

OPERATION OF THE PRIOR INFORMED
CONSENT PROCEDURE FOR BANNED
OR SEVERELY RESTRICTED CHEMICALS
IN INTERNATIONAL TRADE

DECISION GUIDANCE DOCUMENTS

Chlordimeform

JOINT FAO/UNEP PROGRAMME
FOR THE OPERATION OF
PRIOR INFORMED CONSENT



United Nations Environment Programme



Food and Agriculture Organization
of the United Nations

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Food and Agriculture Organization of the United Nations
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Rome - Geneva 1991; amended 1996

DISCLAIMER

The inclusion of these chemicals in the Prior Informed Consent Procedure is based on reports of control action submitted to the United Nations Environment Programme (UNEP) by participating countries, and which are presently listed in the UNEP-International Register of Potentially Toxic Chemicals (IRPTC) database on Prior Informed Consent. While recognizing that these reports from countries are subject to confirmation, the FAO/UNEP Joint Working Group of Experts on Prior Informed Consent has recommended that these chemicals be included in the Procedure. The status of these chemicals will be reconsidered on the basis of such new notifications as may be made by participating countries from time to time.

The use of trade names in this document is primarily intended to facilitate the correct identification of the chemical. It is not intended to imply approval or disapproval of any particular company. As it is not possible to include all trade names presently in use, only a number of commonly used and published trade names have been included here.

This document is intended to serve as a guide and to assist authorities in making a sound decision on whether to continue to import, or to prohibit import, of these chemicals because of health or environmental reasons. While the information provided is believed to be accurate according to data available at the time of preparation of this Decision Guidance Document, FAO and UNEP disclaim any responsibility for omissions or any consequences that may flow therefrom. Neither FAO or UNEP, nor any member of the FAO/UNEP Joint Group of Experts shall be liable for any injury, loss, damage or prejudice of any kind that may be suffered as a result of importing or prohibiting the import of these chemicals.

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ABBREVIATIONS WHICH MAY BE USED IN THIS DOCUMENT

(N.B. : chemical elements and pesticides are not included in this list)

ADI	acceptable daily intake
ai	active ingredient
b.p.	boiling point
bw	body weight
°C	degree Celsius (centigrade)
CCPR	Codex Committee on Pesticide Residues
DNA	Designated National Authority
EC	emulsion concentrate
EEC	European Economic Community
EPA	U.S. Environmental Protection Agency
ERL	extraneous residue limit
FAO	Food and Agriculture Organization of the United Nations
g	gram
µg	microgram
GAP	good agricultural practice
GL	guideline level
ha	hectare
IARC	International Agency for Research on Cancer
i.m.	intramuscular
i.p.	intraperitoneal
IPCS	International Programme on Chemical Safety
IRPTC	International Register of Potentially Toxic Chemicals
JMPR	Joint FAO/WHO Meeting on Pesticide Residues (Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues)
k	kilo- (x 10 ³)
kg	kilogram
l	litre
LC ₅₀	lethal concentration, 50%
LD ₅₀	lethal dose, median

m	metre
mg	milligram
ml	millilitre
m.p.	melting point
MRL	Maximum Residue Limit.
MTD	maximum tolerated dose
ng	nanogram
NOEL	no-observed-effect level
NOAEL	no-observed-adverse-effect level
NS	Not Stated
OP	organophosphorus pesticide
PHI	pre-harvest interval
ppb	parts per billion
ppm	parts per million (Used only in reference to the concentration of a pesticide in an experimental diet. In all other contexts the terms mg/kg or mg/l are used).
ppt	parts per trillion
sp gr	specific gravity
STEL	Short Term Exposure Limit
TADI	Temporary Acceptable Daily Intake
TLV	Threshold Limit Value
TMDI	theoretical maximum daily intake
TMRL	Temporary Maximum Residue Limit
TWA	Time Weighted Average
UNEP	United Nations Environment Programme
WHO	World Health Organization
WP	wettable powder
wt	weight
<	less than
<<	much less than
≤	less than or equal to
>	greater than
≥	greater than or equal to

CHLORDIMEFORM

PRIOR INFORMED CONSENT DECISION GUIDANCE DOCUMENT

1. IDENTIFICATION

- 1.1 Common Name: Chlordimeform
- 1.2 Chemical Type: Formamidine
- 1.3 Use: Insecticide, acaricide and ovicide
- 1.4 Chemical Name: N¹-(4-chloro-o-tolyl)-N N-dimethylformamidine
- 1.5 CAS No.: 6164-98-3
- 1.6 Trade Names and Synonyms: Bermat, C8514, Ent 27567, EP-333, Fundal, Galecron, SN 3626
- 1.7 Mode of Action: Ovicide/larvicide for control of bollworm/tobacco budworm (*Heliothis* spp.)
- 1.8 Formulation Types: Emulsifiable concentrate (4 lb/gal.)(48.5% ai), water soluble powders (95-97%).
- 1.9 Basic Producers: Agro-Quimicas de Guatemala, S.A. (Guatemala); Ciba-Geigy Corp., Agricultural Div. (USA); Ciba-Geigy Ltd. (Switzerland); NOR-AM Chemical Co. (USA); Quimica Estrella (Argentina); Schering AG (West Germany); Sintesul (Brazil)

2. SUMMARY OF CONTROL ACTIONS

- 2.1 General: Control actions to ban or severely restrict chlordimeform have been taken by at least 10 countries. In at least eight, chlordimeform has been completely banned and in the other two, limited use is permitted for specific crops or under emergency government programmes. Specific actions reported by governments are summarized in Annex 1.
- 2.2 Reasons for the Control Action: Chloridimeform and its principal metabolites are considered probable human carcinogens. Studies in mice indicate dose-related increased incidence of hemangiosarcomas and hemangiomas-malignant tumours of the blood vessel. These data are reinforced by human monitoring data which link a chlordimeform metabolite 4-chloro-o-toluidine (5-CAT), with bladder cancer. The primary concern is for manufacturing plant and agricultural workers handling or applying the insecticide who are subject to exposure to residues over several years. Animal data indicating carcinogenic potential are reinforced by human urine monitoring data which implicate a chlordimeform metabolite with bladder cancer.

- 2.3 Uses Banned: In eight of 10 countries reporting, all uses are banned, with control actions beginning in the mid-1970s. In China, uses on vegetables, tea, fruit trees, herbs and against pests directly harmful to humans or animals are prohibited. Venezuela prohibits all uses except as indicated in 2.4. Details provided by reporting countries are given in Annex 1.
- 2.4 Uses Reported to be Continued in Effect: China permits limited use in cotton and rice and in rodenticide formulations. Venezuela permits vector control and emergency agricultural uses under the supervision of appropriate government authorities (see Annex 1). Other uses may be continuing in countries whose governments have not reported a control action to FAO/UNEP.
- 2.5 Alternatives:
- 2.6 Contacts for Further Information: FAO/UNEP Joint Data Base, IRPTC, Geneva; Designated National Authorities in Countries taking control actions.

3. **SUMMARY OF FURTHER INFORMATION ON CHLORDIMEFORM**

- 3.1 Chemical and Physical Properties: Buff-coloured crystals melting at 32 °C. Solubility in water, 250 ppm at 20°C: dissolves readily in organic solvents. Principal human metabolite of concern: 4-chloro-o-toluidine (5-CAT). Chlordimeform is a medium strength base which forms crystalline salts with strong acids, such as hydrochloric acid. The hydrochloride is soluble in water to over 50%.
- 3.2 Toxicological Characteristics:
- 3.2.1 Acute Toxicity: Rat oral LD₅₀: 340 mg/kg bw. Rat dermal LD₅₀: 640 mg/kg bw. WHO Classification: ai: Class II - moderately hazardous. Formulations: 4E and SP (hydrochloride salt), both Class II. EC formulation oral and dermal LD₅₀: 680 mg/kg. SP formulation oral and dermal LD₅₀: 358 mg/kg.
- 3.2.2 Short-term Toxicity: 30 day:rat:NOEL<25mg/kg (lowest dose tested). Effects observed included nervousness, reflex excitability followed by decreased activity, and apathy. Complete recovery occurs three to four hours after dosing.
- 3.2.3 Chronic Toxicity: NOEL:rat (2 year feeding) 0.1 mg/kg (2ppm)(formation of methemoglobin). NOEL:dog=250 ppm. Effects noted in chronic rat and dog studies were similar. Positive for carcinogenicity in male and female mice (increased hemangiosarcomas and hemangiomas). Mutagenicity: variable results from over 50 studies; chlordimeform-negative; N-formyl-4-chloro-o-toluidine and 4-chloro-o-toluidine metabolites are mutagenic, with the latter the more strongly mutagenic of the two.
- 3.2.4 Epidemiological Studies: In 1975 incidence of hematuria in workers in a Tennessee chemical packaging plant was reported. These individuals had packaged chlordimeform. Nine of twenty-two workers involved became severely ill with abdominal pain, dysuria, urgency to void, or hematuria. Bladder biopsy specimens were taken from three of the workers. These biopsies showed severe haemorrhagic cystitis and chlordimeform and its 4-

chloro-toluidine metabolite were detected in urine specimens collected after exposure. All workers involved recovered completely.

Urine monitoring of agricultural workers in the USA has been conducted. Chlordimeform metabolites were detected at levels between 0.05 (limit of detection) and 8.6 ppm. Highest metabolite levels were found from mixer/loaders and equipment maintenance workers. Mean metabolite concentration in urine was calculated to be 0.1 ppm.

A retrospective mortality study of production workers in Germany suggests that the 4-chloro-o-toluidine (5-CAT) metabolite may induce bladder cancer in humans. 5-CAT is both an intermediate chemical used in the production of chlordimeform and a metabolite of the latter. The German study investigated 335 workers employed between 1929 and 1982. Eight individuals were subsequently diagnosed with urothelial carcinomas. Several monocyclic amines were produced at the plant, with approximate exposure distribution to workers of 80% 5-CAT, 10% 6-chloro-o-toluidine (6 COT) and 10% 0-toluidine.

3.3 Environmental Characteristics:

3.3.1 Fate: Half-life: loam soils: <60 days (chlordimeform and HCL salt); hydrolysis is enhanced as temperature and pH increase. Current data are insufficient to fully characterize fate.

3.3.2 Effects: Toxic to fish and wildlife. Relatively non-toxic to honey bees. Chlordimeform is moderately toxic to cold and warm water fish species, shrimp and oysters. Rainbow trout: 96 hr LC₅₀=13.2 mg/l. Channel catfish: 96 hr LC₅₀=20.2 mg/l. The HCL salt appears less toxic to aquatic organisms than the base. End-use formulations may be more toxic to these organisms than the active ingredients. Emulsifiable concentrates are slightly to moderately toxic to birds. Current data are insufficient to fully-characterize effects.

3.4 Exposure:

3.4.1 Food: Residues may occur in harvested agricultural commodities, including animal tissues and milk, as a result of feeding plant material. Plant residues may concentrate in processed food/feed commodities at approximately 2x rate. No market basket studies are available.

3.4.2 Occupational/Use: Skin contact can be a significant route of exposure. In humans, approximately 1/3 of the applied dose is absorbed through the skin with >1/3 of this absorbed dose detected in urine, of which >80% is excreted in 24 hrs. Chlordimeform metabolite has been detected in urine three days after exposure.

3.4.3 Environment: Although data are not adequate, chlordimeform and its HCL salt are considered to have little potential for leaching to groundwater. They are relatively immobile in mulch and loam soils and short-lived. Residues may move from a treated site in run-off sediment.

3.4.4 Accidental Poisoning: No reports are available. No antidote is available or has been identified. Treat symptomatically for organochlorine compounds.

- 3.5 Measures to Reduce Exposures: Protective gear, including body covering, rubber or neoprene gloves and boots, and an appropriate respirator can reduce exposure for workers handling or applying chlordimeform. Thorough bathing with soap and water at the end of each working day is recommended. When transferring spray material from mixing tanks to application systems, closed systems which eliminate human contact should be used. Agricultural workers should not enter treated areas for at least 24 hours following application.
- 3.6 Packaging and Labelling : Follow FAO Guidelines on Good Labelling Practice for Pesticides and Guidelines for the Packaging and Storage of Pesticides.
- 3.7 Waste Disposal Methods: Guidelines are under development. This section will be updated when guidelines are available.
- 3.8 Maximum Residue Limits (MRLs). (mg/kg):

JMPR/Codex Alimentarius: Temporary MRLs withdrawn in 1987.

Chile: Peaches, pears, 5; Citrus fruit, cherries, 2; tomatoes, 1; dairy products (fat), beef carcasses, beef fat, 0.5; hulled rice, 0.1; whole milk (fat), 0.05. The sum of chlordimeform and its metabolites is determined as 4-chloro-o-toluidine and expressed as chlordimeform.

Germany: All foods of plant origin 0.01; Honey 0.01. Chlordimeform and chlordimeform-hydrochloride; total calculated as chlordimeform.

Hungary: Ground cottonseed, cottonseed oil. 2 (in imported produce).

Japan: Fruits, 2; vegetables, tea, 0.6; rice, 0.1.

Netherlands: All 0 (0.02). Residues shall be absent, while the highest concentration at which this requirement is deemed to have been met is indicated between brackets.

Peru: Pears, peaches, 5; apples, strawberries, grapes, 3; citrus fruits, cabbage, Brussels sprouts, broccoli, cauliflower, cottonseed oil (refined and unrefined), 2; beans, milk products, fat of cattle, meat and meat products (fat basis), 0.5; raw whole milk, eggs, 0.05.

USA: Remaining US Tolerances - Cottonseed 5; (Hulls 10); Animal tissues from 0.05-0.25. All US Tolerances have been or are scheduled to be revoked.

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ANNEX 1
SUMMARY OF CONTROL ACTIONS AND REMAINING USES FOR
CLORDIMEFORM
AS REPORTED BY COUNTRIES

BANNED:

Columbia	(1987) Banned as agricultural chemical.
Ecuador	(1985) Banned as agricultural chemical.
Kenya	(1987) Banned as agricultural chemical.
Republic of Korea	(1986) Banned.
Mexico	(1986) Banned as agricultural chemical.
Panama	(1987) Banned as agricultural chemical.
USSR	(NS) Banned as agricultural chemical.

WITHDRAWN:

Yugoslavia (1976) Voluntary withdrawal by the manufacturer.

SEVERELY RESTRICTED:

Only remaining uses allowed:

Venezuela (1983) Only permitted when intended for control vectors for medical reasons by Ministry of Health and control of agricultural pests by Ministry of Agriculture.

Specific uses reported as not allowed:

China (1982) Prohibited for use on vegetables, tea, fruit trees and herbs, against insects harmful to health of humans and animals, for rat control except when formulated as a rodenticide. Permitted for cotton insect and rice insect control, but only to achieve adequate control.

Uses permitted only with special authorization:

None reported.

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