

UNEP/WHO/ILCO/ICS INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

Health and Safety Guide No. 49

**CAPTAFOL
HEALTH AND
SAFETY GUIDE**



UNITED NATIONS
ENVIRONMENT PROGRAMME



INTERNATIONAL
LABOUR ORGANISATION



WORLD HEALTH
ORGANIZATION

WORLD HEALTH ORGANIZATION, GENEVA 1990

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**CAPTAFOL
HEALTH AND
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INTRODUCTION

This Health and Safety Guide is not based on an existing Environmental Health Criteria document, but on critical national reviews. The hazard evaluation in the Health and Safety Guide was made on the basis of carefully selected studies, after scrutiny of the original publications.

In order to assist the peer-review process of the present Health and Safety Guide, a background companion document was prepared by the IPCS and can be obtained from the Manager on request; the IPCS does not intend that the background document should be published.

The first three sections of this Health and Safety Guide present essential technical information and the hazard evaluation. 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. 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.

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

**THE INFORMATION IN THIS GUIDE
SHOULD BE CONSIDERED AS A
STARTING POINT TO A COMPREHENSIVE
HEALTH AND SAFETY PROGRAMME**

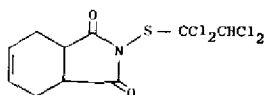
1. PRODUCT IDENTITY AND USES

1.1 Identity

Chemical formula: $C_{10}H_9Cl_4NO_2S$

Common name: captafol

Chemical structure:



Relative molecular mass: 349.1

Common trade names (including formulations): Captafol; Captatol; Captofol; Captaspor; Difolatan; Difosan; Merpafol; Folcid; Ortho-5865; Ortho Difolatan 80W; Ortho Difolatan 4 Flowable; Sanseal; Sanspor; Sulfonimide; Sulpheimide

CAS chemical name: *N*-((1,1,2,2-tetrachloroethyl)thio)-4-cyclohexene-1,2-dicarboximide

Synonyms: *N*-(1,1,2,2-tetrachloroethylthio)-cyclohex-4-ene-1,2-dicarboximide;
N-(1,1,2,2-tetrachloroethylthio)-tetrahydrophthalimid;
N-1,1,2,2-tetrachloroethylmercapto-4-cyclohexene-1,2-carboximide;
N-((1,1,2,2-tetrachloroethyl)-sulfenyl)-*cis*-4-cyclohexene-1,2-dicarboximide;

PRODUCT IDENTITY AND USES

Synonyms: (continued)	<i>N</i> -(1,1,2,2-tetra-chloroethylthio)-4-cyclohexene-1,2-dicarboximide
CAS registry number:	2425-06-1
RTECS registry number:	GW4900000

In the past, captafol was available in a wide range of mixtures and formulations. However, information on currently available formulations is not available.

Technical captafol, previously manufactured in the USA, contained 97–99% active ingredient with tetrahydrophthalimide (4-cyclohexene-1,2-dicarboximide) as the main impurity (0.5–1.5%) together with 0.5–1.5% toluene and 0.1–0.2% of unknown chlorinated substances.

1.2 Physical and Chemical Properties

Technical captafol is a light tan powder with a characteristic odour. It is stable at room temperature in the dry state, but is readily hydrolysed, especially in an alkaline environment. The melting point of the pure compound is 162 °C; a range of 156–161 °C has been recorded for the technical product. The vapour pressure at room temperature is negligible.

Captafol is practically insoluble in water (1.4 mg/litre) and only slightly soluble in aliphatic hydrocarbon solvents: it has a solubility of 25 g/litre at 77 °C in isopropanol, and of 428 g/litre in toluene at 24 °C.

Sulphydryl compounds, such as glutathione and cysteine, cause rapid chemical decomposition of captafol.

1.3 Analytical Methods

Capillary gas-liquid chromatography with electron-capture detection is a multi-residue method suitable for the routine determination of five fungicides including captan, folpet, captafol, vinclozolin, and iprodione.

PRODUCT IDENTITY AND USES

1.4 Production and Uses

Captafol was introduced in 1961; although it was withdrawn in many countries in the late 1980s, production and use continue in some countries.

Captafol is a non-systemic broad-spectrum fungicide, leaving relatively stable deposits when applied to foliage. This pesticide can be combined with commonly used insecticides and fungicides, except for oil sprays and strongly alkaline materials. Captafol is mainly used to control foliage and fruit diseases in various vegetable and fruit crops. It has also been used in the lumber and timber industries for the control of wood rot fungi on logs and wood products.

Captafol is formulated as a wettable powder, dust, emulsifiable concentrate, flowable suspension, and as water-dispersible granules. It is applied by dusting, spraying, and misting, and by dipping under pressure (wood treatment).

2. SUMMARY AND EVALUATION

2.1 Human Exposure to Captafol

The highest exposures to captafol are occupational and are associated with its use in agriculture. Dermal exposure can be important because of local effects on the skin. Low-level exposure of the general population may occur through residues in food. However, captafol is extensively hydrolysed during thermal and other food processing. Because of the nature of the captafol residues, they are readily reduced by, for example, peeling, washing, and blanching.

2.2 Uptake, Metabolism, and Excretion

Captafol may be absorbed through ingestion as well as through inhalation, and to a very limited extent through skin exposure. Following oral administration, captafol appears to be extensively hydrolysed to tetrahydrophthalimide (THPI; 4-cyclohexene-1,2-dicarboximide) and tetrachloroethylmercaptan (TES). Captafol and its metabolites do not accumulate in the tissues of animals and are rapidly eliminated; after a single oral dose of labelled captafol, most of the radioactivity appeared to be excreted within 3-4 days, primarily in the urine. Tetrahydrophthalimide (THPI) has been identified as the major metabolite of captafol in both animals and plants, as is the case for the closely related fungicide, captan. THPI is further metabolized into a large number of metabolites. More important for the toxicity of captafol is the further metabolism of TES. To explain the formation of the end metabolite, 2-chloro-2-methyl-thioethylene sulfonic acid, the formation of a cyclic sulfonium ion is assumed to be a transient intermediate. This intermediate is a potential alkylating agent and is probably responsible for the toxic and carcinogenic action of captafol.

2.3 Effects on Animals

The acute toxicity of captafol, when ingested, is low. However, the inhalation toxicity is considerably higher, and it is irritating to the skin and also to the mucous membranes of the respiratory tract. The substance is

SUMMARY AND EVALUATION

highly irritating to the eye and may cause eye damage. There are several reports indicating that captafol induces sensitization in guinea-pigs.

After repeated administration in the diet to experimental animals, captafol caused toxic effects involving several organs, notably kidney damage, and pathological changes of the gastric mucosa. Long-term administration to rats and mice induced tumours at multiple sites. These results constitute sufficient evidence for the carcinogenicity of captafol. Captafol, which is an alkylating agent, has produced genotoxic effects in several *in vitro* systems, but, so far, it has not been possible to demonstrate any mutagenic effects *in vivo*. Thus, though captafol may induce genotoxic events in somatic cells, the results obtained seem to indicate that the potential for causing heritable effects in mammals is extremely low. There is no evidence that captafol constitutes a teratogenic hazard, but it may induce fetotoxicity at doses toxic for the mother.

2.4 Effects on Human Beings

Captafol has caused allergic and contact dermatitis in man. During occupational exposure, it has also been reported to cause severe irritation of the respiratory tract, eye damage, and other systemic effects. In a limited study of employees involved in the manufacture of captafol, no significant excess in mortality could be associated with exposure to this pesticide.

2.5 Effects on the Environment

Captafol, administered as a single oral dose, or in short-term dietary studies, was not toxic for birds ($LC_{50} > 5620$ mg/kg diet). However, high levels of exposure may cause reproductive impairment. The toxicity of captafol for bees is low. Captafol is highly toxic for fish and moderately to very highly toxic for freshwater invertebrates (96-h LC_{50} s ranged between 0.04 and 3 mg/litre). The 96-h LC_{50} reported in three investigations on rainbow trout ranged from 0.027 to 0.19 mg/litre.

Captafol is not persistent. Its half-life in soil is less than 11 days. The environmental impact of the pesticide is likely to be limited by its high chemical reactivity, high rate of biodegradation, and lack of tendency to

SUMMARY AND EVALUATION

bioaccumulate. However, because of its demonstrated high toxicity, exposure of aquatic organisms to captafol through drift and/or run-off is a cause for concern. Fish kills have been associated with the use of this pesticide.

3. CONCLUSIONS AND RECOMMENDATIONS

In view of the established carcinogenic potential of captafol and the availability of alternatives, it is recommended that this pesticide should not be used.

Captafol is highly toxic for fish, and moderately to highly toxic for freshwater invertebrates. Because of this demonstrated high aquatic toxicity, it is recommended that adequate precautions be taken to prevent contamination of surface and ground water.

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

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

The acute oral toxicity of technical captafol for human beings is low. The compound causes severe irritation of the respiratory tract, and allergic dermatitis. Captafol also has a potential for causing eye damage.

In view of the severe toxicity induced in experimental animals with repeated exposure, including a proven carcinogenic action, exposure of human beings should be kept to a minimum.

4.1.1 *Prevention and protection*

The following precautions should be observed during the handling and use of captafol, in order to reduce the risk of accidental contamination:

- (a) Avoid contact with the skin and eyes.
- (b) Do not smoke, drink, or eat in the work-place. Wash hands and any exposed skin before eating, drinking, or smoking, and after work.
- (c) Avoid raising a dust cloud when handling wettable powder formulations.
- (d) Avoid breathing dust from powder products.
- (e) When unloading and handling containers, wear protective PVC or neoprene gloves.
- (f) When handling leaking containers, or when dealing with leaks and spills, wear overalls, PVC or neoprene gloves, boots, and eye/face protection. If overalls become contaminated, change and wash them thoroughly before re-use.
- (g) Store products in closed original containers, out of reach of children, and away from food, drink, and animal feed.

HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

4.1.2 *First Aid*

Acute poisoning by captafol is unlikely, unless large amounts are ingested. In cases of over-exposure, apply routine first-aid measures. If the compound has been spilled on the skin, immediately remove the patient from the source of contamination, remove all contaminated clothing, and wash affected areas with soap and running water. If the material is in the eyes, flush with clean water for at least 15 minutes. In case of ingestion of significant quantities, if the patient is conscious, give several glasses of water. Do not induce vomiting. In serious cases, medical attention should be sought.

4.2 **Advice to Physicians**

The acute oral toxicity of captafol for human beings is low. There is no specific antidote. Treat symptomatically, paying special attention to respiratory and dermal symptoms when necessary. In cases of ingestion of large amounts, gastric lavage may be indicated.

4.3 **Explosion and Fire Hazards**

Captafol is not flammable but, on heating, may produce toxic fumes, such as sulfur dioxide, hydrochloric acid, and phosgene. Concentrated products react violently with alkali.

Extinguish small fires with carbon dioxide, dry powder, or alcohol-resistant foam. Water spray can be used for larger fires and for the cooling of unaffected stock, but avoid the accumulation of polluted run-off from the site. Fire service personnel should be advised that self-contained breathing apparatus may be required, because of the generation of noxious fumes.

4.4 **Storage and Transport**

All products should be stored in secure buildings, out of reach of children and animals, and local regulations should be complied with. Containers should be sound and adequately labelled.

HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

4.5 Spillage and Disposal

Avoid contact with the solid or dust. Keep spectators away from any leakage. This pesticide is highly toxic for fish. Prevent contamination of other goods or cargo, and of nearby vegetation and waterways.

Absorb spilled liquid products using earth or sand. If available, sawdust, peat, moss, or straw are also suitable absorbents; sweep up and place in a separate container. Empty any product remaining in damaged or leaking containers into a clean empty container, which should be suitably labelled. Sweep up any spilled powder with damp sawdust, taking care not to raise a dust cloud (use a vacuum cleaner). Remove trapped material with suction hoses. Place in a separate container for subsequent disposal. Use mechanical dredges or lifts to remove immobilized masses of pollutants and precipitates.

Before disposal, captafol can be concentrated by gravity separation followed by dual media filtration and activated carbon adsorption. Alkaline treatment of captafol leads to the formation of degradation products of much lower toxicity. For treatment of large spills, or for the decontamination of equipment, the use of an aqueous solution of commercial low-foaming, hard-water detergent in 5% trisodium phosphate or 10–25% sodium hydroxide is recommended. During neutralization, hydrogen sulfide may be formed, if insufficient alkali is used.

Do not deposit in landfill. Captafol is not amenable to biological treatment at municipal sewage plants.

5. HAZARDS FOR THE ENVIRONMENT AND THEIR PREVENTION

Captafol is not persistent and small quantities of the compound are readily hydrolysed in soil and surface waters. However, it is highly toxic for aquatic organisms. Contamination of ponds, waterways, and ditches with captafol should be avoided. In case of spills, and for the decontamination of equipment and containers, apply the methods recommended in section 4.5.

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. A full reference to the original national document from which the information was extracted can be obtained from IRPTC. When no effective date appears in the IRPTC legal file, the year of the reference from which the data are taken is indicated by (r).

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 appropriate regulatory authorities before application.

6.1 Exposure Limit Values

The threshold limit value (TWA) recommended by the US ACGIH for captafol is 0.1 mg/m^3 in air. This value is also enforced in Argentina, Australia, Canada, the Netherlands, and the United Kingdom.

In 1985, the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) recommended that the temporary ADI should be withdrawn, saying that, "In view of the established carcinogenic potential of this compound, the meeting recommended that captafol should not be used where its residues in food can arise."

Some tolerances for food and animal feed are given in the table opposite.

6.2 Specific Restrictions

Captafol has never been granted registration in the German Democratic Republic or Sweden. In 1987, the pesticide was voluntarily withdrawn from the US market by the main producers. It was banned in the Netherlands as from 21 May 1986 and also in Cyprus, the Federal Republic of Germany, Hungary, and Italy.

CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

TOLERANCES AND MAXIMUM RESIDUE LIMITS FOR FOOD PRODUCTS

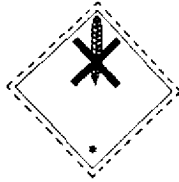
Country/ organization	Food product	Exposure limit description	Value (mg/kg)	Effective date
Brazil	Specified plant products	Acceptable limit	0.04-15	
Czechoslovakia	Plants products	Maximum residue limit	2-15	October 1978
EEC	Specified plant products	Maximum residue limit	0.058 ^a	1988
Sweden	Fruits and vegetables	Maximum acceptable concentration	0.5-3.0	January 1985
USA	Raw agricultural products	Tolerance	0.25-100	May 1986

^a Limit of detection.

CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

6.3 Transport and Labelling

Conveyance labelling should be as follows:



Division 6.1

Poisonous (toxic) substances

Packing Group: III

The bottom half of the label
should bear the inscriptions:

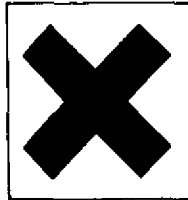
HARMFUL

Stow away from foodstuffs

Symbol (St Andrew's Cross over an
ear of wheat); black; Background:
white

Supply and use labelling

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



Sundhedsskadelig
Mindergiftig
(Gesundheitsschädlich)
Επιβλαβές
Harmful
Nocif
Nocivo
Schadelijk

The label must read:

R20

Harmful by inhalation

R36/37/38

Irritating to eyes, respiratory system and skin

CURRENT REGULATIONS, GUIDELINES, AND STANDARDS

R40	<i>Possible risk of irreversible effects</i>
R41	<i>Risk of serious damage to eyes</i>
R43	<i>May cause sensitization by skin contact</i>
R45	<i>May cause cancer</i>
S2	<i>Keep out of reach of children</i>
S13	<i>Keep away from food, drink, and animal feeding stuffs</i>
S20/21	<i>When using do not eat, drink, or smoke</i>
S22	<i>Do not breathe dust</i>
S24/25	<i>Avoid contact with skin and eyes</i>
S36/37/39	<i>Wear suitable protective clothing gloves and eye/face protection</i>

Price: Sw. fr. 5.-
Price in developing countries: Sw. fr. 3.50

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