Health and Safety Guide No. 61

ISOBENZAN HEALTH AND SAFETY GUIDE



UNITED NATIONS
ENVIRONMENT PROGRAMME



INTERNATIONAL LABOUR ORGANISATION



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WORLD HEALTH ORGANIZATION, GENEVA 1991

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Health and Safety Guide No. 61

ISOBENZAN HEALTH AND SAFETY GUIDE

This is a companion volume to Environmental Health Criteria 129: Isobenzan

Published by the World Health Organization for the International Programme on Chemical Safety
(a collaborative programme of the United Nations Environment Programme, the International Labour Organization, and the World Health Organization)

WORLD HEALTH ORGANIZATION, GENEVA 1991

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the United Nations Environment Programme, the International Labour Organisation, or the World Health Organization

WHO Library Cataloguing in Publication Data

Isobenzan: health and safety guide.

(Health and safety guide; no. 61)

1.Insecticides, Organochlorine - standards

2.Insecticides, Organochlorine - toxicity 3.Hazardous substances I.Series

ISBN 92 4 151061 7

(NLM Classification: WA 240)

ISSN 0259-7268

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Computer typesetting by HEADS, Oxford OX7 2NY, England Printed by Wissenschaftliche Verlagsgesellschaft mbH · D-7000 Stuttgart 10

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INTRODUCTION

The Environmental Health Criteria (EHC) documents produced by the International Programme on Chemical Safety include an assessment of the effects on the environment and on human health of exposure to a chemical or combination of chemicals, or physical or biological agents. They also provide guidelines for setting exposure limits.

The purpose of a Health and Safety Guide is to facilitate the application of these guidelines in national chemical safety programmes. The first three sections of a Health and Safety Guide highlight the relevant technical information in the corresponding EHC. Section 4 includes advice on preventive and protective measures and emergency action; health workers should be thoroughly familiar with the medical information to ensure that they can act efficiently in an emergency. Within the Guide is a Summary of Chemical Safety Information which should be readily available, and should be clearly explained, to all who could come into contact with the chemical. The section on regulatory information has been extracted from the legal file of the International Register of Potentially Toxic Chemicals (IRPTC) and from other United Nations sources.

The target readership includes occupational health services, those in ministries, governmental agencies, industry, and trade unions who are involved in the safe use of chemicals and the avoidance of environmental health hazards, and those wanting more information on this topic. An attempt has been made to use only terms that will be familiar to the intended user. However, sections 1 and 2 inevitably contain some technical terms. A bibliography has been included for readers who require further background information.

Revision of the information in this Guide will take place in due course, and the eventual aim is to use standardized terminology. Comments on any difficulties encountered in using the Guide would be very helpful and should be addressed to:

The Manager
International Programme on Chemical Safety
Division of Environmental Health
World Health Organization
1211 Geneva 27
Switzerland

<u></u>		
	THE INFORMATION IN THIS GUIDE SHOULD BE CONSIDERED AS A STARTING POINT TO A COMPREHENSIVE HEALTH AND SAFETY PROGRAMME	

1. PRODUCT IDENTITY AND USES

1.1 Identity

Common name:

Isobenzan

Molecular formula:

C9H4Cl8O

Chemical structure:

Chemical names:

1,3,4,5,6,7,8,8-octachloro-4,7-methylene-

3a.4,7,7a-tetrahydro-isobenzofuran;

1,3,4,5,6,7,8,8-octachloro-3a,4,7,7a-tetra-

hydro-4.7-endomethylene-naphthalene

(IUPAC)

Developmental

BAS-4402; CP 14957; ENT-25545;

codes:

OMS-206; OMS-618; SD-4402, WL 1650

Trade names:

Telodrin (technical product), Omtan

Purity (technical):

not less than 95% (w/w)

CAS registry

number:

297-78-9

Conversion factors:

1 ppm = 17 mg/m³ at 20 $^{\circ}$ C 1 mg/m³ = 0.06 ppm at 20 $^{\circ}$ C

RTECS registry

number:

PC1225000

PRODUCT IDENTITY AND USES

1.2 Physical and Chemical Properties

Isobenzan is a whitish to light-brown crystalline powder, with a mild chemical odour. It is relatively stable to acids, but liable to dehydrochlorination under strongly alkaline conditions.

Some physical properties of isobenzan are given in Table 1.

Table 1. Physical properties

Relative molecular mass	411.73
Melting point (°C)	120-122
Flash-point	non-flammable
Explosion limits	non-explosive
Specific gravity	1.87
Vapour pressure (20 °C)	6.7×10^{-4} Pa (5 x 10^{-6} mmHg)
Solubility in water	practically insoluble

Solubility in organic solvents: slightly soluble in kerosene and ethanol; soluble in acetone, benzene, toluene, xylene, heavy aromatic naphtha, and ethyl ether.

1.3 Analytical Methods

The method of choice is gas-liquid chromatography with electron-capture detection.

1.4 Production and Uses

Isobenzan is a broad spectrum contact and stomach insecticide, which was manufactured from 1958 to 1965 and was used throughout the world. Its agricultural use was restricted, because of its persistence and toxicity.

2. SUMMARY AND EVALUATION

As far as is known, isobenzan, an organochlorine insecticide, was only manufactured during the period 1958-65. Existing stocks were used for several years after this. At present, the only major sources of exposure are believed to be the original waste-disposal sites of industrial wastes, and dredgings from contaminated sediments.

Following the application of isobenzan to the soil, a rapid initial loss occurs, after which the remaining compound decays at a much slower rate. Isobenzan persists in the soil from 2 to 7 years, depending on the type of soil. Under laboratory conditions, isobenzan decomposes in surface water within a few weeks, when exposed to natural and artificial light.

Soil, ground water, and surface water from polders built up using sediment contaminated with organochlorines, including chlorinated cyclodiene compounds, still contained minor residues of isobenzan some years later. Sediments of rivers in the Netherlands did not contain any detectable isobenzan (less than 0.01 mg/kg dry weight). Crop residues, resulting from soil treatment, are usually low (below 0.05 mg/kg crop), but higher levels may be found in some root crops (up to 0.2 mg/kg in carrots). No residues were detected (less than 0.01 mg/kg) in food items analysed in market surveys that were carried out when isobenzan was being used in agriculture.

When domestic animals were introduced to pastures treated with isobenzan, the dairy products contained residues of the compound. Two samples of butter contained 0.07–0.15 mg isobenzan/kg product. In milk, the levels were 0.005–0.07 mg/kg (whole milk). Dried milk contained only 0.005 mg/kg. Up to 50% of the residue was lost during the processing of dairy products, depending on the type of treatment.

No data were available on the levels of isobenzan in the blood and adipose tissue of the general population. Operators of manufacturing and formulation plants exposed to isobenzan had mean whole blood levels of isobenzan of up to 0.041 mg/litre. In whole blood samples from people living in the neighbourhood of one plant, the concentration of isobenzan was below the limit of detection of 0.001 mg/litre.

SUMMARY AND EVALUATION

Isobenzan is well absorbed through the gastrointestinal wall. It is transported in the blood as the unchanged compound. Hydrophilic metabolites are formed, one of which has been identified as isobenzan lactone. Isobenzan accumulates in the tissues and organs of rats and dogs in the following order: fat > liver = muscle > brain > blood. In general, the concentrations are higher in the tissues of female rats than in those of male rats, especially in the body fat. The biological half-life in the body fat was 10.9 days in male rats and 16.6 days in female rats. A female dog pup that had fed only on its mother's milk (containing 0.7 mg/litre of whole milk) showed convulsions 15 days after birth. The blood of the pup contained 0.09 mg/litre. These effects in the pup were also seen in a rat reproduction study. Isobenzan is excreted via the milk of cows.

Mosquito larvae and soil fungi metabolize isobenzan in the same way as vertebrates, yielding isobenzan-lactone.

Isobenzan is very persistent in the environment and bioaccumulates. It is highly toxic for fish, shrimps, and birds. In the Netherlands, the country where isobenzan was produced, residues in the eggs of terns living along the Dutch coast ranged up to 0.45 mg/kg (mean, 0.09 mg/kg); mean residues in mussels and fish were 0.05 mg/kg in 1965. Earthworm numbers were reduced in field plots treated with isobenzan at 2 kg/ha. Nitrification was reduced, with a consequent increase in inorganic nitrogen, in soils treated with isobenzan in the field at 1 kg/ha; laboratory studies did not show any effects on nitrification at doses equivalent to 250 g/ha.

The acute toxicity of isobenzan is high in mammals exposed via the oral or percutaneous route. The mode of action is an overstimulation of the central nervous system, resulting in convulsions. The acute toxicity of formulations of isobenzan varies according to the percentage of active ingredient present.

Isobenzan is not a skin irritant, but some formulations may cause irritation.

Limited short- and long-term oral studies on mice, rats, and dogs have been carried out. Isobenzan may cause histological changes in the liver of the classical type associated with organochlorine intoxication. In a long-term rat study, a no-observed-effect level (NOEL) of 5 mg/kg diet (\approx 0.25 mg/kg body weight) was found. In a 2-year study on dogs, a NOEL of 0.025 mg/kg body weight was established.

SUMMARY AND EVALUATION

A one-generation reproduction study on rats indicated a NOEL of 0.1 mg/kg diet ($\approx 0.005 \text{ mg/kg}$ body weight). A higher dose level of 1 mg/kg diet ($\approx 0.05 \text{ mg/kg}$ body weight) decreased survival of pups.

No teratogenicity or mutagenicity studies have been reported.

No carcinogenic potential was demonstrated in a 2-year oral study on rats and an oral study on mice; both these studies were inadequate for the evaluation of carcinogenicity.

The toxicological data base for isobenzan is incomplete. The Task Group considered that the quality of the data was generally poor, by today's standards, and that the data were inadequate to make an evaluation of the hazards of isobenzan for human health or for the environment.

Data on exposed human beings are limited to observations on workers in a factory in the Netherlands during the manufacture and formulation of isobenzan and related "drins". No cases of skin irritation were reported. Convulsions occurred in several cases of intoxication, but the changes in the EEG pattern were reversible. The intoxication threshold level (for convulsions) was estimated to be 0.015 mg isobenzan/litre blood. The biological half-life of isobenzan in human blood was estimated to be of the order of 2.8 years.

3. CONCLUSIONS AND RECOMMENDATIONS

Isobenzan is highly toxic and very persistent. The available information on the hazards of isobenzan is incomplete. However, available data are sufficient to indicate that the hazards posed to those handling isobenzan, and to the environment, are such that any human or environmental exposure to this substance, either as an insecticide or for any other purpose, should not be allowed.

4. HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

4.1 Main Human Health Hazards, Prevention and Protection, First Aid

Isobenzan is an organochlorine insecticide. It is highly toxic (rat oral LD50: 5-10 mg/kg) and can be very hazardous for human beings if incorrectly or carelessly handled. It is therefore essential that the correct precautions should be observed in its handling and use.

The human health hazards of isobenzan exposure, together with preventive and protective measures and first aid, are listed in Table 2.

4.1.1 Symptoms of poisoning

Isobenzan is readily absorbed by mouth, by skin contact (especially liquid formulations), and by inhalation (especially dust or mist). It acts as a stimulant of the central nervous system. It is eliminated from the body very slowly.

Following accidental ingestion or gross overexposure, symptoms may include headache, dizziness, nausea, vomiting, weakness in legs, and convulsions.

Respiratory depression may lead to metabolic acidosis and, if necessary, blood gases should be checked. The use of an ECG monitor is recommended, if the symptoms are severe.

4.1.2 Medical advice

Medical treatment is largely symptomatic and supportive, and directed against convulsions and hypoxia.

If isobenzan is swallowed, the stomach should be emptied as soon as possible by careful gastric lavage (with a cuffed endotracheal tube already in place), avoiding aspiration into the lungs. In a rural situation, where this is not feasible, and if the victim is conscious, vomiting should be induced immediately. This should be followed by intragastric administration of 50 g of activated charcoal and 30 g magnesium or sodium sulfate in a 30%

TABLE 2. HUMAN HEALTH HAZARDS, PREVENTIVE AND PROTECTIVE	MEASURES, AND FIRST AID
--	-------------------------

FIRST AID	After contact with skin, wash immediately with plenty of water and soap; remove all contaminated clothing immediately, and launder separately before re-use	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice			If swallowed, seek medical advice immediately and show container or label; keep at rest, and ensure a clear airway; if, in a rural situation, gastric lavage is not possible, and the victim is conscious, induce vomiting
PREVENTION AND PROTECTION FIRST AID	Avoid contact with skin; wear suitable impervious protective clothing and gloves	Avoid contact with eyes; wear eye protection	Wear appropriate dust mask or respirator	Do not eat, drink, or smoke during work; wash hands before eating,	or many, or smooning
HAZARDS/SYMPTOMS	SKIN: may cause poisoning in contact with skin	EYES: may cause irritation to eyes	INHALATION: dusts may cause poisoning by inhalation	INGESTION: unlikely occupational hazard	Accidental or intentional ingestion may cause poisoning

HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

aqueous solution. Oily purgatives are contraindicated. No fats, oils, or milk should be given.

If convulsions occur, anti-convulsants should be given immediately, e.g., 10 mg of diazepam, slowly, intravenously (children 1–5 mg), repeated as necessary; or thiopental sodium or hexobarbital sodium slowly, intravenously, in a dose of 10 mg/kg with a maximum total dose of up to 750 mg for an adult, or paraldehyde 5 ml by intramuscular injection. These short-acting anticonvulsants should always be followed by phenobarbital given orally at 3 mg/kg (up to 200 mg for an adult), or phenobarbital sodium given intramuscularly at 3 mg/kg (also up to 200 mg for an adult).

Morphine and its derivatives, adrenaline, and noradrenaline should never be given.

An unobstructed airway must be maintained. Respiratory inadequacy, which may be accentuated by barbiturate anticonvulsants, should be corrected; oxygen and/or artificial ventilation may be needed.

4.1.3 Health surveillance advice

A complete medical history and physical examination of regularly exposed workers should be made, on an annual basis.

4.2 Explosion and Fire Hazards

4.2.1 Explosion hazard

The explosion hazard will depend on the solvent used in the formulation, or on the characteristics of the dust.

4.2.2 Fire hazard

Liquid formulations containing organic solvents may be flammable. Extinguish fires with alcohol-resistant foam, carbon dioxide, or powder. With sufficient burning or external heat, isobenzan will decompose, emitting toxic fumes. Fire-fighters should be equipped with self-contained breathing apparatus, eye protection, and full protective clothing.

HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION. EMERGENCY ACTION

The use of water spray should be confined to the cooling of unaffected containers, thus avoiding the accumulation of polluted run-off from the site.

4.3 Storage

Products should be stored in locked buildings, preferably dedicated to insecticides, and in compliance with labelling recommendations.

Keep the products out of reach of children and unauthorized personnel. Do not store near foodstuffs or animal feed.

4.4 Transport

Comply with any national or local requirements regarding movement of hazardous goods or wastes. Do not transport in the same compartment as foodstuffs or animal feed. Check that containers are sound, and labels undamaged, before dispatch.

4.5 Spillage and Disposal

4.5.1 Spillage

Before dealing with any spillage, precautions should be taken as required, and appropriate personal protection should be used (Table 2). Empty any product remaining in a damaged or leaking container into a clean empty drum, which should then be tightly closed and suitably labelled.

Prevent liquid from spreading or contaminating other cargo and vegetation, and avoid pollution of surface waters and ground water by using the most suitable available material, e.g., earth or sand.

After emptying, leaking containers should be rinsed with at least 1 litre water per 20-litre drum. Swirl round to rinse the walls of the container, empty, and add the rinsings to the sawdust or earth. Puncture or crush the container to prevent re-use.

HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

As soon as possible after the spillage, and before re-use, cover all contaminated areas with damp sawdust, sand, or earth. Sweep up and place in a closeable container for later transfer to a safe place for disposal.

4.5.2 Disposal

Any surplus product, contaminated absorbents, and containers should be disposed of in an appropriate way. Waste material should be burned in a proper incinerator designed for organochlorine waste disposal, with effluent gas scrubbing. If this is not possible, bury in an approved dump or landfill where there is no risk of contamination of surface or ground water. Comply with any local requirements regarding disposal of toxic wastes. Puncture or crush container to prevent re-use.

5. HAZARDS FOR THE ENVIRONMENT AND THEIR PREVENTION

Isobenzan is toxic for aqu	very persistent in the environment and in biota. It is highly natic and terrestrial organisms.
any spillage	from the manufacture, formulation, or use of isobenzan, and or unused product, must be prevented from spreading to a waterways, and must be treated and disposed of properly 2).

6. CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

The information given in this section has been extracted from the International Register of Potentially Toxic Chemicals (IRPTC) legal file and other United Nations sources. Its intention is to give the reader a representative, but not an exhaustive, overview of current regulations, guidelines, and standards.

The reader should be aware that regulatory decisions about chemicals, taken in a certain country, can only be fully understood in the framework of the legislation of that country. Furthermore, the regulations and guidelines of all countries are subject to change and should always be verified with the appropriate regulatory authorities before application.

6.1 Previous Evaluations by International Bodies

Not available.

6.2 Exposure Limit Values

No data available.

6.3 Specific Restrictions

In the Federal Republic of Germany, isobenzan has been prohibited for use as a plant protectant. It has not been registered as a pesticide in, among others, Canada, the Netherlands, Sweden, the United Kingdom, and the USA (where it had previous approval for use on alfalfa, corn, and tobacco).

6.4 Labelling, Packaging, and Transport

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

Hazard Class 6.1:

poisonous substance;

Packing Group I:

substances and preparations presenting a very severe risk of poisoning, when the

content of active ingredient is 10-100%;

CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

Packing Group II: substances and preparations presenting a

serious risk of poisoning, when the content

of active ingredient is 2-10%;

Packing Group III: substance presenting a relatively low risk of

poisoning in transport, when the content of

active ingredient is 0.4-2%.

The labels should be as follows:

In Packing Group II



Symbol (skull and crossbones): black Background; white In Packing Group III



The bottom half of the label should bear the inscriptions HARMFUL

Stow away from foodstuffs Symbol (St. Andrew's Cross over an ear of wheat; black Background; white

The European Economic Community legislation requires labelling as a dangerous substance using the symbol:



Giftig Giftig Tokic Tokic Tokique Tokico Vergiftig

CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

The label must read:

Very toxic by inhalation, in contact with skin and if swallowed; irritating to eyes and skin; keep locked up; keep away from food, drink and animal feeding stuffs; if you feel unwell, seek medical advice (show the label where possible).

The European Economic Community legislation on the labelling of pesticide preparations classifies isobenzan in Class 1A for the purpose of determining the label for preparations containing isobenzan and other active ingredients.

6.5 Waste Disposal

No information is available.

6.6 Other Measures

The European Economic Community legislation concerning the major accident hazards of certain industrial activities foresees that the manufacturer must take all necessary measures to prevent accidents and to limit their consequences for man and the environment, when processing isobenzan in quantities equal to or over 100 kg. Notification must be made to the competent authorities, giving information on the substance, the installation, information on possible major accident situations, and emergency plans.

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