PIC - Decision Guidance Document for a banned or severely restricted chemical

Bromacil

Published:

Common name	Bromacil (ISO)
Other names/ synonyms	5-Bromo-3-sec-butyl-6-methyluracil (IUPAC); 5-bromo-6-methyl-3-(1-methylpropyl)-uracil; 5-Bromo-6-methyl-3-(1-methylpropyl)-2,4(1H,3H)-pyrimidinedione (CA); Pyrimidinedione.
CAS No.	314-40-9
Use category	Pesticide
Use	Bromacil is a herbicide used for brush control on non-cropland areas. It is especially effective against perennial grasses. It is also used for selective weed control in pineapple and citrus crops.
Trade names	Borea, Bromax 4G, Bromax 4L, Borocil, Rout, Croptex; Cynogan, Du Pont herbicide 976; Isocil; Hyvar L; Hyvar X; Hyvar X 80W; Hyvar X-L; Hyvar XL 2L; Hyvarex; Krovar II; Nalkil; OnyxBorocil 1V; Uragan; Urox 'B'.
Formulation types	Granules (GR), soluble concentrate (SC), and wettable powder (WP) formulations.
Basic manufacturers	Du Pont Agricultural Products.

Reasons for Inclusion in the PIC Procedure

Bromacil is included in the PIC procedure as a pesticide. Inclusion was recommended at the Eighth FAO/UNEP Joint Meeting on PIC following detailed discussions during the Sixth and Seventh Meetings. It is included in the procedure on the basis of the control actions reported by a number of governments.

Summary of Control Actions (see Annex 2 for details)

Control actions were reported by 4 countries. In 3 countries (Germany, Slovenia, Sweden) bromacil was reported as banned. Belize reports to have severely restricted bromacil for use in citrus only. Environmental concerns reported were high persistence in soil, high leaching potential and contamination of ground water. Human health concern reported was suspected carcinogenicity.

Hazard Classification by Organisation

WHO	Unlikely to present acute hazard in normal use *(WHO,1996*).
EPA	Toxicity class IV - practically nontoxic in dry form, and class II - moderately toxic in the liquid form. Bromacil is classified as a general use herbicide.
IARC	Not classified.

Protective Measures that have been Applied Concerning the Chemical

Measures to Reduce Exposures

For the health and welfare of workers and the general public, the handling and application of the substance should be entrusted only to competently supervised and well-trained applicators who must follow adequate safety measures and use the chemical according to good application practices. Regularly exposed workers should receive appropriate monitoring and health evaluations. Protective clothing as indicated in the *FAO Guidelines for Personal Protection when Working with Pesticides in Tropical Climates* (FAO, 1990) is required.

Packaging and Labelling

Follow *FAO Revised Guidelines on Good Labelling Practice for Pesticides* (FAO, 1995).

The labelling requirements of the U. S. Environmental Protection Agency (USEPA) state: Dry formulations containing bromacil must bear the signal word "Caution" and liquid formulations must bear the signal word "Warning".

Alternatives

Germany reported that at present there are no soil acting alternatives registered for weed control on railway tracks (plant protection products containing diurone or glyphosate); on uncultivated land the use of glyphosate is possible. A non-chemical alternative is mechanical weed control (see Annex 2).

It is essential that before a country considers substituting any of the reported alternatives, it ensures that the use is relevant to its national needs. A first step may be to contact the DNA in the country where the alternative has been reported (see addresses of DNAs in Annex 3). It would then be necessary to determine the compatibility with national crop protection practices.

Waste Disposal

Waste should be disposed of in accordance with the provisions of the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal and any guidelines thereunder *(SBC, 1994)*.

See *FAO Guidelines on Prevention of Accumulation of Obsolete Pesticide Stocks* and *The Pesticide Storage and Stock Control Manual* (FAO,1996).

Wear protective clothing and respiratory equipment suitable for toxic dusts. Sweep, scoop or pick up spilled material. Vacuuming or wet sweeping may be used to avoid dust dispersal. Do not flush to surface water or sanitary sewer system. Dispose of empty container in a sanitary landfill or by incineration *(Dupont, MSDS).*

Bromacil should be incinerated in a chemical incinerator unit operating at 850 °C equipped with off gas scrubbing equipment (*IRPTC, 1985*).

It should be noted that the methods recommended in the literature are often not suitable in all countries. High temperature incinerators may not be available. Consideration should be given to the use of alternative destruction technologies.

Exposure Limits

	Type of limit	Value
Food	National MRLs (Maximum Residue Limits in mg/kg) in specified products	0.1 mg/kg citrus and pineapples (USA) 0.05 mg/kg mandarins (Japan) 0.04 mg/kg pineapples (Australia) 0.05 mg/kg citrus (Spain)
	RfD (Reference Dose for Chronic Oral Exposure) *(USEPA, 1989).*	0.13 mg/kg/day
	JMPR ADI (Acceptable Daily Intake) in mg/kg diet.	No value.
Water	*(USEPA , 1983).*	90 µg/l
Workplace	USA (ACGIH) TLV-TWA (Threshold Limit Value, Time-Weighted Average) (1986).	10 mg/m^3
Environment	NIOSH.	1 ppm (10 mg/m^3)

First Aid

Persons who have been poisoned (accidentally or otherwise) should be transported immediately to a hospital and put under surveillance of properly trained medical staff.

Eyes: Immediately flush eyes with plenty of water for at least 15 minutes, occasionally lifting the upper and lower lids. Get medical aid immediately.

Skin: Get medical aid. Flush skin with plenty of soap and water for at least 15 minutes before removing contaminated clothing and shoes. Seek medical attention immediately. Contaminated skin should be washed with soap and water *(Simplot)*.

Ingestion: If victim is conscious and alert, give 2-4 cupfuls of milk or water. Get medical aid immediately.

Inhalation: Get medical aid immediately.

Annexes

Annex 1 **Further Information on the Substance**

Annex 2 **Details on Reported Control Actions**

Annex 3 **List of Designated National Authorities**

Annex 4 **References**

Annex 1 - Further Information on the Substance

1 Chemical and Physical Properties

1.1	**Identity**	Bromacil is an odorless, white crystalline solid *(ACGIH, 1986; Clayton et al., 1981).*
1.2	**Formula**	$C_9H_{13}N_2O_2Br$
	Chemical name	5-Bromo-6-methyl-3-(1-methylpropyl)-2,4(1H,3H)-pyrimidinedione (CA); 5-bromo-3-sec-butyl-6-methyluracil (IUPAC).
	Chemical type	Uracil
1.3	**Solubility**	813 - 815 ppm (0.0815%) at 25 °C *(Worthing, 1983; Meister, 1992)*
	$logP_{ow}$	Log Pow = 2.61 *(Li, 1982)*
1.4	**Vapour pressure**	2,5 x 10^{-4} Torr at 25 °C
1.5	**Melting point**	157.5-160 °C *(ACGIH, 1986; Clayton et al. 1981; Meister, 1992)*
1.6	**Reactivity**	It is chemically stable under normal storage conditions, but may pose a slight fire hazard when exposed to heat or flame. It slowly decomposes in the presence of strong acids and poses a fire and explosion hazard in the presence of strong oxidizers *(Occupational Health Services, Inc. 1991)*. When heated to decomposition, bromacil emits highly toxic and corrosive fumes of bromides and toxic oxides of nitrogen and carbon *(Occupational Health Services, Inc. 1991, Sax, 1984)*. Airborne bromacil dust may ignite *(Gosselin, et al. 1984)*.

2 Toxicity

2.1 General

2.1.1	**Mode of action**	Rapid uptake through the roots. Bromacil inhibits photosynthesis. *(Gosselin, et al. 1984; Meister, 1992).*
2.1.2	**Uptake**	A number of studies show that the substituted uracils, the class of compounds to which bromacil belongs, are absorbed into the body from the gut and excreted primarily in the urine *(National Research Council, 1977; Paulson, 1975, USEPA, 1989)*.
2.1.3	**Metabolism**	Small amounts of bromacil were detected in the milk of lactating cows that were given 5 ppm in their food *(Gosselin, 1984)*. No bromacil was found in the urine or feces of these cows *(Paulson, 1975)*. Experimental animals and humans occupationally exposed to bromacil excreted unchanged bromacil and the metabolite 5-bromo-3-sec-butyl-6-hydroxymethyluracil in the urine *(USEPA, 1989).*

2.2 Known Effects on Human Health

2.2.1 Acute Toxicity

Symptoms of poisoning

Liquid formulations of bromacil are moderately toxic, while dry formulations are relatively non-toxic *(Meister, 1992)*. Hyvar X-L formulation can be harmful or fatal if swallowed *(Gosselin, 1984, Hartley et al., 1983, Meister, 1992)*. The herbicide is irritating to the skin, eyes and respiratory tract *(Morgan, 1982)*.

2.2.2 Short and long term exposure

There are no short and long term exposure studies on effects on human health related to bromacil.

2.2.3 Epidemio-logical studies

There are no epidemiological studies on effects on human health related to bromacil.

2.3 Toxicity studies with laboratory animals and *in vitro* systems

2.3.1 Acute Toxicity

oral

When 100 mg/kg of the herbicide was fed to dogs, it caused vomiting, salivation, muscular weakness, excitability, diarrhoea, and dilation of the pupils of the eyes. Rats fed single doses of bromacil experienced initial weight loss, paleness, exhaustion and rapid breathing *(Occupational Health Services, Inc. 1991)*. Within four hours of being given 250 mg/kg of bromacil, or a related material (isocil), sheep became bloated and walked with a stilted gait *(Gosselin, 1984)*. The oral LD_{50} value for rats was calculated to be 5200 mg/kg *(USEPA, 1989).*

Dermal

Bromacil caused mild dermal irritation when applied to the skin of guinea pigs. Rabbits did not show clinical signs of poisoning or toxicity in response to skin applications of 5000 mg/kg of the herbicide *(ACGIH, 1986, Gosselin, 1984)*.

Bromacil did not produce skin sensitization *(USEPA, 1989).*

Inhalation

Because bromacil has a low vapour pressure, it is unlikely to produce vapours which can be inhaled. No deaths occurred when rats were exposed to approximately 4.8 milligrams of bromacil per litre of air (mg/l) for four hours *(ACGIH, 1986; Occupational Health Services, Inc., 1991).*

Irritation

When bromacil was put in the eyes of rabbits, there was irritation in the conjunctiva, the mucous membrane lining of the eye, but no injury to the cornea, the transparent portion of the eyeball *(Gosselin, 1984)*.

2.3.2 Short and long term exposure

Enlarged livers were revealed in autopsies on rats that died after five days of repeated doses of bromacil at 1500 mg/kg/day *(Gosselin, 1984)*. Sheep that died after being given 250 mg/kg/day of bromacil on four successive days showed the following disease-related findings: inflammation of the mucus membrane that lines the stomach and intestines, or gastroenteritis; congestion and enlargement of the liver; weakened appearance of the adrenal glands; bleeding from the heart; swollen and bleeding lymph nodes *(Gosselin, 1984).*

In a 2-year study rats were fed dietary levels of bromacil of 0, 50, 250 or 1250 ppm bromacil (corresponding to about 0, 2.5, 12.5, or 62.5 mg/kg/day). Females in the highest dose group showed decreased body weight gain. The NOAEL was 12.5 mg/kg/day *(USEPA, 1989).*

In a 78-week study CD-1 mice were fed dietary levels of 0, 250, 1250 and 5000 ppm (corresponding to 0, 39.6, 195 or 871 mg/kg/day for males and 0, 66.5, 329 or 1310 mg/kg/day for females). The LOAEL was 250 ppm for male mice and the NOAEL was 250 ppm for female mice *(USEPA, 1989).*

2.3.3 **Effects on reproduction**

Bromacil did not affect the reproduction and lactation performance of rats fed 0 or 12.5 mg/kg/day for 3 generations *(TOXNET, USEPA, 1988)*. Toxic effects and developmental abnormalities of the musculoskeletal system were seen in the embryos or foetuses of female rats which inhaled 38 mg/m^3 of bromacil for two hours daily, during the 7th to 14th day of pregnancy *(NIOSH).*

2.3.4 **Mutagenicity**

Bromacil was not mutagenic in a number of microbial and fungal gene mutation test systems. A number of indicator tests (for DNA damage) were also negative. In one Ames test, however, bromacil induced revertants in three of six Salmonella strains tested.

Bromacil was weakly mutagenic at the 2000 ppm dose level in a sex-linked recessive lethal test in *Drosophila melanogaster*. It did not cause chromosome aberration in an *in vivo* mouse dominant lethal assay *(USEPA, 1989)*.

2.3.5 **Carcinogenicity**

In a two year study ChR-CD rats were fed dietary levels of 0, 50, 250 or 1250 ppm bromacil. No increased incidence of tumours was found *(USEPA, 1989)*.

An increased incidence of hepatocellular adenomas plus carcinomas was observed in male but not in female CD-1 mice fed bromacil in the diet at dietary levels of 5000, found predominantly in mice that survived to terminal sacrifice *(USEPA, 1989)*. According to USEPA (1989) bromacil has not been determined to be carcinogenic.

The International Agency for Research on Cancer has not evaluated the carcinogenic potential of bromacil.

3 Exposure

3.1 **Food**

Exposure through food is low as major uses of bromacil are on non-cultivated land.

3.2 **Occupational**

Industrial and agricultural workers are exposed to the wettable powders and aqueous emulsions of bromacil through two primary routes of exposure: inhalation of dusts and sprays, and skin contact with dusts, emulsions and sprays *(Clayton et al., 1981)*.

4 Effects on the Environment

4.1 Fate

4.1.1 **Persistence**

Bromacil adsorbs only lightly to soil particles (Koc = 32 g/ml), is soluble in water and has a relatively lengthy soil half-life (60 days). For these reasons, bromacil is expected to move (leach) quite readily through the soil and it can contaminate groundwater *(VanDriesche, 1985)*. Bromacil is persistent and its half-life is greater than 100 days *(Rao et al., 1983)*.

4.1.2 **Bioconcentration** Using a flow-through system and a 17-day exposure period, (14)C labelled bromacil had a BCF of only 3.2 in fathead minnow fish; this indicates that bromacil does not accumulate in fish tissue to a large extent *(Call, 1987).*

4.1.3 **Groundwater concentrations** Monitoring analyses of 10929 wells in California during 1975 to 1989 detected bromacil (detection limit and concentrations not reported) in 4 wells *(Mackay, 1990)*. Bromacil concentrations of 30 to 147 µg/l have been reported for upper ground water samples collected in West Germany *(Frank, 1987)*; concentrations of <0.1-1.8 µg/l were reported for water samples from bore holes (15-40 m deep) in three provinces in the Netherlands *(Leistra, 1989).* In a 1979-1984 analysis of 7 wells in Ontario, Canada that were in the vicinity of bromacil herbicide use, bromacil was detected (detection limit 0.1 µg/l) in only one well *(Frank, 1987).*

4.1.4 **Aquatic fate** Bromacil may degrade in natural water through microbial degradation and photo-sensitized degradation. No degradation occurred in the absence of the sensitizers *(Acher 1980).* The rate of photodegradation in natural water could vary dramatically depending upon concentration of sensitizing agents and sunlight intensity. A two-month half-life is suggested for this herbicide in clean river water which is low in sediment *(VanDriesche, 1985)*.

4.2 Ecotoxicity

4.2.1 **Fish** The median tolerance limit, or the concentration of bromacil that will kill 50% of the exposed fish after 48 hours of exposure, varies from 40 ppm to 164 ppm, depending on the type of fish tested *(Clayton et al., 1981)*. The 48-hour LC_{50} for bromacil in bluegill sunfish is 71 ppm, in rainbow trout is 56-75 ppm, and in carp is 164 ppm *(TOXNET)*. The 96-hour LC_{50} in fathead minnows is 182 mg/l *(Du Pont, 1990)*.

Bromacil is slightly to very slightly toxic to fish with 48-96h LC_{50} values ranging from 28 mg/l for *Oncorhyncus mykiss* to 182 mg/l *Pimephales promelas (RIVM/CSR, 1988).*

4.2.2 **Aquatic invertebrates** Bromacil is slightly toxic to the marine crustacea *Artemia salina* with a 24 hour LD_{50} of 71 mg/l *(Wilkins and Metcalfe, 1993)*.

Aquatic plants For 17 algal strains belonging to the Chlorophyceae EC_{50}-values range from 0.05 to 10 mg/l, indicating that bromacil is toxic to very toxic to algae *(Cullimore, 1975)*.

4.2.3 **Birds** The 8-day oral LD_{50} for bromacil is over 10000 ppm in mallards and quail *(Clayton et al., 1981).*

4.2.4 **Bees** Bromacil is slightly to very slightly toxic to honeybees with the contact and oral LD_{50}s being >16 and >40 µg/bee, respectively *(RIVM/CSR, 1988)*.

Annex 2 - Details on reported control actions

BELIZE

Effective: 1990

Control Action: Severely restricted.

Uses still allowed: For use in citrus only.

GERMANY

Effective: 1993

Control Action: Totally banned for use as plant protection product.

Uses still allowed: No remaining uses allowed.

Reasons: High persistence of bromacil in soil combined with high leaching potential with the likelihood that application of bromacil would exceed a regulatory limit of 0.1 µg/l in ground water. The action is based on a national review of scientific data.

Alternatives: At present there are no soil acting alternatives registered for weed control on railway tracks (plant protection products containing diurone or glyphosate); on uncultivated land the use of glyphosate is possible, a non chemical alternative is mechanical weed control.

SLOVENIA

Effective: 1997

Control Action: Banned for use in agriculture.

Reasons: This chemical was banned from the use in agriculture due to the effect of its toxic properties to human health and the environment according to the opinion given by the Commission on Poisons.

SWEDEN

Effective: 1990

Control Action: The substance is banned for use as pesticide. No remaining uses allowed.

Reasons: Suspended due to the substance's suspected carcinogenic properties and mobility in soil.

Annex 3 - List of Designated National Authorities

BELIZE

P
The Secretary
Department of Agriculture
Pesticides Control Board
Central Farm
Cayo
Mr Mario Fernandez
Fax +501 92 2640
Phone +501 92 2640 / 92 3772
Telex 102 Foreign Bz

C
Sanitation Engineer
Public Health Bureau
Ministry of Health
Belize City

GERMANY

P
Abteilung fuer Pflanzenschutzmittel und Anwendungstechnik Koordinierungsgruppe
Biologische Bundesanstalt für Land- und Forstwirtschaft
Messeweg 11-12
Braunschweig, D-38104
Dr. A. Holzmann
e-mail A.Holzmann@bba.de
Fax +49 531 299 3003
Phone +49 531 299 3452

CP
Anmeldestelle Chemikaliengesetz
Bundesanstalt für Arbeitsschutz und Arbeitsmedizin
Friedrich-Henkel-Weg 1-25
Dortmund, D-44149
Ms. Kowalski
e-mail amst@baua.do.shuttle.de
Fax +49 231 9071679
Phone +49 231 9071516

SLOVENIA

CP
Advisor
Ministry of Health
Stefanova 5
Ljubljana, 1000
Ms. Karmen Krajnc
e-mail karmen.kranjc@mz.sigov.mail.si
Fax +386 61 123 1781
Phone +386 61 178 6054

SWEDEN

CP
The National Chemicals Inspectorate (KemI)
P.O. Box 1384
Solna, S-171 27
Mr. Ule Johansson
Fax +46 8 735 7698
Phone +46 8 730 6004
Telex 10460 AMS S

CP **DNA** Industrial Chemicals and Pesticides
P **DNA** Pesticides
C **DNA** Industrial Chemicals

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