the oral intake route is unknown. Regarding the alternatives and assuming similar release rates after breakage, the short-term peak exposures to Hg will be related to the amount of Hg present. However, peak concentrations of Hg after breakage of lamps with highest Hg concentrations will likely be above long-term occupational limits, but only for a very short time. Therefore, no health risks for adults are expected. Conclusions regarding health risks for children cannot be made due to absence of exposure estimations.

In conclusion, regarding the alternatives, i.e. the six types of lamps listed above, no health risks for adults are expected and the environmental risks are unlikely.

3.3 Question C

Assess the risk to the environment from the mercury liberated upon disposal of CFLs, taking into account the above-mentioned limit of 5 mg mercury per CFL, the requirements for separate collection of the CFLs and for removal of the mercury from the collected CFLs. Would the risk be significantly reduced by strengthening these requirements?

In 3.2 the SCHER concluded that environmental risks due to use and disposal of CFLs are unlikely.

To assess the effect of separate collection (and removal of Hg from the collected Hg - i.e. recycling) and a reduced Hg content of the CFLs on the total Hg release into the environment, SCHER calculated different scenarios (Table 3). In the exposure assessment performed in 3.2, it was assumed that each CFL unit contained 4.5 mg and that 20% of the CFLi units were recycled. Using this scenario and the 2007 sales data, this calculation resulted in an Hg emission of 1592 kg in the EU-27 area. Increasing the recycling efficiency to 100% will result in 71% less Hg being released (reduced from 1592 to 462 kg /y).

A 50% reduction in the Hg content (to 2.25 mg) of the CFL (combined with 20% recycling) will decrease the Hg emission to 660 kg/y.

Table 3: Effect different recycling efficiency and Hg content of the CFL on the total environmental release of Hg.

Recycling efficiency (%)	Hg content of CFL (mg)	Hg release in environment (kg/y)
20	4.5	1592
50	4.5	1027
100	4.5	462
20	2.25	891
50	2.25	660
100	2.25	462

As indicated above, present use and disposal of CFLs are unlikely to pose environmental risks. Separate collection of the CFLs and removal of the mercury from the collected CFLs will reduce Hg emission (Table 3).

3.4 Question D

Weigh the risks identified in A), B) and C) against the reduction of mercury emissions from coal-based power plants due to the lower electricity consumption of CFLs compared to conventional household lamps. Incorporate and consider the potential health risks from mercury when CFLs are broken, accidentally in the household or after disposal, into the life cycle analysis of CFLs, taking into account the reduction of human health and environment risks resulting from the potential reduction in mercury emissions from coal-based power plants and the reduction of

the emission of other pollutants due to the lower electricity consumption of CFLs compared to conventional household lamps.

In A, B, C, the SCHER concluded that the environmental risks of Hg due to the use of CFLs are very low. The VITO (2009) report demonstrated that the amount of Hg emitted over a CFL lifetime per lumen is approximately 10% lower than that of conventional CLS bulbs (Table 2). Considering that this normalized life cycle estimation (per lumen per hour) includes both the Hg emissions from the use and disposal phase, the net emission reduction would be in that order of magnitude, if all conventional household lamps were replaced by CLFs. It is noted that halogen lamps emit even less Hg (up to 39% less) per lumen per hour.

The SCHER would like to point out, that weighing risks to different targets (human health and ecosystems) from different outputs (Hg and greenhouse gases) from different products (various kinds of light bulbs) presents some considerable challenges that are only just now being addressed in risk assessment. Hence, SCHER is only able to give a partial and somewhat tentative response to this question.

That said, from an environmental perspective, the weighing of the adverse effects of mercury emissions on ecosystems and the climate effects of greenhouse gas emissions is made easier by virtue of the mercury emissions per lumen per hour being roughly similar across lamp types (see Table 2). On the other hand the environmental impacts of the CFLi lamps is considerably less than the rest, Thus the VITO (2009) report presents data per lumen per hour for each environmental indicator including two main environmental impact indicators, i.e. total energy consumption (GER) and total global warming potential (GWP). These indicators for CFLi lamps are about 25% of those of GLS-C and GLS-F lamps. Compared to HL-MV-LW, HL-MV-HW and HL-LV lamps, CFLis have 13%, 53% and 22% less impact on the GER indicator and 13, 47 and 25% less impact on the GWP indicator, respectively.

The SCHER is therefore of the opinion that CFLis offer a net environmental benefit as compared with the other light bulbs considered. This could have been more equivocal had the Hg released from disposal caused the life cycle emissions from the CFLis to exceed that of the other light bulbs. And it is more equivocal in weighing the environmental gains from CFLis with any risks to human lives from accidental exposures. Often, weighing different effects across different targets is based on expert judgements.

Another approach is to weigh different effects on the basis of public values and with a common monetary measure. Thus, the variations per lumen per hour across light bulb types would be modulated as follows: for greenhouse gases with the social cost of carbon; for human health with values for life and/or healthy life years; for ecosystems with the values of ecosystem services. That would put all the risks in the same monetary units.

SCHER counsels some caution with this kind of approach but is of the opinion that for the sake of developing transparent assessment that properly informs management and policy the above-described approach to risk-benefit analysis needs to be given more critical attention. For example, without this kind of approach, it would not be possible at this stage for SCHER to give an opinion that weighs the benefits from greenhouse gas reductions with any increased risks of accidental exposure for human health. That has to remain a matter for judgement in the risk management process.

4. LIST OF ABBREVIATIONS

CFL	Compact Fluorescent Lamp
GER	Total Energy Consumption
CLS-C	Incandescent Lamp, Clear
CLS-F	Incandescent Lamp, Frosted
GWP	Global Warming Potential
HL-LV	Halogen Lamp, Low Voltage
HL-MV-LW	Halogen Lamp, Mains Voltage, Low Wattage
HL-MV-HW	Halogen Lamp, Mains Voltage, High Wattage
KWh	Kilowatt hour
NOAEL	No-Adverse-Effect Level
TWh	Terawatt hour

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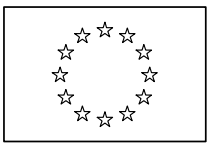

COMMISSION OF THE EUROPEAN COMMUNITIES

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COMMUNICATION FROM THE COMMISSION TO THE COUNCIL AND THE EUROPEAN PARLIAMENT

Community Strategy Concerning Mercury

{SEC(2005) 101}

1. INTRODUCTION

In December 2002 the Commission presented a report to the Council concerning mercury from the chlor-alkali industry[1]. This considered the fate of 12-15 thousand tonnes of surplus mercury resulting from the sector's conversion away from the mercury cell process. The Council reacted by inviting the Commission to present "a coherent strategy ... with measures to protect human health and the environment from the release of mercury based on a life-cycle approach, taking into account production, use, waste treatment and emissions". The strategy also provides a basis for the Community's input to international debate on mercury at the UNEP Governing Council in February 2005.

This Communication is accompanied by an Extended Impact Assessment[2] (ExIA) looking at the mercury problem and policy options in detail. It also takes account of a wide range of expressions on the need to act made during stakeholder consultation on the strategy, the processes and results of which are described in the ExIA.

2. THE MERCURY PROBLEM

2.1. The mercury threat

Mercury and its compounds are highly toxic to humans, ecosystems and wildlife. Initially seen as an acute and local problem, mercury pollution is now also understood to be global, diffuse and chronic. High doses can be fatal to humans, but even relatively low doses can have serious adverse neurodevelopmental impacts, and have recently been linked with possible harmful effects on the cardiovascular, immune and reproductive systems. Mercury also retards microbiological activity in soil, and is a priority hazardous substance under the Water Framework Directive[3].

Mercury is persistent and can change in the environment into methylmercury, the most toxic form. Methylmercury readily passes both the placental barrier and the blood-brain barrier, inhibiting potential mental development even before birth. Hence exposure of women of child-bearing age and children is of greatest concern.

The largest source of mercury exposure for most people in developed countries is inhalation of mercury vapour from dental amalgam. Exposure to methylmercury mostly occurs via diet. Methylmercury collects and concentrates especially in the aquatic food chain, making populations with a high intake of fish and seafood particularly vulnerable.

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1 COM(2002) 489 final, 6.9.2002.

2 SEC(2005) 101.

3 Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy, OJ L 327, 22.12.2000, as amended by Decision 2001/2455/EC of the European Parliament and of the Council of 20 November 2001 establishing the list of priority substances in the field of water policy, OJ L 331, 15.12.2001.

Most people in central and northern Europe show bioindicators of exposure below internationally accepted safe levels for methylmercury. However, most people in coastal areas of Mediterranean countries, and around 1-5% of the population in central and northern Europe, are around these levels, and large numbers among Mediterranean fishing communities and the Arctic population exceed them significantly.

2.2. A global perspective

Although mercury is released by natural sources like volcanoes, additional releases from anthropogenic sources, like coal burning and use in products, have led to significant increases in environmental exposure and deposition. Past releases have also created a "global pool" of mercury in the environment, part of which is continuously mobilised, deposited and re-mobilised. Further emissions add to this global pool circulating between air, water, sediments, soil and biota.

Elevated mercury concentrations occur in many parts of the world. Some are largely due to local sources, especially small scale gold mining in South America, Africa and Asia. But as a transboundary pollutant, mercury also can be transported globally to regions far from its source. This means that some pollution of a local character, viewed in the short term, adds to the global pool in the long term. It has also led to contamination of regions with few or no mercury sources, like the Arctic.

3. OBJECTIVES

A key aim is to reduce mercury levels in the environment and human exposure, especially from methylmercury in fish. But eliminating the problem of methylmercury in fish will probably take decades, as present levels are due to past emissions, and would take time to fall even without further releases. The Community has already taken much action to reduce mercury emissions and uses. This does not mean that no more can be done, but highlights the importance of full implementation of existing measures by Member States, and of making progress at the global level.

The strategy therefore has the following objectives:

- Reducing mercury **emissions**.
- Reducing the entry into circulation of mercury in society by cutting **supply** and **demand**.
- Resolving the long-term fate of mercury **surpluses** and societal **reservoirs** (in products still in use or in storage).
- Protecting against mercury **exposure**.
- Improving **understanding** of the mercury problem and its solutions.
- Supporting and promoting **international action** on mercury.

Progress, gaps and additional actions to be taken are described below for each objective. References to the short and medium terms relate to the next 3 years and 4-6 years respectively. Longer term actions will be identified following review of the strategy.

4. REDUCING EMISSIONS

Mercury releases have generally risen with industrialisation. Global atmospheric emissions grew about 20% from 1990-2000. European emissions fell about 60% over this period, but Europe remains a major source of mercury deposited in other continents and the Arctic.

One of the main source of mercury releases is coal burning. Coal burning in plants above 50 MW_{th} is covered by the IPPC Directive[4] – as are other major sources like the metals, cement and chemical industries – and Directive 2001/80/EC[5].

The IPPC Directive is therefore a key Community tool to reduce emissions of mercury and other pollutants. Permitting of IPPC installations, with limited exceptions for some new Member States, is to be complete by 30 October 2007. The Commission is publishing a series of BAT reference (BREF) documents to support IPPC implementation.

Action 1. The Commission will assess the effects of applying IPPC on mercury emissions, and consider if further action like Community emission limit values is needed, as data under the IPPC and EPER[6] reporting requirements are submitted, and in a broader strategy review by the end of 2010. This will include review of the co-benefit effect of controls to be implemented by 1 January 2008 under Directive 2001/80/EC to reduce sulphur dioxide emissions from large combustion plants.

Action 2. The Commission will encourage Member States and industry to provide more information on mercury releases and prevention and control techniques, so conclusions can be drawn in BREFs helping to reduce emissions further. The second edition of the chlor-alkali BREF will include information to address the risk of releases in decommissioning mercury cells.

Small combustion plants and residential coal burning are also significant mercury sources. Control of such facilities is more likely to be cost-effective when considered on a multi-pollutant, rather than a single substance, basis. This is already being examined in the Clean Air for Europe (CAFE) programme for "classical" air pollutants such as ammonia and sulphur dioxide.

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4 Council Directive 96/61/EC of 24 September 1996 concerning integrated pollution prevention and control, OJ L 257, 10.10.96.

5 Directive 2001/80/EC of the European Parliament and of the Council of 23 October 2001 on the limitation of emissions of certain pollutants into the air from large combustion plants, OJ L 309, 27.11.2001.

6 Commission Decision 2000/479/EC of 17 July 2000 on the implementation of a European pollutant emission register (EPER) according to Article 15 of Council Directive 96/61 concerning integrated pollution prevention and control, OJ L192, 28.7.2000.

Action 3. The Commission will undertake a study in 2005 of options to abate mercury emissions from small scale coal combustion, to be considered alongside the broader CAFE assessment.

Some Member States identify dental amalgam as a significant source of mercury releases, including via dental surgeries and cremation. Treatment of dental amalgam waste is covered by Community waste law[7].

Action 4. The Commission will review in 2005 Member States' implementation of Community requirements on the treatment of dental amalgam waste, and will take appropriate steps thereafter to ensure correct application.

Emissions from crematoria are not covered by Community law, but are regulated in several Member States, and are also the subject of an OSPAR Recommendation. Reports on emissions by parties to this Recommendation, first due by 30 September 2005, will give an indication of effectiveness and whether further action is required. Similar control is encouraged in other Member States where cremation takes place.

More broadly the proposal for a Directive on priority substances under the Water Framework Directive will include quality standards for mercury to be met by 2015, which will be relevant in IPPC permitting, for example. Adoption of the measures will start the framework Directive's 20-year period for cessation or phasing-out of emissions, discharges and losses.

5. REDUCING SUPPLY

Mercury is traded freely on the world market. Current global supply is around 3,600 tonnes per year. The EU is the major exporter, with a net annual export of around 1,000 tonnes. The price of mercury has fallen dramatically since its peak in the 1960s, standing relatively stably at around €5 per kilogramme for most of the past decade. The economic impact of the mercury trade is therefore very small. The low price and ready supply also encourage continued use of mercury outside Europe in activities such as gold mining.

Mercury compounds used as pesticides are subject to the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. This is implemented in the Community by Regulation (EC) No. 304/2003[8], which also bans export of cosmetic soaps containing mercury and requires export notification of mercury compounds for all other uses. There are no Community or international restrictions on trading metallic mercury. However, analysis in the ExIA suggests that the export of mercury from the Community should be phased out.

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[7] Commission Decision (2000/532/EC) of 3 May 2000 replacing Decision 94/3/EC establishing a list of wastes pursuant to Article 1(a) of Directive 75/442 on waste and Council Decision 94/904 establishing a list of hazardous waste pursuant to Article 1(4) of Council Directive 91/689EEC on hazardous waste, OJ L226/3, 6.9.2000 (as amended).

[8] Regulation (EC) No. 304/2003 of the European Parliament and of the Council of 28 January 2003 concerning the export and import of dangerous chemicals, OJ L 63, 6.3.2003.

Action 5. As a pro-active contribution to a proposed globally organised effort to phase out primary production of mercury and to stop surpluses re-entering the market as described in section 10, the Commission intends to propose an amendment to Regulation (EC) No. 304/2003 to phase out the export of mercury from the Community by 2011.

The main global supplier is the Spanish state-owned firm MAYASA. Under an agreement made in 2001, MAYASA buys the EU chlor-alkali sector's surplus mercury for resale. MAYASA also sells mercury that it has made from ore mined in Almadén, Spain. Mercury production in Almadén peaked at around 2,800 tonnes in 1941, but has since fallen as the market has declined, and recently as the chlor-alkali industry has provided an alternative source. The recent total supply by MAYASA has been around 1,000 tonnes of mercury per year.

The ExIA finds that, even without an export ban, the negative environmental impacts of primary mercury mining and production, and their questionable economic viability, support the ending of these particular activities. Spain has stated that mining and production in Almadén had already been stopped temporarily before the adoption of this strategy, and does not anticipate that they will restart.

The Commission recognises the historical economic and social significance of mercury production and trade in Almadén, dating back to Roman times. The Commission also strongly supports the provision of help to develop new areas of business and employment. The area is already eligible for Community support as part of an Objective 1 region (Castile-la-Mancha), and is expected to remain so in the next Structural Fund programming period.

6. REDUCING DEMAND

Mercury demand is around 3,600 tonnes per year globally, and in 2003 was around 300 tonnes in the then 15 EU Member States. Use of mercury is declining, at both global and EU levels, yet some significant uses remain. The main global uses are gold mining, batteries and the chlor-alkali industry, together accounting for over 75% of consumption. Of these, only use in the chlor-alkali industry is presently significant across the EU, but the mercury cell process is not considered to be BAT[9] under the IPPC Directive, and is being phased out. Mercury use in gold mining is known to be significant in French Guyana (where the French authorities are considering a ban) but not in the European region of the EU. Directive 91/157/EEC[10] limits use of mercury in batteries.

[9] Reference Document on Best Available Techniques (BAT) in the Chlor-Alkali Manufacturing Industry adopted by the Commission in December 2001, http://eippcb.jrc.es.

[10] Council Directive 91/157/EEC of 18 March 1991 on batteries and accumulators containing certain dangerous substances, OJ L 078, 26.3.91.

As the chlor-alkali industry phases out mercury cells, dental amalgam will become the EU's major mercury use. It is therefore appropriate to re-examine the scope for substitution. This is especially important as Member States can encourage substitution, but the coverage of dental amalgam under the medical devices Directive[11] limits the scope for restrictive national measures.

Action 6. In the short term the Commission will ask the Medical Devices Expert Group to consider the use of mercury in dental amalgam, and will seek an opinion from the Scientific Committee on Health and Environmental Risks, with a view to considering whether additional regulatory measures are appropriate.

The main mercury product group not covered by Community law is measuring and control equipment. The Commission is due to present proposals to include medical devices and monitoring and control instruments under Directive 2002/95/EC[12], which already covers lighting and other electrical and electronic equipment. However, some of the larger mercury uses in this product group (thermometers, blood pressure gauges and barometers) are not electrical or electronic equipment, so would not be covered. The ExIA finds that additional action in this area is appropriate.

Action 7. The Commission intends to propose in 2005 an amendment to Directive 76/769/EEC[13] to restrict the marketing for consumer use and healthcare of non-electrical or electronic measuring and control equipment containing mercury.

Action 8. The Commission will further study in the short term the few remaining products and applications in the EU that use small amounts of mercury. In the medium to longer term, any remaining uses may be subject to authorisation and consideration of substitution under the proposed REACH Regulation[14], once adopted.

7. ADDRESSING SURPLUSES AND RESERVOIRS

The largest holding of mercury in the EU is that of the chlor-alkali industry. Given the intention to phase out exports, much of this mercury will need to be stored or disposed of. Some Member States are already developing policies in this area[15]. The ExIA finds that permanent disposal would be optimal from an environmental point of view, but is presently too expensive and technically uncertain to pursue at

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11 Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, OJ L 169, 12.7.93.

12 Directive 2002/95/EC of the European Parliament and of the Council of 27 January 2003 on the restrictions of the use of certain hazardous substances in electrical and electronic equipment (RoHS), OJ L 37, 13.2.2003.

13 Directive 76/769/EEC on the approximation of the laws, regulations and administrative provisions of the Member States relating to restrictions on the marketing and use of certain dangerous substances and preparations, OJ L 262, 27.9.76.

14 Proposal for a Regulation of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency and amending Directive 1999/45/EC and Regulation (EC) {on Persistent Organic Pollutants}, COM(2003) 644 final, 29.10.2003.

15 For example, Sweden has introduced a requirement for stabilisation and storage of mercury in deep bedrock, while Germany is examining the idea of storing metallic mercury in disused salt mines.

Community level. The need to find cost-efficient storage arrangements is therefore an important area for further examination.

Action 9. The Commission will take action to pursue the storage of mercury from the chlor-alkali industry, according to a timetable consistent with the intended phase out of mercury exports by 2011. In the first instance the Commission will explore the scope for an agreement with the industry.

There is also a large amount of mercury in products already circulating in society. Once a product becomes "waste", present Community policy generally encourages recovery over disposal. More active collection and recycling of mercury could be considered. However, some Member States argue that mercury should not be recovered for re-use, but rather should be taken out of circulation via storage or disposal.

Action 10. The Commission will undertake further study in the short to medium term of the fate of mercury in products already circulating in society.

8. PROTECTING AGAINST EXPOSURE

A recent opinion of the European Food Safety Authority (EFSA) on the risk from mercury in food[16] found that people who eat a lot of fish and fishery products, in particular large predatory fish, can reach or exceed the established safe levels. The Commission is reviewing risk management options in the light of EFSA's opinion, including the maximum limits in Regulation (EC) No. 466/2001[17] on the mercury content of fishery products. However, the scope to reduce these levels is limited. Other solutions, like the targeted consumer advice issued by the Commission[18] and Member States, are also needed.

Action 11. In the short term, EFSA will investigate further specific dietary intakes of different types of fish and seafood among vulnerable subpopulations (e.g. pregnant women, children).

Action 12. The Commission will provide additional information concerning mercury in food as new data become available. National authorities will be encouraged to give advice in the light of local specificities.

16 http://www.efsa.eu.int/science/contam/contam_opinions/259_en.html.

17 Commission Regulation (EC) No 466/2001 of 8 March 2001 setting maximum levels for certain contaminants in foodstuffs, OJ L 77, 16.3.2001.

18 http://europa.eu.int/comm/food/food/chemicalsafety/contaminants/information_note_mercury-fish_12-05-04.pdf.

Community law also limits the mercury content of drinking water[19]. The recently agreed 4th air quality daughter Directive[20] does not set a target value or quality standard for mercury – levels observed in ambient air are below those believed to have adverse health effects – but concentrations and deposition are to be measured to show geographical and temporal trends.

The existing Community legislation on health and safety at work provides an adequate framework to protect workers against risks to their health and safety from exposure to mercury. Under this framework, the Commission is developing an occupational exposure limit value for mercury.

More broadly, action will be taken under the European Environment and Health Action Plan 2004-2010[21] to improve determination of human exposure, by developing integrated monitoring of the environment and food and investigating the scope for a coherent approach to biomonitoring. This will cover a range of environmental stressors including mercury.

9. IMPROVING UNDERSTANDING

Gaps in knowledge on the mercury problem and its possible solutions can be filled by research, development and pilot projects. Areas for such activities include human health effects, how mercury moves or is retained in the environment, and questions of ecosystem sensitivity and toxicity. Effort should also be directed at addressing issues associated with mercury in products, emissions and wastes, particularly the development of techniques to reduce mercury releases from coal combustion and other major sources, and to treat, stabilise and permanently dispose of surplus mercury and mercury-containing wastes.

Action 13. Priorities for mercury research will be addressed in the 7th RTD Framework Programme and other appropriate funding mechanisms.

10. SUPPORTING AND PROMOTING INTERNATIONAL ACTION

It is important to make progress in addressing the mercury problem globally, in particular to reduce emissions, and also to reduce supply and demand.

There is considerable potential to reduce mercury emissions and foster the use of BAT, especially in the power, metals, cement, chlor-alkali and waste sectors. EU action has already reduced emissions significantly, and can be offered as an example in international, regional and bilateral fora. Technology transfer will also be important.

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19 Council Directive 98/83/EEC of 3 November 1998 on the quality of water intended for human consumption, OJ L 330, 5.12.98.

20 Proposed Directive of the European Parliament and of the Council relating to arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons in ambient air, COM(2003) 423 final, 16.7.2003. Final text not yet published in the Official Journal.

21 COM(2004) 416 final, 9.6.2004.

Global demand for mercury is already decreasing, but the nature of the mercury problem makes it important to take steps to further manage demand downwards. Measures should be taken to phase out mercury use where suitable alternatives are available, and to strictly control it where they are not. The Commission considers that purposeful demand reduction efforts could cut global mercury use significantly – to around 1,000 tonnes or less by 2020. This relies especially on cutting use in the chlor-alkali sector and batteries, where great potential has again been illustrated in the EU, and in gold mining.

However, the fall in global demand will not meet its potential if mercury supply stays high and cost low, stimulating continued and new uses. Parallel action is needed to reduce supply. The US decision to store mercury previously stockpiled for strategic purposes is welcomed.

Action 14. The Community, Member States and other stakeholders should pursue input to international fora and activities, and bilateral engagement and projects with third countries, including technology transfer, to address the mercury problem.

Action 15. The Commission will consider establishing a specific funding scheme for research and pilot projects to reduce mercury emissions from coal combustion in countries with a high dependency on solid fuels, e.g. China, India, Russia, etc., similar to the CARNOT programme that promotes the clean and efficient use of solid fuels.

Action 16. The Community should promote an initiative to make mercury subject to the PIC procedure of the Rotterdam Convention.

Action 17. The Community and Member States should continue to support work under the Heavy Metals Protocol to the UNECE Convention on Long Range Transboundary Air Pollution.

Action 18. The Community, Member States and other stakeholders should also support the UNEP Global Mercury Programme, e.g. through review of materials and provision of technical knowledge and human and financial resources.

Action 19. The Community and Member States should support global efforts contributing to reduced use of mercury in the gold mining sector, e.g. the UNDP/GEF/UNIDO Global Mercury Project. They will also consider possibilities to support individual developing countries through the various instruments related to development cooperation assistance, taking national strategies for development into account.

Action 20. To reduce mercury supply internationally, the Community should advocate a global phase-out of primary production and encourage other countries to stop surpluses re-entering the market, under an initiative similar to that of the Montreal Protocol on substances that deplete the ozone layer. To support this objective, the envisaged amendment of Regulation (EC) No. 304/2003 would phase out the export of mercury from the Community by 2011.

11. REVIEW

The ExIA identifies a number of significant milestones in the short to medium term under current Community and international measures which will enable further review of the mercury problem, the success of policies and possible additional actions. More broadly, the Commission intends to review the mercury strategy as a whole by the end of 2010. This review will also meet the requirement to report under the 4th air quality daughter Directive by this time on the merit of further action on mercury, taking account of measures adopted pursuant to this strategy. The Commission intends to conduct the review using data from various sources and covering all media, rather than just from an air quality perspective.

12. CONCLUSIONS

Mercury poses a threat in the Community and globally. This Communication marks the first step in the implementation of a coherent Community strategy on this subject. It is presented ahead of the intended legislative proposals announced herein, to enable conclusion of a Community position on mercury in time for the UNEP Governing Council of February 2005.

The Commission requests the Council, in response to its invitation to present a mercury strategy, and the European Parliament, to endorse the approach set out in this Communication.

EUROPEAN COMMISSION

Brussels, 7.12.2010
COM(2010) 723 final

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on the review of the Community Strategy Concerning Mercury

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on the review of the Community Strategy Concerning Mercury

1. INTRODUCTION

On 28 January 2005, the Commission adopted the Communication to the Council and the European Parliament on a Community Strategy Concerning Mercury[1]. The Strategy addresses most aspects of the mercury life cycle. Its key aim is to reduce mercury levels both in relation to human exposure and the environment. It identifies twenty priority actions to be undertaken, both within the EU and internationally.

The Strategy was welcomed by Council Conclusions on 24 June 2005 as well as by a European Parliament Resolution on 14 March 2006.

The Commission expressed its intention to "review the mercury strategy as a whole by the end of 2010", as indicated in Section 11 of the Communication. In support of the review, the Commission asked an external consultant to perform a comprehensive study on the implementation of the Strategy.[2] In addition, a stakeholder consultation meeting with Member States, industry and environmental NGOs was held on 18 June 2010 in Brussels. The final report reflects comments received during the meeting as well as written comments submitted between July and August 2010.

This review is based on the findings of this study and other information available to the Commission. It also fulfils the Commission's obligation to report on progress in multilateral activities according to Article 8(5) of Regulation (EC) No 1102/2008 on the banning of exports of metallic mercury and certain mercury compounds and mixtures and the safe storage of metallic mercury[3]. The obligation laid down in Article 8(2) of the Regulation to report on ongoing research activities on safe disposal options is complied with by the study report on "Requirements for facilities and acceptance criteria for the disposal of metallic mercury" available on the Commission's website (see also action 9 below).

2. INTERNATIONAL DEVELOPMENTS

Due to the long range transport properties of mercury, the exposure of people living in the Union as well as the exposure of the EU's environment can not be reduced to an acceptable level through domestic policies alone. Co-ordinated international action is therefore needed to address the mercury problem in a globally effective manner. The Mercury Strategy had this in mind when focusing seven of its actions (actions 14 to 20) on supporting and promoting international activities. The EU

1 COM(2005)20 final
2 http://ec.europa.eu/environment/chemicals/mercury/pdf/review_mercury_strategy2010.pdf
3 OJ L 304, 14.11.2008, p.75

repeatedly requested the UNEP Governing Council to take a decision on the opening of negotiations on a global legally binding instrument on mercury. In February 2009, the Governing Council finally decided to establish an Intergovernmental Negotiating Committee (INC) mandated for developing a global legally binding instrument covering most aspects of the mercury life cycle. The first session of the INC took place in Stockholm, 7-11 June 2010 and the process is aimed at concluding early in 2013. The European Strategy on mercury and its implementation aims at making a significant contribution to this process.

Once the global legally binding instrument is adopted, the Commission will evaluate the need to further review the EU Mercury Strategy in order to fully reflect the new international obligations.

3. THE IMPLEMENTATION OF THE STRATEGY

Overall, there is significant progress in the implementation of the actions decided in 2005. In the following, a short overview on progress is given for all twenty actions. For ease of reference the full text of those actions is reproduced in the Annex.

3.1. Reducing emissions

Action 1: implementation of IPPC

Directive 2008/1/EC[4] on Integrated Pollution Prevention and Control (IPPC – initially adopted in 1996) is a key legal instrument for reducing mercury emissions. However, the way the instrument was applied by Member States' permitting authorities together with a weak application of Best Available Techniques (BAT) in permits have not allowed for making full use of the reduction potential for mercury emissions. The Commission, therefore, has paid particular attention to redress this situation, in the in-depth revision of the IPPC Directive which has taken place and has led to the new Industrial Emissions Directive (IED)

Indeed, in the new Industrial Emissions Directive (IED), adopted on 8 November 2010, which will replace the IPPC Directive, the role of BAT and BAT associated emission levels (AEL) is strongly reinforced. They are now to be adopted by the Commission as BAT Conclusions and will have legal effect. The possibility for permitting authorities to deviate from the AEL levels will be restricted and subject to justification according to strict criteria set out in the Directive. It is expected that this will result in an accelerated replacement of mercury-based technologies and reduction of mercury emissions in a range of industrial sectors, in particular cement production, non-ferrous metal industries, large combustion plants, waste incineration and chlor-alkali manufacturing.

[4] OJ L24/8 of 29.1.2008

Action 2: development of BAT Reference documents (BREFs)

This is an ongoing exercise. The BREFs for the Chlor-Alkali Manufacturing Industry, Large Combustion Plants, and the Non-Ferrous Metals Industry are currently under review in close co-operation with stakeholders. In this context, mercury emissions will be specifically addressed in this process, in particular with regard to the decommissioning of mercury cell plants in the chlor-alkali industry.

Action 3: emissions from small-scale coal combustion

A study on "Costs and environmental effectiveness of options for reducing mercury emissions to air from small-scale combustion installations" was finalised in December 2005[5]. According to the findings of the study, this source was estimated to contribute 16% of the total EU mercury emissions. On the basis of these findings, the European Commission, in its proposal for the IED, suggested reducing the threshold for the application of the rules applying to large combustion plants from a total rated input of 50 MW to 20 MW. However, the EU legislator maintained the 50 MW threshold and introduced in the Directive a clause requiring the Commission to review by end 2012 the need to control emissions below this threshold and if appropriate come forward with a legislative proposal. The Commission will follow up on this in due course.

Action 4: management of dental amalgam waste

Dental amalgam is the second biggest use of mercury in the EU. Commission Decision 2000/532/EC[6] characterises amalgam waste from dental care as hazardous waste, it is therefore subject to the provisions of the recently established Waste Framework Directive[7]. The Commission has reviewed actual practices in dental clinics in Member States through a questionnaire survey carried out in 2005. It was concluded that while in many Member States the installation of amalgam separators is obligatory and appropriate collection schemes have been established, this is not the case throughout the Community.

Mercury emissions from dental cabinets are also subject to EU water legislation. Mercury is classified as priority hazardous substance according to Annex X of the Water Framework Directive (WFD)[8], thus Member States are obliged in the long term to take measures to cease or phase out the emissions, discharges and losses of this substance. In addition and reflecting the combined approach of the WFD, Directive 2008/105/EC[9] establishes Environmental Quality Standards in the field of water policy for certain priority substances including mercury and its compounds. In case these standards are not met, Member States have to take measures to comply with them as foreseen by Article 11 of WFD.

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5 http://ec.europa.eu/environment/chemicals/mercury/
6 OJ L226/3 of 6/9/2000
7 Directive 2008/98/EC, OJ L312/3 of 22.11.2008
8 Directive 2000/60/EC, OJ L327 of 22.12.2000
9 OJ L348/89 of 24.12.2008

3.2. Reducing supply

Action 5: mercury export ban

On 22 October 2008, the EU legislator adopted Regulation (EC) No 1102/2008[10] on the banning of exports of metallic mercury and certain mercury compounds and mixtures and the safe storage of metallic mercury. The export ban enters into force on 15 March 2011. Reporting obligations and an information exchange established under the Regulation will allow for assessing the effectiveness of the ban and its impact on the global mercury market.

3.3. Reducing demand

Dental amalgam and measuring equipment applications have been identified as of particular importance as they represent the major volumes of mercury still present in products.

Action 6: use of dental amalgam

The Commission services consulted two Scientific Committees on the use of dental amalgam, the Committee for Environmental and Health Risks (SCHER) and the Committee for Emerging and Newly Identified Health Risks (SCENIHR). The opinions[11,12] of both Committees were not conclusive regarding the appropriateness of additional regulatory measures to restrict the use of dental amalgam.

However, given that some Member States have already substantially restricted the use of dental amalgam in their national health care systems and given that dental amalgam represents the second largest use of mercury in the EU, the Commission has decided to undertake a full lifecycle assessment of this mercury use. The results of this assessment are expected for the end of 2011.

Action 7: measuring and control equipment containing mercury

The EU legislator adopted on 25 September 2007 Directive 2007/51/EC[13] amending Council Directive 76/769/EEC relating to restrictions on the marketing of certain measuring devices containing mercury. Fever thermometers as well as other mercury-containing measuring devices (e.g. manometers, barometers, sphygmomanometers, thermometers other than fever thermometers) intended for sale to the general public may no longer be placed on the market. The Directive includes a review clause for a possible extension of the existing restrictions to other measuring devices containing mercury.

An extension of this marketing restriction to additional health care devices as well as to measuring devices intended for professional and industrial use is presently under consideration. However, the legal framework has changed with Directive 76/769/EEC being repealed and further marketing restrictions now having to follow

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10 OJ L304/75 of 14.11.2008

11 http://ec.europa.eu/health/archive/ph_risk/committees/04_scher/docs/scher_o_089.pdf

12 http://ec.europa.eu/health/archive/ph_risk/committees/04_scenihr/docs/scenihr_o_016.pdf

13 OL L257 of 3.10.2007

the procedures laid down in the REACH Regulation (EC) No 1907/2006[14]. The above-mentioned directive 2007/51/EC has been included in the Annex XVII "Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles", under the entry 18a, of the REACH Regulation (EC) 1907/2006, as amended by Commission Regulation (EC) No. 552/2009[15]. The European Chemicals Agency (ECHA), further to a request from the European Commission based on its obligation contained in the review clause of the restriction on mercury-containing measuring devices, evaluated new scientific evidence and prepared a report proposing to further restrict mercury in measuring devices in healthcare and in other professional and industrial uses. The opinion building process of the restriction report prepared by ECHA started with a public consultation on 24 September 2010. The opinions of the relevant Committees under REACH are expected to be submitted to the Commission in September 2011. The Commission will subsequently decide whether and when the restrictions will enter into force in the EU. In a related development, SCENIHR has recently issued an opinion[16] confirming that reliable alternatives to mercury sphygmomanometers in health care are available.

Action 8: other products and applications

The study report "Options for reducing mercury use in products and applications and the fate of mercury already circulating in society"[17] addresses most current mercury applications and contains an assessment of options for reducing inputs of mercury to society. This study also covers action 10.

Following the progressive ban of incandescent bulbs from the EU market by the 2005 Eco-design Directive as amended in 2009[18], the Commission addressed the mercury content of increasingly used energy efficient light bulbs. On 24.9.2010, the Commission adopted a Decision amending the Annex to Directive 2002/95/EC (the so-called RoHS Directive) which significantly reduced the limit values for such mercury containing bulbs[19]. These light bulbs are also subject to the provisions on separate collection and treatment of Directive 2002/96/EC[20] on waste electrical and electronic equipment (WEEE). In addition, the Commission asked the Scientific Committee on Health and Environmental Risks (SCHER) for an opinion on mercury in certain energy-saving light bulbs. The SCHER concluded[21] that compact fluorescent lamps (CFLs) offer a net, although limited, decrease in total mercury emissions from the lamps and from coal-fired power plants providing electricity for lighting as compared with the other light bulbs considered. The SCHER was also of the opinion that a human health risk for adults due to breakage of such lamps was unlikely. For children SCHER could not conclude on the risk, since data on exposure are missing.

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14 OJ L396/1 of 30.12.2006

15 OJ L164/7 of 26.6.2009

16 http://ec.europa.eu/health/archive/ph_risk/committees/04_scenihr/docs/scenihr_o_025.pdf

17 http://ec.europa.eu/environment/chemicals/mercury/pdf/study_report2008.pdf

18 Directive 2009/125/EC, OJ L 285, 31.10.2009, p.10

19 OJ L251/28 of 25.9.2010

20 OJ L37/24 of 13.2.2003

21 http://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_124.pdf

In December 2008, the Commission proposed a recast of the WEEE and of the RoHS Directives which aims, inter alia, at a further reduction of the hazardous substances (including mercury) content in waste and enhanced recollection and recycling targets. A first reading agreement was reached in the co-decision process for RoHS in November 2010, whilst the WEEE proposal is still under examination by the European Parliament and the Council. Directive 2000/53/EC on end-of-life vehicles[22] (as last amended in 2010) stipulates a general ban on mercury in materials and components of vehicles. An exemption is still granted for headlight lamps and fluorescent tubes used in instrument panel displays, but this exemption is limited in time until 1 July 2012 (date of vehicle type approval).

Under Directive 2006/66/EC on batteries and accumulators and waste batteries and accumulators[23], the maximum allowed content of mercury in batteries and accumulators was significantly lowered as compared to the previous (repealed) Batteries Directive 91/157/EEC.

3.4. Addressing surpluses and reservoirs

Action 9: storage

Regulation (EC) No 1102/2008 of the European Parliament and of the Council on the banning of exports of metallic mercury and certain mercury compounds and mixtures and the safe storage of metallic mercury stipulates that mercury from selected large-volume sources, in particular the chlor-alkali industry, is to be considered as waste and subject to disposal. Specific criteria for the safe storage of metallic mercury are presently under development and will be adopted by the Commission early 2011. In addition, the European chlor-alkali industry signed a voluntary agreement, committing itself to send surplus mercury only to storage sites that guarantee high safety standards. The reporting obligations under Regulation No 1102/2008 will allow the Commission to monitor closely the implementation of this commitment.

In line with the obligation to keep under review ongoing research activities on safe disposal options, including solidification of metallic mercury (see Article 8(2) of the Regulation), the Commission has commissioned a consultant's report finalised in autumn 2010[24]. Progress in solidification techniques that are about to hit the market are likely to impact on the development of requirements and criteria for the storage of metallic mercury according to Article 4(3). This work is still ongoing by the time of adoption of this Communication.

Action 10: mercury in products already circulating in society

Work undertaken under this action is reported under action 8.

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22 OJ L 269, 21.10.2000, p.34

23 OJ L 266, 26.9.2006, p.1

24 http://ec.europa.eu/environment/chemicals/mercury/

3.5. Protection against exposure

Action 11: mercury in fish and seafood

The European Food Safety Authority (EFSA) has developed refined tools to calculate exposure at a detailed food level and in some specific population groups. The new Comprehensive Food Consumption Database[25] contains information on children and adult consumption at individual level capturing age, gender and weight of each participant. If new data on mercury become available, refined exposure assessments can be carried out using the new food consumption database.

National authorities have given more detailed consumption advice concerning mercury in food using the Information Note from the Commission as a basis (see also below under action 12).

In order to further improve the protection of the health of workers who may be exposed to mercury, the Commission adopted Directive 2009/161/EU[26] establishing a third list of indicative occupational exposure limit values (IOELVs). This includes an IOELV for mercury and divalent inorganic mercury compounds.

Action 12: information on mercury in food

On the basis of the knowledge acquired under Action 11, the Commission issued an Information Note[27] to Member States regarding methylmercury in fish and fishery products on 21 April 2008. This note provides advice on the maximum quantities of certain fish to be consumed by vulnerable groups (pregnant and breast-feeding women and young children), which should be used as guidance by Member States when issuing consumer advice.

3.6. Improving understanding

Action 13: priorities for mercury research

A number of research projects addressing priorities for mercury research have been funded by the EU since 2005. Details of projects funded through the Seventh Framework Programme **(**FP7) and other research funding mechanisms are available through the Community Research and Development Information Service (CORDIS)[28]. A grant agreement for a five-year research project on a Global Mercury Observation System (GMOS) with a total cost of 8,8 million euro and involving 24 partners from 24 countries has been recently signed under the FP7 environment programme. The Commission contributes 6,8 million Euro to the overall cost for this project that officially started on 1 November 2010. The objective of GMOS is to provide key information on the atmospheric transport of mercury at global scale that could be used as a basis for the evaluation of the effectiveness of mercury emissions'

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25 http://www.efsa.europa.eu/en/datex/datexfooddb.htm

26 OJ L338 of 19.12.2009

27 Information note from the EC dated 21 April 2008 on methylmercury in fish and fishery products: ec.europa.eu/food/food/chemicalsafety/contaminants/information_note_mercury-fish_21-04-2008.pdf

28 http://cordis.europa.eu/search

reduction strategies. This will be an important contribution in assessing the long-term success of the relevant policies at European and global level.

The EU's financial instrument for the Environment (LIFE) has been used to fund a pilot project on the safe disposal of metallic mercury[29]. In addition, the European Commission launched in 2009 a study on "Scientific support in relation to the EU Mercury Policy". The objective of the study is to provide the Commission with a solid scientific knowledge base on mercury by analysing and summarising existing research results of policy relevance. It will provide for a consolidated inventory of mercury-related findings from diverse research projects undertaken over the recent years. The results of this study are expected for summer 2011.

3.7. Supporting and promoting international action.

The EU actively supported efforts under the UNEP Global Mercury Programme, in particular those leading to decision 25/5[30] of the UNEP Governing Council in February 2009. Decision 25/5 was the starting point for a 3 to 4 year negotiation process that should lead to a global legally binding instrument on mercury (see also chapter 2 and actions 17 & 18). At the global level, the European Commission has provided support to the Group on Earth Observation that has recently initiated a new Task (Global Monitoring Plan for Mercury) aiming to build a global observation system for mercury.

Action 14: input to international fora and activities

In addition to the above, the European Commission and several Member States have engaged in a number of international activities raising awareness as well as seeking solutions for the mercury problem. In this context, an international conference was organised by the European Commission in October 2006 in Brussels. The EU and its Member States are members and participants in several international fora where the mercury issue is discussed[31]. Initiatives have also been taken at individual Member State level, such as IKIMP[32] (Integrating Knowledge to Inform Mercury Policy), a 3-year knowledge exchange initiative dedicated to mercury issues in the UK.

Action 15: funding to reduce emissions from coal combustion in third countries

The European Commission has provided funding of €1million to UNEP for carrying out a project on "Reducing mercury emissions from coal combustion in the energy sector". The project currently underway is being lead by the International Energy Agency Clean Coal Centre[33] and focuses on countries with a high dependency on solid fuels in particularly China, India, Russia and South Africa. Furthermore, an open call for proposals on clean coal technologies was published by the European Commission in 2010 for grants targeted at coal-dependent countries, emerging

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29 MERSADE project (http://www.mayasa.es/ing/mersade.asp); MERSADE LIFE06 ENV/ES/PREP/03

30 http://www.chem.unep.ch/mercury/GC25/GC25Report_English_25_5.pdf

31 Including the UNEP Mercury Programme, the Heavy Metals Protocol under the UNECE LRTAP Convention, the OSPAR and Basel Conventions etc

32 http://www.mercurynetwork.org.uk/

33 http://www.iea-coal.org.uk

economies and developing countries[34]. These grants are aimed mainly at capacity building activities and studies and comprise a total budget of 3 million euro. While the project will not focus exclusively on mercury it will help identifying co-benefits of emission control techniques in the coal-based power sector.

Action 16: prior informed consent for the import of mercury

Already since 2003, prior informed consent has been made mandatory for the export and import of mercury compounds through Regulation (EC) No 304/2003 (now replaced by Regulation (EC) No 689/2008[35]) concerning the export and import of dangerous substances, thereby implementing the Rotterdam Convention on the Prior Informed Consent (PIC) procedure on certain dangerous chemicals and pesticides in international trade. The PIC procedure was also applied to imports of mercury compounds for use as pesticide.

Action 17: Heavy Metals Protocol to the UNECE Convention on Long Range Transboundary Air Pollution

The EU and 20 Member States are Parties to the Heavy Metals Protocol under the UNECE Convention on Long Range Transboundary Air Pollution (LRTAP). The European Commission strongly encourages Member States that have not ratified the Protocol yet to do so the soonest possible. In September 2008, the EU proposed the addition of a number of mercury-containing products to Annex VI of the Protocol. The Executive Body of the LRTAP Convention will decide in December 2010 on the possible opening of a negotiation process and on the scope of the negotiation mandate. However, it will be important to ensure that negotiations under the Heavy Metals Protocol are in line with developments under the future UNEP legally binding instrument on Mercury.

Action 18: support the UNEP Global Mercury Programme

The European Commission is participating in the Global Mercury Partnership Advisory Group and has formally subscribed to the "Mercury Releases from Coal Combustion" Partnership area, while Germany and Italy are members of the "Mercury Waste Management" and "Mercury Air Transport and Fate Research" areas respectively. UNEP Governing Council Decision 25/5 specified the Global Mercury Partnership as one of the main mechanisms for the delivery of immediate actions on mercury during the negotiation process of the global legally binding instrument on mercury.

Action 19: mercury in the gold mining sector

In 2010 the European Commission will provide a financial contribution of €1,5 million to UNDP for setting up the Guiana Shield Facility[36]. The facility is a multi-donor financial mechanism focused on activities needed to ensure the ecological

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34 https://webgate.ec.europa.eu/europeaid/online-services/index.cfm?ADSSChck=1281432803820&do=publi.detPUB&searchtype=AS&Pgm=7573841&debpub=&orderby=upd&orderbyad=Desc&nbPubliList=15&page=1&aoref=129199

35 OJ L204/14 of 31.7.2008

36 http://ec.europa.eu/europeaid/documents/aap/2010/af_aap_2010_dci-env.pdf

integrity of the Guyana Shield eco-region[37]. It will fund field-based projects addressing (among others) risks caused by illegal and unregulated gold mining by small scale gold miners (*garimpeiros*) spreading into French Guyana, Suriname, Guyana, Venezuela and Colombia.

Action 20: reduction of mercury supply at the international level

The mandate given by UNEP's Governing Council to the INC in form of Decision 25/5 contains inter alia the reduction of mercury supply, capacity-building for the environmentally sound storage of the substance and the reduction of international trade in mercury. The EU has already made a contribution to the overall goal by adopting the Mercury Export Ban Regulation (see action 5). Within the negotiating process, the EU will advocate its policy approach and explore the possibilities of how it could be appropriately reflected in a future legally binding instrument.

4. CONCLUSIONS

The implementation of the Mercury Strategy is in an advanced stage, having delivered on almost all actions.

For the reduction of mercury emissions, a new legal framework is now in place for large point sources. The implementation of the new Industrial Emissions Directive will allow the EU to realise the considerable emission reduction potential that can be achieved through the application of Best Available Techniques. However, this will require an ambitious transposition and implementation practice in the Member States which will be closely followed and supported by the Commission.

Concerning the demand for mercury in products, current work will continue on the extension of the existing marketing restrictions for certain measuring devices containing mercury to additional devices used in the health care sector, in particular sphygmomanometers and for other professional and industrial uses.

The Commission sees in particular the necessity to investigate more the issue of dental amalgam. The Commission therefore intends to undertake in 2011 a study to assess the issue in more detail with due consideration to all aspects of its lifecycle.

International action is a priority for the coming years. Given the global aspect of the mercury problem, internal EU legislation alone cannot guarantee effective protection of the European citizen. The Commission therefore intends to focus its efforts on the negotiation of a global legally binding instrument on mercury under the auspices of UNEP. In this context, the EU has a lot to offer by having already effective instruments at EU level. Once this international instrument has taken shape, the European Commission will assess which aspects of the mercury life cycle should be subject to additional EU-specific action, including if needed additional legislative proposals, and taking into account the 2013 review of the Export Ban Regulation and further progress under the Strategy. This is particularly valid for the additional import and export restrictions suggested by the consultant's review study which need to be assessed against the background of internationally negotiated obligations.

[37] http://www.guianashield.org

ANNEX

The actions of the Community Strategy Concerning Mercury (full text)

1. REDUCING EMISSIONS

Action 1. The Commission will assess the effects of applying IPPC on mercury emissions, and consider if further action like Community emission limit values is needed, as data under the IPPC and EPER[38] reporting requirements are submitted, and in a broader strategy review by the end of 2010. This will include review of the co-benefit effect of controls to be implemented by 1 January 2008 under Directive 2001/80/EC to reduce sulphur dioxide emissions from large combustion plants.

Action 2. The Commission will encourage Member States and industry to provide more information on mercury releases and prevention and control techniques, so conclusions can be drawn in BREFs helping to reduce emissions further. The second edition of the chlor-alkali BREF will include information to address the risk of releases in decommissioning mercury cells.

Action 3. The Commission will undertake a study in 2005 of options to abate mercury emissions from small scale coal combustion, to be considered alongside the broader CAFE assessment.

Action 4. The Commission will review in 2005 Member States' implementation of Community requirements on the treatment of dental amalgam waste, and will take appropriate steps thereafter to ensure correct application.

2. REDUCING SUPPLY

Action 5. As a pro-active contribution to a proposed globally organised effort to phase out primary production of mercury and to stop surpluses re-entering the market as described in section 10, the Commission intends to propose an amendment to Regulation (EC) No. 304/2003 to phase out the export of mercury from the Community by 2011.

3. REDUCING DEMAND

Action 6. In the short term the Commission will ask the Medical Devices Expert Group to consider the use of mercury in dental amalgam, and will seek an opinion from the Scientific Committee on Health and Environmental Risks, with a view to considering whether additional regulatory measures are appropriate.

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[38] Commission Decision 2000/479/EC of 17 July 2000 on the implementation of a European pollutant emission register (EPER) according to Article 15 of Council Directive 96/61 concerning integrated pollution prevention and control, OJ L192, 28.7.2000.

Action 7. The Commission intends to propose in 2005 an amendment to Directive 76/769/EEC[39] to restrict the marketing for consumer use and healthcare of non-electrical or electronic measuring and control equipment containing mercury.

Action 8. The Commission will further study in the short term the few remaining products and applications in the EU that use small amounts of mercury. In the medium to longer term, any remaining uses may be subject to authorisation and consideration of substitution under the proposed REACH Regulation[40], once adopted.

4. ADDRESSING SURPLUSES AND RESERVOIRS

Action 9. The Commission will take action to pursue the storage of mercury from the chlor-alkali industry, according to a timetable consistent with the intended phase out of mercury exports by 2011. In the first instance the Commission will explore the scope for an agreement with the industry.

Action 10. The Commission will undertake further study in the short to medium term of the fate of mercury in products already circulating in society.

5. PROTECTION AGAINST EXPOSURE

Action 11. In the short term, EFSA will investigate further specific dietary intakes of different types of fish and seafood among vulnerable subpopulations (e.g. pregnant women, children).

Action 12. The Commission will provide additional information concerning mercury in food as new data become available. National authorities will be encouraged to give advice in the light of local specificities.

6. IMPROVING UNDERSTANDING

Action 13. Priorities for mercury research will be addressed in the 7th RTD Framework Programme and other appropriate funding mechanisms.

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39 Directive 76/769/EEC on the approximation of the laws, regulations and administrative provisions of the Member States relating to restrictions on the marketing and use of certain dangerous substances and preparations, OJ L 262, 27.9.76.

40 Proposal for a Regulation of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency and amending Directive 1999/45/EC and Regulation (EC) {on Persistent Organic Pollutants}, COM(2003) 644 final, 29.10.2003.

7. SUPPORTING AND PROMOTING INTERNATIONAL ACTION

Action 14. The Community, Member States and other stakeholders should pursue input to international fora and activities, and bilateral engagement and projects with third countries, including technology transfer, to address the mercury problem.

Action 15. The Commission will consider establishing a specific funding scheme for research and pilot projects to reduce mercury emissions from coal combustion in countries with a high dependency on solid fuels, e.g. China, India, Russia, etc., similar to the CARNOT programme that promotes the clean and efficient use of solid fuels.

Action 16. The Community should promote an initiative to make mercury subject to the PIC procedure of the Rotterdam Convention.

Action 17. The Community and Member States should continue to support work under the Heavy Metals Protocol to the UNECE Convention on Long Range Transboundary Air Pollution.

Action 18. The Community, Member States and other stakeholders should also support the UNEP Global Mercury Programme, e.g. through review of materials and provision of technical knowledge and human and financial resources.

Action 19. The Community and Member States should support global efforts contributing to reduced use of mercury in the gold mining sector, e.g. the UNDP/GEF/UNIDO Global Mercury Project. They will also consider possibilities to support individual developing countries through the various instruments related to development cooperation assistance, taking national strategies for development into account.

Action 20. To reduce mercury supply internationally, the Community should advocate a global phase-out of primary production and encourage other countries to stop surpluses re-entering the market, under an initiative similar to that of the Montreal Protocol on substances that deplete the ozone layer. To support this objective, the envisaged amendment of Regulation (EC) No. 304/2003 would phase out the export of mercury from the Community by 2011.

EUROPEAN
COMMISSION

Brussels, 2.2.2016
COM(2016) 39 final

2016/0023 (COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on mercury, and repealing Regulation (EC) No 1102/2008

(Text with EEA relevance)

{SWD(2016) 14 final}
{SWD(2016) 17 final}
{SWD(2016) 18 final}

EXPLANATORY MEMORANDUM

1. CONTEXT OF THE PROPOSAL

General context – Grounds for and objectives of the proposal

The Union and twenty-six Member States signed a new International Convention on Mercury[1], negotiated under the auspices of UNEP. The Convention is named the "Minamata Convention" (hereafter, "Minamata Convention" or "the Convention"), after the name of the town where the worst ever case of mercury pollution occurred between 1950 and 1960. The signature marked the successful end of a negotiation process, involving five sessions of an Intergovernmental Negotiating Committee. All Member States are committed to ratifying the Convention.

The Convention addresses the whole life-cycle of mercury, from primary mercury mining to the management of mercury waste, with the objective to protect human health and the environment from anthropogenic emissions of mercury and mercury compounds to air, water and land. In particular, it sets restrictions on primary mining of mercury and on international trade of mercury, prohibits the manufacture, import and export of a wide range of mercury-added products, foresees prohibitions or operating conditions for several manufacturing processes using mercury, calls for discouraging new uses of mercury in products and industrial processes and measures to be taken to reduce mercury emissions from artisanal and small-scale gold mining (hereafter, "ASGM") and industrial activities, including through the use of best available techniques and requires interim storage of mercury and management of mercury waste to occur in an environmentally sound manner.

Much of the Minamata Convention is already covered by Union legislation. Regulation (EC) No 1102/2008[2] sets an export prohibition on mercury and on several mercury compounds, qualifies mercury from certain sources as waste and establishes rules on the storage of mercury. Other EU instruments contain *ad hoc* provisions on mercury and mercury compounds, including Regulation (EU) No 649/2012[3] that sets a notification system applicable *inter alia*, to imports of mercury and Regulations (EC) 396/2005[4], 1907/2006[5], 1223/2009[6] and Directives 2006/66/EC[7] and 2011/65/EU[8], which address the placing on the

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1 Portugal and Estonia did not sign the Minamata Convention.

2 Regulation (EC) No 1102/2008 of the European Parliament and of the Council of 22 October 2008 on the banning of exports of metallic mercury and certain mercury compounds and mixtures and the safe storage of metallic mercury (OJ L 304, 14.11.2008, p. 75).

3 Regulation (EU) 649/2012 of the European Parliament and of the Council of 4 July 2012 concerning the export and import of hazardous chemicals **(**OJ L 201, 27.7.2012, p. 60).

4 Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC (OJ L 70, 16.3.2005, p. 1)**.**

5 Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC **(**OJ L 396, 30.12.2006, p. 1).

6 Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products **(**OJ L 342, 22.12.2009, p. 59).

7 Directive 2006/66/EC of the European Parliament and of the Council of 6 September 2006 on batteries and accumulators and waste batteries and accumulators and repealing Directive 91/157/EEC (OJ L 266 of 26.9.2006, p. 1).

8 Directive 2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment (OJ L 174 of 1.7.2011, p. 88).

Union market of a range of mercury-added products and set maximum levels of mercury content. Additionally, Directives 2010/75/EU[9], 2012/18/EU[10], 2008/98/EC[11] and 1999/31/EC[12] aim at controlling, reducing and, when mercury-free alternatives exist, eliminating point sources and diffuse emissions of mercury, mercury compounds and mercury waste into the environment.

The assessment of the Union *acquis* has identified a limited number of regulatory gaps that need to be filled in to ensure the full alignment of Union legislation with the Convention.[13] This proposal seeks to address those gaps, which concern the following issues:

- the import of mercury;
- the export of certain mercury-added products;
- the use of mercury in certain manufacturing processes;
- new mercury uses in products and manufacturing processes;
- mercury use in ASGM and
- mercury use in dental amalgam.

In the interest of legal clarity, the obligations resulting from the Convention that are not yet transposed into EU law should be integrated into a single legal act.

For that purpose, Regulation (EC) No 1102/2008, as the only dedicated Union legal act on mercury to date, should serve as the basis for doing so. Yet, given the nature and extent of the necessary modifications to Regulation (EC) No 1102/2008 and the need to enhance consistency and legal clarity, this proposal should repeal and replace it while taking over its substantive obligations whenever still needed.

Consistency with other policies and objectives of the Union

This initiative is consistent with the seventh Environment Action Programme[14] that establishes the long-term objective of a non-toxic environment and that stipulates, for that purpose, that action is needed to ensure the minimisation of significant adverse effects of chemicals on human health and the environment by 2020.

The objectives of this initiative are also consistent with the Europe 2020 objectives on smart, inclusive, and sustainable growth, by stimulating innovation in terms of the development of mercury-free products and manufacturing processes. This proposal, by promoting ratifications of the Convention and its entry into force, will contribute to levelling the global playing-field for industrial processes using or unintentionally emitting mercury and mercury compounds

[9] Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on Industrial Emissions (OJ L 334 of 17.12.2010, p. 17).

[10] Directive 2012/18/EU of the European Parliament and of the Council of 4 July 2012 on the control of major-accident hazards involving dangerous substances, amending and subsequently repealing Council Directive 96/82/EC (OJ L 197 of 24.7.2012, p. 1).

[11] Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain Directives (OJ L 312 of 22.11.2008, p. 3).

[12] Council Directive 1999/31/EC of 26 April 1999 on the landfill of waste (OJ L 182 of 16.7.1999, p. 1).

[13] Commission Staff Working Document, Impact Assessment *Accompanying the documents* Proposal for a Regulation of the European Parliament and of the Council on mercury, and repealing Regulation (EC) No 1102/2008 and Proposal for a Council Decision on the conclusion of the Minamata Convention on Mercury, SWD [2016] 17 final.

[14] Decision No 1386/2013/EU of the European Parliament and of the Council of 20 November 2013 on a General Union Environment Action Programme to 2020 'Living well, within the limits of our planet' (OJ L 354, 28.12.2013, p. 171).

and the manufacturing and trading of mercury-added products, thereby promoting the competitiveness of Union industry, all the more as most its provisions mirror the Union *acquis*.

Additionally, simplification and clarification of the *acquis* to enable better implementation is pursued where possible.

2. RESULTS OF CONSULTATIONS WITH THE INTERESTED PARTIES AND IMPACT ASSESSMENTS

Consultations with interested parties

Member State authorities and stakeholders were consulted within the framework of two studies conducted by the Commission[15,16] and at a workshop held in Brussels on 7 July 2014 following which a request for additional information on specific issues was also published[17]. All written contributions received were made publicly available on the Commission's website[18]. A broad on-line public consultation was also run from 14 August 2014 until 14 November 2014 and publicised on the basis of a questionnaire[19] on the *"Your voice in Europe"* webpage[20]. The objective of this survey was to get a better understanding of the views of the public stakeholders and Member States concerning the ratification of the Convention and specific issues related to its transposition and implementation, in particular in relation to the areas where Union legislation needs to be aligned with the Convention. The target groups were citizens, public authorities, research organisations, academia, non-profit/non-governmental organisations, consultancies and private companies and their representative organisations. There was broad consensus among stakeholders and the public in general that the Union should ratify the Minamata Convention. Specific issues raised by stakeholders were taken into account in the preparation of this proposal.

Result of the impact assessment

The impact assessment (hereafter: "IA") concluded that the ratification and implementation of the Minamata Convention will provide the EU with significant environmental and human health benefits, mainly due to the expected reduction of mercury emissions originating in other parts of the world. In particular:

- Once implemented, important provisions of the Convention concerning among others the application of the best available techniques (hereafter, "BAT") to abate emissions from large industrial plants, the phase out of existing primary mining combined with the prohibition of new primary mining or the establishment of restrictions on ASGM are expected to have a great positive environmental impact both globally and for the Union. Such activities practically do not exist within the EU or are already regulated. This will allow the Union to meet its objectives on the protection of the environment and human health, as outlined in the 2005 Community Strategy Concerning Mercury ('the Strategy')[21].

[15] ICF, COWI, BiPRO, Garrigues (2015). Study on EU Implementation of the Minamata Convention on Mercury (March 2015)

[16] COWI, BiPRO (2015). Ratification of the Minamata Convention by the EU - Complementary Assessment of the Mercury Export Ban (June 2015).

[17] http://ec.europa.eu/environment/chemicals/mercury/pdf/InfoRequest.pdf

[18] http://ec.europa.eu/environment/chemicals/mercury/ratification_en.htm

[19] Questionnaire available at: http://ec.europa.eu/environment/consultations/pdf/MinamataConvention.pdf

[20] http://ec.europa.eu/yourvoice/consultations

[21] Communication of 28 January 2005 from the Commission to the Council and the European Parliament "Community Strategy Concerning Mercury", COM(2005) 20 final.

- By implementing the Convention, third countries will apply similar standards as those currently in force within the Union to many industrial activities. This will help address potential competitive advantages benefitting companies in non-EU Member States that are subject to less strict (or even non-existing) environmental standards and possibly open new markets for Union companies specialising in environmental technology. As an illustrative example, the provisions of the Convention on mercury emissions from certain industrial activities will make numerous industrial facilities emitting mercury on the global scale subject to the use of BAT that are already applied by the Union industry.
- The IA examined different policy options to address the above-listed six regulatory gaps affecting EU law: a baseline option corresponding to "No EU action", and at least two different options for each of the relevant policy areas, i.e. one option consisting in transposing the obligations set out in the Convention and one option consisting in laying down requirements going beyond what is required by the Convention.

With regard to the use of dental amalgam, the IA assessed the need for measures and their potential impacts:

- Commission Decision 2000/532/EC[22] characterises amalgam waste from dental care as hazardous waste, it is therefore subject to the provisions of the Waste Framework Directive[23]. Mercury emissions from dental cabinets are also subject to Union water legislation. Mercury is classified as priority hazardous substance according to Annex X of the Water Framework Directive[24] and hence the release of this substance to water has to be drastically reduced. As amalgam is the second biggest use of mercury within the Union with an estimated pollution potential of about 75t of mercury per year and a long-term pollution potential of more than 1000t[25], specific measures addressing this source are necessary.
- The IA concludes, in the light of the available scientific information, that a prohibition of the use of dental amalgam would not be proportionate as the health risks of dental amalgam are not clearly demonstrated and the cost of a prohibition would be high. Furthermore, the assessment shows that two measures included in the list of measures proposed in the Convention, and from which Parties should take at least two, would deliver environmental and health benefits at a low cost, i.e. the restriction of the use of dental amalgam to its encapsulated form and the promotion of the use of best environmental practices in dental facilities. Such measures are in line with Action 4 of the Mercury Strategy that was confirmed as a priority area for further action by the review of the Strategy in 2010. They would reduce exposure of dentists and patients to mercury emissions and ensure a drastic reduction of mercury releases to sewage systems and to the environment via urban wastewater treatment plants. Furthermore, the generation of new jobs is expected in companies involved in the manufacturing, installation and maintenance of amalgam separators and in companies specialising in the collection and treatment of mercury-containing waste.

[22] Commission Decision 2000/532/EC of 3 May 2000 replacing Decision 94/3/EC establishing a list of wastes pursuant to Article 1(a) of Council Directive 75/442/EEC on waste and Council Decision 94/904/EC establishing a list of hazardous waste pursuant to Article 1(4) of Council Directive 91/689/EEC on hazardous waste (OJ L 226, 6.9.2000, p. 3).0

[23] *Supra*, No 11.

[24] Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy (OJ L 327 of 22.12.2000, p. 1).

[25] Quantity of mercury estimated in people's mouths in the form of dental amalgam within the EU.

- Although the majority of the businesses concerned would qualify as microenterprises, they would not be disproportionally affected by the proposed measures as (1) given the type of activity they would not suffer from competition with larger undertakings, (2) the implementation cost of the measure is limited and would require only low investment, and (3) no jobs loss is expected in the dentistry sector. Furthermore, those measures are good practice promoted[26] by the Council of European Dentists and the majority have already implemented them. However, as such undertakings would need time to adapt to the obligations set out in this Regulation, the compliance date proposed for these measures is one year later than for the other measures covered in this Regulation. Finally, the requirement to use amalgam in an encapsulated form would not cause any additional burden to dentists who have opted out from using dental amalgam.

With regard to the other gaps, the analysis carried out in the IA concludes as follows:

- Import restrictions on mercury: trade restrictions that would go beyond the requirements of the Convention, i.e. to set an unconditional mercury import prohibition (rather than allowing imports of mercury under certain conditions related to the place of origin and to the source of the imported mercury) would not be justified as they would be more costly for Union industry and would not have any significant environmental benefits.
- Export restrictions on certain mercury-added products: trade restrictions that would go beyond the ones established in the Convention, i.e. to prohibit the export of mercury-added products subject to stricter Union rules regarding their mercury content than those laid down in the Convention (rather than prohibiting only exports of mercury-added products that do not meet the requirements of the Convention) would not be justified given that mercury input and releases into the environment would remain largely unchanged and that mercury emissions could, as a consequence of such a prohibition, increase in third countries.
- To restrict the use of mercury in certain manufacturing processes: the establishment of an absolute prohibition on the use of mercury for the production of sodium or potassium ethylate or methylate (instead of requirements limiting mercury use and emissions as foreseen in the Convention) would not be justified given the need for industry to be supplied with certain chemicals for which the availability of mercury-free production processes could not be demonstrated.
- To restrict mercury use in new manufacturing processes and products: the Convention provides only for Parties to take measures to discourage the development of new manufacturing processes using mercury and the production and placing on the market of new mercury-added products. Setting up a conditional prohibition applicable to those processes and products would result in the best environmental and economic outcome as it would have a strong signal value and thus reduce the risk that economic operators engage in costly development of such products or processes that would likely be subsequently prohibited.
- To restrict mercury use in ASGM: as the only Member State concerned, France, has already taken measures to prohibit the use of mercury in ASGM, it is therefore sufficient for the Union to simply transpose the obligation to develop and review a national action plan in accordance with the Convention.

[26] CED resolution on responsible practice (2011).

Economically-wise, the total cost of above-mentioned options, that have been singled out in the IA as the preferred ones ranges between 13-135 million EUR/y, mainly reflecting the costs of measures relating to the use of mercury in manufacturing processes and dental amalgam.

3. LEGAL ELEMENTS OF THE PROPOSAL

Summary of the proposed action

While Regulation (EC) No 1102/2008 constitutes the starting point for this Proposal, it is appropriate to repeal and replace it for the sake of legal clarity. Annex IV contains the correlation table.

Articles 1 and 2 specify the subject-matter of the proposal and provide definitions of key terms used therein.

Article 3 read in combination with Annex I sets a prohibition on the export from the Union of mercury, of several mercury compounds and of mixtures of mercury with other substances, save in respect of those mercury compounds that can still be exported when aimed at laboratory-scale research. This prohibition is already established since March 2011 in accordance with Article 1 of Regulation (EC) No 1102/2008 and complements the one provided for in Regulation (EU) No 649/2012. It transposes Article 3 (6), of the Minamata Convention read in combination with its Article 3 (1) ((a) and (b)), and (2) (a).

Article 4 prohibits the import into the Union of mercury when intended for ASGM and puts up a conditional prohibition on the import into the Union of mercury and of mixtures when planned for other uses. Such a prohibition does not apply to imports of mercury and of mixtures for final disposal as waste, to imports of mercury from countries that are Parties to the Minamata Convention when it originates from a primary mining source that is still allowed under Article 3(4) of the Convention, to imports of mercury from countries that are not Parties to the Convention provided that imported mercury is neither from primary mining nor from the chlor-alkali sector and that an import written consent has been granted. For the purpose of streamlining administrative activity and preventing an increased administrative burden, Article 4(3) specifies that the national competent authorities designated under Regulation (EU) No 649/2012 shall also be those in charge of the implementation and control of such a prohibition.

Article 5 read in combination with Annex II transposes Article 4(1) and Annex A (Part I) of the Minamata Convention. It sets a prohibition, which shall start on 1st January 2021, on the export, import and manufacturing of a range of mercury-added products. Article 5 applies both as a complement and without prejudice to provisions of the EU *acquis* that establish already restrictions on the placing on the market and that set stricter requirements in terms, for instance, of the maximum mercury content of these products, as laid down, among others, in Directive 2006/66/EC.

Article 6 foresees the possible adoption of Commission Implementing Decisions specifying the trade forms to be used by the Member States' competent authorities to implement Articles 3 and 4, as a follow up of Decisions that will be adopted by the Conference of the parties of the Minamata Convention ('CoP') in accordance with Article 3(12) of the Convention.

Article 7 read in combination with Annex III transposes Article 5 (2 and 3) and Annex B of the Convention. It prohibits the use of mercury and mercury compounds as catalyst for the production of acetaldehyde and of vinyl chloride monomer as from 1st January 2019. Regarding installations producing sodium or potassium methylate or ethylate using a mercury-based process, it establishes restrictions on the use of mercury from primary mining

and on releases of mercury and mercury compounds to the environment while prohibiting, as from the date of entry into force of this Regulation, any increase of production capacity or new establishment of installations. Article 7(3) foresees the possible adoption of Commission Delegated Acts as a means to transpose Decisions of the CoP establishing requirements for the interim storage of mercury and mercury compounds when supported by the Union, thereby maintaining the application of the ordinary legislative procedure in the absence of a Union position in favour of the concerned CoP decision or when the Union would have opposed to it.

Article 8 transposes Articles 4(6 and 7) and 5(4 and 9) of the Convention. It sets a prohibition on the manufacturing and placing on the market of mercury-added products not covered by any known use prior to the date of application of this proposal and on the implementation of manufacturing processes that did not exist prior to this date. Article 8(3 and 4) establishes a mechanism by which such new mercury-added products and manufacturing processes could still be allowed by means of a Commission Implementing Act taken on the basis of an assessment of their environmental and human health benefits and of the availability of mercury-free alternatives that are technically and economically feasible.

In accordance with Article 7 of the Convention, Article 9 read in combination with Annex IV provides that Member States where ASGM occurs shall take steps to reduce, and where feasible eliminate, the use and emissions of mercury and mercury compounds resulting from such an activity and shall develop and implement a relevant national plan.

Article 10 transposes Article 4(3) and Annex A (Part II) of the Minamata Convention. It requires that dental amalgam be used only in an encapsulated form and that dental facilities be equipped with amalgam separators to retain and collect mercury-containing amalgam residues, as from 1st January 2019. It calls upon Member States to make use of relevant EN standards, as last updated, including EN ISO 138987[27], EN ISO 24234[28] and EN 1641:2009[29] or of any other national or international standards ensuring an equivalent level of amalgam residue retention and quality of amalgam capsules.

Article 11 reproduces Article 2 of Regulation (EC) 1102/2008 by providing that mercury that is no longer used in the chlor-alkali industry or generated from the cleaning of natural gas or from non-ferrous metals mining and smelting or extracted from cinnabar ore qualifies as waste that must be disposed of.

Article 12 is based upon Article 6 of Regulation (EC) 1102/2008 and provides that the companies operating activities referred to in Article 11 shall have to provide annually to national competent authorities information regarding notably the amount of mercury stored within each installation concerned and the amount of mercury sent to temporary or permanent mercury waste storage facilities. Article 12(2) provides that information must be reported by using the relevant waste category and NACE codes, as established in Regulation (EC) No 2150/2002[30]. Article 12(3) specifies that installations producing chlor-alkali using mercury cells shall cease reporting once all those cells will have been decommissioned in accordance

[27] European standard EN ISO 13897, *Dentistry – Amalgam capsules (ISO 1397:2003)*, May 2004.
[28] European standard EN ISO 24234:2015, *Dentistry – Dental amalgam (ISO 24234:2015)*, January 2015.
[29] European standard EN 1641:2009, *Dentistry – Medical devices for dentistry – Materials*, October 2009.
[30] Regulation (EC) No 2150/2002 of the European Parliament and of the Council of 25 November 2002 on waste statistics (OJ L 332, 9.12.2002, p. 1).

with Commission Implementing Decision 2013/732/EU[31] and all mercury waste has been transferred to a storage facility.

Article 13 provides that mercury waste can be temporarily or permanently stored in underground storage facilities and temporarily stored in above-ground storage facilities and specifies, for that purpose what requirements established in Council Directive 1999/31/EC for the temporary storage of mercury waste are applicable to the permanent storage of mercury waste in underground storage facilities.

Articles 14 and 20 lay down the provisions on penalties applicable to breaches of this proposal and on its entry into force and date of application.

Article 15 transposes Article 21 of the Minamata Convention by providing for an obligation for Member States to prepare, update and publish a report containing all relevant information on the implementation of this proposal, information that needs to be reported to comply with above-cited Article 21, a summary of the information gathered under Article 12 of this proposal on mercury waste from large sources and information on the significant individual stocks of mercury that may exist on the territory of each Member State. This provision specifies that the Commission must be informed of such a report and updates within one month of their publication. Article 15(2) provides for the adoption by the Commission of an Implementing Act establishing questionnaires to assist Member States to report relevant information to the Commission by specifying what precise information will have to be submitted, including information on key performance indicators, under what format and by when.

Article 16 foresees the possible adoption by the Commission of delegated acts that would amend Annexes I to IV of this proposal in order to transpose relevant Decisions adopted by the CoP when supported by the Union, thereby maintaining the application of the ordinary legislative procedure in the absence of a Union position in favour of the concerned CoP decision or when the Union would have opposed to it.

Articles 17 and 18 are standard texts for the exercise of the delegation granted to the Commission under Articles 7(3) and 16 and for the Committee procedure as a means to adopt Implementing Acts under Articles 6, 8(4) and 15(2).

Article 19 stipulates that Regulation (EC) No 1102/2008 will be replaced and repealed by 1st January 2018, date where this proposal shall start to apply and that references to Regulation (EC) No 1102/2008 shall be construed as references to this proposal.

Legal basis

Alike Regulation (EC) No 1102/2008, this proposal seeks both to protect the environment and human health and to ensure uniformity in respect of its trade aspects (export and import prohibition and restrictions affecting mercury, mercury compounds and mercury-added products). Accordingly, this proposal has a twofold legal basis, i.e. Articles 192(1) and 207 of the Treaty on the Functioning of the European Union.

Subsidiarity and proportionality principles and choice of instrument

This proposal aims at transposing into the Union *acquis* the provisions of the Minamata Convention that are not yet covered by EU legal requirements in order to enable the Union and the Member States to ratify and implement that Convention.

[31] Commission implementing Decision 2013/732/EU of 9 December 2013 establishing the best available techniques (BAT) conclusions, under Directive 2010/75/EU of the European Parliament and of the Council on industrial emissions, for the production of chlor-alkali (OJ L 332, 11.12.2013, p. 34).

In this respect, the subsidiarity principle applies insofar as this proposal does not entirely fall under the exclusive competence of the Union.

The objectives of this proposal cannot be sufficiently achieved by the Member States. To address the issue of mercury pollution and exposure in the Union, each Member State must *inter alia* implement an export prohibition on mercury and several mercury compounds and on certain mercury-added products and a conditional import prohibition applicable to mercury. Such trade-related measures can only be transposed and implemented on the basis of Union provisions as measures in the field of common commercial policy fall within the exclusive competence of the Union in accordance with Article 3(e) of the Treaty on the Functioning of the European Union.

Regarding the non-trade provisions of this proposal on the use of mercury in existing and new manufacturing pocesses and in new products, on the control of mercury emissions into the environment and on the storage of mercury and management of mercury waste, they belong to the category of the shared competence between the Union and the Member States, i.e. environmental and human health protection. Considering, as specified above, that the protection of the environment and of human health from mercury pollution and exposure is already extensively regulated at Union level, action by the Union is justified. As to the provisions of the Convention on ASGM, this proposal provides the concerned Member State with the choice of the optimum combination of measures to implement to achieve the relevant requirements.

This proposal therefore respects the subsidiarity principle.

The chosen legal instrument is a Regulation as the proposal lays down provisions on e.g. trade and mercury-added products, which require uniform implementation across the Union, while leaving sufficient flexibility to the Member States as regards the choice of measures for compliance with provisions on manufacturing processes and ASGM and their detailed implementation. The proposal therefore complies with the proportionality principle.

4. BUDGETARY IMPLICATION

This legislative Proposal has no budgetary implications.

2016/0023 (COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on mercury, and repealing Regulation (EC) No 1102/2008

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 192(1) and Article 207 thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national Parliaments,

Having regard to the opinion of the European Economic and Social Committee[32],

Having regard to the opinion of the Committee of the Regions[33],

Acting in accordance with the ordinary legislative procedure,

Whereas:

(1) Mercury is a highly toxic substance which represents a global and major threat to human health, including by methylmercury in fish and seafood resources, the ecosystems and wildlife. Due to the transboundary nature of mercury pollution, between 40% and 80% of total mercury deposition in the Union originates from outside of the Union and therefore warrants action at local, regional, national and international levels.

(2) Most mercury emissions and associated exposure risks result from anthropogenic activities, including primary mercury mining and processing, the use of mercury in products, industrial processes and artisanal and small-scale gold mining ("ASGM") and mercury emissions originating in particular from coal combustion and the management of mercury waste.

(3) The seventh Environment Action Programme adopted by Decision No 1386/2013/EU of the European Parliament and of the Council[34] establishes the long-term objective of a non-toxic environment and, for that purpose, stipulates that action is needed to ensure the minimisation of significant adverse effects of chemicals on human health and the environment by 2020.

(4) The Communication from the Commission to the European Parliament and the Council 'Community Strategy Concerning Mercury'[35] ("the Strategy"), as reviewed in

[32] OJ C , , p. .

[33] OJ C , , p. .

[34] Decision No 1386/2013/EU of the European Parliament and of the Council of 20 November 2013 on a General Union Environment Action Programme to 2020 'Living well, within the limits of our planet' (OJ L 354, 28.12.2013, p. 171).

[35] Communication of 28 January 2005 from the Commission to the Council and the European Parliament "Community Strategy Concerning Mercury", COM(2005) 20 final.

2010[36], aims at minimising and, where feasible, ultimately eliminating global anthropogenic mercury releases to air, water and land.

(5) Significant progress has been achieved in the Union in the past 10 years in the field of mercury management following the adoption of the Strategy and of a wide range of measures concerning mercury emissions, supply, demand and use and the management of mercury surplus and stocks.

(6) The Strategy establishes that the negotiation and conclusion of an international legally-binding instrument should be a priority as Union action alone cannot guarantee effective protection of the citizens of the Union against the negative health effects of mercury.

(7) The Union and 26 Member States have signed in Kumamoto on 11 October 2013 the Minamata Convention on Mercury ("the Convention").[37] The Union and all its Member States are therefore committed to its conclusion, transposition and implementation[38].

(8) Swift ratification of the Convention by the Union and its Member States will encourage major global mercury users and emitters, that are signatories of the Convention, to ratify and implement it.

(9) As Union legislation already transposes many of the obligations of the Convention, this Regulation should only lay down provisions that complement the Union *acquis* and that are needed to ensure its full alignment with the Convention and, accordingly, to enable the Union and its Member States to ratify and implement it.

(10) The mercury export ban set out in Regulation (EC) No 1102/2008 of the European Parliament and of the Council[39] should be complemented by restrictions on the import of mercury depending on the source, the intended use and the place of origin of mercury. The national authorities designated in accordance with Regulation (EU) No 649/2012 of the European Parliament and of the Council[40] should perform the administrative functions linked to the implementation of such restrictions.

(11) The export, import and manufacturing of a range of mercury-added products accounting for a significant share of the use of mercury and mercury compounds within the Union and globally should be prohibited.

(12) This Regulation should therefore have a twofold legal basis, Articles 192(1) and 207 of the TFEU, as it seeks to protect both the environment and human health and to ensure uniformity in respect of its trade aspects through the export and import prohibition and restrictions affecting mercury, mercury compounds and mercury-added products.

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36 Communication of 7 December 2010 from the Commission to the European Parliament and the Council "Review of the Community Strategy Concerning Mercury", COM(2010) 723 final.

37 https://treaties.un.org

38 Council Decision XXX of XX/XX/XX on the conclusion of the Minamata Convention on Mercury (OJ L , , p.).

39 Regulation (EC) No 1102/2008 of the European Parliament and of the Council of 22 October 2008 on the banning of exports of metallic mercury and certain mercury compounds and mixtures and the safe storage of metallic mercury (OJ L 304, 14.11.2008, p. 75).

40 Regulation (EU) No 649/2012 of the European Parliament and of the Council of 4 July 2012 concerning the export and import of hazardous chemicals (OJ L 201, 27.7.2012, p. 60).

(13) This Regulation applies without prejudice to the provisions of the applicable Union *acquis* that set stricter requirements for such products, including in terms of their maximum content of mercury.

(14) In the absence of relevant available mercury-free production processes, operating conditions for the production of sodium or potassium methylate or ethylate involving the use of mercury should be set.

(15) The manufacturing and placing on the market of new mercury-added products and the establishment of new mercury-based manufacturing processes would increase the use of mercury and of mercury compounds and mercury emissions within the Union. Such new activities should therefore be prohibited unless an assessment demonstrates that these uses would provide significant environmental and health benefits and that no technically and economically feasible mercury-free alternatives providing such benefits are available.

(16) The use of mercury and mercury compounds in ASGM accounts for a significant share of mercury use and emissions worldwide, and should therefore be regulated.

(17) The use of dental amalgam in an encapsulated form and the implementation of amalgam separators should be made mandatory to protect dental practitioners and patients from mercury exposure and to ensure that resulting mercury waste are not released into the environment, but are collected and subjected to sound waste management. Given the size of the undertakings from the dentristy sector concerned by this change, it is appropriate to provide sufficient time to adapt to the new provision.

(18) Most of the criteria established in Council Directive 1999/31/EC[41] for the temporary storage of mercury waste should apply to the permanent storage of mercury waste in underground storage facilities. The applicability of some of those criteria should depend on the specific characteristics of each underground storage facility, as determined by the competent authorities of the Member States in charge of the implementation of Directive 1999/31/EC.

(19) In order to align Union legislation with Decisions of the Conference of the Parties of the Convention supported by the Union, the power to adopt acts in accordance with Article 290 of the TFEU should be delegated to the Commission in respect of amending the annexes to this Regulation and supplementing this Regulation with technical requirements for environmentally sound interim storage of mercury and mercury compounds. It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level. The Commission, when preparing and drawing-up delegated acts, should ensure a simultaneous, timely and appropriate transmission of relevant documents to the European Parliament and Council.

(20) In order to ensure uniform conditions for the implementation of this Regulation with regard to prohibiting or allowing new mercury using products and processes and reporting obligations, implementing powers should be conferred on the Commission. Those powers should be exercised in accordance with Regulation (EU) No 182/2011 of the European Parliament and the Council[42].

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[41] Council Directive 1999/31/EC of 26 April 1999 on the landfill of waste (OJ L 182 of 16.7.1999, p. 1).

[42] Regulation (EU) No 182/2011 of the European Parliament and of the Council of 16 February 2011 laying down the rules and general principles concerning mechanisms for control by Member States of the Commission's exercise of implementing powers (OJ L 55, 28.2.2011, p. 13).

(21) Member States should lay down rules on penalties applicable to infringements of the national provisions adopted pursuant to this Regulation and ensure that they are implemented. Those penalties should be effective, proportionate and dissuasive.

(22) Given the nature and extent of the modifications which need to be made to Regulation (EC) No 1102/2008/EC and to enhance legal certainty, clarity, transparency and legislative simplification, that Regulation should be replaced.

(23) In order to allow for the competent authorities of the Member States and the economic operators concerned by this Regulation sufficient time to adapt to the new regime lays down by this Regulation, it should apply from 1 January 2018.

(24) Since the objective of this Regulation, namely to ensure a high level of protection of human health and the environment from mercury, by means of a mercury and mercury-added product export and import prohibition, of restrictions on mercury use in manufacturing processes, products, ASGM and dental amalgam and of obligations applicable to mercury waste, cannot be sufficiently achieved by Member States, but can rather, by reason of the transboundary nature of mercury pollution and the nature of the measures to be taken, be better achieved at Union level, the Union may adopt measures in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty on European Union. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve that objective,

HAVE ADOPTED THIS REGULATION:

Chapter I
General provisions

Article 1
Subject matter

This Regulation establishes measures and conditions concerning the trade, manufacture, use and interim storage of mercury, mercury compounds, mixtures, mercury-added products and the management of mercury waste.

Article 2
Definitions

For the purposes of this Regulation, the following definitions shall apply:

1. 'mercury' means metallic mercury (Hg, CAS RN 7439-97-6);

2. 'mercury-added product' means a product or product component that contains mercury and/or mercury compounds that were intentionally added;

3. 'mercury waste' means mercury that qualifies as waste, in accordance with Article 3(1), of Directive 2008/98/EC of the European Parliament and of the Council[43];

4. 'export' means any of the following:

   (a) the permanent or temporary export of a chemical meeting the conditions of Article 28(2) of the Treaty on the Functioning of the European Union;

   (b) the re-export of a chemical not meeting the conditions of Article 28(2) of the Treaty on the Functioning of the European Union which is placed under a customs procedure other than the external Union transit procedure for movement of goods through the customs territory of the Union;

5. 'import' means the physical introduction into the customs territory of the Union of a chemical that is placed under a customs procedure other than the external Union transit procedure for movement of goods through the customs territory of the Union;

6. 'primary mercury mining' means mining in which the principal material sought is mercury.

Chapter II
Trade and manufacturing restrictions concerning mercury, mercury compounds and mercury-added products

Article 3
Export restrictions

1. The export of mercury and of the mercury compounds and of mixtures listed in Annex I shall be prohibited.

   The first subparagraph shall not apply to the export of the mercury compounds listed in Annex I for laboratory-scale research.

2. The export of mixtures of mercury not listed in Annex I for the purposes of recovering the mercury shall be prohibited.

Article 4
Import restrictions

1. The import of mercury and of mixtures listed in Annex I for uses other than disposal as waste shall be prohibited.

   By way of derogation from the first subparagraph, import shall be allowed in any of the following circumstances:

   – the exporting country is a Party to the Convention and the exported mercury is not from primary mercury mining as set out in Article 3(3) and (4), of that Convention;

[43] Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain Directives (OJ L 312 of 22.11.2008, p. 3).

– the exporting country not being a Party to the Convention has provided certification that the mercury is not from primary mercury mining and not from the chlor-alkali industry, and the importing Member State has granted its written consent to the import.

2. The import of mercury for use in artisanal and small-scale gold mining shall be prohibited.

3. The national authority or authorities designated in accordance with Article 4 of Regulation (EU) No 649/2012 shall carry out the administrative functions resulting from the requirements laid down in paragraphs 1 and 2 of this Article.

Article 5
Export, import and manufacturing of mercury-added products

1. Without prejudice to stricter requirements set out in other applicable Union legislation, the export, import and the manufacturing in the Union of the mercury-added products as set out in Annex II shall be prohibited from 1 January 2021.

2. The prohibition laid down in paragraph 1 shall not apply to the following mercury-added products:

– products essential for civil protection and military uses;

– products for research, calibration of instrumentation, for use as reference standard.

Article 6
Forms for Import and Export

The Commission shall adopt decisions, by means of implementing acts, to specify the forms to be used for the purpose of implementing Articles 3 and 4.

Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 18(2).

Chapter III
Restrictions on use and storage of mercury and mercury compounds

Article 7
Industrial activities

1. The use of mercury and mercury compounds in the manufacturing processes listed in Part I of Annex III is prohibited as from the dates indicated therein.

2. The use of mercury and mercury compounds in the manufacturing processes listed in Part II of Annex III shall only be allowed under the conditions set out therein.

3. Interim storage of mercury and mercury compounds shall be carried out in an environmentally sound manner.

The Commission shall be empowered to adopt delegated acts in accordance with Article 17 in order to set out requirements for environmentally sound interim storage of mercury and mercury compounds adopted by the Conference of the Parties to the Convention, where the Union has supported the Decision concerned**.**

Article 8

New mercury-added products and new manufacturing processes

1. The manufacture and placing on the market of mercury-added products not covered by any known use prior to 1 January 2018 shall be prohibited.

2. Manufacturing processes involving the use of mercury and/or mercury compounds that did not exist prior to 1 January 2018 shall be prohibited.

This paragraph shall not apply to processes manufacturing and/or using mercury-added products others than those falling under paragraph 1.

3. By way of derogation from paragraphs 1 and 2, where an economic operator intends to manufacture and/or place on the market a new mercury-added product or to operate a new manufacturing process, the operator shall notify the competent authorities of the Member State concerned and provide them, with the following:

– a technical description of the product or process concerned;

– an assessment of its environmental and health risks;

– a detailed explanation of the manner in which such product or process must be manufactured, used and operated to ensure a high level of protection of the environment and of human health.

4. Upon notification by the Member State concerned, the Commission shall verify in particular whether it has been demonstrated that the new mercury-added product or new manufacturing process would provide significant environmental and health benefits and that no technically and economically feasible mercury-free alternatives providing such benefits are available.

The Commission shall adopt decisions, by means of implementing acts, in view of specifying whether the relevant new mercury-added product or new manufacturing process is allowed.

Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 18(2).

Article 9

Artisanal and small-scale gold mining

Member States on the territory of which more than insignificant artisanal and small-scale gold mining and processing activities are carried out shall:

– take steps to reduce, and where feasible eliminate, the use of mercury and mercury compounds in, and the emissions and releases to the environment of mercury from, such mining and processing;

– develop and implement a national plan in accordance with Annex IV.

Article 10
Dental amalgam

1. From 1 January 2019 onwards dental amalgam shall only be used in an encapsulated form.

2. From 1 January 2019 onwards dental facilities shall be equipped with amalgam separators aimed at retaining and collecting amalgam particles. Those separators shall be maintained as required to ensure a high level of retention.

3. Capsules and amalgam separators complying with harmonised EN standards or with other national or international standards that ensure an equivalent level of quality and of level retention shall be presumed to satisfy the requirement set out under paragraphs 1 and 2.

Chapter IV
Storage and disposal of mercury waste

Article 11
Mercury waste

Without prejudice to Commission Decision 2000/532/EC[44], the following shall be considered as waste and be disposed of without endangering human health or harming the environment in accordance with Directive 2008/98/EC:

(a) mercury that is no longer used in the chlor-alkali industry;

(b) mercury generated from the cleaning of natural gas;

(c) mercury generated through non-ferrous mining and smelting operations;

(d) mercury extracted from cinnabar ore in the Union.

Article 12
Reporting on mercury waste from large sources

1. The companies operating within the industry sectors referred to in points (a), (b) and (c) of Article 11 shall send each year by 31 May to the competent authorities of the Member States concerned data related to the total amount of mercury waste stored in

[44] Commission Decision 2000/532/EC of 3 May 2000 replacing Decision 94/3/EC establishing a list of wastes pursuant to Article 1(a) of Council Directive 75/442/EEC on waste and Council Decision 94/904/EC establishing a list of hazardous waste pursuant to Article 1(4) of Council Directive 91/689/EEC on hazardous waste (OJ L 226, 6.9.2000, p. 3).

each installation and sent to individual temporary or permanent storage facilities as well as the location and contact details of those facilities.

2. The data referred to in paragraph 1 shall be expressed using the codes laid down in Regulation (EC) No 2150/2002 of the European Parliament and of the Council[45].

3. The obligation established in paragraphs 1 and 2 shall cease to apply to companies operating chlor-alkali installations the year after all mercury cells will have been decommissioned in accordance with Commission Implementing Decision 2013/732/EU[46] and all mercury has been handed over to waste management facilities.

Article 13
Disposal of mercury waste

1. By way of derogation from point (a) of Article 5(3) of Directive 1999/31/EC, mercury waste may be stored in one of the following ways:

   (a) temporarily stored for more than one year or permanently stored in salt mines that are adapted for the disposal of mercury, or in deep underground hard rock formations providing a level of safety and confinement equivalent to that of those salt mines;

   (b) temporarily stored in above-ground facilities dedicated to and equipped for the temporary storage of mercury.

2. The specific requirements for the temporary storage of mercury waste, as laid down in Annexes I, II and III to Directive 1999/31/EC shall apply to the permanent storage facilities referred to in point (a) of paragraph 1 of this Article under the following conditions laid down in the following Annexes to that Directive:

   (a) Annex I, Section 8 (first, third and fifth indents) and Annex II to Directive 1999/31/EC shall apply;

   (b) Annex I, Section 8 (second, fourth and sixth indents) and Annex III, Section 6, to Directive 1999/31/EC shall only apply where deemed appropriate by the competent authorities of the Member States in charge of implementing that Directive.

Chapter V
Penalties and reporting

Article 14
Penalties

[45] Regulation (EC) No 2150/2002 of the European Parliament and of the Council of 25 November 2002 on waste statistics (OJ L 332, 9.12.2002, p.1).

[46] Commission implementing Decision 2013/732/EU of 9 December 2013 establishing the best available techniques (BAT) conclusions, under Directive 2010/75/EU of the European Parliament and of the Council on industrial emissions, for the production of chlor-alkali (OJ L 332, 11.12.2013, p. 34).

Member States shall lay down the rules on penalties applicable to infringements of the provisions of this Regulation and shall take all measures necessary to ensure that they are applied. The penalties provided for must be effective, proportionate and dissuasive. The Member States shall notify those provisions to the Commission by [xxx] and shall notify it without delay of any subsequent amendment affecting them.

Article 15
Report

1. Member States shall prepare, update and publish online a report with the following information:

   (a) information concerning the implementation of this Regulation;

   (b) information needed for the fulfilment by the Union and by the Member States of its reporting obligation established under Article 21 of the Minamata Convention;

   (c) a summary of the information gathered in accordance with Article 12;

   (d) a list of individual stocks of mercury exceeding 50 metric tonnes, which are located in their territory and, where Member States are made aware, a list of sources of mercury supply generating annual stocks of mercury exceeding 10 metric tonnes.

   Member States shall inform the Commission of their report and of their updates within one month of their publication.

2. The Commission shall adopt appropriate questionnaires in order to specify the content, the information and the key performance indicators to be included in the report referred to in paragraph 1 as well as the format of this report and the timing of its publication and of its updates.

   The questionnaires may also organise reporting in such a way as to enable the Union to provide the Secretariat of the Convention with a single report submitted on behalf of the Union and its Member States.

   The Commission shall adopt decisions, by means of implementing acts, to provide a template for those questionnaires and to make an electronic reporting tool available to the Member States.

   Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 18(2).

Chapter VI
Delegated and implementing powers

Article 16
Amendment of Annexes

The Commission shall be empowered to adopt delegated acts in accordance with Article 17 in order to amend Annexes I, II, III and IV to transpose Decisions adopted by the Conference of the Parties to the Convention, where the Union has supported the Decision concerned**.**

Article 17
Exercise of the delegation

1. The power to adopt delegated acts is conferred on the Commission subject to the conditions laid down in this Article.
2. The delegation of powers referred to in Articles 7(3) and 16 shall be conferred on the Commission for an indeterminate period of time from the date of entry into force of this Regulation.
3. The delegation of power referred to in Articles 7(3) and 16 may be revoked at any time by the European Parliament or by the Council. A decision of revocation shall put an end to the delegation of the power specified in that decision. It shall take effect the day following the publication of the decision in the *Official Journal of the European Union* or at a later date specified therein. It shall not affect the validity of any delegated acts already in force.
4. As soon as it adopts a delegated act, the Commission shall notify it simultaneously to the European Parliament and to the Council.
5. A delegated act adopted pursuant to Articles 7(3) and 16 shall enter into force only if no objection has been expressed either by the European Parliament or the Council within a period of two months of notification of that act to the European Parliament and the Council or if, before the expiry of that period, the European Parliament and the Council have both informed the Commission that they will not object. That period shall be extended by 2 months at the initiative of the European Parliament or the Council.

Article 18
Committee procedure

1. For the adoption of forms for import and export under Article 6, of a decision under Article 8(4), and of questionnaires in accordance with Article 15(2) the Commission shall be assisted by a Committee. That Committee shall be a committee within the meaning of Regulation (EU) No 182/2011.
2. Where reference is made to this paragraph, Article 5 of Regulation (EU) No 182/2011 shall apply.

Chapter VII
Final provisions

Article 19
Repeal

Regulation (EC) No 1102/2008 is hereby repealed.

References to the repealed Regulation shall be construed as references to this Regulation.

Article 20
Entry into force

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 1st January 2018.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels,

For the European Parliament	*For the Council*
The President	*The President*

I

(Legislative acts)

REGULATIONS

REGULATION (EU) 2017/852 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 17 May 2017

on mercury, and repealing Regulation (EC) No 1102/2008

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 192(1) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee ([1]),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure ([2]),

Whereas:

(1) Mercury is a very toxic substance which represents a global and major threat to human health, including in the form of methylmercury in fish and seafood resources, ecosystems and wildlife. Due to the transboundary nature of mercury pollution, between 40 % and 80 % of total mercury deposition in the Union originates from outside the Union. Action is therefore warranted at local, regional, national and international levels.

(2) Most mercury emissions and associated exposure risks result from anthropogenic activities such as primary mercury mining and processing, the use of mercury in products and industrial processes, artisanal and small-scale gold mining and processing, coal combustion and the management of mercury waste.

(3) The Seventh Environment Action Programme adopted by Decision No 1386/2013/EU of the European Parliament and of the Council ([3]) establishes the long-term objective of a non-toxic environment and, for that purpose, stipulates that action is needed to ensure the minimisation of significant adverse effects of chemicals on human health and the environment by 2020.

([1]) OJ C 303, 19.8.2016, p. 122.
([2]) Position of the European Parliament of 14 March 2017 (not yet published in the Official Journal) and decision of the Council of 25 April 2017.
([3]) Decision No 1386/2013/EU of the European Parliament and of the Council of 20 November 2013 on a General Union Environment Action Programme to 2020 'Living well, within the limits of our planet' (OJ L 354, 28.12.2013, p. 171).

(4) The Communication of 28 January 2005 from the Commission to the European Parliament and the Council entitled 'Community Strategy Concerning Mercury', as reviewed on 7 December 2010 ('the Strategy'), aims at minimising and, where feasible, ultimately eliminating global anthropogenic mercury releases to air, water and land.

(5) In the past 10 years, significant progress has been achieved in the Union in the field of mercury management following the adoption of the Strategy and of a wide range of measures concerning mercury emissions, supply, demand and use, and the management of mercury surplus and stocks.

(6) The Strategy recommends that the negotiation and conclusion of an international legally-binding instrument on mercury should be a priority as Union action alone cannot guarantee effective protection of the citizens of the Union against the negative health effects of mercury.

(7) The Union and 26 Member States have signed the Minamata Convention on Mercury of 2013 ('the Convention'). The two Member States that did not sign the Convention, Estonia and Portugal, have expressed their commitment to ratify it. The Union and all its Member States are therefore committed to its conclusion, transposition and implementation.

(8) Swift approval of the Convention by the Union and its ratification by Member States will encourage the major global mercury users and emitters, which are signatories of the Convention, to ratify and implement it.

(9) This Regulation should complement the Union *acquis* and lay down the provisions that are needed to ensure the complete alignment of the Union *acquis* with the Convention so that the Union and its Member States are able to respectively approve or ratify and implement the Convention.

(10) Further action undertaken by the Union, going beyond the Convention requirements, would lead the way, as was the case with Regulation (EC) No 1102/2008 of the European Parliament and of the Council ([1]), for mercury-free products and processes.

(11) In accordance with Article 193 of the Treaty on the Functioning of the European Union (TFEU), this Regulation does not prevent Member States from maintaining or introducing more stringent protective measures, provided that such measures are compatible with the Treaties and the Commission has been notified thereof.

(12) The mercury export ban laid down in Regulation (EC) No 1102/2008 should be complemented by restrictions on the import of mercury which vary depending on the source, the intended use and the place of origin of the mercury. Regulation (EC) No 1013/2006 of the European Parliament and of the Council ([2]) should continue to apply as regards imports of mercury waste, particularly as regards the powers of the competent authorities under that Regulation.

(13) The provisions of this Regulation on the import of mercury and of mixtures of mercury are aimed at ensuring the fulfilment by the Union and the Member States of the obligations of the Convention concerning trade of mercury.

(14) The export, import and manufacturing of a range of mercury-added products accounting for a significant share of the use within the Union and globally of mercury and mercury compounds should be prohibited.

(15) This Regulation should apply without prejudice to the provisions of the applicable Union *acquis* that set stricter requirements for mercury-added products, including as regards maximum mercury content.

(16) The use of mercury and mercury compounds in manufacturing processes should be phased out and, to that end, incentives should be provided for research into alternative substances with characteristics that are innocuous, or, in any event, less dangerous for the environment and for human health.

([1]) Regulation (EC) No 1102/2008 of the European Parliament and of the Council of 22 October 2008 on the banning of exports of metallic mercury and certain mercury compounds and mixtures and the safe storage of metallic mercury (OJ L 304, 14.11.2008, p. 75).

([2]) Regulation (EC) No 1013/2006 of the European Parliament and of the Council of 14 June 2006 on shipments of waste (OJ L 190, 12.7.2006, p. 1).

(17) Regulation (EC) No 1907/2006 of the European Parliament and of the Council ([1]) prohibits, as from 10 October 2017, the manufacture, placing on the market and use of the five phenylmercury compounds known to be used, especially as catalysts, in the production of polyurethane. The use of other mercury-containing catalysts in polyurethane production should also be prohibited as from 1 January 2018.

(18) The production of alcoholates involving the use of mercury as an electrode should be phased out and such manufacturing processes should be replaced by feasible mercury-free manufacturing processes as soon as possible. In the absence of relevant available mercury-free manufacturing processes, operating conditions for the production of sodium or potassium methylate or ethylate involving the use of mercury should be laid down. Measures should be taken to reduce the use of mercury so as to phase out its use in such production as soon as possible and in any event before 1 January 2028.

(19) The manufacturing and placing on the market of new mercury-added products and the use of new manufacturing processes involving the use of mercury or mercury compounds would increase the use of mercury and of mercury compounds, and mercury emissions within the Union. Such new activities should therefore be prohibited unless an assessment demonstrates that the new mercury-added product or new manufacturing process would provide significant environmental or health benefits and pose no significant risks either to the environment or to human health, and that no technically practicable mercury-free alternatives providing such benefits are available.

(20) The use of mercury and mercury compounds in artisanal and small-scale gold mining and processing accounts for a significant share of mercury use and emissions worldwide with negative effects both for local communities and at a global level. Such use of mercury and mercury compounds should therefore be prohibited under this Regulation and regulated at international level. Without prejudice to the prohibition of such use and in addition to the implementation of effective, proportionate and dissuasive penalties by Member States in respect of infringements of this Regulation, it is also appropriate to provide for a national plan in the event of there being more than isolated cases of non-compliance with that prohibition, in order to tackle the problem of artisanal and small-scale gold mining and processing in which mercury amalgamation is used to extract gold from ore.

(21) The use of mercury in dental amalgam is the largest use of mercury in the Union and a significant source of pollution. The use of dental amalgam should therefore be phased down in accordance with the Convention and with national plans based, in particular, upon the measures listed in Part II of Annex A to the Convention. The Commission should assess and report on the feasibility of a phase out of the use of dental amalgam in the long term, and preferably by 2030, taking into account the national plans required by this Regulation and whilst fully respecting Member States' competence for the organisation and delivery of health services and medical care. Furthermore, particular preventive health protection measures should be taken for vulnerable members of the population, such as children and pregnant or breastfeeding women.

(22) Only pre-dosed encapsulated dental amalgam should be allowed for use, and the use of amalgam separators in dental facilities in which dental amalgam is used or dental amalgam fillings or teeth containing such fillings are removed should be made mandatory, in order to protect dental practitioners and patients from mercury exposure and to ensure that the resulting waste is collected and disposed of in accordance with sound waste management and under no circumstances released into the environment. In this respect, the use of mercury in bulk form by dental practitioners should be prohibited. Amalgam capsules such as those described in European standards EN ISO 13897:2004 and EN ISO 24234:2015 are considered to be suitable for use by dental practitioners. Furthermore, a minimum level of retention efficiency for amalgam separators should be set. Compliance of amalgam separators should be based on relevant standards, such as European standard EN ISO 11143:2008. Given the size of economic operators in the dentistry sector affected by the introduction of those requirements, it is appropriate to provide sufficient time to adapt to the new requirements.

([1]) Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L 396, 30.12.2006, p. 1).

(23) The training of dentistry students and dental practitioners on the use of mercury-free alternatives, in particular for vulnerable members of the population such as children and pregnant or breastfeeding women, as well as the carrying out of oral health research and innovation in order to improve knowledge of existing materials and restoration techniques, and to develop new materials, can help in reducing the use of mercury.

(24) Over 6 000 metric tonnes of liquid mercury waste will have been generated in the Union by the end of 2017, mainly as a result of the mandatory decommissioning of mercury cells in the chlor-alkali industry in accordance with Commission Implementing Decision 2013/732/EU ([1]). Given the limited available capacity for undertaking the conversion of liquid mercury waste, the temporary storage of liquid mercury waste should still be allowed under this Regulation for a period of time sufficient for ensuring the conversion and, if applicable, solidification of all such waste produced. Such storage should be carried out in accordance with the requirements set out in Council Directive 1999/31/EC ([2]).

(25) Given that mercury is an extremely hazardous substance in its liquid form, the permanent storage without pre-treatment of mercury waste should be prohibited owing to the risks that such disposal poses. Therefore, mercury waste should undergo appropriate conversion, and if applicable, solidification operations prior to permanent storage. For that purpose and in order to reduce the associated risks, Member States should take into account the technical guidelines on mercury of the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal.

(26) In order to ensure that the provisions on waste of this Regulation are properly implemented, measures should be taken to ensure an effective traceability system throughout the whole mercury waste management chain whereby the producers of mercury waste and the operators of waste management facilities that store and treat such waste are required to establish an information register, as part of the record-keeping required under Directive 2008/98/EC of the European Parliament and of the Council ([3]).

(27) The Convention requires Parties to endeavour to develop appropriate strategies for identifying and assessing sites contaminated by mercury or mercury compounds. Directive 2010/75/EU of the European Parliament and of the Council ([4]) requires operators of industrial installations to address soil contamination. Furthermore, Directive 2000/60/EC of the European Parliament and of the Council ([5]) requires Member States to address soil contamination where it adversely affects the status of a water body. Therefore, an exchange of information between the Commission and the Member States should take place to share experiences on the initiatives and measures taken at national level.

(28) In order to reflect the current scientific understanding of the risks posed by methylmercury, the Commission should, when undertaking the review of this Regulation, evaluate the current health-based intakes and should establish new mercury health benchmarks.

(29) In order to align Union legislation with decisions of the Conference of the Parties to the Convention supported by the Union by means of a Council decision adopted in accordance with Article 218(9) TFEU, the power to adopt acts in accordance with Article 290 TFEU should be delegated to the Commission in respect of amending the annexes to this Regulation and in respect of an extension of the period allowed for the temporary storage of mercury waste. It is of particular importance that the Commission carry out appropriate consultations during its preparatory work, including at expert level, and that those consultations be conducted in accordance with the principles laid down in the Interinstitutional Agreement of 13 April 2016 on Better Law-Making ([6]). In particular, to ensure equal participation in the preparation of delegated acts, the European Parliament and the Council receive all documents at the same time as Member States' experts, and their experts systematically have access to meetings of Commission expert groups dealing with the preparation of delegated acts.

([1]) Commission Implementing Decision 2013/732/EU of 9 December 2013 establishing the best available techniques (BAT) conclusions, under Directive 2010/75/EU of the European Parliament and of the Council on industrial emissions, for the production of chlor-alkali (OJ L 332, 11.12.2013, p. 34).
([2]) Council Directive 1999/31/EC of 26 April 1999 on the landfill of waste (OJ L 182, 16.7.1999, p. 1).
([3]) Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain Directives (OJ L 312, 22.11.2008, p. 3).
([4]) Directive 2010/75/EU of the European Parliament and of the Council of 24 November 2010 on industrial emissions (integrated pollution prevention and control) (OJ L 334, 17.12.2010, p. 17).
([5]) Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy (OJ L 327, 22.12.2000, p. 1).
([6]) OJ L 123, 12.5.2016, p. 1.

(30) In order to ensure uniform conditions for the implementation of this Regulation with regard to specifying forms for import and export, setting out technical requirements for environmentally sound interim storage of mercury, mercury compounds and mixtures of mercury, prohibiting or authorising new mercury-added products and new manufacturing processes involving the use of mercury or mercury compounds and specifying reporting obligations, implementing powers should be conferred on the Commission. Those powers should be exercised in accordance with Regulation (EU) No 182/2011 of the European Parliament and of the Council ([1]).

(31) Member States should lay down rules on penalties applicable to infringements of this Regulation and should ensure that they are implemented. Those penalties should be effective, proportionate and dissuasive.

(32) Given the nature and extent of the modifications which need to be made to Regulation (EC) No 1102/2008, and to enhance legal certainty, clarity, transparency and legislative simplification, that Regulation should be repealed.

(33) In order to allow the competent authorities of the Member States and the economic operators affected by this Regulation sufficient time to adapt to the new regime laid down by this Regulation, it should apply from 1 January 2018.

(34) Since the objective of this Regulation, namely to ensure a high level of protection of human health and the environment from anthropogenic emissions and releases of mercury and mercury compounds, by means, inter alia, of a mercury and mercury-added product export and import prohibition, of restrictions on mercury use in manufacturing processes, products, artisanal and small-scale gold mining and processing and in dental amalgam, and of obligations applicable to mercury waste, cannot be sufficiently achieved by Member States, but can rather, by reason of the transboundary nature of mercury pollution and the nature of the measures to be taken, be better achieved at Union level, the Union may adopt measures in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty on European Union. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve that objective,

HAVE ADOPTED THIS REGULATION:

CHAPTER I

GENERAL PROVISIONS

Article 1

Subject matter and objective

This Regulation establishes measures and conditions concerning the use and storage of and trade in mercury, mercury compounds and mixtures of mercury, and the manufacture and use of and trade in mercury-added products, and the management of mercury waste, in order to ensure a high level of protection of human health and the environment from anthropogenic emissions and releases of mercury and mercury compounds.

Member States may, where appropriate, apply stricter requirements than those laid down in this Regulation, in accordance with the TFEU.

Article 2

Definitions

For the purposes of this Regulation, the following definitions apply:

(1) 'mercury' means metallic mercury (Hg, CAS RN 7439-97-6);

(2) 'mercury compound' means any substance consisting of atoms of mercury and one or more atoms of other chemical elements that can be separated into different components only by chemical reactions;

([1]) Regulation (EU) No 182/2011 of the European Parliament and of the Council of 16 February 2011 laying down the rules and general principles concerning mechanisms for control by Member States of the Commission's exercise of implementing powers (OJ L 55, 28.2.2011, p. 13).

(3) 'mixture' means a mixture or solution composed of two or more substances;

(4) 'mercury-added product' means a product or product component that contains mercury or a mercury compound that was intentionally added;

(5) 'mercury waste' means metallic mercury that qualifies as waste as defined in point (1) of Article 3 of Directive 2008/98/EC;

(6) 'export' means any of the following:

(a) the permanent or temporary export of mercury, mercury compounds, mixtures of mercury and mercury-added products meeting the conditions of Article 28(2) TFEU;

(b) the re-export of mercury, mercury compounds, mixtures of mercury and mercury-added products not meeting the conditions of Article 28(2) TFEU which are placed under a customs procedure other than the external Union transit procedure for movement of goods through the customs territory of the Union;

(7) 'import' means the physical introduction into the customs territory of the Union of mercury, mercury compounds, mixtures of mercury and mercury-added products that are placed under a customs procedure other than the external Union transit procedure for movement of goods through the customs territory of the Union;

(8) 'disposal' means disposal as defined in point (19) of Article 3 of Directive 2008/98/EC;

(9) 'primary mercury mining' means mining in which the principal material sought is mercury;

(10) 'conversion' means the chemical transformation of the physical state of mercury from a liquid state to mercury sulfide or a comparable chemical compound that is equally or more stable and equally or less soluble in water and that presents no greater environmental or health hazard than mercury sulfide;

(11) 'placing on the market' means supplying or making available, whether in return for payment or free of charge, to a third party. Import shall be deemed to be placing on the market.

CHAPTER II

TRADE AND MANUFACTURING RESTRICTIONS CONCERNING MERCURY, MERCURY COMPOUNDS, MIXTURES OF MERCURY AND MERCURY-ADDED PRODUCTS

Article 3

Export restrictions

1. The export of mercury shall be prohibited.

2. The export of the mercury compounds and of the mixtures of mercury listed in Annex I shall be prohibited as from the dates set out therein.

3. By way of derogation from paragraph 2, the export of the mercury compounds listed in Annex I for the purposes of laboratory-scale research or laboratory analysis shall be allowed.

4. The export, for the purpose of reclaiming mercury, of mercury compounds and of mixtures of mercury that are not subject to the prohibition laid down in paragraph 2 shall be prohibited.

Article 4

Import restrictions

1. The import of mercury and the import of the mixtures of mercury listed in Annex I, including mercury waste from any of the large sources referred to in points (a) to (d) of Article 11, for purposes other than disposal as waste shall be prohibited. Such import for disposal as waste shall only be allowed where the exporting country has no access to available conversion capacity within its own territory.

Without prejudice to Article 11 and by way of derogation from the first subparagraph of this paragraph, the import of mercury and the import of the mixtures of mercury listed in Annex I for a use allowed in a Member State shall be allowed where the importing Member State has granted written consent to such import in either of the following circumstances:

(a) the exporting country is a Party to the Convention and the exported mercury is not from primary mercury mining that is prohibited under Article 3(3) and (4) of the Convention; or

(b) the exporting country not being a Party to the Convention has provided certification that the mercury is not from primary mercury mining.

Without prejudice to any national measures adopted in accordance with the TFEU, a use allowed pursuant to Union legislation shall be deemed to be a use allowed in a Member State for the purposes of this paragraph.

2. The import of mixtures of mercury that do not fall under paragraph 1 and of mercury compounds, for the purpose of reclaiming mercury, shall be prohibited.

3. The import of mercury for use in artisanal and small-scale gold mining and processing shall be prohibited.

4. Where the import of mercury waste is allowed in accordance with this Article, Regulation (EC) No 1013/2006 shall continue to apply in addition to the requirements of this Regulation.

Article 5

Export, import and manufacturing of mercury-added products

1. Without prejudice to stricter requirements set out in other applicable Union legislation, the export, import and manufacturing in the Union of the mercury-added products set out in Annex II shall be prohibited as from the dates set out therein.

2. The prohibition laid down in paragraph 1 shall not apply to any of the following mercury-added products:

(a) products that are essential for civil protection and military uses;

(b) products for research, for calibration of instrumentation, or for use as a reference standard.

Article 6

Forms for import and export

The Commission shall adopt decisions, by means of implementing acts, to specify forms to be used for the purpose of implementing Articles 3 and 4. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 22(2).

CHAPTER III

RESTRICTIONS ON USE AND STORAGE OF MERCURY, MERCURY COMPOUNDS AND MIXTURES OF MERCURY

Article 7

Industrial activities

1. The use of mercury and mercury compounds in the manufacturing processes listed in Part I of Annex III shall be prohibited as from the dates set out therein.

2. The use of mercury and mercury compounds in the manufacturing processes listed in Part II of Annex III shall only be allowed subject to the conditions set out therein.

3. Interim storage of mercury and of the mercury compounds and mixtures of mercury listed in Annex I to this Regulation shall be carried out in an environmentally sound manner, in accordance with the thresholds and requirements set out in Directive 2012/18/EU of the European Parliament and of the Council [1] and in Directive 2010/75/EU.

[1] Directive 2012/18/EU of the European Parliament and of the Council of 4 July 2012 on the control of major-accident hazards involving dangerous substances, amending and subsequently repealing Council Directive 96/82/EC (OJ L 197, 24.7.2012, p. 1).

In order to ensure the uniform application of the obligation laid down in the first subparagraph of this paragraph, the Commission may adopt implementing acts setting out technical requirements for environmentally sound interim storage of mercury, mercury compounds and mixtures of mercury in line with decisions adopted by the Conference of the Parties to the Convention in accordance with Article 10(3) and Article 27 of the Convention, provided that the Union has supported the decision concerned by means of a Council decision adopted in accordance with Article 218(9) TFEU. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 22(2) of this Regulation.

Article 8

New mercury-added products and new manufacturing processes

1. Economic operators shall not manufacture or place on the market mercury-added products that were not being manufactured prior to 1 January 2018 ('new mercury-added products') unless authorised to do so by means of a decision taken pursuant to paragraph 6 of this Article or allowed to do so under Directive 2011/65/EU of the European Parliament and of the Council ([1]).

The first subparagraph shall not apply to any of the following:

(a) equipment which is necessary for the protection of the essential interests of the security of Member States, including arms, munitions and war material intended for specifically military purposes;

(b) equipment designed to be sent into space;

(c) technical improvements made to or the redesign of mercury-added products that were being manufactured prior to 1 January 2018 provided that such improvements or redesign lead to less mercury being used in those products.

2. Economic operators shall not use manufacturing processes involving the use of mercury or mercury compounds that were not processes used prior to 1 January 2018 ('new manufacturing processes') unless authorised to do so by means of a decision taken pursuant to paragraph 6.

The first subparagraph of this paragraph shall not apply to processes manufacturing or using mercury-added products other than those subject to the prohibition laid down in paragraph 1.

3. Where an economic operator intends to apply for a decision pursuant to paragraph 6 in order to manufacture or place on the market a new mercury-added product, or to use a new manufacturing process, that would provide significant environmental or health benefits and pose no significant risks either to the environment or to human health, and where no technically practicable mercury-free alternatives providing such benefits are available, that economic operator shall notify the competent authorities of the Member State concerned. That notification shall include the following information:

(a) a technical description of the product or process concerned;

(b) an assessment of its environmental and health benefits and risks;

(c) evidence demonstrating the absence of technically practicable mercury-free alternatives providing significant environmental or health benefits;

(d) a detailed explanation of the manner in which the process is to be operated or the product is to be manufactured, used and disposed of as waste after use, in order to ensure a high level of protection of the environment and of human health.

4. The Member State concerned shall forward to the Commission the notification received from the economic operator if it considers on the basis of its own assessment of the information provided therein that the criteria referred to in the first subparagraph of paragraph 6 are fulfilled.

The Member State concerned shall inform the Commission of cases in which it considers that the criteria referred to in the first subparagraph of paragraph 6 were not fulfilled.

5. Where the Member State forwards a notification pursuant to the first subparagraph of paragraph 4 of this Article, the Commission shall immediately make the notification available to the committee referred to in Article 22(1).

([1]) Directive 2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment (OJ L 174, 1.7.2011, p. 88).

6. The Commission shall examine the notification received and assess whether it has been demonstrated that the new mercury-added product or new manufacturing process would provide significant environmental or health benefits and pose no significant risks either to the environment or to human health, and that no technically practicable mercury-free alternatives providing such benefits are available.

The Commission shall inform the Member States of the outcome of the assessment.

The Commission shall adopt decisions, by means of implementing acts, specifying whether the relevant new mercury-added product or new manufacturing process is authorised. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 22(2).

7. By 30 June 2018, the Commission shall make publicly available on the internet an inventory of manufacturing processes involving the use of mercury or mercury-compounds that were processes used prior to 1 January 2018 and of mercury-added products that were being manufactured prior to 1 January 2018 and of any applicable marketing restrictions.

Article 9

Artisanal and small-scale gold mining and processing

1. Artisanal and small-scale gold mining and processing in which mercury amalgamation is used to extract gold from ore shall be prohibited.

2. Without prejudice to paragraph 1 of this Article and to Article 16, where there is evidence of there being more than isolated cases of non-compliance with the prohibition laid down in paragraph 1 of this Article, the competent authority of the Member State concerned shall develop and implement a national plan in accordance with Annex IV.

Article 10

Dental amalgam

1. From 1 January 2019, dental amalgam shall only be used in pre-dosed encapsulated form. The use of mercury in bulk form by dental practitioners shall be prohibited.

2. From 1 July 2018, dental amalgam shall not be used for dental treatment of deciduous teeth, of children under 15 years and of pregnant or breastfeeding women, except when deemed strictly necessary by the dental practitioner based on the specific medical needs of the patient.

3. By 1 July 2019, each Member State shall set out a national plan concerning the measures it intends to implement to phase down the use of dental amalgam.

Member States shall make their national plans publicly available on the internet and shall transmit them to the Commission within one month of their adoption.

4. From 1 January 2019, operators of dental facilities in which dental amalgam is used or dental amalgam fillings or teeth containing such fillings are removed, shall ensure that their facilities are equipped with amalgam separators for the retention and collection of amalgam particles, including those contained in used water.

Such operators shall ensure that:

(a) amalgam separators put into service from 1 January 2018 provide a retention level of at least 95 % of amalgam particles;

(b) from 1 January 2021, all amalgam separators in use provide the retention level specified in point (a).

Amalgam separators shall be maintained in accordance with the manufacturer's instructions to ensure the highest practicable level of retention.

5. Capsules and amalgam separators complying with European standards, or with other national or international standards that provide an equivalent level of quality and retention, shall be presumed to satisfy the requirements set out in paragraphs 1 and 4.

6. Dental practitioners shall ensure that their amalgam waste, including amalgam residues, particles and fillings, and teeth, or parts thereof, contaminated by dental amalgam, is handled and collected by an authorised waste management establishment or undertaking.

Dental practitioners shall not release directly or indirectly such amalgam waste into the environment under any circumstances.

CHAPTER IV

DISPOSAL OF WASTE AND MERCURY WASTE

Article 11

Waste

Without prejudice to point (5) of Article 2 of this Regulation, mercury and mercury compounds, whether in pure form or in mixtures, from any of the following large sources shall be considered to be waste within the meaning of Directive 2008/98/EC and be disposed of without endangering human health or harming the environment, in accordance with that Directive:

(a) the chlor-alkali industry;

(b) the cleaning of natural gas;

(c) non-ferrous mining and smelting operations;

(d) extraction from cinnabar ore in the Union.

Such disposal shall not lead to any form of reclamation of mercury.

Article 12

Reporting on large sources

1. Economic operators within the industry sectors referred to in points (a), (b) and (c) of Article 11 shall send, each year by 31 May, the following to the competent authorities of the Member States concerned:

(a) data on the total amount of mercury waste stored in each of their installations;

(b) data on the total amount of mercury waste sent to individual facilities undertaking the temporary storage, the conversion and, if applicable, solidification of mercury waste, or the permanent storage of mercury waste that underwent conversion and, if applicable, solidification;

(c) the location and contact details of each facility referred to in point (b);

(d) a copy of the certificate provided by the operator of the facility undertaking the temporary storage of mercury waste, in accordance with Article 14(1);

(e) a copy of the certificate provided by the operator of the facility undertaking the conversion and, if applicable, the solidification of mercury waste, in accordance with Article 14(2);

(f) a copy of the certificate provided by the operator of the facility undertaking the permanent storage of mercury waste that underwent conversion and, if applicable, solidification, in accordance with Article 14(3).

2. The data referred to in points (a) and (b) of paragraph 1 shall be expressed using the codes laid down in Regulation (EC) No 2150/2002 of the European Parliament and of the Council [1].

3. The obligations laid down in paragraphs 1 and 2 shall cease to apply to an economic operator of chlor-alkali installations from one year after the date that all mercury cells operated by the economic operator have been decommissioned in accordance with Implementing Decision 2013/732/EU and all mercury has been handed over to waste management facilities.

Article 13

Storage of mercury waste

1. By way of derogation from point (a) of Article 5(3) of Directive 1999/31/EC, mercury waste may be temporarily stored in liquid form provided that the specific requirements for the temporary storage of mercury waste as laid down in Annexes I, II and III to that Directive are complied with and that such storage occurs in above-ground facilities dedicated to and equipped for the temporary storage of mercury waste.

The derogation set out in the first subparagraph shall cease to apply as from 1 January 2023.

2. The Commission is empowered to adopt delegated acts in accordance with Article 21 in order to amend this Regulation by extending the period allowed for temporary storage of mercury waste referred to in paragraph 1 of this Article by up to three years.

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[1] Regulation (EC) No 2150/2002 of the European Parliament and of the Council of 25 November 2002 on waste statistics (OJ L 332, 9.12.2002, p. 1).

3. Prior to being permanently disposed of, mercury waste shall undergo conversion and, where intended to be disposed of in above-ground facilities, conversion and solidification.

Mercury waste that underwent conversion and, if applicable, solidification shall only be permanently disposed of in the following permanent storage facilities licensed for disposal of hazardous waste:

(a) salt mines that are adapted for the permanent storage of mercury waste that underwent conversion, or deep underground hard rock formations providing a level of safety and confinement equivalent to or higher than that of such salt mines; or

(b) above-ground facilities dedicated to and equipped for the permanent storage of mercury waste that underwent conversion and solidification and that provide a level of safety and confinement equivalent to or higher than that of the facilities referred to in point (a).

Operators of permanent storage facilities shall ensure that mercury waste that underwent conversion and, if applicable, solidification is stored separately from other waste and in disposal batches in a storage chamber that is sealed. Those operators shall further ensure that the requirements set out in Directive 1999/31/EC, including the specific requirements for the temporary storage of mercury waste established in the third and fifth indents of Section 8 of Annex I and in Annex II to that Directive, are complied with in relation to the permanent storage facilities.

Article 14

Traceability

1. Operators of facilities undertaking the temporary storage of mercury waste shall establish a register including the following:

(a) for each shipment of mercury waste received:

(i) the origin and amount of that waste;

(ii) the name and contact details of the supplier and the owner of that waste;

(b) for each shipment of mercury waste leaving the facility:

(i) the amount of that waste and its mercury content;

(ii) the destination and intended disposal operation of that waste;

(iii) a copy of the certificate provided by the operator of the facility undertaking the conversion and, if applicable, the solidification of that waste, as referred to in paragraph 2;

(iv) a copy of the certificate provided by the operator of the facility undertaking the permanent storage of the mercury waste that underwent conversion and, if applicable, solidification, as referred to in paragraph 3;

(c) the amount of mercury waste stored at the facility at the end of each month.

Operators of facilities undertaking the temporary storage of mercury waste shall, as soon as the mercury waste is taken out of temporary storage, issue a certificate confirming that the mercury waste was sent to a facility undertaking disposal operations covered by this Article.

Once a certificate as referred to in the second subparagraph of this paragraph is issued, a copy thereof shall be transmitted without delay to the economic operators concerned referred to in Article 12.

2. Operators of facilities undertaking the conversion and, if applicable, the solidification of mercury waste shall establish a register including the following:

(a) for each shipment of mercury waste received:

(i) the origin and amount of that waste;

(ii) the name and contact details of the supplier and the owner of that waste;

(b) for each shipment of mercury waste that underwent conversion and, if applicable, solidification leaving the facility:

(i) the amount of that waste and its mercury content;

(ii) the destination and intended disposal operation of that waste;

(iii) a copy of the certificate provided by the operator of the facility undertaking the permanent storage of that waste, as referred to in paragraph 3;

(c) the amount of mercury waste stored at the facility at the end of each month.

Operators of facilities undertaking the conversion and, if applicable, the solidification of mercury waste shall, as soon as the conversion and, if applicable, the solidification operation of the entire shipment is completed, issue a certificate confirming that the entire shipment of mercury waste has been converted and, if applicable, solidified.

Once a certificate as referred to in the second subparagraph of this paragraph is issued, a copy thereof shall be transmitted without delay to the operators of the facilities referred to in paragraph 1 of this Article and to the economic operators concerned referred to in Article 12.

3. Operators of facilities undertaking the permanent storage of mercury waste that underwent conversion and, if applicable, solidification shall, as soon as the disposal operation of the entire shipment is completed, issue a certificate confirming that the entire shipment of mercury waste that underwent conversion and, if applicable, solidification has been placed into permanent storage in compliance with Directive 1999/31/EC, including information on the storage location.

Once a certificate as referred to in the first subparagraph of this paragraph is issued, a copy thereof shall be transmitted without delay to the operators of the facilities referred to in paragraphs 1 and 2 of this Article as well as to the economic operators concerned referred to in Article 12.

4. Each year by 31 January, the operators of the facilities referred to in paragraphs 1 and 2 shall transmit the register for the previous calendar year to the competent authorities of the Member States concerned. The competent authorities of the Member States concerned shall annually communicate each transmitted register to the Commission.

Article 15

Contaminated sites

1. The Commission shall organise an exchange of information with the Member States regarding the measures taken at national level to identify and assess sites contaminated by mercury and mercury compounds and to address the significant risks such contamination may pose to human health and the environment.

2. By 1 January 2021, the Commission shall make the information gathered pursuant to paragraph 1, including an inventory of sites contaminated by mercury and mercury compounds, publicly available on the internet.

CHAPTER V

PENALTIES, COMPETENT AUTHORITIES AND REPORTING

Article 16

Penalties

Member States shall lay down the rules on penalties applicable to infringements of this Regulation and shall take all measures necessary to ensure that they are implemented. The penalties provided for shall be effective, proportionate and dissuasive. Member States shall, by the respective dates of application of the relevant provisions of this Regulation, notify the Commission of those rules and of those measures and shall notify it, without delay, of any subsequent amendment affecting them.

Article 17

Competent authorities

Member States shall designate the competent authorities responsible for carrying out obligations arising from this Regulation.

Article 18

Report

1. By 1 January 2020 and at appropriate intervals thereafter, Member States shall prepare, provide to the Commission and make publicly available on the internet a report with the following:

(a) information concerning the implementation of this Regulation;

(b) information needed for the fulfilment by the Union of its reporting obligation under Article 21 of the Convention;

(c) a summary of the information gathered in accordance with Article 12 of this Regulation;

(d) information regarding mercury located in their territories:

(i) a list of sites where stocks of more than 50 metric tonnes of mercury other than mercury waste are located as well as the amount of mercury at each site;

(ii) a list of sites where more than 50 metric tonnes of mercury waste is accumulated as well as the amount of mercury waste at each site; and

(e) a list of sources supplying more than 10 metric tonnes of mercury per year, where Member States are made aware of such sources.

Member States may decide not to make any of the information referred to in the first subparagraph publicly available on any of the grounds mentioned in Article 4(1) and (2) of Directive 2003/4/EC of the European Parliament and of the Council ([1]), subject to the second subparagraph of Article 4(2) of that Directive.

2. For the purposes of the report referred to in paragraph 1, the Commission shall make an electronic reporting tool available to the Member States.

The Commission shall adopt implementing acts to establish appropriate questionnaires in order to specify the content, the information and the key performance indicators needed to meet the requirements under paragraph 1 as well as the format and the frequency of the report referred to in paragraph 1. Those questionnaires shall not duplicate reporting obligations of the Parties to the Convention. The implementing acts referred to in this paragraph shall be adopted in accordance with the examination procedure referred to in Article 22(2).

3. The Member States shall, without delay, make available to the Commission reports they provide to the Secretariat of the Convention.

Article 19

Review

1. By 30 June 2020, the Commission shall report to the European Parliament and to the Council on the outcome of its assessment regarding:

(a) the need for the Union to regulate emissions of mercury and mercury compounds from crematoria;

(b) the feasibility of a phase out of the use of dental amalgam in the long term, and preferably by 2030, taking into account the national plans referred to in Article 10(3) and whilst fully respecting Member States' competence for the organisation and delivery of health services and medical care; and

(c) the environmental benefits and the feasibility of a further alignment of Annex II with relevant Union legislation regulating the placing on the market of mercury-added products.

2. By 31 December 2024, the Commission shall report to the European Parliament and to the Council on the implementation and the review of this Regulation, inter alia, in the light of the effectiveness evaluation undertaken by the Conference of the Parties to the Convention and of the reports provided by the Member States in accordance with Article 18 of this Regulation and Article 21 of the Convention.

3. The Commission shall, if appropriate, present a legislative proposal together with its reports referred to in paragraphs 1 and 2.

([1]) Directive 2003/4/EC of the European Parliament and of the Council of 28 January 2003 on public access to environmental information and repealing Council Directive 90/313/EEC (OJ L 41, 14.2.2003, p. 26).

CHAPTER VI

DELEGATED AND IMPLEMENTING POWERS

Article 20

Amendment of Annexes

The Commission is empowered to adopt delegated acts in accordance with Article 21 of this Regulation in order to amend its Annexes I, II, III and IV to align them with decisions adopted by the Conference of the Parties to the Convention in accordance with Article 27 of the Convention, provided that the Union has supported the decision concerned by means of a Council decision adopted in accordance with Article 218(9) TFEU.

Article 21

Exercise of the delegation

1. The power to adopt delegated acts is conferred on the Commission subject to the conditions laid down in this Article.

2. The power to adopt delegated acts referred to in Article 13(2) and Article 20 shall be conferred on the Commission for a period of five years from 13 June 2017. The Commission shall draw up a report in respect of the delegation of power not later than nine months before the end of the five-year period. The delegation of power shall be tacitly extended for periods of an identical duration, unless the European Parliament or the Council opposes such extension not later than three months before the end of each period.

3. The delegation of power referred to in Article 13(2) and Article 20 may be revoked at any time by the European Parliament or by the Council. A decision to revoke shall put an end to the delegation of the power specified in that decision. It shall take effect the day following the publication of the decision in the *Official Journal of the European Union* or at a later date specified therein. It shall not affect the validity of any delegated acts already in force.

4. Before adopting a delegated act, the Commission shall consult experts designated by each Member State in accordance with the principles laid down in the Interinstitutional Agreement of 13 April 2016 on Better Law-Making.

5. As soon as it adopts a delegated act, the Commission shall notify it simultaneously to the European Parliament and to the Council.

6. A delegated act adopted pursuant to Article 13(2) and Article 20 shall enter into force only if no objection has been expressed either by the European Parliament or the Council within a period of two months of notification of that act to the European Parliament and the Council or if, before the expiry of that period, the European Parliament and the Council have both informed the Commission that they will not object. That period shall be extended by two months at the initiative of the European Parliament or of the Council.

Article 22

Committee procedure

1. For the adoption of forms for import and export under Article 6, of technical requirements for environmentally sound interim storage of mercury, mercury compounds or mixtures of mercury under Article 7(3), of a decision under Article 8(6), and of questionnaires under Article 18(2), the Commission shall be assisted by a committee. That committee shall be a committee within the meaning of Regulation (EU) No 182/2011.

2. Where reference is made to this paragraph, Article 5 of Regulation (EU) No 182/2011 shall apply.

Where the committee delivers no opinion, the Commission shall not adopt the draft implementing act and the third subparagraph of Article 5(4) of Regulation (EU) No 182/2011 shall apply.

CHAPTER VII

FINAL PROVISIONS

Article 23

Repeal

Regulation (EC) No 1102/2008 is repealed with effect from 1 January 2018.

References to the repealed Regulation shall be construed as references to this Regulation and shall be read in accordance with the correlation table in Annex V.

Article 24

Entry into force

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 1 January 2018.

However, point (d) of Part I of Annex III shall apply from 11 December 2017.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Strasbourg, 17 May 2017.

For the European Parliament	*For the Council*
The President	*The President*
A. TAJANI	C. ABELA

ANNEX I

Mercury compounds subject to Article 3(2) and (3) and Article 7(3) and mixtures of mercury subject to Article 3(2), Article 4(1) and Article 7(3)

Mercury compounds prohibited for export from 1 January 2018:

— Mercury (I) chloride (Hg_2Cl_2, CAS RN 10112-91-1)

— Mercury (II) oxide (HgO, CAS RN 21908-53-2)

— Cinnabar ore

— Mercury sulfide (HgS, CAS RN 1344-48-5)

Mercury compounds prohibited for export from 1 January 2020:

— Mercury (II) sulphate ($HgSO_4$, CAS RN 7783-35-9)

— Mercury (II) nitrate ($Hg(NO_3)_2$, CAS RN 10045-94-0)

Mixtures of mercury prohibited for export and import from 1 January 2018:

— Mixtures of mercury with other substances, including alloys of mercury, with a mercury concentration of at least 95 % by weight.

ANNEX II

Mercury-added products referred to in Article 5

Part A — Mercury-added products

Mercury-added products	Date from which the export, import and manufacturing of the mercury-added products are prohibited
1. Batteries or accumulators that contain more than 0,0005 % of mercury by weight.	31.12.2020
2. Switches and relays, except very high accuracy capacitance and loss measurement bridges and high frequency radio frequency switches and relays in monitoring and control instruments with a maximum mercury content of 20 mg per bridge, switch or relay.	31.12.2020
3. Compact fluorescent lamps (CFLs) for general lighting purposes: (a) CFL.i ≤ 30 watts with a mercury content exceeding 2,5 mg per lamp burner; (b) CFL.ni ≤ 30 watts with a mercury content exceeding 3,5 mg per lamp burner.	31.12.2018
4. The following linear fluorescent lamps (LFLs) for general lighting purposes: (a) Triband phosphor < 60 watts with a mercury content exceeding 5 mg per lamp; (b) Halophosphate phosphor ≤ 40 watts with a mercury content exceeding 10 mg per lamp.	31.12.2018
5. High pressure mercury vapour lamps (HPMVs) for general lighting purposes.	31.12.2018
6. The following mercury-added cold cathode fluorescent lamps and external electrode fluorescent lamps (CCFLs and EEFLs) for electronic displays: (a) short length (≤ 500 mm) with mercury content exceeding 3,5 mg per lamp; (b) medium length (> 500 mm and ≤ 1 500 mm) with mercury content exceeding 5 mg per lamp; (c) long length (> 1 500 mm) with mercury content exceeding 13 mg per lamp.	31.12.2018
7. Cosmetics with mercury and mercury compounds, except those special cases included in entries 16 and 17 of Annex V to Regulation (EC) No 1223/2009 of the European Parliament and of the Council ([1]).	31.12.2020
8. Pesticides, biocides and topical antiseptics.	31.12.2020
9. The following non-electronic measuring devices: (a) barometers; (b) hygrometers; (c) manometers; (d) thermometers and other non-electrical thermometric applications; (e) sphygmomanometers; (f) strain gauges to be used with plethysmographs;	31.12.2020

Mercury-added products	Date from which the export, import and manufacturing of the mercury-added products are prohibited
(g) mercury pycnometers; (h) mercury metering devices for determination of the softening point. This entry does not cover the following measuring devices: — non-electronic measuring devices installed in large-scale equipment or those used for high precision measurement where no suitable mercury-free alternative is available; — measuring devices more than 50 years old on 3 October 2007; — measuring devices which are to be displayed in public exhibitions for cultural and historical purposes.	

([1]) Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products (OJ L 342, 22.12.2009, p. 59).

Part B — Additional products excluded from the list in Part A of this Annex

Switches and relays, cold cathode fluorescent lamps and external electrode fluorescent lamps (CCFLs and EEFLs) for electronic displays and measuring devices, when they are used to replace a component of larger equipment and provided that no feasible mercury-free alternative for that component is available, in accordance with Directive 2000/53/EC of the European Parliament and of the Council ([1]) and Directive 2011/65/EU.

([1]) Directive 2000/53/EC of the European Parliament and of the Council of 18 September 2000 on end-of life vehicles (OJ L 269, 21.10.2000, p. 34).

ANNEX III

Mercury-related requirements applicable to manufacturing processes referred to in Article 7(1) and (2)

Part I: Prohibited use of mercury or mercury compounds, whether in pure form or in mixtures, in manufacturing processes

(a) from 1 January 2018: manufacturing processes in which mercury or mercury compounds are used as a catalyst;

(b) by way of derogation from point (a), the production of vinyl chloride monomer shall be prohibited from 1 January 2022;

(c) from 1 January 2022: manufacturing processes in which mercury is used as an electrode;

(d) by way of derogation from point (c), from 11 December 2017: chlor-alkali production in which mercury is used as an electrode;

(e) by way of derogation from point (c), the production of sodium or potassium methylate or ethylate shall be prohibited from 1 January 2028;

(f) from 1 January 2018: the production of polyurethane, to the extent not already restricted or prohibited in accordance with entry 62 of Annex XVII to Regulation (EC) No 1907/2006.

Part II: Manufacturing processes subject to restrictions on use and releases of mercury and mercury compounds

Production of sodium or potassium methylate or ethylate

The production of sodium or potassium methylate or ethylate shall be carried out in accordance with point (e) of Part I and subject to the following conditions:

(a) no use of mercury from primary mercury mining;

(b) reduction of direct and indirect release of mercury and of mercury compounds into air, water and land in terms of per unit production by 50 % by 2020 as compared to 2010;

(c) supporting research and development in respect of mercury-free manufacturing processes; and

(d) as from 13 June 2017, the capacity of installations using mercury and mercury compounds for the production of sodium or potassium methylate or ethylate that were in operation before that date shall not be increased and no new installations shall be allowed.

ANNEX IV

Content of the national plan on artisanal and small-scale gold mining and processing referred to in Article 9

The national plan shall include the following information:

(a) national objectives and reduction targets to eliminate the use of mercury and mercury compounds;

(b) actions to eliminate:

  (i) whole ore amalgamation;

  (ii) open burning of amalgam or processed amalgam;

  (iii) burning of amalgam in residential areas; and

  (iv) cyanide leaching in sediment, ore or tailings to which mercury has been added without first removing the mercury;

(c) steps to facilitate the formalization or regulation of the artisanal and small-scale gold mining and processing sector;

(d) baseline estimates of the quantities of mercury used and the practices employed in artisanal and small-scale gold mining and processing within its territory;

(e) strategies for promoting the reduction of emissions and releases of, and exposure to, mercury in artisanal and small-scale gold mining and processing, including mercury-free methods;

(f) strategies for managing trade and preventing the diversion of mercury and mercury compounds from both foreign and domestic sources to use in artisanal and small-scale gold mining and processing;

(g) strategies for involving stakeholders in the implementation and continuing development of the national plan;

(h) a public health strategy on the exposure of artisanal and small-scale gold miners and their communities to mercury which shall include, inter alia, the gathering of health data, training for health-care workers and awareness-raising through health facilities;

(i) strategies to prevent the exposure of vulnerable populations, particularly children and women of child-bearing age, especially pregnant women, to mercury used in artisanal and small-scale gold mining and processing;

(j) strategies for providing information to artisanal and small-scale gold miners and affected communities; and

(k) a schedule for the implementation of the national plan.

ANNEX V

Correlation table

Regulation (EC) No 1102/2008	This Regulation
Article 1(1)	Article 3(1) and (2)
Article 1(2)	Article 3(3)
Article 1(3)	Article 3(4)
Article 2	Article 11
Article 3(1)(a)	Article 13(3)(a)
Article 3(1)(b)	Article 13(1)
Article 3(1), second subparagraph	Article 13(1), first subparagraph and Article 13(3), third subparagraph
Article 3(2)	—
Article 4(1)	Article 13(1)
Article 4(2)	Article 13(1)
Article 4(3)	—
Article 5(1)	—
Article 5(2)	—
Article 5(3)	—
Article 6(1)(a)	—
Article 6(1)(b)	Article 12(1)(a)
Article 6(1)(c)	Article 12(1)(b) and (c)
Article 6(2)(a)	Article 12(1)(a)
Article 6(2)(b)	Article 12(1)(b) and (c)
Article 6(3)	Article 12(1)
Article 6(4)	—
Article 7	Article 16
Article 8(1)	—
Article 8(2)	—
Article 8(3)	—
Article 8(4)	—
Article 8(5)	—
Article 9	—