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

DECISION GUIDANCE DOCUMENTS

Chlorobenzilate

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

United Nations Environment Programme

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

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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.

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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
^{o}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 103)
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

Prior Informed Consent Decision Guidance Document

Chlorobenzilate

1 Identification

1.1	**Common Name**	Chlorobenzilate
	Other names/synonyms	ENT 18596
1.2	**Chemical Type**	Organochlorine
1.3	**Use**	Pesticide (Acaricide)
1.4	**Chemical Name**	Ethyl 4,4'-dichlorobenzilate (IUPAC) Ethyl 4-chloro-α-(4-chlorophenyl)- α -hydroxybenzene-acetate (CA)
1.5	**CAS No.**	510-15-6
1.6	**Trade Names**	Acaraben (Ciba Geigy), Akar (Ciba Geigy), Benzilan (Makhteshim Agan), Benz-O-Chlor (Tower), Folbex (Ciba Geigy), G 23992 (Ciba Geigy), Kopmite
1.7	**Mode of action as Pesticide**	Effector of ion permeability (nerve poison)
1.8	**Formulation Types**	Emulsifiable concentrate (EC) 25%, 45.5% and 50%; Wettable powder (WP) 25 %
1.9	**Basic Manufacturers**	(Makhteshim-Agan, Israel, production ceased); Nippon Kayaku Co., Japan; Baldock, Poland; (Ciba Geigy, the original manufacturer has ceased production)

2 Summary of Control Actions

2.1 General

Control actions to ban or severely restrict chlorobenzilate use as a pesticide or in agriculture have been reported in a total of seven countries. Cyprus reported that chlorobenzilate was severely restricted with a single use retained that represented < 30% of the previous use level.

The actions reported by governments to IRPTC/UNEP are listed in Annex 1.

2.2 Reasons for the Control Actions

Four of the five countries identified carcinogenicity as a primary concern. Cuba and the United States also listed potential reproductive hazards in male workers as an issue. Morocco cited persistence in the environment and the bioaccumulation of residues in the food chain as the basis for their control action.

2.3 Bans and restrictions

With the exception of Cyprus and India, all countries reported that no pesticide uses were permitted.

2.4 Uses Reported to be Continued in Effect

Cyprus has retained a use on citrus for the control of citrus rust mite. India reports the use of Folbex strips in beehives.

2.5 Alternatives

Specific alternatives were suggested by the United Sates and Cuba (Annex 2). Morocco indicated that alternatives were available but made no specific suggestions.

It is important to remember that the effectiveness of any alternative pesticide needs to be established under conditions of use in specific crops and countries.

2.6 Contacts for Further Information

FAO/UNEP Joint Data Base, IRPTC, Geneva; Designated National Authorities (DNAs) in countries taking control actions and reporting alternatives (Annex 3).

3 Summary of Further Information on Chlorobenzilate

3.1 Chemical and Physical Properties

Pure chlorobenzilate is a colourless solid with a melting point of 35-37^{o}C, and a boiling point for pure material of 156-158 ^{o}C. Technical material (94 %) is a brownish viscous liquid with a boiling point of 141-142^{o}C. The compound is virtually insoluble in water (10 mg/l) and is infinitely miscible (1 kg/kg) in acetone, dichloromethane, methanol and toluene; 600 g/l hexane and 700 g/kg octan-1-ol, all at 20^{o}C. Vapour pressure, 0.12 mPa at 20^{o}C. Chlorobenzilate is hydrolysed by alkalis and strong acids to free carboxylic acid or its salts (Royal Society of Chemistry, 1991).

3.2 Toxicological Characteristics

3.2.1 Classification

WHO Class III, slightly hazardous based on acute oral toxicity in the rat (WHO, 1994)

EU Harmful

3.2.2 General

Metabolism In animals: In rats, following oral administration the principal metabolites identified were p,p'-dichlorobenzilic acid, p,p'dichlorobenzylhydrol, p-chlorobenzoic acid and p,p'-dichlorobenzophenone.

3.2.3 Acute Toxicity

Oral Reported rat oral LD_{50}s include 700 mg/kg; 960-1200 mg/kg; 2784-3880 mg TC/kg; mouse oral LD_{50}: 729 mg/kg.

Dermal Rat dermal LD_{50} greater than 10,200 mg/kg.

Irritation — Irritating to eyes; non-irritating to skin (rabbits).

3.2.4 Short-term Toxicity

Teratogenicity

IARC, 1983 — Although no adverse effect was observed on reproduction in a three-generation study in rats (Bartsch *et al*., 1971), the teratogenic potential of chlorobenzilate has not been fully determined. On the basis of this study it was concluded that data are insufficient to determine if chlorobenzilate is a developmental toxin (IARC ,1983).

JMPR — The WHO Group of Experts re-evaluated the potential for chlorobenzilate to induce testicular damage as noted previously in chronic and reproduction studies and concluded that insufficient evidence exists to suggest that testicular damage would result from chlorobenzilate exposure. Further evidence and supportive claims for safety with respect to male reproduction have been made with an *in vivo* cytogenic study in mice (Hool and Muller, 1978) that revealed no mutagenic effects in the germinal epithelium and on spermatocytes in animals exposed to chlorobenzilate (JMPR, 1981).

3.2.5 Chronic Toxicity

Carcinogenicity

IARC 1983 — Chlorobenzilate was tested for carcinogenicity by administration in the diet in three strains of mice and in two strains of rats.

It induced hepatocellular carcinomas in both sexes of mice in one strain (National Cancer Institute, 1978) and in males of the other two strains (National Technical Information Service, 1968; Innes *et a*l., 1969).

The data on rats were inadequate for evaluation (Horn *et al*., 1955; National Cancer Institute, 1978).

Results of the experiments in mice provide *limited evidence* that chlorobenzilate is carcinogenic to experimental animals. The available data are insufficient to evaluate the carcinogenicity of chlorobenzilate to humans (IARC ,1983).

JMPR 1980 — In a review of the same studies in mice (Innes *et al*., 1969; National Cancer Institute, 1978) and rats (National Cancer Institute, 1978) the WHO Panel of the 1980 JMPR concluded that the available data suggested a correlation between the administration of chlorobenzilate at high dietary dosages and the development of hepatomas in mice. In studies on rats a carcinogenic potential was not observed (JMPR ,1981).

Mutagenicity

IARC 1983 — Chlorobenzilate was not mutagenic to *Salmonella typhimurium* with or without exogenous metabolic activation (Rinkus and Legator, 1980). Data from studies on other organisms (Fahrig, 1974) were considered insufficient for evaluation. No overall evaluation of the mutagenicity of chlorobenzilate could be made (IARC, 1983).

3.2.6 Epidemiological Data

No epidemiological studies are available.

3.3 Environmental Characteristics

3.3.1 Fate

The available data are insufficient to fully assess the environmental fate of chlorobenzilate.

Residues on treated fruit are stable to atmospheric and biological influences and, except on leaves which are growing fairly rapidly, the residue levels decline with a half-life of more than 14 days (JMPR,1978).

When chlorobenzilate was applied to a bare silty loam soil at 5 kg a.i/ha disappearance was rapid, with a half-life of less than 30 days, and residues could not be detected after 61 days. Vertical movement was confined to the upper 5 cm of soil. The concentration of the metabolites 4,4'-dichlorobenzilic acid and 4,4'-dichlorobenzophenone reached a maximum after 20 and 61 days, respectively, and rapidly decreased thereafter (JMPR ,1978).

3.3.2 Effects

Fish LC_{50s} Rainbow trout 0.60 mg/l: Bluegill sunfish 1.80 mg/l (Pesticide Manual ,1994)

Birds Practically non-toxic to birds (Pesticide Manual,1994)

Bees Non-toxic to bees (JMPR, 1969). Honey bee LD_{50} 1.01 µg/bee in laboratory (48 hr. 65% relative humidity, 26.7°C)

3.4 Exposure

3.4.1 Food

Humans may be exposed to chlorobenzilate through consumption of food commodities that have been treated with the pesticide. Chlorobenzilate is non-systemic so that residues remain mainly on the outside of fruit and migrate to a very small extent or not at all into the pulp. The principal component of the residue is the parent compound. Washing and peeling of treated fruit should remove most of the residue. No data were available on the fate of residues during storage and processing or on the effect of cooking (JMPR, 1969).

3.4.2 Occupational/Use

No information.

3.4.3 Environment

Chlorobenzilate degrades fairly rapidly and both it and its degradates have low mobility; groundwater contamination is considered unlikely.

3.4.4 Accidental Poisoning

One case of systemic poisoning due to exposure to chlorobenzilate was reported in a worker involved in mixing and spraying the compound on trees; he developed muscle pains, ataxia, mild delirium and fever (Ravindran, 1978, reported in IARC ,1983).

There were four human exposures identified in the USA; however, in all cases other pesticides were also implicated. Only two resulted in any hospitalisation.

3.5 Measures to Reduce Exposures

Protective clothing and gloves will protect those handling and applying chlorobenzilate. Additionally, goggles or a face shield should be worn.

3.6 Packaging and Labelling

Labels should include precautions and warnings related to applicator, handler and worker exposure, as well as hazards to aquatic organisms. Refer to the FAO Guidelines on Good Labelling Practice for Pesticides (1995).

3.7 Waste Disposal Methods (WHO/IPCS, 1990)

Incineration at above 1200°C in a unit equipped with an effluent gas scrubber to absorb any hydrogen chloride (IRPTC, Data Profile Series No.5).

3.8 Maximum Residue Limits (mg/kg)

Codex. ADI:	0.02 mg/kg body weight (confirmed 1980)
Codex MRLs:	All Codex maximum residue levels were recommended for withdrawal by the Codex Committee on Pesticide Residues (CCPR) in 1993.(ALINORM 93/24A, para . 50).

4 Major References

FAO (1969). Evaluations of Some Pesticide Residues in Food 1968, Monographs. FAO/WHO Joint Meeting on Pesticide Residues (JMPR) . WHO, Geneva

FAO (1978). Pesticide Residues in Food 1977: Evaluations 1977, Monographs. FAO/WHO Joint Meeting on Pesticide Residues (JMPR). FAO, Rome

FAO (1981). Pesticide Residues in Food 1980: Evaluations 1980 .Monographs. FAO/WHO Joint Meeting on Pesticide Residues (JMPR) . FAO, Rome

Associated references:

Hool, G. and Müller, D. (1978): Chromosome studies in male germinalepithelium - mouse

National Cancer Institute (1978): Bioassay of Chlorobenzilate for possible carcinogenicity. NCI Carcinogenesis Technical Report series No. 75. DHEW Publication No. (NIH) 78-1325

FAO (1995). Revised Guidelines for good labelling practices for pesticides. Food and Agriculture Organization, Rome

Farm Chemical Handbook '90 (1990). Meister Publishing. Willoughby, Ohio, USA

IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans, miscellaneous pesticides, Vol. 30 pp 73-85. IARC, Lyons, France. (January 1983).

Associated references:

Bartsch, *et al*.(1971). The carbinole acaricides: Chlorobenzilate and chlropropylate. Residue Rev., 39, 1-88

Fahrig, R. (1974). Comparative Mutagenicity Studies with Pesticides in Chemical Carcinogenesis Essays, IARC Scientific Publication No. 10, International Agency for Research on Cancer, Lyons, p.161-181

Horn, H.J. *et al*. (1955). Toxicology of chlorobenzilate. Agric. Food Chem., 3, 752-765

Innes, J.R. M. *et al.* (1969). Bioassay of Pesticides and Industrial Chemicals for Tumorigenicity in mice: A

preliminary Note. J. Natl. Cancer Inst. 42: 1101-1114

National Cancer Institute (1978). Bioassay of Chlorobenzilate for possible carcinogenicity (NCI-CG-TR-75; DHEW Publ. No. (NIH) 78-1325, Bethesda, MD

Ravindran, M. (1978). Toxic encephalopathy from chlorobenzilate poisoning: Report of a case. Clin. Encephalography, 9, 170-172

IRPTC. Treatment and Disposal Methods for Waste Chemicals. IRPTC, Data Profile Series No.5, UNEP/IRPTC, Geneva

Royal Society of Chemistry (1991). The Agrochemicals Handbook (3rd ed.). Cambridge, United Kingdom

US Department of Interior. Manual of acute toxicity: interpretations and data base for 410 chemicals and 66 species of freshwater animals. Washington DC, USA

US Environmental Protection Agency (1983). Pesticide fact sheet no 15: Chlorobenzilate. USEPA, Washington, DC, USA

US Environmental Protection Agency (1985). Guidance for the re-registration of pesticide products containing chlorobenzilate as an active ingredient. USEPA, Washington, DC, USA

WHO (1996). The World Health Organization Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1996-1997. World Health Organization, Geneva, WHO/PCS/96.3

Worthing, C.R. and R.J. Hance (Eds.) (1994). The Pesticide Manual: A World Compendium. (10th ed.). British Crop Protection Council, Surrey, United Kingdom

ANNEX 1

Summary of Control Actions and Remaining Uses as Reported by Countries

Actions taken and year effective

Bans

Argentina	
Control Action	Import, production, fractionation, commercialisation and use of products for agricultural use containing this active ingredient are banned
Effective	16/10/1990
Uses still allowed	
Reasons for control action	Carcinogenic effect on mammals, risk of cancer and adverse testicular effect

Cuba	
Control Action	Substance banned for import, production and use by Res. 268 of the Minister of Public Health of 28/12/90
Effective	28/12/1990
Uses still allowed	
Reasons for control action	Some factors indicated an adverse effect on the human reproductive system and a carcinogenic effect on various species of mammals

Morocco	
Control Action	Banned for use in agriculture since 1984.
Effective	19/031984
Uses still allowed	No remaining uses allowed.
Reasons for control action	Persistence in the environment, bioaccumulation of residues in the food chain

Voluntary Withdrawals

Sweden	
Control Action	This substance has been withdrawn after mutual discussion between the national chemicals inspectorates and the importers because of its carcinogenic effects on experimental animals.
Effective	31/12/1979
Uses still allowed	
Reasons for control action	Carcinogenic effects on experimental animals

United States	
Control Action	EPA initiated a special review of the substance in May 1976, based on possible risks to pesticide applicators. In March 1986, EPA issued a final rule revoking tolerances on almonds, apples, cotton seed, melons, pears, and walnuts. In 1987, Ciba Geigy (basic producer) requested voluntary cancellation and this became effective in 1988. Chlorobenzilate is no longer registered for use in the USA nor are there any tolerances
Effective	December 1988
Uses still allowed	No remaining uses allowed
Reasons for control action	Animal studies indicated that exposure to chlorobenzilate could pose risks of cancer and adverse testicular effects to certain exposed groups

Severely Restricted

Cyprus	
Control Action	Severely restricted for use as a pesticide
Effective	09/01/1982
Uses still allowed	Only remaining use allowed: as acaricide on citrus only, for the control of citrus rust mite. Use allowed constitutes about 30% of the previously allowed uses
Reasons for control action	Health risk because of its carcinogenic effects in experimental animals; human exposure to the chemical poses a risk of cancer

India	
Control Action	Banned for use in agriculture
Effective	
Uses still allowed	Folbex strips in beehives
Reasons for control action	

ANNEX 2

Alternatives

The following alternatives were noted by countries reporting import decisions under the PIC procedure:

Country	
Cuba	Bromopropylate
United States	Dicofol, propagite, carbofenthion, fenbutatin-oxide, ethion, formetanate hydrochloride, aldicarb, dicrotophos, disulfoton, methidathion, methyl parathion, phorate, phosalone, tetradifon

It is essential that before a country considers substituting any of these 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 address: Annex 3). It will then be necessary to determine the compatibility with national crop protection practices.

ANNEX 3

List of Pesticide DNAs in Countries Reporting Control Actions or Alternatives

Argentina	P	Director General Instituto Argentino de Sanidad y Calidad Vegetal Ing. Huergo No 1001 C.P. 1060 Buenos Aires	Tlx: 27 637 DGAAGAR Fax: 541 1615
	C	Dr. M.A. Craviotto Dirección Nacional de Calidad Ambiental Subsecretaria de Vivenda y Calidad Ambiental Av. 9 de Julio 1925-Piso 17 C.P. 1332 Buenos Aires	Tel: 54-1 381 1949 54-1 383 8741 Fax: 54-1 331 0680
Cuba	P	Registro Central de Plaguicidas Calle 150 #, 2125 e/ 21 A y 25 Siboney Playa, Ciudad de La Habana (Ing. Juan C. Amor)	Tel: (537) 21-9665 Fax: 005-37-330535/335086
Cyprus	P	The Chairman Pest Control Products Bd. Department of Agriculture,, Ministry of Agriculture & Natural Resources Nicosia,	Tel: 30-2250/30-2254 Tlx: 4660 Minagri CY Cab: MINAGRI CYPRUS Fax: 361425 Nicosia
	C	Director Environment Service Ministry of Agriculture, Natural Resources & Environment Nicosia	Tel: 30-2883 Tlx: 4660 Minagri CY Cab: MINAGRI CYPRUS Fax: 363945 Nicosia
India	P	The Director/Deputy Secretary Plant Protection Division Dept. of Agriculture & Co-op. Room No. 244-A Krishi Bhavan, New Delhi	
	C	Adviser (Chemicals) Dept. of Chemicals & Petrochemicals Ministry of Chemicals & Fertilizers Shastri Bhavan Rajendra Prasaid Road New Delhi - 110 001	Tel: 91 (11) 385736/382575 Tlx: 62455 Fax: 91 (11) 382604/337223
Morocco	P	M. le secrétaire général Ministère de l'agriculture et de la mise en valeur agricole Direction de la protection des végétaux,des contrôles techniques et de la répression des fraudes Avenue de la Victoire BP 1308 Rabat	Tel. 212 (7) 771078
Sweden		National Chemicals Directorate Attn.: Mr. Ule Johansson P.O. Box 1384 171 27 Solna	Tel: 46 (8) 730 6004 Tlx: 10460 AMS S Fax: 46 (8) 735 7698
USA	CP	The Assistant Administrator for Pesticides and Toxic Substances - Environmental Protection Agency 401 M St. S.W. Washington DC 20460	Tel: 1 202 260 2902 Fax: 1 202 260 1847 Tlx: 892758 EPA WSH

	C	Industrial and consumer product chemicals	
	P	Pesticides	
	CP	Pesticides, industrial and consumer product chemicals	