INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

Health and Safety Guide No. 18

DICHLORVOS HEALTH AND SAFETY GUIDE



UNITED NATIONS ENVIRONMENT PROGRAMME



INTERNATIONAL LABOUR ORGANISATION



WORLD HEALTH ORGANIZATION

WORLD HEALTH ORGANIZATION, GENEVA

IPCS

Other HEALTH AND SAFETY GUIDES available:

Acrylonitrile Kelevan Methylene Chloride Tetrachloroethylene 1-Butanol 2-Butanol

tert-Butanol

Isobutanol

2,4-D

Epichlorohydrin

Tetradifon

- 12. Tecnazene
- 13. Chlordane
- 14. Heptachlor
- 15. Propylene Oxide
- 16. Ethylene Oxide
- 17. Endosulfan

IPCS

Health and Safety Guide No. 18

DICHLORVOS HEALTH AND SAFETY GUIDE

This is a companion volume to Environmental Health Criteria 79: Dichlorvos

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 1988

ISBN 92 4 154337 X ISSN 9259 - 7268 © World Health Organization 1988

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. For rights of reproduction or translation of WHO publications, in part or in toto, application should be made to the Office of Publications, World Health Organization, Geneva, Switzerland. The World Health Organization welcomes such applications.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

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

CONTENTS

INTROD	UCTION	Page 5
1. PROD	UCT IDENTITY AND USES	7
1.1	Identity	7
1.2	Physical and chemical properties	8
1.3	Analytical methods	8
1.4	Production and uses	8
2. SUMM	IARY AND EVALUATION	9
2.1	Evaluation of effects on animals and human health	9
2.2	Evaluation of effects on the environment	11
3. CONC	LUSIONS AND RECOMMENDATIONS	13
3.1	Conclusions	13
3.2	Recommendations	13
4. HUMA	AN HEALTH HAZARDS, PREVENTION AND	
PROTI	ECTION, EMERGENCY ACTION	15
4.1	Main human health hazards, prevention and	
	protection, first aid	15
	4.1.1 Advice to physicians	15
	4.1.1.1 Symptoms of poisoning	15
	4.1.1.2 Medical treatment	15
	4.1.2 Health surveillance advice	16
4.2	Explosion and fire hazards	17
4.3	Storage	17
4.4	Transport	17

CONTENTS

		Page
4.5	Spillage and disposal	17
	4.5.1 Spillage	17
	4.5.2 Disposal	18
5. HAZ	ARDS FOR THE ENVIRONMENT AND THEIR	
PREV	/ENTION	19
6. INTE	RNATIONAL CHEMICAL SAFETY CARD	21
7. CURI	RENT REGULATIONS, GUIDELINES, AND	
STAN	IDARDS	26
7.1	Previous evaluations by international bodies	26
7.2	Exposure limit values	27
7.3	Specific restrictions	27
7.4	Labelling, packaging, and transport	27
BIBLIO	GRAPHY	34
ANNEX	I. Treatment of organophosphate insecticide poisoning	
	in man	36

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 an International Chemical Safety Card 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, it is inevitable that sections 1 and 2 contain 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

THE INFORMATION IN THIS GUIDE	
SHOULD BE CONSIDERED AS A STARTING POINT TO A COMPREHENSIVE	
HEALTH AND SAFETY PROGRAMME	
6	

1. PRODUCT IDENTITY AND USES

1.1 Identity

Common name:

Dichloryos

Primary constituent

Chemical structure:

$$\begin{array}{c} \operatorname{CH_3O} \\ \\ \operatorname{P-O-CH} = \operatorname{CC1_2} \end{array}$$

Chemical formula:

C₄H₇Cl₂O₄P

Relative molecular

mass:

221

Chemical name:

2,2-dichloroethenyl dimethylphosphate

(CAS);

2.2-dichlorovinyl dimethylphosphate

(IUPAC)

Common synonyms:

Bayer-19149, DDVF, DDVP,

ENT-20738, OMS-14, SD 1750, C-177

CAS registry

62 - 73 - 7

number:

Technical product

Common trade

Dedevap, Nogos, Nuvan, Phosvit,

Vapona a

names: Purity:

Not less than 97%

Impurities:

Depends on the manufacturing process

Additives:

On standing, in the presence of traces of moisture, dichlorvos breaks down with the formation of acidic products

The Shell trademark Vapona was formerly used exclusively for dichlorvos and dichlorvos-containing formulations. Now, this trademark is used more widely to include formulations containing other active ingredients.

PRODUCT IDENTITY AND USES

that catalyse further decomposition of the compound. In the past, 2-4% epichlorohydrin was added to stabilize the technical grade product. Other stabilizers may now be used in some products, but improved technology and purity has largely eliminated the need for them.

1.2 Physical and Chemical Properties

Technical dichlorvos is a colourless to amber liquid with a mild chemical odour. It is hydrolysed by water at a rate of 3% per day at room temperature. It is corrosive to iron and mild steel.

For some physical properties see the International Chemical Safety Card on pp.22–25.

1.3 Analytical Methods

Dichlorvos residues can be determined by gas liquid chromatography. The same method can be used for product analysis; alternative methods include infrared spectrometry, or reaction with an excess of iodine, which is estimated by titration.

1.4 Production and Uses

Dichlorvos, an organophosphate, is a direct-acting cholinesterase (ChE) inhibitor. Since 1961, it has been commercially manufactured and used throughout the world as a contact and stomach insecticide.

At present, the global production of dichlorvos is of the order of 4 million kg per year. It is used to protect stored products, to protect crops (mainly in greenhouses), to control internal and external parasites in livestock (granules of impregnated resin), and to control insects in houses, buildings, and outdoor areas (as aerosols or liquid sprays or as impregnated cellulose, ceramic, or resin strips).

2. SUMMARY AND EVALUATION

2.1 Evaluation of Effects on Animals and Human Health

Dichlorvos is readily absorbed by the body of mammals via all routes of exposure, and readily metabolized in the liver. Within 1 h of oral administration, dichlorvos is found in the liver, kidneys, and other organs of experimental animals. The substance is rapidly eliminated via the kidneys, with a half-life of 14 min.

The metabolism of dichlorvos in various species, including man, follows similar pathways and differences between species relate only to the rate of metabolism, but this is always rapid.

Dichlorvos is moderately to highly toxic in mammals (oral LD₅₀ for the rat is 30-110 mg/kg body weight). The classification of dichlorvos by WHO (1986b) is based on an oral LD₅₀ for the rat of 56 mg/kg body weight. Signs of intoxication usually occur shortly after exposure and are typical of an organophosphorus pesticide. A sensitive criterion of exposure is inhibition of cholinesterase (ChE) activity. In short-term toxicity studies on mammals, it has been shown that ChE activity is not decreased at oral doses below about 0.5 mg/kg body weight. In long-term oral studies on rats at dose levels of 2.5 mg/kg body weight or more, hepatocellular fatty vacuolization was seen. A dose level of 0.25 mg/kg body weight did not induce ChE inhibition or any other effects.

The results of reproduction and teratogenicity studies, over a wide range of dose levels (6.25–500 mg/kg body weight), were negative. Dichlorvos showed alkylating properties in *in vitro* studies, but not in *in vivo* studies. The results of many *in vitro* mutagenicity studies with bacteria and yeast were positive, while those of *in vivo* studies were mainly negative.

On the basis of available mutagenicity studies, it is unlikely that dichlorvos constitutes a mutagenic hazard for man.

Negative results were obtained in carcinogenicity studies on mice and rats administered dichlorvos via the oral route (dose levels up to 234 mg/kg diet). Two recent carcinogenicity studies were carried out on mice and rats in which dichlorvos was administered by intubation at dose levels of between 10 and 40 mg/kg body weight (mice) and 4 and 8 mg/kg body weight (rats) for up to 2 years. Only preliminary

SUMMARY AND EVALUATION

information is available. The evidence for carcinogenicity in these new studies is difficult to interpret at this time. Only when complete and final reports become available will it be possible to draw more definite conclusions.

The results of studies on hens have neither established nor refuted the suspicion of delayed neurotoxicity arising from exposure to dichlorvos. Furthermore, there have been two clinical reports of four patients suffering from severe poisoning after oral ingestion of dichlorvos who survived following treatment and who then displayed neurotoxic effects. Thus, the possibility of delayed neurotoxicity in man cannot be entirely discounted, but it is likely to occur only following excessive oral doses.

Human volunteers given single or repeated oral doses of 2 mg dichlorvos/kg body weight or more showed significant inhibition of erythrocyte-ChE activity. No inhibition was found at 1 mg/kg body weight.

Application of dichlorvos to crops and animals results in residues that rapidly disappear through volatilization and hydrolysis. In general, residues of dichlorvos and its break-down product, dichloroacetaldehyde, in food commodities are low and will be further reduced during processing. The exposure of the general population to dichlorvos through food and drinking-water is negligible, as has been confirmed in total diet studies.

In short-term inhalation studies on mammals, 1 or 2 mg dichlorvos/m³ did not inhibit ChE activity.

In a 2-year inhalation study on rats, whole-body exposure to 0.48 mg dichlorvos/m³ for 23 h/day caused inhibition of plasma- and red cell-ChE activity, but AchE activity in the brain was not inhibited and there were no clinical signs. An unquantified, but considerable, increase in exposure resulting from the grooming of contaminated fur, and the contamination of food and drinking-water, had contributed to this effect. The no-observed-adverse-effect level was 0.05 mg/m³. There was no evidence of carcinogenicity.

After 6-7-h exposure of human volunteers to concentrations of approximately 1 mg/m³, only inhibition of plasma-ChE activity was

SUMMARY AND EVALUATION

found. This is generally considered as an indication of exposure. The red cell-AChE activity, taken to be representative of the AChE activity in the nervous tissue, was not affected.

Residents exposed to an average air concentration of dichlorvos of 0.1 mg/m³, arising from slow-release strips for over one year, did not show any inhibition of plasma- or erythrocyte-ChE activity, or any deleterious effects on health.

The main exposure of the general population is through the inhalation of dichlorvos, when used indoors to control insects. The recommended use (one slow-release strip/ 30 m³) will give concentrations in the air of up to 0.1–0.3 mg/m³ within the first few days, decreasing thereafter to below 0.1 mg/m³. The air concentration depends on temperature, humidity, and ventilation.

As long as approved slow-release strips are used according to the instructions on the label, no health hazard can be expected for man. However, special care may need to be taken with young children and sick or elderly people, who are especially vulnerable when continuously exposed (24 h a day) in poorly ventilated rooms. Other methods of indoor application should be safe, if the instructions on the label are followed.

There is some indication that dichlorvos may induce dermatitis and cross- sensitization in workers also handling other types of pesticides.

Under occupational conditions, the main route of exposure to organophosphorus pesticides is, generally, the dermal route. In the case of dichlorvos, with its high vapour pressure, exposure through inhalation is also important. In such occupational situations, the dichlorvos concentrations in air are generally below 1 mg/m³ but, under certain circumstances, they may rise considerably above this level. This stresses the need for adequate protection measures to be taken during occupational exposure and regular monitoring of ChE activity.

2.2 Evaluation of Effects on the Environment

The presence of dichlorvos as a result of accidental loss or direct application on soil or in water will not lead to long-term effects,

SUMMARY AND EVALUATION

because of its fast breakdown and evaporation. Furthermore, dichlorvos will be converted by microorganisms to a number of compounds including dichloroacetic acid. Certain bacteria can use dichlorvos as a sole source of carbon. Other strains cannot and are inhibited in their growth. Thus, the influence of dichlorvos on microorganisms is rather complex.

Dichlorvos is moderately to highly toxic (range, 0.2-10 mg/litre) for fresh-water and estuarine species of fish and invertebrates. In certain fish, concentrations of 0.25-1.25 mg/litre cause inhibition of brain-and liver-ChE activity. Concentrations of 0.05 mg/litre may already have deleterious effects, particularly in invertebrates. Dichlorvos is highly toxic for birds and bees. Caution is advised in the use and handling of dichlorvos where these species might be exposed.

No bioaccumulation occurs in the different compartments and organisms.

3. CONCLUSIONS AND RECOMMENDATIONS

3.1 Conclusions

- (a) Exposure of the general population to dichlorvos through food and drinking-water is negligible and does not constitute a health hazard.
- (b) The in-house use of dichlorvos as an insecticide in the form of sprays or slow-release strips, at recommended levels of use, does not constitute a short- or a long-term hazard for the general population. However, continuous (24 h per day) exposure of young children and sick or elderly people in non- or poorly-ventilated rooms should be avoided.
- (c) Notwithstanding their toxicity, dichlorvos and its formulations do not present an undue hazard for those occupationally exposed, when adequate ventilation and skin protection are used.
- (d) Except in the case of gross spillage, the recommended use of dichlorvos as an insecticide does not pose any acute or long-term hazards for aquatic and terrestrial organisms, though there may be an acute hazard for birds and bees.

3.2 Recommendations

(a) Continuous (24 h/day) exposure of young children and sick or elderly people to dichlorvos in non- or poorly-ventilated rooms should be avoided.

CONCLUSIONS AND RECOMMENDATIONS

(b) As dichlorvos from various sources may differ in purity and impurities, attention should be paid to its composition. This should conform to FAO and WHO specifications. In the case of formulations, other components, such as solvents and stabilizers, should also be considered.

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

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

Dichlorvos is an organophosphorus insecticide. Technical dichlorvos and concentrated formulations are moderately to highly toxic and can be hazardous for human beings, if incorrectly handled. Dichlorvos has a relatively high vapour pressure and is therefore hazardous through inhalation; it is also hazardous through ingestion and skin contact, because of fast absorption. Typical signs and symptoms of organophosphorus poisoning may occur rapidly with overexposure.

The human health hazards associated with certain types of exposure to dichlorvos, together with preventive and protective measures and first aid are listed on the International Chemical Safety Card on pp. 22–25.

4.1.1 Advice to physicians

4.1.1.1 Symptoms of poisoning

Dichlorvos is a direct inhibitor of cholinesterase. Initially, there may be feelings of exhaustion, headache, weakness, and confusion. Then, vomiting, abdominal pain, excessive sweating, and salivation may develop. The pupils are small. Difficulty in breathing may be experienced, due to either congestion of the lungs or weakness of the respiratory muscles. In severe cases of poisoning, muscle spasms, unconsciousness, and convulsions may develop. Respiration may stop. For a more complete treatise on the effects of organophosphorus insecticides, especially their short- and long-term effects on the nervous system, refer to EHC 63: Organophosphorus insecticides—a general introduction (WHO, 1986a).

4.1.1.2 Medical treatment

If ingested and the formulation does not contain petroleum distillates, induce vomiting, or preferably perform gastric lavage using 5% sodium bicarbonate. In the case of ingestion of liquid formulations containing hydrocarbon solvents, vomiting involves a risk of aspiration pneumonia. Instead, the stomach should be emptied as soon as possible by careful gastric lavage (using a cuffed endotracheal

HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

tube). If possible, identify the solvents present in the formulation and observe the victim for additional toxic effects. As early as possible, administer 2 mg of atropine sulfate i.v. and 1000–2000 mg of pralidoxime chloride or 250 mg of obidoxime chloride (adult dose) intramuscularly or intravenously to patients suffering from severe respiratory difficulties, convulsions, and unconsciousness. Repeated doses of 2 mg of atropine sulfate should be given, as required, based on the respiration, blood pressure, pulse frequency, salivation, and convulsion conditions. For children, the doses are 0.04–0.08 mg of atropine/kg body weight, 250 mg of pralidoxime chloride per child or 4–8 mg of obidoxime chloride kg body weight.

Artificial respiration should be applied if required.

Morphine, barbiturates, phenothiazine derivatives, tranquillizers, and all kinds of central stimulants are contraindicated.

The diagnosis of intoxication should be confirmed as soon as possible by determination of the cholinesterase activity in venous blood.

For more information on the treatment of organophosphorus insecticides see EHC No. 63: Organophosphorus insecticides: - a general introduction (WHO 1986a). The section on therapy from this publication is attached as Annex 1 of this guide.

4.1.2 Health surveillance advice

Occupational exposure to organophosphorus insecticides can be monitored by measurement of erythrocyte- and whole blood-ChE activity. Physiological variations in erythrocyte- and blood-ChE values occur in healthy persons.

Inhibition of AChE or ChE activity of less than 20–25% is considered diagnostic of exposure but not necessarily indicative of hazard. However, work procedures and hygiene should be checked. Inhibition of 30–50% or more is considered an indication that an exposed individual should be removed from further contact with ChE-inhibiting pesticides, until values return to normal. Work procedures and hygiene should also be checked.

HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

4.2 Explosion and fire hazards

Liquid formulations may be flammable. Inform the fire service that skin contamination and the breathing of fumes must be avoided. Protective clothing and self-contained breathing apparatus must be worn.

Extinguish fires with alcohol-resistant foam or powder. The use of water spray should be confined to the cooling of unaffected stock, to avoid polluted run-off from the site.

4.3 Storage

Technical dichlorvos and its formulations should be stored in locked, well ventilated buildings preferably specifically used for insecticide storage. Do not expose to direct sunlight. Keep products out of reach of children and unauthorized personnel. Do not store near feed or foodstuffs.

4.4 Transport

Comply with any local regulations regarding movement of hazardous goods. Do not load with feed or foodstuffs. Check that containers are sound and labels undamaged before despatch.

4.5 Spillage and Disposal

4.5.1 Spillage

Stay upwind, avoid skin contamination and inhalation of vapour. Absorb spilled liquid and cover contaminated areas with 1:3 mixture of sodium carbonate crystals and damp sawdust, lime, sand, or earth. Sweep up and place in a closeable impervious container. Ensure that container is tightly closed and suitably labelled before transfer to a safe place for disposal.

Prevent liquid from spreading and contaminating other cargo, vegetation, or waterways with a barrier of the most suitable material available, e.g., earth or sand. If the spill occurs into a waterway and

HUMAN HEALTH HAZARDS, PREVENTION AND PROTECTION, EMERGENCY ACTION

the dichlorvos-containing material is immiscible in water and sinks, dam the waterway to stop flow and to retard dissipation by water movement. Use a bottom pump, dredging, or underwater vacuum equipment to remove undissolved material.

Empty any of the product remaining in the damaged/leaking container into a clean empty container, which should then be tightly closed and suitably labelled.

Decontaminate emptied leaking containers with a 10% sodium carbonate solution added at the rate of at least 1 litre per 20-litre drum. Swirl round to rinse walls, empty, and add rinsings to sawdust, etc. Puncture empty containers to prevent re-use.

4.5.2 Disposal

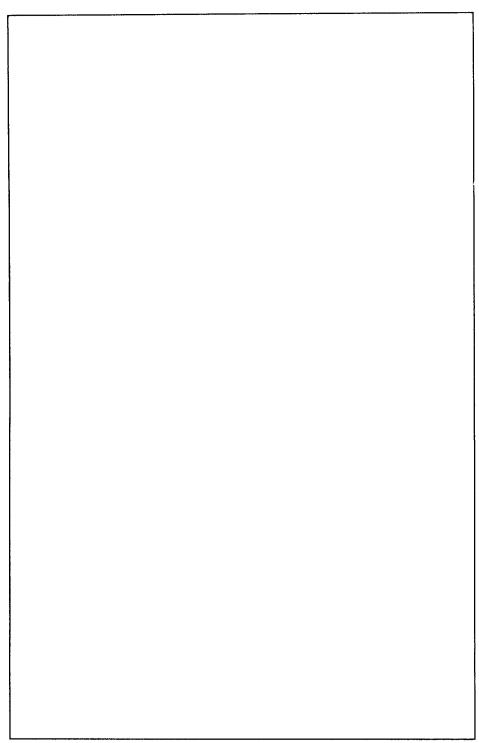
Contaminated absorbents, containers, surplus product, etc., should be burnt in a proper incinerator at high temperatures in a unit with effluent gas scrubbing. When no incinerator is available, bury in an approved dump, or in an area where there is no risk of contamination of surface or ground water. Before burying, liberally mix with sodium carbonate (washing soda) crystals to help neutralize the product and with soil rich in organic matter. Comply with any local legislation.

5. HAZARDS FOR THE ENVIRONMENT AND THEIR PREVENTION

Dichlorvos is highly toxic for honey bees, birds, and fish. It does not bioaccumulate and it breaks down rapidly in the environment.

Avoid contamination of soil, water, and the atmosphere by proper methods of storage, transport, handling, and waste disposal. Caution is advised in the use and handling of dichlorvos where sensitive non-target animal species might be exposed.

In case of spillage, use the methods advised in section 4.5.1.



6. INTERNATIONAL CHEMICAL SAFETY CARD

This card should be easily available to all health workers concerned with, and users of, dichlorvos. It should be displayed at, or near, entrances to areas where there is potential exposure to dichlorvos, and on processing equipment and containers. The card should be translated into the appropriate language(s). All persons potentially exposed to the chemical should also have the instructions on the chemical safety card clearly explained.

Space is available on the card for insertion of the National Occupational Exposure Limit, the address and telephone number of the National Poison Control Centre, and for local trade names.

INTERNATIONAL CHEMICAL SAFETY CARD	DICHLORVOS	Chemical formula: C4H7Cl204P CAS chemical name: (2,2-Dichloroethenyl dimethylphosphate) CAS: registry number: 62-73-7	OTHER CHARACTERISTICS	35 °C (0.05 mmHg) Colourless to amber liquid with a mild chemical odour; stable to heat, but is hydrolysed by water at a rate of 3% per day at room temperature; 1.415 corrosive to iron and mild steel 221 10 g/litre 2-3 g/litre 1.47
Z		O	PHYSICAL PROPERTIES	Boiling point (°C) Vapour pressure Density (25 °C) g/ml Relative molecular mass Solubility: in water (20 °C) in kerosine miscible with most organic solvents Log n-octanol/water partition coefficient

	HAZARD/SYMPTOM	PREVENTION AND PROTECTION	FIRST AID
	GENERAL: readily absorbed via skin, ingestion, and inhalation; may cause organophosphate poisoning: weakness, headache, vomiting, excessive sweating and salivation, pinpoint pupils; in severe cases: convulsions, unconsciousness, and death due to respiratory paralysis		
23	SKIN: irritation; redness; extensive contamination may cause poisoning	Wear PVC or neoprene gloves and apron; rubber boots	Remove and wash contaminated clothing; wash contaminated skin with water and soap; obtain medical attention immediately
	EYES: irritation; redness	Wear safety goggles or face shield	Flush eyes with clean water for at least 15 min; if irritation persists, obtain medical attention immediately

INTERNATIONAL CHEMICAL SAFETY CARD (continued)	HAZARD/SYMPTOM PREVENTION AND PROTECTION FIRST AID	INHALATION: overexposure may Avoid inhaling the vapour; use In case of signs and symptoms, remove cause poisoning proper (exhaust) ventilation or medical attention immediately	INGESTION: an unlikely Wash hands before eating, drink- occupational hazard mg, using the toilet, and after work	Accidental or intentional ingestion medical attention immediately; if breathing has stopped, apply artificial respiration.	REPEATED EXPOSURE BY INHALATION OR INGESTION, OR THROUGH SKIN may grad- ually lead to signs and symptoms of inhibition of cholinesterase
	HAZ	INHA	dnooo 24	Accid	REPE INHA OR T ually I

activity

		owder; otect-	3	308
	FIRE AND EXPLOSION	Use alcohol-resistant foam or powder; cool unaffected stock; wear protective clothing and self-contained breathing apparatus		UN: 2783, 2784, 3017, 3018
The state of the s	STORAGE	Store in locked, well-ventilated storeroom, away from feed and foodstuffs, children, and unauthorized personnel		National Occupational Exposure Limit: National Poison Control Centre: Local trade names:
	SPILLAGE	Absorb spilled liquid and cover contaminated area with 1:3 mixture of sodium carbonate crystals and damp sawdust, lime, sand, or earth; sweep up and place in closed and suitably labelled container	WASTE DISPOSAL	Burn at high temperature in incinerator with effluent scrubbing, comply with local legislation; when allowed, treat with washing soda mixed with soil rich in organic matter and bury in an approved dump

The information given in this section has been extracted from the International Register of Potentially Toxic Chemicals (IRPTC) legal file and other UN sources. Its intention is to give the reader a representative but non-exhaustive overview of current regulations, guidelines, and standards.^a

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.

7.1 Previous Evaluations by International Bodies

Dichlorvos was evaluated by the Joint FAO/WHO Expert Committee on Pesticide Residues (JMPR) in 1965, 1966, 1967, 1969, 1970, 1974, and 1977. In 1966, the JMPR established an Acceptable Daily Intake (ADI) for man of 0–0.004 mg/kg body weight, a level still maintained as acceptable.

The Pesticide Development and Safe Use Unit, Division of Vector Biology and Control, WHO, classified technical dichlorvos as "highly hazardous" (Class IB) (Plestina, 1984; WHO, 1986a). This division has also issued a data sheet on dichlorvos (WHO/FAO, 1975).

In 1979, IARC came to the following conclusion in considering the carcinogenicity of dichlorvos:

- Dichlorvos was tested in different animal species via different routes;
 no conclusive evaluation on the basis of these studies could be made;
- Dichlorvos is an alkylating agent and binds to bacterial and mammalian nucleic acids;
- It is a mutagen in a number of microbial systems, but there is no evidence of its mutagenicity in mammals, in which it is rapidly degraded.

^a The regulations and guidelines of all countries are subject to change and should always be verified with the appropriate regulatory authorities before application.

IRPTC has published a volume on Dichlorvos, in its series "Scientific Reviews of Soviet Literature on Toxicity and Hazards of Chemicals".

7.2 Exposure Limit Values

Some exposure limit values are given in the table on pp. 28-30.

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).

7.3 Specific Restrictions

Dichlorvos has been officially approved for use as a pesticide in many countries, in each of which specific uses are defined as well as limitations and precautions. Absorption through the skin is indicated as a potentially hazardous route in the regulatory documents in Argentina, the countries of the European Community, the USA, and the USSR.

In Brazil, the maximum concentration of the active substance authorized for use as an insecticide is 1-5% (weight/weight).

In the USSR, the presence of dichlorvos in fishing waters is not allowed, but a level of 0.1 mg/litre is allowed in other surface waters. The preliminary safety limit for soil is 0.1 mg/kg.

7.4 Labelling, Packaging, and Transport

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

- Hazard Class 6.1: poisonous substance;
- Packing Group II: a substance presenting a serious risk of poisoning in transport, for material containing 35-100% dichlorvos;
- Packing Group III: a substance presenting a relatively low risk of poisoning in transport, for material containing 7-35% dichlorvos.

	CURREN	T REGULAT	JRRENT REGULATIONS, GUIDELINES, AND STANDARDS	DARDS	
EXPOSURE LIMI	RE LIMIT VALUES	SS			
Medium	Specification	Country/ organization	Exposure limit description	Value	Effective Date
AIR	Work-place	Argentina	Maximum permissible concentration - Time-weighted average (TWA) - Short-term exposure limit (STEL)	1 mg/m ³ 3 mg/m ³	1979
		Germany, Federal Republic of	Maximum work-site concentration (MAK) -Time-weighted average (TWA) - 30-min short-term exposure limit (STEL)	1 mg/m^3 10 mg/m^3	
·		United Kingdon	United Kingdom Recommended limit (RECL) - Short-term exposure limit (STEL)	1 mg/m ³ 3 mg/m ³	
		USA	Permissible exposure limit - Time-weighted average (TWA)	1 mg/m ³	
		USSR	Maximum allowable concentration (MAC) - Ceiling value	0.2 mg/m ³	1977

AIR	Ambient	USSR	Maximum allowable concentration (MAC) (average per day)	$0.002~\mathrm{mg/m}^3$	···
FOOD	General	FAO/WHO	Acceptable daily intake(ADI)	0-0.004 mg/kg body weight	1966
FOOD	Plant	Brazil	Acceptable limit (AL) - Safety interval	0.1–5 mg/kg 30 days	1981
		Czechoslovakia	Czechoslovakia Maximum residue limit (MRL)	0.02-2 mg/kg	1978
		European Community	Maximum residue limit (MRL)	0.1 mg/kg	1984
		FAO/WHO	Maximum residue limit (MRL)	0.02-5 mg/kg	1978
		India	Maximum tolerable concentration (MTC)	0.1-1 mg/kg	1976
		Јарап	Acceptable residue limit (ARL)	0.1 mg/kg	
		Sweden	Maximum tolerable concentration (MTC)	0.1-2 mg/kg	1985

EXPOSURI	EXPOSURE LIMIT VALUES (continued)	2S (continued)			
Medium	Specification	Country/ organization	Exposure limit description	Value	Effective Date
FOOD	Plant	USSR	Maximum residue limit (MRL) for specific food items	0-0.3mg/kg	1983
			Acceptable daily intake (ADI)	0.04 mg/kg	
FOOD	Animal	Kenya	Maximum limit	0.02-5 mg/kg	
		Sweden	Maximum tolerable concentration (MTC)	$0.02-0.1~\mathrm{mg/kg}$	1983
		USA	Acceptable residue limit (ARL)	0.05-10 mg/kg	

The label 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 Community Legislation requires labelling as dangerous substance using the symbol:



Giftig Giftig Tokiko Toxic Toxique Tossico Vergiftig

The label must read:

Toxic by inhalation, in contact with skin and if swallowed; keep out of reach of children; keep away from food, drink and animal feeding stuffs — if you feel unwell, seek medical advice (show the label where possible).

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

WHO gives the following product specification for dichlorvos for use in public health:

Technical dichlorvos: the material shall consist of dichlorvos together with related manufacturing compounds and shall be a pale amber-coloured liquid free from extraneous impurities or added modifying agents. It shall contain at least 970 g of dichlorvos per kg. Acidity and water content are specified and analytical methods for checking are given.

Technical dichlorvos shall be packed in suitable clean containers, and all packages shall bear, durably and legibly marked on the container, the following:

- Manufacturer's name
- Technical dichlorvos to specification WHO/SIT/16.R2
- Batch or reference number, and date of test
- Net weight of contents
- Date of manufacture

and the following minimum cautionary notice:

"POISON (skull-and-crossbones emblem): dichlorvos is an organophosphorus compound that inhibits cholinesterase. It is poisonous if swallowed, inhaled, or absorbed through the skin. Wear protective gloves, clean protective clothing, goggles, and a respirator of the organic-vapour type when handling this material. Avoid prolonged exposure to fumes. Wash hands and exposed skin after handling and before eating, and bathe immediately afterwork.

Keep the material out of the reach of children and well away from foodstuffs, animal feed and their containers. Ensure that containers are tightly sealed, and stored and disposed of in such a way as to prevent accidental contact.

In case of contact, immediately remove contaminated clothing and wash the skin thoroughly with soap and water; for eyes, flush with water for 15 minutes.

If poisoning occurs, call a physician. Atropine and pralidoxime are specific antidotes and artificial respiration may be needed."

Similar specifications and instructions are given for dichlorvos emulsifiable concentrate. FAO gives similar product specifications for dichlorvos for its use in plant protection. In this case, the technical material should contain at least 95% active material.

Containers must comply with pertinent national and international transport and safety regulations.

BIBLIOGRAPHY

FAO (1985a) Guidelines for the packaging and storage of pesticides. Rome, Food and Agriculture Organization of the United Nations.

FAO (1985b) Guidelines for the disposal of waste pesticides and pesticide containers on the farm. Rome, Food and Agriculture Organization of the United Nations.

FAO (1985c) Guidelines on good labelling practice for pesticides. Rome, Food and Agriculture Organization of the United Nations.

FAO (1986a) International code of conduct on the distribution and use of posticides. Rome, Food and Agriculture Organization of the United Nations.

FAO/WHO (1986b) Guide to Codex recommendations concerning pesticide residues. Part 8. Recommendations for methods of analysis of pesticide residues. 3rd ed. Rome, Codex Committee on Pesticide Residues.

GIFAP (1982) Guidelines for the safe handling of pesticides during their formulation, packing, storage and transport, Brussels, Groupement International des Associations Nationales des Fabricants de Produits Agrochimiques.

GIFAP (1983) Guidelines for the safe and effective use of pesticides. Brussels, Groupement International des Associations Nationales des Fabricants de Produits Agrochimiques.

GIFAP (1984) Guidelines for emergency measures in cases of pesticide poisoning. Brussels, Groupement International des Associations Nationales des Fabricants de Produits Agrochimiques.

GIFAP (1987) Guidelines for the safe transport of pesticides. Brussels, Groupement International des Associations Nationales des Fabricants de Produits Agrochimiques.

IARC (1972-present) L4RC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Lyons, International Agency for Research on Cancer.

BIBLIOGRAPHY

IRPTC (1985) IRPTC file on treatment and disposal methods for waste chemicals. Geneva, International Register of Potentially Toxic Chemicals, United Nations Environment Programme.

IRPTC (1987) IRPTC legal file 1986. Geneva, International Register of Potentially Toxic Chemicals, United Nations Environment Programme.

PLESTINA, R. (1984) Prevention, diagnosis, and treatment of insecticide poisoning. Geneva, World Health Organization (Unpublished report No. VBC/84.889).

SAX, N.I. (1984) Dangerous properties of industrial materials. New York, Van Nostrand Reinhold Company, Inc.

UNITED NATIONS (1986) Recommendations on the transport of dangerous goods. 4th ed. New York, United Nations.

US NIOSH/OSHA (1981) Occupational health guidelines for chemical hazards. 3 Vols. Washington DC, US Department of Health and Human Services, US Department of Labor (Publication No. DHHS(NIOSH) 01-123).

WHO (1986a) EHC No. 63. Organophosphorus Insecticides: a general introduction. Geneva, World Health Organization, 181 pp.

WHO (1986b) The WHO recommended classification of pesticides by hazard. Guidelines to classification 1986-87. Geneva, World Health Organization (Unpublished report VBC/86.1).

WHO (1988) EHC No. 79: Dichlorvos. Geneva, World Health Organization.

WHO/FAO (1975-87) Dichlorvos. Data sheets on pesticides, Geneva, World Health Organization (Unpublished documents).

WORTHING, C.R. & WALKER, S.B. (1983) The pesticide manual. 7th ed. Lavenham, Lavenham Press Limited, British Crop Protection Council.

TREATMENT OF ORGANOPHOSPHATE INSECTICIDE POISONING IN MAN

(From EHC 63: Organophosphorus Insecticides - A General Introduction)

All cases of organophosphorus poisoning should be dealt with as an emergency and the patient sent to hospital as quickly as possible. Although symptoms may develop rapidly, delay in onset or a steady increase in severity may be seen up to 48 h after ingestion of some formulated organophosphorus insecticides.

Extensive descriptions of treatment of poisoning by organophosphorus insecticides are given in several major references (Kagan, 1977; Taylor, 1980; UK DHSS, 1983; Plestina, 1984) and will also be included in the IPCS Health and Safety Guides to be prepared for selected organophosphorus insecticides.

The treatment is based on:

- (a) minimizing the absorption;
- (b) general supportive treatment; and
- (c) specific pharmacological treatment.

I.1 Minimizing the Absorption

When dermal exposure occurs, decontamination procedures include removal of contaminated clothes and washing of the skin with alkaline soap or with a sodium bicarbonate solution. Particular care should be taken in cleaning the skin area where venupuncture is performed. Blood might be contaminated with direct-acting organophosphorus esters and, therefore, inaccurate measures of ChE inhibition might result. Extensive eye irrigation with water or saline should also be performed. In the case of ingestion, vomiting might be induced, if the patient is conscious, by the administration of ipecacuanha syrup (10–30 ml) followed by 200 ml water. This treatment is, however, contraindicated in the case of pesticides dissolved in hydrocarbon solvents. Gastric lavage (with addition of

bicarbonate solution or activated charcoal) can also be performed, particularly in unconscious patients, taking care to prevent aspiration of fluids into the lungs (i.e., only after a tracheal tube has been put in place).

The volume of fluid introduced into the stomach should be recorded and samples of gastric lavage frozen and stored for subsequent chemical analysis. If the formulation of the pesticide involved is available, it should also be stored for further analysis (i.e., detection of toxicologically relevant impurities). A purgative can be administered to remove the ingested compound.

I.2 General Supportive Treatment

Artificial respiration (via a tracheal tube) should be started at the first sign of respiratory failure and maintained for as long as necessary.

Cautious administration of fluids is advised, as well as general supportive and symptomatic pharmacological treatment and absolute rest.

I.3 Specific Pharmacological Treatment

I.3.1 Atropine

Atropine should be given, beginning with 2 mg i.v. and given at 15–30-min intervals. The dose and the frequency of atropine treatment varies from case to case, but should maintain the patient fully atropinized (dilated pupils, dry mouth, skin flushing, etc.). Continuous infusion of atropine may be necessary in extreme cases and total daily doses up to several hundred mg may be necessary during the first few days of treatment.

1.3.2 Oxime reactivators

Cholinesterase reactivators (e.g., pralidoxime, obidoxime) specifically restore AChE activity inhibited by organophosphates. This is not the case with enzymes inhibited by carbamates. The treatment should begin as soon as possible, because oximes are not effective on "aged" phosphorylated ChEs. However, if absorption, distribution, and metabolism are thought to be delayed for any reasons, oximes can be

administered for several days after intoxication. Effective treatment with oximes reduces the required dose of atropine. Pralidoxime is the most widely available oxime. A dose of 1 g pralidoxime can be given either i.m. or i.v. and repeated 2–3 times per day or, in extreme cases, more often. If possible, blood samples should be taken for AChE determinations before and during treatment. Skin should be carefully cleansed before sampling. Results of the assays should influence the decision whether to continue oxime therapy after the first 2 days.

There are indications that oxime therapy may possibly have beneficial effects on CNS-derived symptoms.

I.3.3 Diazepam

Diazepam should be included in the therapy of all but the mildest cases. Besides relieving anxiety, it appears to counteract some aspects of CNS-derived symptoms, which are not affected by atropine. Doses of 10 mg s.c. or i.v. are appropriate and may be repeated as required (Vale & Scott, 1974). Other centrally acting drugs and drugs that may depress respiration are not recommended in the absence of artificial respiration procedures.

I.3.4 Notes on the recommended treatment

I.3.4.1 Effects of atropine and oxime

The combined effect far exceeds the benefit of either drug singly.

I.3.4.2 Response to atropine

The response of the eye pupil may be unreliable in cases of organophosphorus poisoning. A flushed skin and drying of secretions are the best guide to the effectiveness of atropinization. Although repeated dosing may well be necessary, excessive doses at any one time may cause toxic side-effects. Pulse-rate should not exceed 120/min.

I.3.4.3 Persistence of treatment

Some organophosphorus pesticides are very lipophilic and may be taken into, and then released from, fat depots over a period of many days. It is therefore quite incorrect to abandon oxime treatment after 1–2 days on the supposition that all inhibited enzyme will be aged. Ecobichon et al. (1977) noted prompt improvement in both condition and blood-ChEs in response to pralidoxime given on the 11th–15th days after major symptoms of poisoning appeared due to extended exposure to fenitrothion (a dimethyl phosphate with a short half-life for aging of inhibited AChE).

I.3.4.4 Dosage of atropine and oxime

The recommended doses above pertain to exposures, usually for an occupational setting, but, in the case of very severe exposure or massive ingestion (accidental or deliberate), the therapeutic doses may be extended considerably. Warriner et al. (1977) reported the case of a patient who drank a large quantity of dicrotophos, in error, while drunk. Therapeutic dosages were progressively increased up to 6 mg atropine i.v. every 15 min together with continuous i.v. infusion of pralidoxime chloride at 0.5 g/h for 72 h, from days 3 to 6 after intoxication. After considerable improvement, the patient relapsed and further aggressive therapy was given at a declining rate from days 10 to 16 (atropine) and to day 23 (oxime), respectively. In total, 92 g of pralidoxime chloride and 3912 mg of atropine were given and the patient was discharged on the thirty-third day with no apparent sequelae.

References to Annex I

ECOBICHON, D.J., OZERE, R.L., REID, E., & CROCKER, J.F.S (1977) Acute fenitrothion poisoning. *Can. Med. Assoc. J.*,116: 377-379.

KAGAN, JU.S. (1977) [Toxicology of organophosphorus pesticides.] Moscow, Meditsina, pp. 111-121, 219-233, 260-269 (in Russian).

PLESTINA, R. (1984) Prevention, diagnosis, and treatment of insecticide poisoning. Geneva, World Health Organization (Unpublished report No. VBC/84.889).

TAYLOR, P. (1980) Anticholinesterase agents. In: Goodman, L.S. & Gilman, A., ed. *The phannacological basis of therapeutics*. 6th ed. New York, Macmillan Publishing Company, pp. 100-119.

UK DHSS (1983) Pesticide poisoning: notes for the guidance of medical practitioners, London, United Kingdom Department of Health and Social Security, pp. 41-47.

VALE, J.A. & SCOTT, G.W. (1974) Organophosphorus poisoning. Guy's Hosp. Rep., 123: 13-25,

WARRINER, R.A., III, NIES, A.S., & HAYES, W.J., Jr (1977) Severe organophosphate poisoning complicated by alcohol and terpentine ingestion. *Arch. environ. Health*, 32: 203-205.

WHO publications may be obtained, direct or through booksellers, from:

- Al.GERIA: Enterprise nationale du Livre (ENAL), 3 bd. Zirout Youcef, Al GIERS
- ARGENTINA: Carlos Hirsch, SRL, Florida 165, Galerias Güemes, Escritorio 453/465, BUENOS AIRES
- AUSTRALIA: Hunter Publications, 58A Gipps Street, COLLINGWOOD, VIC 3066 Australian Government Publishing Service (Mail order sales), P.O. Box 84, CANBERRA A.C.T. 2601: ar over the conator from: Australian Government Publishing Service Bookshops at: 70 Alinga Street, CANBERRA CITY A.C.T. 2600; 294 Adelaide Street, BRISBANE, Queensland 4000, 347 Swanston Street, MELBOURNE, VIC 3000, 309 Pitt Street, SYDNEY, N.S.W. 2000; Mt Newman House, 200 St. George's Terrace, PERTH, WA 6000; Industry House, 12 Pirle Street, ADEL AIDE, SA 5000; 156—162 Macquarie Street, HOBART, TAS 7000 R. Hill & Son Ltd., 608 St. Kilda Road, MELBOURNE, VIC 3004; Lawson House, 10–12 Clark Street, CROW'S NEST, NSW 2065
- AUSTRIA: Gerold & Co., Graben 31, 1011 VIENNA I
- BANGLADESH: The WITO Representative, G.P.O. Box 250, DHAKA 5
- BELGIUM: For imoks: Office International de Librairie s.a., avenue Marnis 30, 1050 BRUSSELS. For perudicals and subscriptions: Office International des Périodiques, avenue Louise 485, 1050 BRUSSELS Subscriptions to World Health only: Jean de Lannoy, 202 avenue du Roi, 1000 BRUSSELS
- BHUTAN: vee India, WHO Regional Office
- BOTSWANA: Botsalo Books (Pty) 1.td., P.O. Box 1532. GARORONE
- BRAZIL: Biblioteca Regional de Medicina OMS/OPS, Sector de Publicações, Caixa Postal 20,381, Vila Clementino, 04023 SÃO PAULO, S.P.
- BURMA: see India, WHO Regional Office
- CANADA; Canadian Public Health Association, 1335 Carling Avenue, Suite 210, OTTAWA, Ont. KIZ 8N8
- CHINA: China National Publications Import & Export Corporation, P.O. Box 88, BEIJING (PEKING)
- DEMOCRATIC PEOPLE'S REPUBLIC OF KOREA: see India, WHO Regional Office
- DENMARK: Munksgaard Export and Subscriptions Service, Norre Sogade 35, 1370 COPFNHAGEN K
- FIJI: The WHO Representative, P.O. Box 113, SUVA
- FINLAND: Akateeminen Kirjakauppa, Keskuskatu 2, 00401 HELSINKI 10
- FRANCE: Librairie Arnette, 2 rue Casimir-Delavigne, 75,006 PARIS
- GERMAN DEMOCRATIC REPUBLIC: Buchhaus Leipzig, Postfach 140, 701 LEIPZIG
- GERMANY, FEDERAL REPUBLIC OF: Govi-Verlag GmbH, Ginnheimer Straße 20, Postfach 5360, 6236 ESCHBORN
 - Buchhandlung Alexander Horn, Friedrichstraße 3, Postfach 3340, 6200 WIESBADEN
- GHANA: Fides Enterprises, P.O. Box 1628, ACCRA
- GREECE: G. C. Eleftheroudakis S.A., Librairie internationale, rue Nikis 4, ATHENS (T. 126)

- HONG KONG: Hong Kong Government Information Services, Beaconsfield House, 6th Floor, Queen's Road, Central, VICTORIA
- HUNGARY: Kultura, P.O. Box 149, BUDAPEST 62
- INDIA: WHO Regional Office for South-Fast Asia, World Health House, Indraprastha Estate, Mahatmu Gandhi Road, NEW DELHI 110002
- INDONESIA: P.1. Kalman Media Pusaka, Pusat Perdagangan Senen, Block I, 4th Floor, P.O. Box 3433/Jkt. LAKARTA
- **IRAN (ISLAMIC REPUBLIC OF):** Iran University Press. 85 Park Avenue P.O. Box 54/551, TEHERAN
- IRELAND: TDC Publishers, 12 North Frederick Street, DUBLIN
- ISRAEL: Heiliger & Co., 3 Nathan Strauss Street, JERU-SALEM 94227
- TTALY: Edizioni Minerva Medica. Corso Bramante 83-85, 10 126 TURIN, Via Lamarmora 3, 20 100 MILAN; Via Spallanzani 9, 00 161 ROME
- JAPAN: Maruzen Co. Ltd., P.O. Box 5050, TOKYO International, 300-31
- JORDAN: Jordan Book Centre Co. Ltd., University Street, P.O. Box 301 (Al-Jubeiha), AMMAN
- KUWAIT: The Kuwait Bookshops Co, Ltd., Thunayan Al-Ghanem Bldg., P.O. Box 2942. KUWAIT
- LAO PEOPLE'S DEMOCRATIC REPUBLIC: The WHO Representative, P.O. Box 343, VIENTIANE
- LUXEMBOURG: Librairie du Centre, 49 bd Royal, LUXEMBOURG
- MALAWI: Malawi Book Service, P.O. Box 30044. Chichiti, BLANTYRE 3
- MALAYSIA: The WHO Representative, Room 1004, 10th Floor, Wisma Lim Foo Yong (formerly Fitzpatrick's Building), Jalan Raja Chulan, KUALA LUMPUR 05-10; P.O. Box 2550, KUALA LUMPUR 01-02; Parry's Book Center, 124-1 Jalan Tun Sambanthan, P.O. Box 10960, 50730 KUALA LUMPUR
- MALDIVES: see India, WHO Regional Office
- MEXICO: Librería International, S.A. de CV., Av. Sonora 206, 06100-MEXICO, D.E.
- MONGOLIA; see India, WHO Regional Office
- MOROCCO: Editions La Porte, 281 avenue Mohammed V. RABAT
- NEPAL: see India, WHO Regional Office
- NETHERLANDS: Medical Books Europe BV. Noorderwal 38, 7241 BL LOCHEM
- NEW ZEALAND: New Zealand Government Printing Office, Publishing Administration, Private Bag, WELLINGTON: Walter Street, WELLINGTON: World Trade Building, Cubacade, Cuba Street, WELLINGTON, Government Bookshops at: Hannaford Burton Building, Rutland Street, Private Bag, AUCKLAND; 159 Hereford Street, Private Bag, CHRISTCHURCH; Alexandra Street, P.O. Box 857, HAMILTON; T.& G. Building, Prince Street, P.O. Box 1104, DUNFDIN-R. Hill & Son Ltd., Ideal House, Cnr Gillies Avenue & Eden Street, Newmarket, AUCKLAND 1
- NORWAY: Tanum Karl Johan A.S., P.O. Box 1177, Sentrum, N-0107 OSLO 1

- PAKISTAN: Mirza Book Agency, 65 Shahrah-E-Quaid-E-Azam, P.O. Box 729, LAHORE 3
- PAPUA NEW GUINEA: The WHO Representative, P.O. Box 646, KONEDOBU
- PHILIPPINES: World Health Organization, Regional Office for the Western Pacific, P.O. Box 2932, MANILA
- PORTUGAL: Livraria Rodrigues, 186 Rua do Ouro, LIS-BON 7
- REPUBLIC OF KOREA: The WHO Representative, Central P.O. Box 540, SEOUI.
- SINGAPORE: The WIIO Representative, 144 Moulmein Road, SINGAPORE 1130; Newton P.O. Box 31, SIN-GAPORE 9122
- SOUTH AFRICA: Commet major book stores
- SPAIN: Ministerio de Sanidad y Consumo, Centro publicaciones, Documentación y Biblioteca, Paseo del Prado 18, 28014 MADRID Comercial Atheneum S.A., Consejo de Ciénto 130-136, 08015 BARCE-LONA; General Moscardó 29, MADRID 20 Libreria Díaz de Santos, P. O. Box 6050, 28006 MADRID; Balmes 417 y 419, 08022 BARCELONA.
- SRI LANKA: see India. WHO Regional Office
- SWEDEN: For booky: Akticholaget C.F. Fritzes Kungl, Hoybokhandel, Regeringsgatan 12, 10327 STOCK-HOLM. For periodicals: Wennergren-Williams AB, Box 30004, 10425 STOCKHOLM

- SWITZERLAND: Medizinischer Verlag Hans Huber, Länggassstrasse 76, 3012 BLRN 9
- THAILAND: we India, WHO Regional Office
- UNITED KINGDOM: H. M. Stationery Office: 49 High Holborn, JONDON WCIV 6HB: 13a Castle Street, EDINBURGH EHZ 3AR, 80 Chichester Street, BELENST BTI 4TY; Brazennose Street, MANCHESTER M60/8/AS; 258 Broad Street, BIRMINGHAM B12HE; Southey House, Wine Street, BRISTOL BS12RQ, 4H multi-orders should be sent in: HMSO Publications Centre, 51 Nine Elms Lane, LONDON SW8/519R
- UNITED STATES OF AMERICA: Copies of individual publications (not subscriptions): WHO Publications Center USA, 49 Sheridan Avenue, ALBANY, NY 12210, Subscription orders and correspondence concerning subscriptions should be addressed to the World Health Organization, Distribution and Sales, 1211 GENEVA 27, Switzerland, Publications are also available from the United Nations Bookshops, NEW YORK, NY 10017 (retail only)
- USSR: For readers in the USSR requiring Russian editions: Komsomolskij prospekt 18, Medicinskaja Kniga, MOSCOW – For readers outside the USSR requiring Russian editions. Kuzneckij most 18, Meždunarodnaja Kniga, MOSCOW G-200
- VENEZUELA: Libreria Medica Paris, Apartado 60.681, CARACAS 106
- YUGOSLAVIA: Jugoslovenska Knijga, Terazije 27/II, 11000 BELGRADF

Special terms for developing countries are obtainable on application to the WHO Representatives or WHO Regional Offices listed above or the World Health Organization, Distribution and Sales Service, 1211 Geneva 27, Switzerland. Orders from countries where sales agents have not yet been appointed may also be sent to the Geneva address, but must be paid for in pounds sterling, US dollars, or Swiss francs. UNESCO book coupons may also be used. Prices are subject to change without notice.

