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INTERGOVERNMENTAL NEGOTIATING COMMITTEE FOR AN INTERNATIONAL LEGALLY BINDING INSTRUMENT FOR THE APPLICATION OF THE PRIOR INFORMED CONSENT PROCEDURE FOR CERTAIN HAZARDOUS CHEMICALS AND PESTICIDES IN INTERNATIONAL TRADE
Sixth session
Rome, 12-16 July 1999
Item 4 (c) of the provisional agenda*

IMPLEMENTATION OF THE INTERIM PRIOR INFORMED CONSENT PROCEDURE: ADOPTION OF DECISION GUIDANCE DOCUMENTS FOR ALREADY IDENTIFIED CHEMICALS

Note by the secretariat

Addendum

The secretariat has the honour to submit, in the annex to the present addendum, the draft decision guidance document for the following chemical:

Chemical	CAS number	Category
Binapacryl	485-31-4	Pesticide

* UNEP/FAO/PIC/INC.6/1/Rev.1.

Annex

PIC - Decision guidance document for a banned or severely restricted chemical

Binapacryl

Published:

Common name	Binapacryl (ISO)
Other names/ synonyms	2-*sec*-butyl-4,6-dinitrophenyl 3-methylcrotonate (IUPAC); 2-(1-methylpropyl)-4,6-dinitrophenyl-3-methyl-2-butenoate (CA).
CAS No.	485-31-4
Use category	Pesticide
Use	Binapacryl is used as a fungicide and miticide.
Trade names	Morocide, Endosan, Dapacryl, Ambox, Acricid, Morrocid, Hoe 2784, Niagara 9044
Formulation types	Wettable powders (WP), emusifiable concentrates (EC).
Basic manufacturers	Marman USA, Inc.

Reasons for inclusion in the PIC procedure

Binapacryl is included in the PIC procedure as a pesticide. Inclusion was recommended at the eighth meeting of the FAO/UNEP Joint Group of Experts on Prior Informed Consent 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 10 countries and the European Union. In 7 countries (Angola, Cyprus, India, Kuwait, Pakistan, Slovenia and Thailand) and in the European Union binapacryl was reported as banned. In 3 countries (Australia, Austria and New Zealand) the substance was reported as withdrawn by the producer. No remaining uses were reported. All countries listed concern about the effects of binapacryl on human health as a primary reason for the control actions.

Hazard classification by Organization

<table>
<tr><td>WHO

(WHO,1996)</td><td>Technical product: Class II (moderately hazardous),classification based on an oral LD_{50} of 421 mg/kg bw.

Classification of formulations
<table>
<tr><td></td><td colspan="2">oral toxicity</td><td colspan="2">dermal toxicity</td></tr>
<tr><td></td><td colspan="2">LD_{50}: 58 mg/kg bw (see Ann. 1)</td><td colspan="2">LD_{50}: 750 mg/kg bw (see Ann. 1)</td></tr>
<tr><td>Formulation</td><td>a.i. (%)</td><td>Hazard class</td><td>a.i. (%)</td><td>Hazard class</td></tr>
<tr><td>Solid</td><td>>10
<10</td><td>II
III</td><td>>70
<70</td><td>II
III</td></tr>
</table></td></tr>
<tr><td>EPA</td><td>Not classified.</td></tr>
<tr><td>EU</td><td>Toxic, teratogen cat.2. (classification in accordance with Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances).</td></tr>
<tr><td>IARC</td><td>Not classified.</td></tr>
</table>

Protective measures that have been applied concerning the chemical

Measures to reduce exposure

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

The United Nations Committee of Experts on the Transportation of Dangerous Goods classifies the chemical in:

Hazard class 6.1 Poisonous substance.

Packing group 3 Harmful substances and preparations presenting a relatively low risk of poisoning.

Alternatives

India indicated specific alternatives (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 designated national authority in the country where the alternative has been reported (see addresses of designated national authorities 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 the *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 materials. 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 containers in a sanitary landfill or by incineration.

It should be noted that the methods recommended in literature are often not suitable in a specific country. 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	MRLs (Maximum Residue Limits in mg/kg) in specified products *(FAO/WHO, 1983).*	MRL withdrawn.
	JMPR ADI (Acceptable Daily Intake) in mg/kg diet *(FAO/WHO, 1983).*	ADI withdrawn.

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.

Skin: Flush skin with plenty of soap and water for at least 15 minutes before removing contaminated clothing and shoes. Seek medical attention immediately.

Ingestion: Do not induce vomiting. Have the victim rinse his or her mouth and then drink 2-4 cupfuls of water, and seek medical advice.

Inhalation: Remove from exposure into fresh air immediately.

Annexes

Annex 1 - Further information on the substance

1 Chemical and physical properties

1.1	Identity	Pale yellow to brownish crystals.
1.2	Formula	$C_{15}H_{18}N_2O_6$
	Chemical name	2-(1-methylpropyl)-4-,6-dinitrophenyl-3-methyl-2-butenoate (CA)
	Chemical type	Nitrophenol
1.3	Solubility	Solubility in water is low to moderate (11%) in ethanol, but exceeds 50 percent in heavy aromatic naphta and acetone.
	$\log K_{ow}$	4.75 (estimate)
1.4	Vapour pressure	1 x 10^4 Torr at 60 °C *(JMPR, 1969)*
1.5	Melting point	66 °C
1.6	Reactivity	It is readily hydrolized by strong acids or dilute alkalis; a small degree of hydrolysis will occur in water after prolonged contact. Decomposes slowly by UV irradiation *(JMPR, 1969).* Further information in Tomlin (1994).

2 Toxicity

2.1 General

2.1.1	Mode of action	Binapacryl is a dinitrophenol and acts by uncoupling or inhibiting oxidative phosphorylation, which basically prevents the formation of the high-energy phosphate molecule, adenosine triphosphate (ATP) *(Ware, 1997)*.
2.1.2	Uptake	Most nitrophenols and nitrocresols are well absorbed from the gastrointestinal tract through the skin, and by the lungs when fine droplets are inhaled. Fatal poisonings have occurred as a result of dermal contamination.
2.1.3	Metabolism	Nitrophenols and nitrocresols undergo some biotransformation in humans, mainly reduction (one nitro group to an amino group) and conjugation at the phenolic site. Although nitrophenols and metabolites appear consistently in the urine of poisoned individuals, hepatic excretion is probably the main route of disposition. Elimination is slow: residence half-life in humans is 5-14 days. Blood and tissue concentrations tend to increase progressively if an individual is substantially exposed on successive days *(Morgan, 1989)*.

2.2 Known effects on human health

2.2.1 Acute toxicity

Symptoms of poisoning	Nitroaromatic compounds are highly toxic to humans and animals. Nitrophenols and nitrocresols are toxic to the liver, kidney and nervous system. The basic mechanism of toxicity is stimulation of oxidative metabolism in cell mitochondria by interference with the normal coupling of carbohydrate oxidation to phosphorylation (ADP to ATP). Increased oxidative metabolism leads to hyperthermia, tachycardia and dehydration and in time depletes carbohydrate and fat stores. Most severe poisonings from absorption of these compounds have occurred in workers working in hot environments.

Hyperthermia and direct action on the brain cause cerebral oedema, manifesting clinically as a toxic psychosis and sometimes as convulsions. Liver parenchyma and renal tubules show degenerative changes. Albuminuria, pyuria, hematuria and azotemia are prominent signs of renal injury.

Neutropenia has occurred in humans following heavy exposure to dinitrophenol. Cataracts occur in laboratory animals given nitrophenols, and have occurred in humans, both as a result of ill-advised medicinal use and as a consequence of occupational exposure. Cataract formation is sometimes accompanied by glaucoma *(Morgan, 1989)*.

Yellow staining of skin and hair often signifies contacts with a nitroaromatic chemical. Staining of the sclerae and urine indicates absorption of potentially toxic amounts. Profuse sweating, headache, thirst, fever, confusion, malaise and lassitude are common early symptoms of poisoning. Warm, flushed skin, tachycardia and tachypnea indicate a serious degree of poisoning. Restlessness, apprehension, anxiety, manic behaviour or unconsciousness reflect cerebral injury. Convulsions signify an immediate life-threatening intoxication. Laboured breathing and cyanosis are consequences of stimulated metabolism and tissue anoxia. Weight loss occurs in persons continually exposed to relatively low doses of nitrophenols or nitrocresols *(Morgan, 1989)*.

2.2.2 Short and long-term exposure: There are no short and long-term exposure studies on effects on human health related only to binapacryl.

2.2.3 Epidemio-logical studies: There are no epidemiological studies on effects on human health related only to binapacryl.

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

2.3.1 Acute Toxicity

oral: LD_{50} (mg/kg): 58–200 (different test species), *(Gaines, 1969); (Spencer, E. Y., 1982)*.

dermal: LD_{50} (a.i.; mg/kg): 720 in rats *(World review of pest control, 1970),* LD_{50} (mg/kg): 750 in rabbits (*Spencer, E. Y. 1982).*

inhalation: Inhalation may result in toxic effects on humans *(Sax N.I, 1975).*

irritation: Except in a few sensitive individuals, it is only moderately irritating to the skin and mucous membranes.

2.3.2 Short and long-term exposure: Six-month studies with rats fed with binapacryl concentrations up to 500 ppm in the diet showed pathological alterations at concentrations higher than 200 ppm *(JMPR, 1969).*

2.3.3 Long-term exposure: Rats were fed with a diet containing binapacryl up to 200 ppm for two years. No effect on morbidity or mortality due to binapacryl was found *(JMPR, 1969)*.

2.3.4 Effects on reproduction: In a multigeneration study on binapacryl in rats the reproductive performance, as measured by the indices of mating, pregnancy, fertility, parturition and lactation, was not influenced by feeding with the substance *(Kennedy et al., 1965)*. In rat studies, where three generations were fed with a diet containining up to 60 ppb binapacryl, no effect on reproduction could be observed *(JMPR, 1969).*

2.3.5 Embryotoxicity and: In groups of 11-12 pregnant female New Zealand rabbits, which received binapacryl by gavage, there were no statistically significant differences

	teratogenicity	between control and treated groups with respect to mean values of *corpora lutea*, implantations, live and dead foetuses, early and late resorptions or live foetal weight. Placenta weight was slightly decreased in the 5.0 mg/kg b.w. group, but the difference was not toxicologically relevant because all other findings were normal. Foetuses with externally visible malformations were one in the control and one in the 5.0 mg/kg b.w. group *(FAO, 1983)*.
2.3.6	Mutagenicity	Binapacryl was positive in *Salmonella typhimurium* TA100 without metabolic activation *(Agrochemicals Handbook, 1987)*.
2.3.7	Carcinogenicity	Rats administered 500 mg/kg in diet for 2 years and dogs receiving 50 mg/kg in diet for 2 years showed no ill effects *(Agrochemicals Handbook, 1987)*.

3 Exposure

3.1	Occupational	Two workers developed headache, nausea, vomiting, abdominal pain, diarrhea, and breathing difficulties after spraying tomatoes with binapacryl for 2 hours. Fever, weak pulse, and tremor were noted later. Recovery was complete within a week.

4 Effects on the environment

4.1	Fate	If released to soil, binapacryl may undergo slow hydrolysis in basic soils *(RSC, 1983; Goring et al., 1975).* If released to water, binapacryl is expected to undergo slow hydrolysis under basic conditions *(RSC, 1983).* Binapacryl is known to slowly decompose under the influence of UV light *(RSC, 1983)* and it may undergo photolysis in the atmosphere. An estimated rate constant for the gas-phase reaction of binapacryl with photochemically produced hydroxyl radicals leads to an estimated half-life of 4.63 hours in the ambient atmosphere *(Goring, 1975).*
4.1.1	Persistence	Binapacryl, a dinitrophenol ester, probably hydrolyzes to form free phenol, identical in structure to the herbicide dinoseb. Only after such a transformation might there be some potential for leaching *(McBride).*
4.1.2	Bioconcentration	Based on an estimated log octanol/water partition coefficient of 4.75, a calculated bioconcentration factor of 2400 can be calculated for binapacryl using an appropriate regression equation. The magnitude of this value indicates that binapacryl may significantly bioconcentrate in fish and aquatic organisms *(Lyman, 1982).*

4.2 Ecotoxicity

4.2.1	Fish	Binapacryl is highly toxic to fish ; (LC_{50} : 0.04 – 0.06 mg/l).
4.2.2	Aquatic invertebrates	Binapacryl is toxic to aquatic organisms. *Asellus brevicaudus* (96 hr) 29 μg/l at 16 °C as the technical material.
4.2.3	Birds	There are no studies on effects on birds related only to binapacryl.
4.2.4	Bees	Not toxic to bees (*Spencer, 1982).*

Annex 2 - Details on reported control actions

ANGOLA

Effective:	1990
Control action:	Banned for use. No remaining uses allowed.
Reasons:	Banned for use in agriculture for toxicological reasons.
Alternatives:	Currently not known.

AUSTRALIA

Effective:	1987
Control action:	Withdrawn by industry. No remaining uses allowed.
Reasons:	Inadequate toxicology available. Several invalidated IBT studies without acceptable replacements.
Alternatives:	Various.

AUSTRIA

Effective:	1993
Control action:	Voluntarily withdrawn by manufacturer since July 1991. All uses banned as of1 January 1993.
Reasons:	High acute human toxicity (probable oral lethal dose 5-50 mg/kg; for a 70 kg person: between 7 drops and 1 teaspoon).
Alternatives:	Many alternatives for designated purposes.

CYPRUS

Effective:	1987
Control action:	Banned for all use as a pesticide. No remaining uses allowed.
Reasons:	Risk associated with birth defects and male sterility.

EUROPEAN UNION

Effective:	1990
Control action:	The placing on the market and the use of all plant protection products containing binapacryl as a active ingredient is prohibited.
Reasons:	Binapacryl is likely to give rise to harmful effects on human and animal health (close chemical relationship to dinoseb). The chemical showed mutagenic effects in animal testing. Binapacryl has been classified by the EC as a category 2 reproductive toxin (probably causing developmental damage to humans).

(Member States of the European Union are: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, United Kingdom.)

INDIA

Effective:	1975
Control action:	Refused registration.
Reasons:	Since it is moderately irritant to eyes and its effective and safer substitutes are available.
Alternatives:	Dicofol, Dinocap, Tridemorph.

KUWAIT

Effective:	1975
Control action:	Banned for use as a pesticide. No remaining uses allowed.
Reasons:	Action was taken because safe alternatives are available.

NEW ZEALAND

Effective:	1986
Control action:	Voluntary withdrawal of all products, registrations cancelled. No uses allowed.
Reasons:	Human health reasons (teratogenicity and possible carcinogen).

PAKISTAN

Effective:	1990
Control action:	Prohibited. No remaining uses allowed.

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.

THAILAND

Effective:	1995
Control action:	All use categories have been banned.
Reasons:	Possibly carcinogenic and teratogenic in test animals.

Annex 3 – List of designated national authorities

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Le Coordinateur
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Ministère de l'Agriculture, Cabinet technique
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CP DNA Industrial chemicals and pesticides
P DNA Pesticides
C DNA Industrial chemicals

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