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

Environmental Health Criteria 40

ENDOSULFAN

Published under the joint sponsorship of
the United Nations Environment Programme,
the International Labour Organisation,
and the World Health Organization

World Health Organization
Geneva, 1984

The **International Programme on Chemical Safety (IPCS)** is a joint venture of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. The main objective of the IPCS is to carry out and disseminate evaluations of the effects of chemicals on human health and the quality of the environment. Supporting activities include the development of epidemiological, experimental laboratory, and risk-assessment methods that could produce internationally comparable results, and the development of manpower in the field of toxicology. Other activities carried out by IPCS include the development of know-how for coping with chemical accidents, coordination of laboratory testing and epidemiological studies, and promotion of research on the mechanisms of the biological action of chemicals.

ISBN 92 4 154180 6

PRINTED IN FINLAND

84/6230 – VAMMALA – 5500

CONTENTS

TASK GROUP MEETING ON ENVIRONMENTAL HEALTH CRITERIA FOR ORGANOCHLORINE PESTICIDES OTHER THAN DDT (ENDOSULFAN, QUINTOZENE, TECNAZENE, TETRADIFON)

Members

Dr E. Astolfi, Faculty of Medicine of Buenos Aires, Buenos Aires, Argentina

Dr I. Desi, Department of Environmental Hygienic Toxicology, National Institute of Hygiene, Budapest, Hungary (Vice-Chairman)

Dr R. Drew, Department of Clinical Pharmacology, Flinders University of South Australia, Bedford Park, South Australia

Dr S.K. Kashyap, National Institute of Occupational Health, Ahmedabad, India

Dr A.N. Mohammed, University of Calabar, Calabar, Nigeria

Dr O.E. Paynter, Office of Pesticide Programs, US Environmental Protection Agency, Washington DC, USA

Dr W.O. Phoon, Department of Social Medicine and Public Health, Faculty of Medicine, University of Singapore, Outram Hill, Singapore (Chairman)

Dr D. Wassermann, Department of Occupational Health, The Hebrew University, Hadassah Medical School, Jerusalem, Israel

Representatives of Other Organizations

Dr H. Kaufmann, International Group of National Associations of Agrochemical Manufacturers (GIFAP)

Dr V.E.F. Solman, International Union for Conservation of Nature and Natural Resources (IUCN), Ottawa, Ontario, Canada

Secretariat

Dr S. Dobson, Institute of Terrestrial Ecology, Monks Wood Experimental Station, Abbots Ripton, Huntingdon, United Kingdom (Temporary Adviser)

Secretariat (contd).

Dr M. Gilbert, International Register for Potentially Toxic Chemicals, United Nations Environment Programme, Geneva, Switzerland

Dr K.W. Jager, Division of Environmental Health, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland (Secretary)

Dr D.C. Villeneuve, Health Protection Branch, Department of National Health and Welfare, Tunney's Pasture, Ottawa, Ontario, Canada (Temporary Adviser) (Rapporteur)

Mr J.D. Wilbourn, Unit of Carcinogen Identification and Evaluation, International Agency for Research on Cancer, Lyons, France

NOTE TO READERS OF THE CRITERIA DOCUMENTS

While every effort has been made to present information in the criteria documents as accurately as possible without unduly delaying their publication, mistakes might have occurred and are likely to occur in the future. In the interest of all users of the environmental health criteria documents, readers are kindly requested to communicate any errors found to the Manager of the International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda, which will appear in subsequent volumes.

In addition, experts in any particular field dealt with in the criteria documents are kindly requested to make available to the WHO Secretariat any important published information that may have inadvertently been omitted and which may change the evaluation of health risks from exposure to the environmental agent under examination, so that the information may be considered in the event of updating and re-evaluation of the conclusions contained in the criteria documents.

* * *

A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Palais des Nations, 1211 Geneva 10, Switzerland (Telephone no. 988400 - 985850).

ENVIRONMENTAL HEALTH CRITERIA FOR ENDOSULFAN

Following the recommendations of the United Nations Conference on the Human Environment held in Stockholm in 1972, and in response to a number of World Health Resolutions (WHA23.60, WHA24.47, WHA25.58, WHA26.68), and the recommendation of the Governing Council of the United Nations Environment Programme, (UNEP/GC/10, 3 July 1973), a programme on the integrated assessment of the health effects of environmental pollution was initiated in 1973. The programme, known as the WHO Environmental Health Criteria Programme, has been implemented with the support of the Environment Fund of the United Nations Environment Programme. In 1980, the Environmental Health Criteria Programme was incorporated into the International Programme on Chemical Safety (IPCS). The result of the Environmental Health Criteria Programme is a series of criteria documents.

A WHO Task Group on Environmental Health Criteria for Organochlorine Pesticides other than DDT (Endosulfan, Quintozene, Tecnazene, Tetradifon) was held at the Health Protection Branch, Department of National Health and Welfare Ottawa from 28 May - 1 June, 1984. The meeting was opened by Dr E. Somers, Director- General, Environmental Health Directorate, and Dr K.W. Jager welcomed the participants on behalf of the three co-sponsoring organizations of the IPCS (UNEP/ILO/WHO). The Task Group reviewed and revised the draft criteria document and made an evaluation of the health risks of exposure to endosulfan.

The drafts of this document were prepared by Dr D.C. Villeneuve of Canada and Dr S. Dobson of the United Kingdom.

The efforts of all who helped in the preparation and finalization of the document are gratefully acknowledged.

* * *

Partial financial support for the publication of this criteria document was kindly provided by the United States Department of Health and Human Services, through a contract from the National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA - a WHO Collaborating Centre for Environmental Health Effects.

1. SUMMARY AND RECOMMENDATIONS

1.1 SUMMARY

1.1.1 Identity, analytical methods, and sources of exposure

Technical endosulfan (6,7,8,9,10, 10-hexachloro-1,5,5a,6, 9,9a, hexahydro 6,9-methano-2,4,3-benzodioxathiepin, 3-oxide) is a brown crystalline substance consisting of alpha- and beta-isomers in the ratio of approximately 70:30. It is used in a formulated form as a broad-spectrum contact and stomach insecticide mainly in agriculture and, in some countries, in public health.

The method of choice for its determination is gas chromatography combined with electron capture detection. In considering residue levels, the sum of the alpha- and beta-isomers plus the endosulfan sulfate metabolite, which is similar in toxicity to the parent compound, have to be considered.

The main source of exposure of the general population is food, but residues have generally been found to be well below the FAO/WHO maximum residue limits. Because of its use in tobacco farming, smoking may be an additional source of endosulfan exposure.

1.1.2 Environmental concentrations and exposures

Both endosulfan isomers are fairly resistant to photodegradation, but the metabolites endosulfan sulfate and endosulfan diol are susceptible to photolysis. Its half-life in water is estimated to be 4 days, but anaerobic conditions and/or a low pH will lengthen the half-life. In water, it is mainly degraded to endosulfan diol. Fish are extremely sensitive to endosulfan and fish kills have been reported as a result of the discharge of endosulfan into rivers. Agricultural run-off has not caused such a problem.

In soil, the alpha-isomer disappears more rapidly than the beta isomer. Endosulfan sulfate is the major degradation product in soil. These compounds are not prone to leaching.

Biodegradation in soil and water is dependent on climatic conditions and on the type of microorganisms present.

1.1.3 Kinetics and metabolism

Endosulfan can be absorbed following ingestion, inhalation, and skin contact. Following oral or parenteral dosing, it is rapidly excreted via faeces and urine. Following acute over-exposure, high endosulfan concentrations

can temporarily be found in the liver; the concentration in plasma decreases rapidly. The major metabolities are endosulfan sulfate and endosulfan diol.

1.1.4 Studies on experimental animals

Endosulfan is moderately to highly toxic according to the scale of Hodge & Sterner (1956). The oral LD_{50} in the rat ranges from 18 to 355 mg/kg body weight. WHO (1984) classified endosulfan in Class II: technical products moderately hazardous. One of its metabolites, endosulfan sulfate, has the same order of toxicity as endosulfan.

Signs of acute intoxication include neurological manifestations, such as hyperactivity, muscular twitching, and convulsions, sometimes followed by death.

In rats, induction of hepatic mixed-function oxidases was observed after administration of endosulfan for 7 days at 2.5 mg/kg body weight per day. At higher doses (100 mg/kg in the diet for 104 weeks), testicular atrophy and renal tubular damage with interstitial nephritis were observed. The long-term, no-observed-adverse-effect level in rats was 30 mg/kg of diet (1.5 mg/kg body weight) and 0.75 mg/kg body weight in dogs. Protein-deficient rats are more sensitive to acute toxic effects of endosulfan.

Adequate data were not available on effects on reproduction, or teratogenic or embryotoxic effects. Negative or conflicting results were obtained in short-term tests for genetic activity. Carcinogenicity studies on mice and rats were difficult to evaluate because of inadequate reporting or early death in males; however, there was no indication of carcinogenic activity in females.

1.1.5 Effects on man

Several cases of accidental and suicidal poisoning have been reported. In fatal cases, death occurred within a few hours of ingestion. Signs of poisoning included vomiting, restlessness, irritability, convulsions, pulmonary oedema, and cyanosis. EEG changes have been reported in occupationally overexposed persons. Cases of poisoning in production workers have been reported, but occurred only when safe handling procedures were neglected.

1.1.6 Effects on the environment

Endosulfan is not readily bioaccumulated and it is not persistent in biological tissues. It is hazardous as an acute poison for some aquatic species, particularly fish, even at application rates recommended for wetland areas. It is

moderately toxic for honey bees. It is moderately to highly toxic for birds in a laboratory setting, but no poisonings have been reported under field conditions.

1.2 Recommendations

1. Precautions should be taken to avoid contamination of surface and drinking-water supplies during spraying. Where necessary, residue levels of endosulfan in drinking-water should be reduced by proper water treatment.

2. In countries where endosulfan is used for tsetse fly control, exposed populations should be monitored for potential adverse health effects.

3. Research is required to determine whether biological monitoring can be used as an early warning of endosulfan exposure.

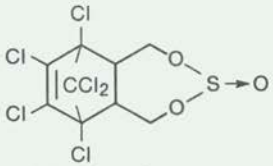
4. Further research is required to investigate possible reproductive, teratological, and embryotoxic effects.

5. An adequate carcinogenicity study should be carried out.

2. IDENTITY, ANALYTICAL METHODS AND SOURCES OF EXPOSURE

2.1 Identity

Chemical structure:



Molecular formula: $C_9H_6Cl_6O_3S$

CAS chemical name: 6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxa-thiepin-3-oxide

Common trade names: Benzoepin, Beosit, Chlorthiepin, Cyclodan, FMC 5462, Insectophene, Kop-thiodan, HOE 2671, Malix, NCI-C00566, NIA 5462, Thifor, Thimul, Thiodan, Thiofor, Thiomul, Thionex, Thiosulfan, Tionel, Tiovel. Formulations under other trade names may also exist.

CAS registry number: 115-29-7

Relative molecular mass: 406.9

Endosulfan was developed and introduced in the mid 1950s (Maier-Bode, 1968). Technical endosulfan is obtained through the Diels-Alder addition of hexachlorocylopentadiene and cis-butene-1,4-diol, followed by reaction of the addition-product with thionyl chloride (Canada, National Research Council, 1975). Technical endosulfan consists of a mixture of alpha- and beta-isomers in the approximate ratio of 70:30.

2.2 Properties and Analytical Methods

2.2.1 Physical and chemical properties

Technical endosulfan is usually sold in the form of brown crystalline flakes with a terpene odour (Maier-Bode, 1968). It has a melting point of 79 - 100 °C (Canada, National Research Council, 1975) and a vapour pressure of $1 \cdot 10^{-5}$ mm Hg at 25 °C. Its solubility in water is low: 60 -

150 µg/litre (Canada, National Research Council, 1975), and increases with decreasing pH (Shuttleworth, 1971). Solubility in other solvents varies from 5 - 65% (Maier-Bode, 1968; Canada, National Research Council, 1975).

Endosulfan is available as a wettable powder, granules, emulsifiable concentrates, dusts, and as ultra-low-volume (ULV) formulations.

2.2.2 Analytical methods

Methods for the clean-up and determination of endolsulfan have been summarized by Maier-Bode (1968), Canada, National Research Council (1975), and Goebel et al., (1982), but the sensitivities and recoveries for the various methods are not always given. Although colorimetric techniques, thin-layer chromatography, and bio-assays have been used for the determination of endosulfan, the most recent method involves a combination of gas chromatography with electron capture detection (GC-EC).

The sensitivity of assays in water ranged from 0.01 - 2.0 g/litre with recoveries generally greater than 90% (Wegman & Greve, 1978; 1980; Frank et al., 1979a). In soil and sediment, assays were not as sensitive, ranging from 0.001 to 0.1 mg/kg with recoveries between 80 - 110% but usually less than 90% (Miles & Harris, 1973; Frank et al., 1976; Carey et al., 1979). Biological samples such as animal and plant tissues, milk, etc., normally require more extensive clean-up procedures (i.e., column methods). Sensitivities from 0.2 to 10 µg/kg were usual with most recoveries greater than 90% (Cheng & Braun, 1977; Chopra & Mahfouz, 1977; Frank et al., 1979a; Zanini et al., 1980). Samples with a high sugar content gave erroneous results, but methods have been developed to overcome the problem (Shuttleworth, 1971). Clean-up methods employing high-pressure liquid chromatography (HPLC) have been used, which reduce the time involved in the preparation of such samples (Demeter & Heyndrickx, 1979).

It should be noted that detection limits for the alpha- and beta-isomers of endosulfan usually differ, the alpha-isomer being easiest to detect (Goebel et al., 1982). At low concentrations, the identification of endosulfan residues can be hampered by a variety of other pesticides or plant components. Endosulfan residues in environmental samples can only be considered to be valid if alpha- and beta- together with endosulfan sulphate are found simultaneously. Validation can be achieved by methods summarized by Goebel et al. (1982).

3. USES, ENVIRONMENTAL SOURCES, TRANSPORT AND DISTRIBUTION

3.1 Uses

Endosulfan is a contact and stomach poison that has been used to control insects such as the Colorado potato beetle, flea beetle, cabbageworm, peach tree borer, and tarnished plant bug, as well as several species of aphid and leafhopper (Canada, National Research Council, 1975). It is used in countries throughout the world to control pests on fruit, vegetables, tea, and on non-food crops such as tobacco and cotton (FAO/WHO, 1968). Depending on the type of crop and the area in which it is grown, application rates usually range between 0.45 kg ai and 1.4 kg/ha, but both smaller and larger doses have occasionally been used. Minimum time intervals between the last application and harvesting are prescribed in most countries and vary between 0 and 42 days, depending on the crop, type of formulation used, the mode of application, tolerances, and agronomic needs (Hoechst, 1977).

In addition to its agricultural use, and its use in the control of the tsetse fly, endosulfan is used as a wood preservative and for the control of home garden pests (Canada, National Research Council, 1975). A list of uses together with respective quantities used in some countries appear in Table 1.

Figures for world production are not available but, after DDT was banned, the use of endosulfan in Canada increased quite rapidly until the mid 1970s (Canada, National Research Council, 1975). At present, world production might be in the order of 10 000 tonnes per year.

An estimated several tens of thousands of drums containing chemical waste including endosulfan, which have been found in and along the North Sea, are a potential source of pollution (Greve, 1971b).

3.2 Transport and Distribution

Air

Endosulfan is most frequently applied using air-blast equipment or boom sprayers with a resulting potential for local drift and air pollution. Keil et al. (1972) included 4-metre guard rows between treated and control plots. The day after treatment, endosulfan levels of 0.091 - 0.529 mg/kg were found in the control plots, indicating a considerable drift of the insecticide between the plots. Eighteen days after treatment, an endosulfan level of 0.037 mg/kg was still detectable in the control plots. Endosulfan was also found in

Table 1. Usage data for endosulfan from selected countries[a]

Area	Quantity	Year	Uses
Colombia	21 834 kg	1982	agricultural insecticide recommended
	15 918 kg	1981	in the growth of cotton, rice,
	16 868 kg	1980	corn, cabbage, sorghum
Malaysia			insecticide
Sweden	2000 kg	1981	horticultural use against insects and mites
Tanzania	2130 tonne	1980-83	applied to various crops to control chewing, mining, and sucking pests
Thailand	63 420 kg	1982	insecticide
	114 800 kg	1981	
	99 550 kg	1980	
	27 587 kg	1979	
	24 519 kg	1978	
	18 482 kg	1977	
	1540 kg	1976	
United Kingdom	27.58 tonne per year	1975-79	insecticide and acaricide
USA	511-704 tonne	1980	insecticide on various crops;
	454 tonne	1971	insecticide on potatoes, tobacco, and fruits

[a] From: IRPTC, personal communication, 1984.

the water and sediments of streams adjacent to sprayed crops (Canada, National Research Council, 1975).

Residues of alpha- and beta-endosulfan have been detected in ambient air samples in the USA (Alabama, Arkansa, Illinois, Kansas, Kentucky, Louisiana, Maine, Montana, New Mexico, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, South Dakota, Tennessee), though not frequently (Kutz et al., 1976). Between 1970 and 1972, alpha-endosulfan was found in 2.11% of samples tested in the USA at a mean concentration of 111.9 ng/m^3 and a maximum of 2256 ng/m^3. During the same period, beta-endosulfan was present in 0.32% of the samples at a mean of 22.0 ng/m^3 and a maximum concentration of 54.5 ng/m^3. This information suggests that the alpha-isomer is more persistent in air. Both alpha- and beta- endosulfan have been detected at levels up to 12 ng/litre in precipitation in the Great Lakes area of Canada and the USA (Strachan et al., 1980).

Water

Endosulfan contamination does not appear to be widespread in the aquatic environment but has been found in agricultural run-off and rivers in industrialized areas where it is manufactured or formulated. Estimates for the aquatic half-life of both isomers of endosulfan range from 4 days in river water subjected to municipal and industrial runoff (Eichelberger & Lichtenberg, 1971) to 7 days (Greve, 1971a) in normal water (pH 7, with normal oxygen saturation). However, the half-life was profoundly affected by pH and oxygen content; a drop in either of these two parameters inhibited endosulfan degradation. Under anaerobic conditions at pH 7, the half-life increased to approximately 5 weeks, and at pH 5.5, the half-life was nearly 5 months (Greve, 1971a). More than 80% of the endosulfan present can be removed from water by filtration and almost all by treatment with activated charcoal (Greve, 1971a).

Studies of endosulfan in agricultural run-off, in the USA, indicate that, if rain follows within 4 days of application (0.35 kg/ha), residues can average 16 µg/litre run-off (Epstein & Grant, 1968).

A widespread fish kill was observed in 1969, when an estimated quantity of 30 kg of endosulfan was discharged into the section of the Rhine river that runs through the Federal Republic of Germany (Sievers et al., 1972). Annual monitoring of endosulfan (drinking water, ground water, rain water, surface water) since 1969 in the Netherlands has revealed that maximum levels have dropped approximately 3 orders of magnitude, with maximum concentrations in 1977 of 0.03 µg/litre (Wegman & Greve, 1980).

Endosulfan was found only once in rivers draining orchard areas in Ontario, during 2-week sampling periods in 1973 at levels ranging from 0.47 to 0.083 µg/litre (Frank, unpublished data, 1973). Studies on water samples from Lake Erie, Ontario, and the St. Lawrence River showed that approximately 15% of the samples contained endosulfan at levels ranging from 0.005 to 0.060 µg/litre (Natural Research council, 1975). In recent work in Western Canada, endosulfan was found (0.011 µg/litre) in one out of 1400 surface water samples, indicating that water contamination by this insecticide was not widespread (Gummer, 1980).

No alpha- or beta-endosulfan or endosulfan sulfate residues were detected (method sensitivity, 10 µg/litre) in well waters located near treated fields in Wisconsin and Florida, USA, 282 and 100 days, respectively, after the last endosulfan application. The treated fields in Wisconsin received seven foliar applications of endosulfan at 0.56 kg/ha (2 in 1966 and 5 in 1969), while the fields in Florida were

treated with 10 - 16 foliar applications of endosulfan at 1.12 kg/ha over a 5-year period (Niagara Chemical Division, 1971).

Soil

Early work by Byers et al. (1965) indicated that the alpha-isomer dissipated more rapidly in the soil than the beta-isomer. The authors suggested that the latter was more strongly adsorbed on soil than the former. The results of field studies have since confirmed that the alpha-isomer has a shorter half-life (60 days) than the beta-isomer (900 days) (Steward & Cairns, 1974).

It was also suggested that endosulfan sulfate (the major degradation product in soil) accumulated at a rate comparable to the rate of loss of alpha- and beta-endosulfan. Endosulfan sulfate tended to be more stable than either of the 2 endosulfan isomers, but none of the 3 compounds was prone to leaching in soil (Stewart & Cairns, 1974).

The degradation of endosulfan, which was substantially reduced when the compound was incorporated into soil, halted during winter months (Niagara Chemical Division, 1966, Stewart & Cairns, 1974). A survey of agricultural soils in North America showed that endosulfan residue levels were typically below 1 mg/kg, with a few exceptions (4.78 mg/kg, 4.93 mg/kg) (Frank et al., 1976; Harris et al., 1977). A study from Italy revealed endosulfan soil residues ranging from 0.23 to 3.88 mg/kg (Sanna et al., 1979). Endosulfan has been detected in the sediments of drainage ditches (Miles & Harris, 1971; Niagara Chemical Division, 1971), rivers (Miles, 1976), and lakes (Canada, National Research Council, 1975). Concentrations ranged from trace amounts to 0.64 mg/kg dry weight (Miles et al., 1971).

Degradation of endosulfan appears to be different in sediments and in soil. Martens (1977) studied soil samples under a variety of conditions, including flooding, and demonstrated that the percentage of endosulfan diol was increased in the flooded soil samples and that a lower percentage of the sulfate was observed. Carbon dioxide production was measured in all samples and was highest under aerobic condition (Martens, 1977).

Abiotic degradation and bioaccummulation

Both alpha- and beta-endosulfan are fairly resistant to photodegradation (Schumacher et al., 1971; Schuphan et al., 1972), but the 2 dominant break-down products, endosulfan sulfate and endosulfan diol, are susceptible to photolysis (Fig. 1) (Schuphan et al., 1972). Technical endosulfan is

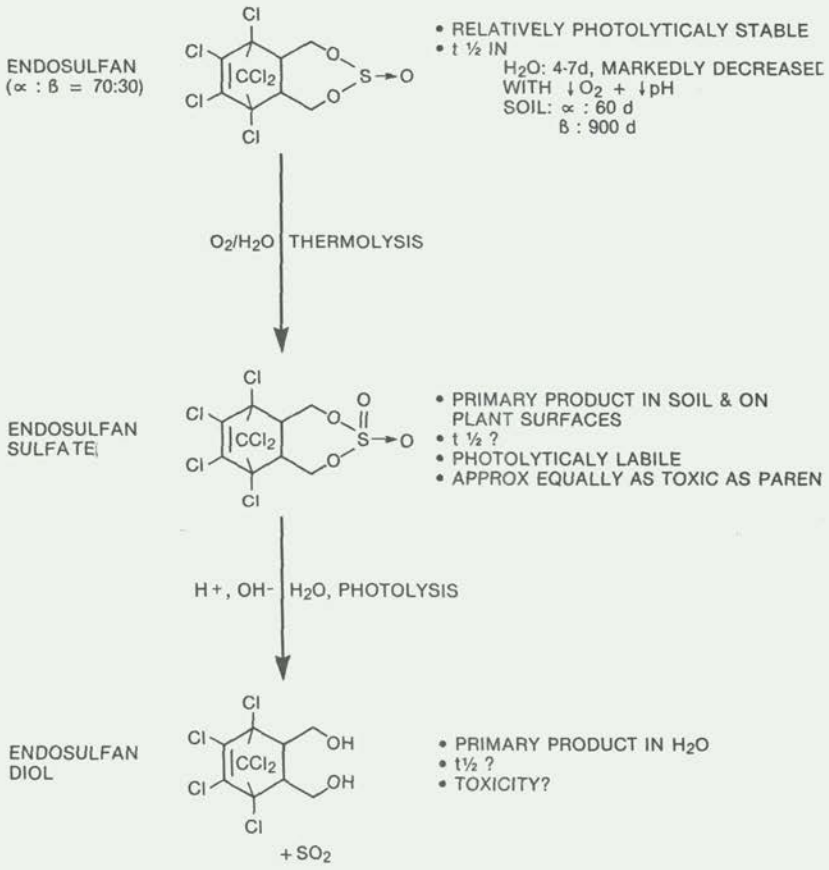


Fig. 1. Chemical degradation of endosulfan in the environment.

sensitive to moisture, acids, and alkali and will undergo slow hydrolyses producing sulfur dioxide (SO_2) and endosulfan alcohol via the intermediate endosulfan sulfate (FAO/WHO, 1968; Martens, 1977).

In soil and on plant surfaces, endosulfan sulfate is the primary degradation product of endosulfan (Cassil & Drummond, 1965; Martens, 1977) with lesser amounts of endosulfan diol and endosulfan lactone being produced. Although sunlight may be involved in the initiation of sulfate production, Archer et al. (1972) felt that thermolysis was the principle formation mechanism.

In aquatic environments (water and sediment), endosulfan diol was present together with smaller amounts of the sulfate and other compounds (Eichelberger & Lichtenberg, 1971; Martens, 1977).

Martens (1972) demonstrated the production of endosulfan and endosulfan diol by fungi, but the role that these and other microorganisms play in environmental degradation is not clear.

As a result of the higher solubility in water of endosulfan compared with most other organochlorine pesticides, it does not have the affinity for lipids that most related compounds have. Consequently, biomagnification and accumulation of endosulfan in food chains is less likely to occur. The typical response for most organisms exposed to endosulfan at below lethal levels, is to accumulate the compound up to a plateau, but clear the residues fairly rapidly once the source of contamination is removed. The higher the exposure level, the longer it takes to reach a plateau and the higher the plateau is. This response was demonstrated in mussels (Roberts, 1972), fish (Schoettger & Bier, 1970; Oeser & Knauf, 1973), and algae (Oeser & Knauf, 1973). An estimate of the half-life of endosulfan in fish was 3 days (Oeser & Knauf, 1973). Similar results have been found in mammals; summaries of data have been made by Maier-Bode (1968), Goebel et al. (1982), and US EPA (1982). Endosulfan sulfate was generally the only compound detected in tissues of animals exposed to endosulfan. In cattle (FAO/WHO, 1967), the concentration factors were small (0.5 in milk, 0.05 in muscle tissue, and 0.15 in fat), and residues cleared quite rapidly when endosulfan was removed from the diet. Other diet studies have produced similar results in sheep (Maier-Bode, 1968) and dogs (FMC Corp., unpublished data, 1963). No reports of endosulfan residues in human adipose tissue or breast milk were available.

In plants sprayed with endosulfan, initial residues on fruits and vegetables can vary from about 1 to 100 mg/kg; after 1 week, residues generally decrease to 20% or less of the initial amount (Canada, National Research Council, 1975).

3.3 Levels of Exposure

Air

Human exposure during endosulfan spraying for tsetse fly control using a helicopter in the Ivory Coast was assessed by means of exposure pads worn over or under light overalls (Copplestone et al., 1979). Three male volunteers were positioned within a village and three more in the area deliberately being sprayed. The men walked in the area during spraying and for 1 h afterwards. The application rate of the compound is not stated. Five cm square sections of 7 pads, 6 worn over and 1 worn under clothing, were analysed from each volunteer and the total exposure to endosulfan calculated assuming that all endosulfan measured on the pads was absorbed into the body, irrespective of clothing. An addition of 10% was made to the calculation as an estimate of respiratory absorption. Calculated values were compared with the dermal LD_{50} for rat of 74 mg/kg body weight. The men outside the village received 0.27% and those in the village 0.007% of the rat LD_{50}. The exposure calculated was an overestimate as it assumed that clothing offered no protection. The authors showed that the cotton overalls reduced the dose of endosulfan by the pads by a factor of at least 20.

Endosulfan has been shown to be released from a wood preservative into a room atmosphere over a 1-year period of observation (Zimmerli et al., 1979).

It is well-known that the respiratory route is a potential route of exposure to endosulfan (Oudbier et al., 1974; Wolfe, 1976), and a TLV has been established at 0.1 mg/m^3 (ACGIH, 1982).

Food

In the USA, endosulfan has been reported to be present in the market basket survey since 1967. Between the 1967 and the 1974-75 studies, the level of contamination decreased, but the proportion of food samples containing endosulfan increased. Endosulfan (alpha-, beta-isomer and the sulfate derivative) was present in 3 out of 360 food samples in the 1967-68 survey, at a concentration range of 0.008 - 0.134 mg/kg and was found in 1 sample of each of 3 food groups: garden fruits, leafy vegetables, and oils and fats (Corneliussen, 1969). The 1968-69 survey revealed that endosulfan was present in 16 out of 360 food samples with a range from 0.01 to 0.042 mg/kg. It was present in 7 out of 20 food samples, but only in 2 food groups, leafy vegetables and garden fruits (Johnson & Manske, 1977). Similar results for the above

food groups were found in Canada (Canada, National Research Council, 1975).

Endosulfan sulfate was also present in cow's milk from tobacco farming areas at levels of up to 0.010 mg/litre (Frank et al., 1970, 1979). Beck et al. (1966) reported that endosulfan could not be detected in the milk of cows that had been fed forage containing endosulfan at 0.41, 0.70, or 2.35 mg/kg for 21 days.

No endosulfan residues have been reported in market basket surveys from other countries and there are no reports of the daily human intake of endosulfan exceeding the FAO/WHO temporary ADI of 0.008 mg/kg body weight (FAO/WHO, 1982).

In general, endosulfan residues in food are well below the tolerance levels established for various food types by the FAO/WHO (1975a) (Table 2). These residue tolerances refer to the total residue of alpha- and beta-endosulfan and endosulfan sulfate.

Table 2. Endosulfan tolerances in food[a]

Food	FAO/WHO tolerance[b]
Tea (dry, manufactured)	30 mg/kg
Fruits and vegetables (other than exceptions noted)	2 mg/kg
Carrots, potatoes, sweet potatoes, bulb onions	0.2 mg/kg
Cottonseed	1.0 mg/kg
Cottonseed oil (crude)	0.4 mg/kg
Rice (in husk)	0.1 mg/kg
Milk and milk products (fat basis)	0.5 mg/kg
Fat and meat	0.2 mg/kg

[a] From: FAO/WHO (1975a).
[b] Calculated as the total of α- and β-endosulphan plus endosulfan sulfate.

High endosulfan residues have been found in tobacco leaves in both Canada and the USA. Pyrolysis studies on tobacco indicate that the alpha- and beta-isomers, the sulfate derivative, and a variety of other products are present in contaminated tobacco smoke (Chopra et al., 1978). Levels as high as 30.9 and 20 $\mu g/m^3$ were detected in Canada and the USA , respectively (Dorough, 1973; Cheng & Braun, 1977). Residues seem to consist primarily of endosulfan sulfate followed by the beta-isomer, then the alpha-isomer (Cheng & Braun, 1977).

Relative importance of different sources

With good agricultural practice, endosulfan residues in food should not be significant. Its use in tobacco farming has been discouraged (Cheng & Braun, 1977) but, if not regulated, could provide a significant route of exposure. As a rule, endosulfan concentrations in air and water are very low and localized, and accordingly of no significance as far as risk for general population is concerned.

No reports of endosulfan in breast milk have appeared in the literature. However, since endosulfan is used as a wood preservative and garden pesticide in some countries, direct exposure of infants and children remains a possibility.

Occupational exposure

Only 2 reports on occupational exposure were found; both involved workers who filled sacks with endosulfan powder. A total of 11 people were poisoned, all of whom experienced difficulties in concentration, vertigo, followed by epileptiform convulsions or stupor (FAO/WHO, 1975b). No further information on workers exposed during the production or spraying of endosulfan was available.

4. KINETICS AND METABOLISM

4.1 Animal Studies

Five days after a single oral administration (by gavage) of ^{14}C-labelled alpha-endosulfan in corn oil at 2 mg/kg body weight to female albino rats, totals of 75% and 13% of the dose were eliminated in the faeces and urine, respectively. With the same dose of ^{14}C-labelled beta-endosulfan, and under the same conditions, the values were 68% and 18.5%, respectively. When radio-labelled endosulfan was fed to rats at 5 mg/kg diet for 14 days, 56% was eliminated in the faeces and 8% in the urine. Maximum residues of endosulfan, which occurred in the kidney and liver, were 3 and 1 mg/kg, respectively. Metabolism studies using alpha- and beta-endosulfan did not reveal any appreciable differences in the fate of the 2 isomers in the rat (Dorough et al., 1978). Endosulfan was metabolized in rats to endosulfan diol, endosulfan hydroxyethers, endosulfan lactone, endosulfan sulfate, and some unidentified polar metabolites (Dorough et al., 1978). Similar metabolites of endosulfan were identified in mice (Deema et al., 1966; Schuphan et al., 1968).

Sheep given daily doses of endosulfan at 15 mg/kg body weight for 28 days, eliminated 20% of the dose in the faeces as the unchanged compound; only a small amount of endosulfan diol was detected in the urine. Endosulfan sulfate (0.1 mg/kg) was found in perirenal and mesenteric adipose tissues (Gorbach, 1965).

In rabbits, after a single intravenous (iv) injection of endosulfan at 2.0 mg/kg, the concentration in plasma declined rapidly. Thirty-seven percent of the dose was excreted in the urine as alpha-endosulfan and 11% as beta-isomer in the first 5 days (Gupta & Ehrnebo, 1979).

The distribution pattern of endosulfan in the plasma and brain was studied when rats were administered daily doses of 5 or 10 mg/kg body weight in peanut oil by gavage (approximately 1/20 and 1/10 LD_{50}) (2 alpha-:1 beta-isomer ratio) for 15 days (Gupta, 1978). On day 16, the rats that were dosed with 5 mg/kg had the following concentrations of the alpha-isomer in the brain: cerebrum, 3.76 mg/kg, cerebellum, 2.04 mg/kg; remaining parts of the brain, 2.66 mg/kg. The concentrations of the beta-isomer were 0.06 mg/kg in the cerebrum and 0.02 mg/kg in the cerebellum; no beta-isomer was detected in the other parts of the brain (Gupta, 1978). When the rats were fed the higher dose level the same pattern of isomers and metobolite was found, the only difference being that the concentrations were higher than in rats receiving the lower dose. Distribution of endosulfan was also investigated in the

cat brain. Following a single iv administration of 3 mg/kg body weight, groups of animals were sacrificed at selected time intervals and analysed for endosulfan content. The cerebrum had the highest concentration followed by the spinal cord, cerebellum, and the brain stem (Khanna et al., 1979).

4.2 Human Studies

Some human data were obtained following the analysis of a case of suicide in which an unknown amount of endosulfan was ingested (Demeter et al., 1977) in combination with alcohol. The individual died within 6 h after ingestion of the chemical. The tissue distribution of endosulfan is given in Table 3. It could not be concluded that death was due solely to the effects of endosulfan.

Table 3. Tissue distribution of endosulfan

Tissue	α-endosulfan (mg/kg)	β-endosulfan (mg/kg)
Liver	12.4	5.2
Kidney	2.48	1.8
Blood	0.06	0.015
Urine	1.78	0.87
Stomach content	2610	1900
Small intestinal content	190	99

5. STUDIES ON EXPERIMENTAL ANIMALS

The toxicity and the residue data on endosulfan have been reviewed by the Joint Meeting on Pesticide Residues (JMPR) in 1965, 1967, 1968, 1971, 1974, and 1982 (FAO/WHO, 1965, 1968, 1969, 1972, 1975a, 1983). For their conclusion, refer to section 8. We refer to these reports, which contain more detailed information on the toxicity studies and residue data than the present report. Moreover, several unpublished studies have been evaluated and reported there.

5.1 Short-Term Exposures

5.1.1 Single exposure

The LD_{50} of endosulfan varied widely depending on the route of administration, species, vehicle, and sex of the animal. The available acute toxicity data are summarized in Table 4. The clinical signs of toxicity include hyperactivity, tremors, and convulsions, followed by death (Boyd, 1972; Gosselin et al., 1976; Gupta, 1976).

Limited short-term studies on the dog showed that as little as 30 mg/kg body weight could be fatal (Canada, National Research Council, 1975), and 2.5 mg/kg body weight per day for 3 days induced toxic symptoms (FAO/WHO, 1968). The 2 stereoisomers have comparable LD_{50} values for the rat (Lindquest & Dahm, 1957).

Male rats given a single oral dose of endosulfan at 40 mg/kg body weight displayed acute neurotoxic manifestations and showed a significant increase in blood glucose, blood ascorbic acid, and blood and brain glutathione (Garg et al., 1980). There have been no published data on skin irritation or sensitization.

5.1.2 Repeated exposures

Endosulfan sulfate was fed to rats in the diet for 3 months at levels as high as 500 mg/kg (Canada, National Research Council, 1975); no effects were detected other than increased liver or kidney weight.

The same compound was administered to dogs for 3 months at levels ranging from 0.75 to 2.5 mg/kg body weight per day. The lowest dose did not have any effect, but the highest dose was not tolerated and the 1.5 mg/kg dose induced occasional signs of toxicity. It was concluded that endosulfan sulfate appeared to have the same order of toxicity as endosulfan (Canada, National Research Council, 1975).

Table 4. Acute toxicity of endosulfan in different animal species

Species	Sex	Route	Vehicle	LD_{50} (mg/kg body weight)	Reference
Rat	NS	oral	olive oil	64	Truhaut et al. (1974)
Rat	NS	oral	95% alcohol	40 - 50	FAO/WHO (1968)
Rat	M	oral	peanut oil	43	Gaines (1969)
Rat	M	oral	cottonseed oil	121	Boyd (1972d)
Rat	F	oral	peanut oil	18	Gaines (1969)
Rat	NS	oral	NS	355	Boyd & Dobos (1969)
Rat	NS	ip	95% alcohol	8	FAO/WHO (1965)
Rat	N	dermal	xylene	130	Gaines (1969)
Rat	F	dermal	xylene	74	Gaines (1969)
Rat	NS	dermal	cottonseed oil	681	Gupta & Gupta (1979)
Rat	NS	inhalation	NS	350 (mg/m^3)[a]	Gupta & Gupta (1979)
Mouse	F	ip	95% alcohol	7.5	Gupta (1976)
Mouse	F	ip	alcohol & peanut oil	13.5	Gupta (1976)
Mouse	M	ip	95% alcohol	6.9	Gupta (1976)
Mouse	M	ip	alcohol & peanut oil	12.6	Gupta (1976)
Rabbit	NS	dermal	cottonseed oil	147	Gupta & Gupta (1979)
Rabbit	NS	percutaneous	cottonseed oil	360	Gupta & Gupta (1979)
Rabbit	NS	dermal	oil solvent	359	Martin (1968)
Rabbit	NS	dermal	chloroform	187	Gupta & Chandra (1975)
Guinea-pig	NS	dermal	cottonseed oil	1000	Gupta & Gupta (1979)
Hamster	NS	oral	olive oil	118	Truhaut et al. (1974)

[a] Value represents the LC_{50} in mg/m^3 for a 4-h exposure period.

NS = Not stated.
M = Male.
F = Female.

When rats were treated with daily oral doses of endosulfan at 1.6 - 3.2 mg/kg body weight, for 12 weeks, no effects were observed on growth-rate (FAO/WHO, 1967). Administration of dietary levels of endosulfan ranging from 2 to 200 mg/kg to male rats for 2 weeks, resulted in changes in mixed-function oxidase activity (Den Tonkelaar et al., 1974). Endosulfan at the highest level (200 mg/kg, approximately 10 mg/kg body

weight per day) was found to induce mixed-function oxidases activity (aniline hydroxylase and aminopyrine demethylase).

Endosulfan was administered to female rats at daily oral doses of 1.0, 2.5, or 5.0 mg/kg body weight for 7 or 15 days (Gupta & Gupta, 1977). No changes were observed in body, ovary, or adrenal weights. Liver weight increased and pentobarbital sleeping time decreased at the 2 highest dose levels and both time intervals. The results of subsequent studies (Agarwal et al., 1978) showed that the 2 highest levels resulted in induction of aminopyrine demethylase and aniline hydroxylase activities as well as a dose-related increase in amino-transferase activity and spontaneous lipid peroxidation.

Male rats were dosed by oral intubation with endosulfan at levels of 5 or 10 mg/kg body weight per day for 15 days (Gupta, 1978). A reduction in body weight gain was observed at the higher dose, and 3 out of 12 animals died during testing.

In a separate study (Garg et al., 1980), male rats were dosed orally with endosulfan at 0.625, 5.0, or 20 mg/kg body weight, 6 days per week, for 7 weeks. Animals receiving the highest dose showed a slight increase in blood glucose and a decrease in plasma calcium levels.

Endosulfan was administered orally to 4 dogs for 3 days at 2.5 mg/kg body weight (FAO/WHO, 1967). Vomiting was observed in one dog and vomiting, tremors, convulsions, rapid respiration, and mydriasis in the 3 remaining animals. Three other groups of dogs, 2 males and 2 females per group, were administered endosulfan orally at levels of 0.075, 0.25, or 0.75 mg/kg body weight for 6 days a week over a 1-year period (FAO/WHO, 1968). No signs of toxicity were observed. At autopsy, gross and microscopic examination of the tissues did not reveal any differences between treated and control animals.

When endosulfan was administered to cats (Misra et al., 1980) at levels of 2, 3, or 4 mg/kg body weight, muscular twitching was observed in all treatment groups, followed by convulsions. At the 2 higher dose levels, there was a marked rise in blood glucose levels after 15 and 30 min with a gradual fall up to 4 h. Adrenalectomy prevented this rise. Cats were fasted for 1 - 2 h before this study and were then injected with a single intravenous dose of endosulfan (2, 3, or 4 mg/kg) through a cannula inserted into the femoral vein. Blood was drawn from the femoral vein after 0, 15, and 30 min, and 1, 2, and 4 h.

Endosulfan is able to inhibit sodium-, potassium-, and magnesium-dependent ATPase enzymes in rainbow trout brain (Davis & Wedemeyer, 1971).

5.2 Long-Term Exposures

Groups of 25 male and 25 female rats received technical grade endosulfan at 10, 30, and 100 mg/kg diet for 104 weeks (FAO/WHO, 1968). Survival of the female rats in the 10 and 30 mg/kg groups was lower than that in the female control group, during the second year of exposure. In the 100 mg/kg female group, survival was significantly lower after 26 weeks and abnormalities were observed in weight gain and haematological parameters. At autopsy, the relative weight of the testes in the 10 mg/kg male group was significantly lower than in the control group. Significant histopathological findings were apparent only in the 100 mg/kg male group. In these animals, the kidneys were enlarged and there were signs of renal tubular damage with interstitial nephritis. Hydropic changes were seen in liver cells. The tumor incidence in all test groups was within the range of the control group.

In a study reported by the Commission of European Communities (CEC, 1981), male and female dogs were dosed with endosulfan (by capsule), 6 days a week for 10 months. The dose levels ranged from 0.075 to 0.75 mg/kg body weight. No gross or microscopic evidence of toxicity was noted.

The Joint Meeting on Pesticide Residues (JMPR) reviewed the toxicity data on endosulfan in its 1982 meeting (FAO/WHO, 1983) and concluded that the following levels did not cause any toxicological effects:

rat: 30 mg/kg diet, equivalent to 1.5 mg/kg body weight; and

dog: 0.75 mg/kg body weight per day (administered by capsules)

5.3 Reproduction Studies

Adequate data are not available.

5.4 Mutagenicity

Endosulfan was not mutagenic in E. coli or S. typhimurium (Fahrig, 1974; Moriya et al., 1982). It did not induce mitotic conversion in Saccharomyces cerevisae (Fahrig, 1974). However, in one study, technical grade endosulfan was reported to induce reverse mutations, cross overs, and mitotic gene conversions in Saccharomyces cerevisiae (Yadav et al., 1982).

Endosulfan did not induce chromosomal abberations in bone marrow cells or spermatogonia of male rats treated with 5

daily oral doses of 11 - 55 mg/kg body weight (Dikshith & Datta, 1978).

An increased number of micronuclei induced in the bone marrow erythrocytes of mice treated with endosulfan in the drinking-water (43.3 mg/litre) for 2 consecutive days was not statistically significant (Usha Rani et al., 1980). Negative results were observed in a dominant lethal test in mice (Canada, National Research Council, 1975).

5.5 Teratogenicity

Adequate data are not available.

5.6 Carcinogenicity

The carcinogenicity of technical grade endosulfan was tested using Osborne-Mendel rats and B6C3F1 mice (NCI Tech. Series, 1978). The time-weighted average high and low endosulfan concentrations in the diet for male rats were 952 and 408 mg/kg; for female rats 445 and 223 mg/kg; for male mice 6.9 and 3.5 mg/kg; and for female mice 3.9 and 2.0 mg/kg. Testing of high-dose male rats was terminated during week 82 and low dose male rats during week 74.

Female rats were administered endosulfan for 78 weeks followed by a 33-week observation period. Mice were administered the chemical for 78 weeks and observed for an additional 14 weeks. A high early mortality rate in male rats and mice precluded any conclusions concerning carcinogenicity. Under the conditions of the assay, it was concluded that endosulfan was not carcinogenic for female Osborne-Mendel rats or female B6C3F1 mice.

In a large scale screening study, 2 strains of male and female hybrid mice [(C57BL/6 x C3H/Anf)F_1] and [(C57BL/6 x AKR)F_1] were given 2.15 or 3.0 mg/kg body weight endosulfan by oral intubution on days 7 - 28 of age followed by the feeding of diets containing concentrations of 3 or 6 mg/kg diet for 78 weeks (Innes et al., 1969). Although no conclusion could be drawn about its carcinogenic potential, endosulfan was reported as being one of the compounds requiring further study.

5.7 Factors Influencing Toxicity

Rats subjected to protein-deficient diets were more susceptible to the acute toxic effects of endosulfan (Boyd, 1972). The LD_{50} for rats on normal lab chow was reported to be 121 mg/kg body weight, compared with 5 mg/kg for rats on a protein-deficient diet.

6. EFFECTS ON MAN

6.1 Poisoning Incidents

A report from Bulgaria described the circumstances, clinical symptoms, and morphological changes in 5 cases associated with endosulfan poisoning (Terziev et al., 1974). These cases comprised 2 suicides and 3 accidental poisonings. Death generally followed a few hours after ingestion. The clinical symptoms included vomiting, agitation, convulsions, cyanosis, dyspnoea, foaming at the mouth, and noisy breathing.

Another report lists the findings on 2 cases (apparently suicides) of men who died after ingesting endosulfan (Demeter & Heyndrickx, 1978). Again, death was noted to occur within a few hours of ingestion, and significant post-mortem findings included congested and oedematous lungs and cyanosis. Tissue analysis for residues indicated the possible synergistic effect of endosulfan and alcohol in one patient (Demeter et al., 1977) and endosulfan, alcohol, and dimethoate, an organophosphorous insecticide, in the second.

6.2 Occupational Exposure

Three cases of poisoning in workers employed in a chemical factory have been reported (Israeli et al., 1969; Tiberin et al., 1970). Poisoning occurred when the men filled bags with insecticide without wearing protective clothing and masks. Symptoms developed after 3 weeks, 1 month, and 18 months, respectively, following daily exposure, and consisted of headaches, restlessness, irritability, vertigo, stupor, disorientation, and epileptiform convulsive seizures.

Electroencephalogram changes were noted. Endosulfan has been shown to persist on the hands of pest control operators for up to 31 days after exposure. No clinical symptoms were observed (Kazen et al., 1974).

6.3 Treatment of Poisoning

In case of overexposure, medical advice should be sought immediately.

If the pesticide has been ingested, gastric lavage should be performed with 2 - 4 litres of tap water followed by saline purgatives (30 g sodium sulfate in 250 ml of water). Barbiturates or diazepam should be given intraveneously in sufficient dosage to control restlessness or convulsions. Mechanical respiratory assistance with oxygen may be required. Calcium gluconate (10% in 10 ml) should be injected

4-hourly. Contraindications are oily purgatives, epinephrine, and other adrenergic drugs and central stimulants of all types (FAO/WHO, 1975b).

7. EFFECTS ON THE ENVIRONMENT

7.1 Toxicity for Aquatic Organisms

The most representative studies on the toxicity of endosulfan for aquatic organisms are summarized in Table 5. A more comprehensive table, listing different conditions and exposure times, is available on request from IRPTC, Geneva, Switzerland.

Ramachandran et al. (1981) looked at the effects of a low concentration of endosulfan (50 µg/litre) on photosynthesis and respiration in some common seaweeds. The red alga Gracilaria verrucosa showed the highest tolerance to endosulfan. Photosynthesis was 96.2% of control levels and respiration was stimulated to 112.32%. The 3 other algal species Gratiloupia, Enteromorpha intestinalis, and Cheatomorpha linum showed photosynthetic rates of 80.4, 83.6, and 84.6% of control levels and respiration rate of 107.38, 86.97, and 93.6%, respectively. The respiration to photosynthesis ratio was lower than control levels for all 4 species.

The toxic effects of endosulfan, determined for 1 freshwater and 2 seawater species of crustacea, are summarized in Table 5. McLeese & Metcalfe (1980) studied the effects of including sediment in test vessels. For the shrimp Crangon, 96-h LC_{50} values for endosulfan increased from 0.2 µg/litre to 6.9 µg/litre with the inclusion of sediment. The mortality rate estimate of Butler (1963) for the brown shrimp included animals immobilized by the material and showing no clear signs of life. Twenty-four- and 48-h LC_{50} values for the freshwater scud Gammarus lacustris were 9.2 and 6.4 µg/litre, respectively (Sanders, 1969).

McLeese et al. (1982) tested the toxicity of endosulfan for the ragworm Nereis virens with and without sediment in the test vessels. The LC_{50} for endosulfan in 288-h tests were 100 µg/litre with sea water and 340 µg/kg with sediment. Symptoms of stress in the worms included eversion of the proboscis, lost equilibrium, and immobilization. Stressed worms in sediment tests emerged from the sediment and subsequently did not burrow, even after the sediment was changed.

Nair (1981) tested endosulfan toxicity with a range of concentrations from 2.6 and 2.9 µg/litre on the freshwater mite Hydrachna trilobata viets and reported a 48-h LC_{50} value of 2.8 µg/litre. The small difference between the no-effect and lethal dosages of endosulfan is typical for many different aquatic organisms. A 96-h LC_{50} of 1890 µg/litre was reported by Holcombe et al. (1983) for adult freshwater

Table 5. Toxicity of endosulfan for aquatic organisms

Organism	Size/ age	Grade	Temp (°C)	pH	Stat/ flow	Sal (°/00)	Effect	Parameter	Conc. (µg/litre)	Reference
eastern oyster (Crassostrea virginica)			28			22	decrease in shell growth	96-h EC50	65	Butler (1963)
polychaete worm (Nereis nereis)	adult		9-10		stat		death	12-day LC_{50}	100	McLeese et al. (1982)
	adult		9-10		stat		death	12-day LC_{50}	340[a]	McLeese et al. (1982)
Cladoceran (Daphnia magna)			10	7.4		45[b] 38[c]	death	96-h LC_{50}	52.9	Schoettger (1970)
shrimp	adult		20		stat		death	96-h LC_{50}	0.2	McLeese & Metcalfe (1980)
(Crangon septemspinosa)	adult		10		stat		death	96-h LC_{50}	6.9[a]	McLeese & Metcalfe (1980)
blue crab (Callinectes sapidus)	juv.		30		stat		death or loss of equilibrium	24-h EC_{50}	55	Butler (1963)
								48-h EC_{50}	35	Butler (1963)
freshwater mite (Hydrachna trilobata)	adult	tech	25-31	7.8-8	stat		immobilisation	48-h EC_{50}	2.8	Nair (1981)
stonefly (Pteronarcys californica)	nymph		15.5	7.1	stat		death	96-h LC_{50}	2.3	Sanders & Cope (1968)
rainbow trout (Salmo gairdneri)	1.3g	tech 96%					death	96-h LC_{50}	1.4	Johnson & Finley (1980)
fathead minnow	0.7g	tech 96%					death	96-h/LC_{50}	1.5	Johnson & Finley (1980)

Table 5 (contd).

Organism	Size/ age	Grade	Temp (°C)	pH	Stat/ flow	Sal (°/00)	Effect	Parameter	Conc. (µg/litre)	Reference
channel catfish (Ictalurus punctatus	1.7g	tech 96%					death	96-h LC_{50}	1.5	Johnson & Finley (1980)
catfish (Mystusvittatus)	6-10 g 80-100 mm	35% EC	18.2	6.9-7.4	stat		death	96-h LC_{50}	0.67	Verma et al. (1980)
	6-10 g 80-100mm	35% EC	18.2	6.9-7.4	stat		death	96-h LCO	0.06	Verma et al. (1980)
	6-10 g 80-100mm	35% EC	18.2	6.9-7.4	stat		death	96-h LC_{50}	3.50	Verma et al. (1980)
				8.4	flow	152[b] 330[c]	death	96-h LC_{50}	2.2	Rao & Murty (1982)
catfish (Heteropneustes fossilis)				8.4	flow	152[b] 330[c]	death	96-h LC_{50}	1.1	Rao & Murty (1982)
	41.8±4.7 g 197±8 mm	35% EC		7.8	stat	120[c]	death	96-h/LC_{50}	14.7	Singh & Narain (1982)
	11.3±1.6 g 102±5 mm	35% EC		7.8	stat	120[c]	death	96-h/LC_{50}	7.3	Singh & Narain (1982)
catfish (Mystuscavasius)				8.4	flow	152[b] 330[c]	death	96-h LC_{50}	1.9	Rao & Murty (1982)
catfish (Ophiocephalus punctatus)	40-55 g 90-100 mm	35% EC	18.2	6.9-7.4	stat		death	96-h LC_{50}	22	Verma et al. (1981)

[a] Sediment present in test vessel. [b] Hardness mg CO_3/litre. [c] Alkalinity mg HCO_3-/litre.

snails Aplexa hypnorum. Roberts (1972) reported that endosulfan at a concentration of 1000 µg/litre delayed the onset of spawning and prolonged the spawning period for the common mussel Mytilus edulis. At a lower dose of 100 µg/litre, a slight reduction in the length of the spawning period was considered by the author to reflect the experimental tank conditions rather than the endosulfan treatment.

Endosulfan has a high acute toxicity for fish. There have been studies on many species of teleosts with 96-h LC_{50} values ranging from 0.67 µg/litre to 4.8 µg/litre. Where commercial preparations of endosulfan have been used, it is not always clear how the dose is presented. Where LC_{50} values exceed 4.8, it seems clear that the values given are for a preparation that usually contains only 35% endosulfan.

Singh & Narain (1982) looked at variations in LC_{50} values in 96-h tests on the catfish Heteropneustes fossilis in relation to season, and size and weight of the fish. Tolerances of the fish to the Thiodan preparation (35% endosulfan) showed a significant seasonal variation. Fish were more tolerant to endosulfan during the colder months of the year. The toxicity of endosulfan was directly proportional to the length and weight of fish; LC_{50} values increased from 5 to 4.7 µg/litre with an increase in fish weight from 4.8 to 41.8 g and an increase in length from 6.2 to 19.7 cm. The relative toxicity of technical endosulfan, endosulfan isomers, and formulations, was investigated in the freshwater fish Labeo rohita by Rao et al. (1980), and in Channa punctata, a catfish, by Devi et al. (1981). In Labeo rohita, endosulfan-A was 3.33 times and endosulfan-B 0.16 times more toxic than technical endosulfan; the α-isomer was 30 times and the β-isomer 0.7 times more toxic than technical material in Channa punctata. Rao & Murty (1982) demonstrated in 3 species of catfish that the relative toxicity between species could not be determined using LC_{50} values alone. The slopes of endosulfan toxicity curves were different for different species. The same authors (Rao & Murty, 1980), reported that endosulfan metabolites were eliminated mainly with faeces and urine, the principal sites of detoxification of endosulfan being the liver and kidney. Using the freshwater catfish Saccobranchus fossilis, Verma et al. (1982a) calculated the safe levels of 2 preparations of endosulfan to be 0.14 µg/litre (Thiotox) and 0.23 µg/litre (Thiodan). Verma et al. (1980) looked for synergism and antagonism between endosulfan, dichlorvos and carbofuran on the test fish Mystus vittatus and Ophiocephalus punctatus, but did not find any evidence of either.

Histopathological, biochemical, and physiological changes in fish after exposure to endosulfan have been reported in a

large number of studies. Gopal et al. (1981a) measured blood glucose levels in catfish during 96-h of exposure to endosulfan at 10 µg/litre. A marked rise, at 4 h, of 66.4% over control levels increased to a peak of 101.6% at 48 h compared with control levels and then declined to match control levels at 72 h. At the end of the study, after 95 h, the glucose level was not significantly different from controls. Singh & Srivastava (1981) exposed Indian catfish to a high sublethal concentration of endosulfan of 1.5 µg/litre (representing 75% of the 96-h LC_{50} for the species). The average mortality rate for all fish groups was 5% over the 96-h experimental period. Muscle glycogen was depressed for most of the experimental period. Liver glycogen was the least affected of all the variables measured. Blood glucose was significantly elevated at 3, 6, 48, and 96 h of exposure, but not at 12 h. Blood pyruvate was elevated at 6 and 48 h only, whereas blood lactate was significantly elevated for the first 6 h of exposure and significantly depressed for the remainder of the observation period. Endosulfan was shown by Sastry & Siddiqui (1982) to reduce intestinal uptake of glucose by the fish Channa punctatus at doses of 1 mg/litre and above. Using endosulfan concentrations of between 0.17 and 2.3 µg/litre on 3 species of Indian catfish, Verma et al. (1983) found elevation of blood glucose ranging from 67.31% to 98.36%. The concentrations of endosulfan used represent 25% of the 96-h LC_{50} for each species. Murty & Devi (1982) demonstrated that changes in tissue protein, glycogen, and lipid levels in the fish Channa punctatus were greater with exposure to the alpha- than to the beta-isomer of endosulfan.

A clear dose-related reduction in both oxygen consumption and total nitrogen excretion was shown by Rao et al. (1981) in the fish Macrognathus aculeatum with endosulfan concentrations ranging from 1 to 15 µg/litre. Verma et al. measured the activity of 3 phosphatases in the liver, brain, and gills of Saccobranchus fossilis after 30 days exposure to endosulfan at concentrations from 0.63 µg/litre. The depression in the activity of these enzymes was increased by the addition of ascorbic acid to the food of the fish. Dalela et al. (1979) reported that acute (5 h of exposure) and short-term exposure (up to 32 days) of the fish Channa gachua to endosulfan at respectively 11.76 and 3.5 µg/litre produced histological changes in the gills. On acute exposure to 11.76 µg/litre, there was separation of the respiratory gill epithelium from the basement membrane, pronounced hyperaemia, necrosis, fusion of adjacent gill lamellae, erosion at the distal end of gill filaments, and loss of cell membrane. With exposure to a sub-lethal dose of 3.5 µg endosulfan/litre, damage to the gill was not as severe after 8 days, but was found to be progressively more pronounced with increasing exposure time.

A detailed field study was conducted in relation to tsetse fly control operations in the Okavango delta region of Botswana. Fox & Matthiessen (1982) reported that in laboratory studies, 24-h LC_{50} values for Okavango fish ranged from 1.2 to 7.4 µg/litre, depending on species. Field concentrations of endosulfan after spraying at 9.5 g/ha ranged between 0.2 and 4.2 µg/litre. The authors determined pre-spraying population densities and, thereby, the apparent mortality rate in a variety of fish species after spraying. Estimated mortality rates ranged from 0.2 to 4.3% for individual species with an overall estimate of 0.9%. Matthiessen & Roberts (1982) reported pathological changes in the liver and brain of fish exposed to endosulfan spray, and Matthiessen (1981) reported a significant elevation in blood cell counts during spraying.

7.2 Toxicity for Terrestrial Organisms

The toxicity of endosulfan for terrestrial organisms is summarized in Table 6.

7.2.1 Plants

Some phytotoxic effects of endosulfan have been reported. Gentile et al. (1978) reported that 24% endosulfan reduced the germination of cucumber pollen to 54.6% of control levels at a concentration of 1000 mg ai/litre, half the recommended concentration for field use. At the same concentration, pollen-tube length was only 8.1% of controls. Morey & Singh (1980) examined the effects of endosulfan on several species of Cucurbitae and found that it was phytotoxic to all but one species and moderately phytotoxic to the latter. Concentrations ranged from 0.035 to 0.14%. Phytotoxicity was estimated by necrotic spots on leaves. Agarwal & Beg (1982a) studied the effects of endosulfan on the germination and seedling growth of Cicer arietinum. They found reduced viability and delayed germination with endosulfan treatment. Inhibition, at lower concentrations of 0.01, 0.1, and 1 mg/litre in an agar bed used as the germination medium, was reversed as germination progressed, whereas at 10 mg/litre inhibition persisted. Endosulfan affected all major stages of germination and seedling growth. The results of a simple in vitro experiment suggested that endosulfan changed the permeability of root membranes. Gupta & Gupta (1977) examined 4 concentrations of endosulfan between 0.35 g/kg and 3 g/kg for effects on Green Gram, Vigna radiata. Toxic effects were dose-dependent. At 0.35 g/kg and 0.7 g/kg, no adverse effects were observed in any of the parameters studied, but, at higher concentrations of 1.5 g/kg and 3 g/kg, symptoms of toxicity

Table 6. Toxicity of endosulfan for terrestrial organisms

Organism	Size/ age	Grade	Temp (°C)	Route	Parameter	Concentration (mg/kg)[a]	Reference
braconoid parasite (*Apanteles ornigis*)	adult	technical	24	contact	24-h LC_{50}	494 mg/litre	Hagley et al. (1981)
ladybird beetle	adult	technical		contact	72-h LC_{83}	200 mg/litre	Makar & Jadhav (1981)
(*Menochilus sexmaculatus*)	1-day-old larva 3rd instar	technical		contact	72-h LC_{78}	200 mg/litre	Makar & Jadhav (1981)
honey bee, worker (*Apis mellifera*)		95%		contact	LD_{50}	7.1 g/bee	Stevenson et al. (1978)
				oral	LD_{50}	6.9 g/bee	
mallard (*Anas platyrhynchos*)	36 h	96%		oral	acute LD_{50}	27.8 (22.8-33.8)	Hudson et al. (1972)
	7 day	96%		oral	acute LD_{50}	6.47 (5.19-9.05)	Hudson et al. (1972)
	30 day	96%		oral	acute LD_{50}	7.89 (5.77-10.8)	Hudson et al. (1972)
	3 - 4 month	96%		oral	acute LD_{50}	33 (23.8-45.8)	Tucker & Crabtree (1970)
	6 month	96%		oral	acute LD_{50}	34.4	Hudson et al. (1972)
	16 day	96%		diet	5-day LC_{50}	1053 (781-1540)	Hill et al. (1975)
	young	35%[b]		diet	< 10-day LC_{50}	1000	DeWitt et al. (1963)
	adult	35%[b]		diet	< 10-day LC_{50}	> 5000	DeWitt et al. (1963)
	adult	35%[b]		diet	< 100-day LC_{50}	1000	DeWitt et al. (1963)

Table 6 (contd).

Organism	Size/ age	Grade	Temp (°C)	Route	Parameter	Concentration (mg/kg)[a]	Reference
ringnecked pheasant	10 day	96%		diet	5-day LC_{50}	1275 (1098-1482)	Hill et al. (1975)
(*Phasianus colchicus*)	young	35%[b]		diet	< 10-day LC_{50}	500	DeWitt et al. (1963)
	young	35%[b]		diet	< 100-day LC_{50}	> 300	DeWitt et al. (1963)
	adult	35%[b]		diet	< 100-day LC_{50}	1000	DeWitt et al. (1963)
Japanese quail (*Coturnix coturnix japonica*)	14-d	96%		diet	5-day LC_{50}	1250	Hill et al. (1975)
bobwhite quail	9-day	96%		diet	5-day LC_{50}	805(690-939)	Hill et al. (1975)
(*Colinus virginianus*)	young	35%[b]		diet	< 10-day LC_{50}	300	DeWitt et al. (1963)
	young	35%[b]		diet	< 100-day LC_{50}	100	DeWitt et al. (1963)
	adult	35%[b]		diet	< 100-day LC_{50}	> 250	DeWitt et al. (1963)
cowbird		35%[b]		diet	10-day LC_{50}	1000	DeWitt et al. (1963)

[a] Concentrations are mg/kg body weight for oral dosing and mg/kg diet for dietary dosing.
[b] Preparation used is "thiodan", which is a 35% formulation of endosulfan.

were visible. These included coiling of the radical, inhibition of root growth, stunting of shoots, and burning of the tips and margins of leaves. Plants were dwarfed and chlorotic, having damaged pollen grains and low productivity. Agarwal & Beg (1982b) reported that exposure of germinating Cicer arietinum seeds to endosulfan resulted in a fall in the pectin, hemicellulose, and cellulose contents of cell walls at all stages of germination compared with untreated controls. It must be stated that these were very isolated phytotoxic effects. In normal usage, endosulfan has not been shown to be significantly toxic to plants.

7.2.2 Honey bees

Endosulfan is considered of moderate or low toxicity for honey bees. Stevenson et al. (1978) reported a contact LD_{50} of 7.1 µg/bee and an oral LD_{50} of 6.9 µg/bee for endosulfan. Endosulfan has never been implicated in episodes of poisoning of bees investigated in Great Britain (Stevenson et al., 1978).

7.2.3 Birds

The toxicity of endosulfan for birds is summarized in Table 6. Hudson et al. (1972) examined the effects of age of mallard ducks on their sensitivity to endosulfan. The acute oral LD_{50}s for ducks at 36 h, 7 days, 30 days, and 6 months of age were 27.8, 6.47, 7.89, and 34.4 mg/kg body weight, respectively.

Field studies on birds in the Okavango delta of Botswana related to endosulfan sprays for tsetse fly control failed to show any change in bird numbers or species diversity (Douthwaite, 1980). Douthwaite (1982) looked specifically at kingfishers that fed on fish killed or incapacitated by the spray. The feeding rates of kingfishers were greatly increased by the availability of debilitated fish, but these rates fell when spraying ended. The kingfisher population in the study area survived and numbers at a communal roost were steady.

7.3 Toxicity for Microorganisms

Endosulfan is toxic for a wide variety of microorganisms. Srivastava & Misra (1981) found a dose-related increase in oxygen consumption by the yeast Rhodotorula gracilis at concentrations of endosulfan between 10 and 200 mg/litre medium. Further increases in dose up to 400 mg/litre did not show any increased effects. The authors suggested that endosulfan affects membrane components. Butler (1963)

reported that endosulfan (thiodan) at a concentration of 1 mg/litre, decreased productivity in a natural phytoplankton community by 86.6% during a 4-h exposure. The bacterial insecticide, Bacillus thuringiensis, was reported by Kahlon et al. (1981) to show reduced viable count and spore count on incubation with solutions of endosulfan at 0.5 or 1 µg/litre. Endosulfan was the most effective inhibitor of sporulation of the 3 insecticides tested. Tarar & Salpekar (1980) reported that endosulfan was the most toxic of 6 organochlorines for soil algae. Of algal species present in the soil (18 species present in the control soil), 17 were eliminated by endosulfan concentrations of 2 g/kg. Only 1 species survived endosulfan at 4 and 6 g/kg. This species, Chlorococcum humicolo, was unaffected by any of the organochlorines with which the soil was treated. El Beit et al. (1981) examined the microbial metabolism of pesticides and effects of the pesticides on the growth of bacterial and actinomycete colonies. Endosulfan either as the α- or β-isomer applied at 4000 mg/litre prevented the growth of any bacterial or actinomycete colonies from any soil type tested. Alpha-endosulfan seemed to be broken down by both bacteria and fungi whereas the beta-isomer was degraded more by bacteria than by fungi. Results suggest that while both isomers can be degraded by microbial organisms, the degradation materials released counteract the growth of the microorganisms.

7.4 Bioaccumulation

In aquatic ecosystems, endosulfan residues tend to reach a plateau level in tissues. Schoettger (1970) exposed western white suckers to water containing ^{14}C-labelled endosulfan at 29 µg/litre for 12 h. In the tissues concentrating the most endosulfan, a plateau level of the compound was reached within 12 h. A plateau was maintained over a prolonged period in studies on goldfish exposed to endosulfan solutions at 7 µg/litre. Residue levels in muscle were 2.54 mg/kg after 5 days and 1.09 mg/kg after 20 days (Schoettger, 1970). Accumulation appeared to be transitory, because endosulfan disappeared rapidly in mussels (Roberts, 1972) and goldfish after the source was removed (Schoettger, 1970). Oeser & Knauf (1973) calculated the half-life for the elimination of endosulfan from goldfish to be 2 - 3 days. This followed a 5-day exposure to 1 µg of the pesticide/litre, during which time residues reached a mean level of 0.35 mg/kg. Little accumulation of endosulfan seems to have been reported in the field. The mean residue level in fish living in endosulfan-contaminated natural surface water was 0.4 mg/kg (Gorbach & Knauf, 1971).

Roberts (1972) reported concentration factors of 17, 11, and 8.1 after exposing mussels to 0.1, 0.5, and 1.0 mg endosulfan/litre, respectively, for 112 days. Although the mussels assimilated more pesticide at higher dose levels, the greatest concentration factors were achieved with the lowest dose of 0.1 mg/litre, a maximum BCF of 22.5 being reached after 70 days. Roberts (1972) found that the major storage site for endosulfan in scallops was the digestive gland. He suggested this would also be the case for mussels and other bivalves.

In a study by Ernst (1977) on the uptake and elimination of endosulfan, a somewhat higher BCF value of 600 was measured in mussels, with an initial concentration of endosulfan in the water of 2.05 µg/litre. The concentration factor is based on a steady state concentration of 0.14 µg endosulfan/litre water. If the BCF is calculated on the initial concentration, a BCF of 41, a more typical value for aquatic organisms, is obtained. Bioaccumulation data are summarized in Table 7.

Koeman et al. (1974) measured residues in animal species in Java, following BIMAS programmes for the control of paddy-stem borer that had continued over several years. No residues were found (detection limit 0.03 mg/kg); animals used included fish, molluscs, crabs, and shrimps. Matthiessen et al. (1982) studied the accumulation of endosulfan in fish and their predators following aerial spraying to control the tsetse fly in Botswana. Residue levels in fish predators, birds, and crocodiles, were similar to those in their prey. Risk to predators was consequently deemed to be low. Although endosulfan residues in insects were not measured, low residues in insectivorous birds suggested rapid degradation and little accumulation. According to Matthiessen et al. (1982), lean fish have a lower survival rate than fat ones at subacute concentrations of endosulfan in the water.

There do not seem to be any accumulation data available for wild mammals.

Table 7. Bioaccumulation of endosulfan

Organism	Grade	Temp (°C)	Organ	Exposure time	Concentration factor BCF	Dose (µg/litre)	References
green alga (*Chlorella* sp.)			WB[c]	initial BCF	2500		Oeser et al. (1971)
mussel (*Mytilus edulis*)			WB	112 day	17	100	Roberts (1972)
			WB	112 day	11	500	Roberts (1972)
			WB	112 day	8.1	1000	Roberts (1972)
	α-isomer		WB		600[a] (41)[b]	0.14[a] (2.05)[b]	Ernst (1977)
goldfish (*Carassius auratus*)			liver	11-20 day	781	7	Schoettger (1970)
			muscle	5-20 day	314	7	Schoettger (1970)
western white sucker (*Catostomus commersoni*)		19	muscle	12 h	65	20	Schoettger (1970)
		19	muscle	9 h	55	20	Schoettger (1970)
		19	liver	12 h	550	20	Schoettger (1970)
		19	liver	9 h	695	20	Schoettger (1970)

[a] Higher BCF based on steady state concentration of endosulfan.
[b] Values in () based on original concentration of endosulfan (static test).
[c] WB = whole body.

8. PREVIOUS EVALUATIONS OF ENDOSULFAN BY INTERNATIONAL BODIES

The Joint Meeting on Pesticide Residues (JMPR) have reviewed residues and toxicity data on endosulfan on several occasions in the past: 1965, 1967, 1968, 1971, 1974, and 1982 (FAO/WHO, 1965, 1968, 1969, 1972, 1975a, 1983).

In 1982, the estimate of a temporary acceptable daily intake for man was made at 0 - 0.008 mg/kg body weight (total of alpha- and beta-endosulfan and endosulfan sulfate). This was based on no-observed-adverse-effect levels of:

rat: 30 mg/kg diet, equivalent to 1.5 mg/kg body weight; and

dog: 0.75 mg/kg body weight per day (administered by capsules).

The FAO/WHO (1975b) in its series of "Data sheets on chemical pesticides" issued one on Endosulfan. Based on a brief review of use, exposure, and toxicity, practical advice is given on labelling, safe-handling, transport, storage, disposal, decontamination, selection, training, and medical supervision of workers, and first aid and medical treatment.

WHO (1984), classified endosulfan in the list of technical products being moderately hazardous.

Regulatory standards established by national bodies in 12 different countries (Argentina, Brazil, Czechoslovakia, Federal Republic of Germany, India, Japan, Kenya, Mexico, Sweden, the United Kingdom, the USA, and the USSR) and the EEC can be found in the IRPTC (International Register of Potentially Toxic Chemicals) Legal file (IRPTC, 1983).

9. EVALUATION OF HEALTH RISKS FOR MAN AND EFFECTS ON THE ENVIRONMENT

9.1 Evaluation of Health Risks for Man

Endosulfan toxicity

Endosulfan is moderately to highly toxic according to the scale of Hodge & Sterner (1956). The oral LD_{50} in the rat ranges from 18 - 355 mg/kg body weight, depending on such parameters as sex, strain, and vehicle used.

WHO (1984) classified endosulfan in the category of technical products that are moderately hazardous.

Endosulfan can be absorbed following ingestion, inhalation, and skin contact. It is readily metabolized and excreted and does not accumulate in the body.

On acute intoxication, neurological manifestations may occur, such as irritability, restlessness, muscular twitchings, and convulsions. Lung oedema and cyanosis may precede death.

Endosulfan was negative or produced conflicting results in short-term tests for genetic activity. It showed no carcinogenic activity in mice or rats but studies were limited by inadequate reporting or survival.

Several cases of suicidal and occupational poisoning have been reported, the latter resulting, in most cases, from neglect of safety precautions.

Exposure to endosulfan

Food is the main source of exposure of the general population to endosulfan. Endosulfan residues in food (the sum of its alpha- and beta-isomers and endosulfan sulfate) have been found to be generally well below FAO/WHO maximum residue limits.

In occupationally-exposed persons, both skin contact and inhalation can be important routes of absorption when adequate safety precautions are not taken.

Hazard assessment

The main hazard associated with endosulfan is acute intoxication through overexposure. Such situations may be due to intentional or accidental overexposure or to gross negligence in occupational situations.

In all other exposure situations, especially as far as the general population is concerned, the toxicity profile and the present exposure pattern do not indicate any appreciable hazard.

9.2 Evaluation of Overall Environmental Effects

Degradation of endosulfan in soil and water by photolysis, chemical reactions, and biotransformation is governed by a wide range of climatic factors and the type of microorganisms present.

Endosulfan does not appear to be a problem with regard to persistence. It is not readily bioaccumulated. In aquatic organisms, loss soon balances uptake and a fairly low plateau level of residues is achieved.

Endosulfan is hazardous in acute overexposure for some aquatic species, especially fish. There has been large-scale field experience with endosulfan without any long-term adverse effects on the environment.

Careful application to avoid overexposure of non-target organisms does not eliminate kills in local fish populations when endosulfan is applied to wetland areas at recommended rates. Because there is little or no biomagnification, endosulfan, when applied at recommended rates, is not hazardous to terrestial animals. Toxicity for bees is low to moderate.

The reported toxicity of endosulfan for microorganisms in the laboratory is low; it is unlikely to have an appreciable effect in the field.

9.3 Conclusions

1. The general population does not appear to be at risk from endosulfan residues in food. Exposure of the general population via air and drinking-water is generally low.

2. Occupational exposure has resulted in some incidents of poisoning. These appear however, only to have occurred when adequate safety precautions were not taken.

3. In terms of the general environment, endosulfan is highly toxic for some aquatic species, particularly fish. Endosulfan is moderately toxic for honey bees.

4. Endosulfan does not accumulate in food chains and is excreted from the body rapidly.

REFERENCES

ACGIH (1982) TLV's (R) threshold limit values for chemical substances and physial agents in the work environment, American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio.

AGARWAL, S. & BEG, M.U. (1982a) Biochemical changes in Cicer arietinum seedling on exposure to endosulfan. Indian J. Biochem. Biophys., 19: 247-252.

AGARWAL, S. & BEG, M.U. (1982b) Effect of endosulfan on endogenous IAA, cell wall polysaccharide peroxidase activity and its isoenzymatic pattern in germinating Cicer arietinum seeds. Indian J. exp. Biol., 20: 319-323.

AGARWAL, D.K., SETH, P.K., & GUPTA, P.K. (1978) Effect of endosulfan on drug metabolizing enzymes and lipid peroxidation in rat. J. environ. Sci. Health, Part C, Environ. Health Sci., 13: 49-62.

ALABASTER, J.S. (1969) Survival of fish in 164 herbicides, insecticides, fungicides wetting agents and miscellaneous substances. Int. Pest Control, 11: 29-35.

ARCHER, T.E., NAZER, I.K., & CROSBY, D.G. (1972) Photodecomposition of endosulfan and related products in thin films by ultraviolet light irradiation. J. agric. food Chem., 20: 547-555.

BECK, E.W., JOHNSON, J.C., WOODHAM, D.W. Jr, LEUCK, D.B., DAWSEY, L.H., ROBBINS, J.E., & BOWMAN, M.C. (1966) Residues of endosulfan in meat and milk of cattle fed treated forages. J. econ. Entomol., 59: 1444-1450.

BEYERS, R.A., WOODHAM, D.W., & BOWMAN, M.C.G. (1965) Residues on coastal Bermuda grass, trash and soil treated with endosulfan. J. econ. Entomol., 58: 160-161.

BOYD, E.M. (1972) Protein deficiency and pesticide toxicity, Springfield, Illinois, Charles C. Thomas Publisher, pp. 195-205.

BOYD, E.M. & DOBOS, I. (1969) Protein deficiency and tolerated oral doses of endosulfan. Arch. int. pharmacodyn. Ther., 178: 152-165.

BUTLER, P.A. (1963) A review of fish and wildlife service investigations during 1961-1962. In: George, J.L., ed. Commercial fisheries investigations, pesticide-wildlife series, US Department of the Interior, Fish and Wildlife Service, Gulf Breeze, Florida, pp. 11-25 (Circular 167).

BYERS, R.A., WOODHAM, D.W., & BOWMAN, M.C.G. (1965) Residues on coastal Bermuda grass, trash, and soil treated with endosulfan. J. econ. Entomol., 58: 160-161.

CANADA, NATIONAL RESEARCH COUNCIL (1975) Endosulfan: its effects on environmental quality (NRC Associate Committee on Scientific Criteria for Environmental Quality, Report No. 11, Subcommittee of Pesticides on Related Compounds, Subcommittee Report No. 3, Publication No. NRCC 14098 of the Environmental Secretariat).

CAREY, A.E., DOUGLAS, P., TAI, H., MITCHELL, W.G., & WIERSMA, G.B. (1979) Pesticide residue concentrations in soils of five United States cities, 1971: urban soils monitoring program. Pestic. Monit. J., 13: 17-22.

CASSIL, C.C. & DRUMMOND, P.E.G. (1965) A plant surface oxidation product of endosulfan. J. econ. Entomol., 58: 356-357.

CEC (1981) Criteria (dose/effect relationships) for organochlorine Pesticides, Oxford, Pergamon Press.

CHENG, H.H. & BRAUN, H.E. (1977) Chlorpyrifos, carbaryl, endosulfan, leptophos and trichlorfon residues on cured tobacco leaves from field-treated tobacco in Ontario. Can. J. plant Sci., 57: 689-695.

CHOPRA, N.M. & MAHFOUZ, A.M. (1977) Metabolism of endosulfan I, endosulfan II, and endosulfan I sulfate in tobacco leaf. J. agric. food Chem., 25: 32-36.

CHOPRA, N.M., CAMPBELL, B.S., & HURLEY, J.C. (1978) Systematic studies on the breakdown of endosulfan in tobacco smokes: isolation and identification of the degradation products from the pyrolysis of endosulfan in a nitrogen atmosphere. J. agric. food Chem., 26: 255-258.

COPPLESTONE, J.F., WEIJAND, B., & EVERTS, J.W. (1979) Observations on side-effects of helicopter spraying against tsetse flies in the Bouafle sleeping sickness focus. In: Everts, J.W., ed. Side effects of aerial insecticide applications against tsetse flies near Bouafle, Ivory Coast,

Wageningen, The Netherlands, Department of Toxicology, Agricultural University.

CORNELIUSSEN, P.E. (1969) Pesticide residues in total diet samples (IV). Pestic. Monit. J., 2: 140-152.

CORNELIUSSEN, P.E. (1970) Pesticide residues in total diet samples (V). Pestic. Monit. J., 4: 89-105.

DALELA, R.C., BHATNAGAR, M.C., TYAGI, A.K., & VERMA, S.R. (1979) Histological damage of gills in Channa gachua after acute and subacute exposure to endosulfan and rogor. Mikroskopie, 35: 301-307.

DAVIS, P.W. & WADEMEYER, G.A. (1971) Na-, K-activated ATPase inhibition in rainbow trout: a site for organochlorine pesticide toxicity. Comp. Biochem. Physiol., 40: 823-827.

DEEMA, P.,THOMPSON E., & WARE, G.W. (1966) Metabolism, storage and excretion of ^{14}C-endosulfan in the mouse. J. econ. Entomol., 59: 546-550.

DEMETER, J. & HEYNDRICKX, A. (1978) Two lethal endosulfan poisonings in man. Anal. Toxicol., 2: 68-74.

DEMETER, J. & HEYNDRICKX, A. (1979) Selection of a high performance liquid chromatographic cleanup procedure for the determination of organochlorine pesticides in fatty biological extracts. Vet. hum. Toxicol., 21: 151-155.

DEMETER, J., HEYNDRICKX, A., TIMPERMAN, J., LEFEVERE, M., & DEBEER, J. (1977) Toxicological analysis in a case of endosulfan suicide. Bull. environ. Contam. Toxicol., 18: 110-114.

DEN TONKELAAR, E.M. & VAN ESCH, G.J. (1974) No-effect-levels of organochlorine pesticides based on induction of microsomal liver enzymes in short-term toxicity experiments. Toxicology, 2: 371-380.

DEVI, A.P., RATO, D.M.R., TILAK, K.S., & MURTY, A.S. (1981) Relative toxicity of the technical grade material, isomers, and formulations of endosulfan to the fish Channa punctata. Bull. environ. Contam. Toxicol., 27: 239-243.

DEWITT, J.B., STICKEL, W.H., & SPRINGER, P.F. (1963) Wildlife studies, Patuxent Wildlife Research Center. In: Pesticide-wildlife studies. A review of Fish and Wildlife Service investigations during 1961 and 1962, Gulf Breeze,

Florida, US Department of the Interior, Fish and Wildlife Service, pp. 74-96 (Circular 167).

DIKSHITH, T.S.S. & DATTA, K.K. (1978) Lack of cytogenetic effects in male rats. Bull. environ. Contam. Toxicol., 20: 826-833.

DOROUGH, H.W. (1973) Fate of insecticides in tobacco plants and factors influencing their levels in tobacco products. In: Proceedings of the Tobacco and Health Workshop Conference No. 4, Lexington, pp. 796-828.

DOROUGH, H.W., HUHTANEN, K., MARSHALL, T.C., & BRYANT, H.E. (1978) Fate of endosulfan in rats and toxicological considerations of apolar metabolites. Pestic. Biochem. Physiol., 8: 241-252.

DOUTHWAITE, R.J. (1980) Occurrence of birds in Acacia woodland in northern Botswana related to endosulfan sprayed for tsetse fly control. Environ. Pollut., 22: 273-279.

DOUTHWAITE, R.J. (1982) Changes in pied kingfisher (Ceryle rudis) feeding related to endosulfan pollution from tsetse fly control operations in the Okavango Delta, Botswana. J. appl. Ecol., 19: 133-142.

EICHELBERGER, J.W. & LICHTENBERG, J.J. (1971) Persistence of pesticides in river water. Environ. Sci. Technol., 5: 541-544.

EL BEIT, I.O.D., WHEELOCK, J.V., & COTTON, D.E. (1981) Pesticide-microbial interaction in the soil. Int. J. environ. Stud., 16: 171-180.

ENVIRONMENTAL QUALITY COORDINATION UNIT (1973) Pesticide survey in Lakes Erie and Ontario, Burlington, Ontario (Prepublication manuscript prepared by Canada Center for Inland Waters).

EPSTEIN, E. & GRANT, W.J. (1968) Chlorinated insecticides in run-off water as affected by croprotation. Soil Soc. Am. Proc., 32: 423-426.

ERNST, W. (1977) Determination of the bioconcentration potential of marine organisms: a steady state approach. Chemosphere, 6: 731-740.

FAHRIG, R. (1974) In: Montesano, R. & Tomatis, L., ed. Comparative mutagenicity studies with pesticides. Proceedings of a Workshop on Approaches to Assess the Significance of

Experimental Chemical Carcinogenesis Data for Man, Brussels, Belgium, Dec. 10-12, 1973, Lyons, France, International Agency for Research on Cancer (XIV + pp. 230. Illus.) pp. 161-181 (Scientific Publications, No. 10, Chemical Carcinogenesis Essays).

FAO/WHO (1965) Endosulfan. In: 1965 Evaluations of some pesticide residues in food, Rome, Food and Agriculture Organization of the United Nations.

FAO/WHO (1968) Endosulfan. In: 1967 Evaluations of some pesticide residues in food, Rome, Food and Agriculture Organization of the United Nations.

FAO/WHO (1969) Endosulfan. In: 1968 Evaluations of some pesticide residues in food, Rome, Food and Agriculture Organization of the United Nations.

FAO/WHO (1973) Endosulfan. In: 1971 Evaluations of some pesticide residues in food, Rome, Food and Agriculture Organization of the United Nations.

FAO/WHO (1975a) Endosulfan. In: 1974 Evaluations of some pesticide residues in food, Rome, Food and Agriculture Organization of the United Nations.

FAO/WHO (1975b) Data sheets on pesticides: endosulfan, Rome, Food and Agriculture Organization of the United Nations (VBC/DS/75.15, No 15).

FAO/WHO (1983) Endosulfan. In: 1982 Evaluations of some pesticide residues in food, Rome, Food and Agriculture Organization of the United Nations.

FOX, P.J. & MATTHIESSEN, P. (1982) Acute toxicity to fish of low-dose aerosol applications of endosulfan to control tsetse fly in the Okavango Delta, Botswana. Environ. Pollut., 27: 129-142.

FRANK, R., BRAUN, H.E., & MCWADE, J.W. (1970) Chlorinated hydrocarbon residues in the milk supply of Ontario, Canada. Pestic. Monit. J., 4: 31-41.

FRANK, R., BRAUN, H.E., ISHIDA, K., & SUDA, P. (1976) Persistent organic and inorganic pesticide residues in orchard soils and vineyards of southern Ontario. Can. J. Soil Sci., 56: 463-484.

FRANK, R., BRAUN, H.E., HOLDRINET, M., SIRONS, G.J., SMITH, E.H., & DIXON, D.W. (1979a) Organochlorine insecticide and industrial pollutants in the milk supply of southern Ontario, Canada, 1977. J. food Prot., 42: 31-37.

FRANK, R., BRAUN, H.E., & MCWADE, J.W. (1979b) Chlorinated hydrocarbon residues in the milk supply of Ontario, Canada. Pestic. Monit. J., 4: 31-41.

GAINES, T.B. (1969) Acute toxicity of pesticides. Toxicol. appl. Pharmacol., 14: 515-534.

GARG, A., KUNWAR, K., DAS, N., & GUPTA, P.K. (1980) Endosulfan intoxication: blood glucose electroyltes, Ca levels, ascorbic acid and glutathione in rats. Toxicol. Lett., 5(2): 119-123.

GENTILE, A.G., VAUGHAN, A.W., & PFEIFFER, D.G. (1978) Cucumber pollen germination and tube elongation inhibited or reduced by pesticides and adjuvants. Environ. Entomol., 7: 689-691.

GOEBEL, H., GORBACH, S., KNAUF, W., RIMPAU, R.H., & HUTTENBACH, H. (1982) Properties, effects, residues, and analytics of the insecticide endosulfan. Residue Rev., 83: 1-165.

GOPAL, K., ANAND, M., KHANNA, R.N., & MISRA, D. (1980) Endosulfan induced changes in blood glucose of catfish, Clarias batrachus. J. Adv. Zool., 1: 68-71.

GOPAL, K., KHANNA, R.N., ANAND, M., & GUPTA, G.S.D. (1981) The acute toxicity of endosulfan to fresh-water organisms. Toxicol. Lett., 7: 453-456.

GORBACH, S.G. (1965) [Investigations on thiodan in the metabolism of milk sheep,] Farbwerke Hoechst AG (Unpublished internal report) (in German).

GORBACH, S.G. & KNAUF, W. (1971) [Endosulfan and the environment. The behaviour of endosulfan in water and its effects on organisms that live in water.] Schriftenr. Ver. Wasser-, Boden, -Lufthyg. (Berlin-Dahlem), 34: 85 (in German).

GOSSELIN, R.E., HODGE, H.C., SMITH, R.P., GLEASON, M.N., ed. (1969) Clinical toxicology of commercial products: acute poisoning, 3rd ed., Baltimore, Williams & Wilkins, (Section II, Ingredients Index).

GREVE, P.A. (1971a) [The persistence of endosulfan in surface water.] Meded. Fac. Landbouwwet. Rijksuniv. Gent., 36: 439-447 (in Dutch).

GREVE, P.A. (1971b) Chemical wastes in the sea: new forms of marine pollution. Science, 173: 1021-1022.

GUMMER, W.D. (1980) Pesticide monitoring in the prairies of Western Canada. In: Afghan, B.K. & McKay, D., ed. Hydrocarbons and halogenated hydrocarbons in the aquatic environment, New York, London, Plenum Press.

GUPTA, P.K. (1976) Endosulfan-induced neurotoxicity in rats and mice. Bull. environ. Contam. Toxicol., 15: 708-713.

GUPTA, P.K. (1978) Distribution of endosulfan in plasma and brain after repeated oral administration to rats. Toxicology, 9: 371-378.

GUPTA, P.K. (1979) Pharmacology, toxicology and degradation of endosulfan, Toxicology, 13: 115-130.

GUPTA, P.K. & CHANDRA, S.V. (1975) The toxicity of endosulfan in rabbits. Bull. environ. Contam. Toxicol., 14: 513-519.

GUPTA, P.K. & EHRNEBO, M. (1979) Pharmacokinetics of α- and β-isomers of racemic endosulfan following intravenous administration in rabbits. Drug Metab. Disp., 7: 7-100.

GUPTA, P.K. & GUPTA, R.C. (1977) Effect of endosulfan pretreatment on organ weights and on pentobarbital hypnosis in rats. Toxicology, 8: 283-288.

GUPTA, P.K. & GUPTA, R.C. (1979) Pharmacology, toxicology, and degradation of endosulfan. A review. Toxicology, 13: 115-130.

GUPTA, R.C. & GUPTA, P.K. (1980) Phytotoxic effects of endosulfan on green gram Vigna radiata (Linns) Wilezek. Indian J. Biochem. Biophys., 17: 20.

GUPTA, P.K., CHANDRA, S.V., & SAXENA, D.K. (1978) Teratogenic and embryonic effects on endosulfan in rats. Acta pharmacol. toxicol., 42: 150-152.

HAGLEY, E.A.C., PREE, D.J., SIMPSON, C.M., & HIKICHI, A. (1981) Toxicity of insecticides to parasites of the spotted tentiform leafminer (Lepidoptera: Gracillariidae). Can. Entomol., 113: 899-906.

HARRIS, C.R., CHAPMAN, R.A., & MILES, J.R.W. (1977) Insecticide residues in soils on fifteen farms in southwestern Ontario, 1964-1974. J. environ. Sci. Health, B12(3): 163-177.

HILL, E.F., HEATH, R.G., SPANN, J.W., & WILLIAMS, J.D. (1975) Lethal dietary toxicities of environmental pollutants to birds, p. 61 (US Department of the Interior Fish and Wildlife Service (Special Science Report (Wildlife No. 191).

HODGE, H.C. & STERNER, J.H. (1956) Combine and tabulation of toxicity classes. In: Spector, W.B., ed. Handbook of toxicology, Philadelphia, W.B. Saunders Company, Vol. 10.

HOECHST A.G. (1977) Thiodan: the versatile but selective insecticide. Instructions for its use, Frankfurt, West Germany Hoechst Aktiengesellschaft.

HOLCOMBE, G.W., PHIPPS, G.L., & FIANDT, J.T. (1983) Toxicity of selected priority pollutants to various aquatic organisms. Ecotoxicol. environ. Saf., 7: 400-409.

HUDSON, R.H., TUCKER, R.K., & HAEGELE, M.A. (1972) Effect of age on sensitivity: acute oral toxicity of 14 pesticides to mallard ducks of several ages. Toxicol. appl. Pharmacol., 22: 556-561.

INDUSTRIAL BIO-TEST LABORATORIES INC. (1965) Three generation reproduction study on thiodan-albino rats (Unpublished Report).

INNES, J.R.M., ULLAND, B.M., VALERIO, M.G., PETRUCELLI, L., FISHBEIN, L., HART, E.R., PALLOTTA, A.J., BATES, R.R., FALK, H.L., GART, J.J., KLEIN, M. MITCHELL, I., & PETERS, J. (1969) Bioassay of pesticides and industrial chemicals for tumorgenicity in mice: a preliminary note. J. Natl Cancer Inst., 42: 1101-1114.

IRPTC (1983) IRPTC legal file 1983, Geneva, International Register of Potentially Toxic Chemicals, United Nations Environment Programme.

IRPTC (1984) IRPTC data profile on endosulfan, Geneva, International Register of potentially Toxic Chemicals, United Nations Environment Programme.

ISRAELI, R., KRISTAL, N., & TIBERIN, P. (1969) Endosulfan poisoning, a preliminary report on three cases. Zentralbl. Arbeitsmed. Arbeitsschutz, 19: 1.

JOHNSON, R.D. & MANSKE, D.D. (1977) Pesticide and other chemical residues in total diet samples. XI. Pestic. Monit. J., 11: 116-131.

JOHNSON, W.W. & FINLEY, M.T. (1980) Handbook of acute toxicity of chemicals to fish and aquatic invertebrates, Gulf Breeze, Florida, US Department of the Interior, Fish and Wildlife Services, p. 56 (Res. Publication No. 137).

JOSHI, A.G. & REGE, M.S. (1980) Acute toxicity of some pesticides and a few inorganic salts to the mosquito fish Gambusia affinis (Baird & Girard). Indian J. exp. Biol., 18: 435-437.

KAHLON, R.S., SIDHU, R.S., & KALRA, M.S. (1981) Compatibility of Bacillus thuringiensis with chemical insecticides. Indian J. Ecol., 8: 306-307.

KAZEN, C., BLOOMER, A., WELCH, R., OUDBIER, A., & PRICE, H. (1974) Persistence of pesticides on the hands of some occupationally-exposed people. Arch. environ. Health, 29: 315-318.

KEIL, J.E., LOADHOLT, C.B., BROWN, B.L., SANDIFER, S.H., & SITTERLY, W.N. (1972) Decay of parathion and endosulfan residues on field-treated tobacco, South Carolina, 1971. Pestic. Monit. J., 6: 73-75.

KHANNA, R.N., MISRA, D., ANAND, M., & SHARMA, H.K. (1979) Distribution of endosulfan in cat brain. Bull. environ. Contam. Toxicol., 22: 72-79.

KOEMAN, J.H., PENNINGS, J.H., ROSANTO, R., SOEMARWOTO, O., TJIOE, P.S., BLANCKE, S., KUSUMADINATA, S., & DJAJADIREDJA, P.R. (1974) Metals and chlorinated hydrocarbon pesticides in samples of fish, Sawah-duck eggs, crustaceans, and molluscs. Collected in Indonesia in April and May 1972, Wageningen, The Netherlands, Department of Toxicology, Agricultural University of Wageningen.

KUTZ, F.W., YOBS, A.R., & YANG, H.S.C. (1976) National Pesticide Monitoring Programs, 95-135. In: Lee, R.E., ed. Air pollution from pesticides and agricultural processes, Florida, CRC Press, pp. 95-135.

LINDQUIST, D.A. & DAHN, P.A. (1957) Some chemical and biological experiments with thiodan. J. econ. Entomol., 50: 483.

LUSSEM, H. & SCHLIMME, E. (1971) [Localization of the pesticide endosulfan, and its effects in the Rhine.] Gas-Wasser Fach, Wasser-Abwasser, 112: 18-21 (in German).

MAIER-BODE, H. (1968) Properties, effect, residues and analytics of the insecticide endosulfan. Residue Rev., 22: 1-44.

MAKAR, P.V. & JADHAV, L.D. (1981) Toxicity of some insecticides to the aphid predator Menochilus sexmaculatus Fabricius. Indian J. Entomol., 43: 140-144.

MARTENS, R. (1972) [Degradation of endosulfan by microorganisms in soil and ground water.] Boden. Lufthyg. Beolen, (Dahlem), 37: 167-173 (in German).

MARTENS, R. (1977) Degradation of endosulfan-8,9-Carbon-14 in soil under different conditions. Bull. environ. Contam. Toxicol., 17: 438-446.

MARTIN, H. (1968) Pesticide manual, Croydon, British Crop Protection Council.

MATTHIESSEN, P. (1981) Haematological changes in fish following aerial spraying with endosulfan insecticide for tsetse fly control in Botswana. J. Fish Biol., 18: 461-469.

MATTHIESSEN, P. & ROBERTS, R.J. (1982) Histopathological changes in the liver and brain of fish exposed to endosulfan insecticide during tsetse fly control operations in Botswana. J. Fish Dis., 5: 153-160.

MATTHIESSEN, P., FOX, P.J., DOUTHWAITE, R.J., & WOOD, A.B. (1982) Accumulation of endosulfan residues in fish and their predators after aerial spraying for the control of tsetse fly in Botswana. Pestic. Sci., 13: 39-48.

MCLEESE, D.W. & METCALFE, C.D. (1980) Toxicities of eight organochlorine compounds in sediment and seawater to Crangon septemspinosa. Bull. environ. Contam. Toxicol., 25: 921-928.

MCLEESE, D.W., BURRIDGE, L.E., & VAN DINTER, J. (1982) Toxicities of 5 organochlorine compounds in water and sediment to Nereis virens. Bull. environ. Contam. Toxicol., 28: 216-220.

MILES, J.R.W. (1976) Insecticide residues on stream sediments in Ontario, Canada, Pestic. Monit. J., 10: 87-91.

MILES, J.R.W. & HARRIS, C.R. (1971) Insecticide residues in a controlled drainage system in agricultural areas of south-western Ontario, 1970. Pestic. Monit. J., 5: 289-294.

MILES, J.R.W. & HARRIS, C.R. (1973) Pesticides in water-organochlorine insecticide residues in streams draining agricultural, urban-agricultural, and resort areas of Ontario, Canada, 1971. Pestic. Monit. J., 6: 363-368.

MISRA, D., KHANNA, R.N., AMAND, M., & GOPAL, K. (1980) Effect of endosulfan on blood glucose. Chemosphere, 9: 119-121.

MOREY, R.J. & SINGH, Z. (1980) Studies on phytotoxic effects of some modern insecticides to cucurbits. Haryana Agric. Univ. J. Res., 10: 509-516.

MORIYA, M., OHTA, T., WATANABE, K., MIYAZAWA, T., KATO, K., & SHIRASU, Y. (1983) Further mutagenicity studies on pesticides in bacterial reversion assay systems. Mutat. Res. 116: 185-216.

MURTY, A.S. & DEVI, A.P. (1982) The effect of endosulfan and its isomers on tissue protein, glycogen, and the lipids in the fish Channa punctata. Pestic. Biochem. Physiol., 17: 280-286.

NAIR, G.A. (1981) Toxic effects of certain biocides on a fresh water mite, Hydrachna trilobata viets (Arachnida: Hydrachnoidea: Hydrachnidae). J. environ. Biol., 2: 91-96.

NCI (1978) Bioassay of endosulfan for possible carcinogenicity, Washington, DC, National Cancer Institute (Technical Report Series No. 621) (CAS No. 115-29-7).

NIAGARA CHEMICAL DIVISION FMC CORP. (1966) Determination of thiodan I, II, and sulfate residues in soil, Middleport, New York, Research and Development Department (Project 105) (Unpublished report).

NIAGARA CHEMICAL DIVISION FMC CORP. (1971) Determination of endosulfan I, endosulfan II and endosulfan sulfate residues in soil, pond, mud, and water, Middleport, New York, Research and Development Department (Unpublished report).

NIAGARA CHEMICAL DIVISION FMC CORP. (1972) Thiodan residues in soil and irrigation run off water, Richmond, California, Research & Development Deptartment (Submitted in fulfillment of pesticide requisition notice 70-15. Project 015-Thion residues in soil and irrigation run-off water) (Unpublished report).

NICHOLSON, S.S. & COOPER, G.W. (1977) Apparant endosulfan toxicities in wolves. Am. J. Vet. Med. Assoc., 170: 319.

OESER, F. & KNAUF, W. (1973) Studies of impact of endosulfan on the environment. In: The effect of sublethal concentrations of endosulfan to gold fish (Submitted in fulfillment of pesticide registration notice 70-15; TAB 20).

OESER, H., GORBACH, S.G., & KNAUF, W. (1971) Endosulfan and the environment. In: Proceedings of the Workshop on Phytopathology, Udine, Italy, May 1971.

OUDBIER, A.J., BLOOMER, A.W., PRICE, H.A., & WELCH, R.L. (1974) Respiratory route of pesticide exposure as a potential health hazard. Bull. environ. Contam. Toxicol., 12(1): 1-9.

PHILLIPS, W.E.J. (1975) Endosulfan: its effects on environmental quality. Rep. Monogr. Non. Ser., 100.

RAMACHANDRAN, S., RAJENDRAN, N., NANDAKUMAR, R., & VENUGOPALAN, V.K. (1981) Inhibition of photosynthesis and respiration by chlorinated hydrocarbons in some marine algae. Mahasagar, 14: 317-319.

RAO, D.M.R. & MURTY, A.S. (1980) Toxicity, biotransformation, and elimination of endosulfan in Anabas testudineus (Bloch). Indian J. exp. Biol., 18: 664-665.

RAO, D.M.R. & MURTY, A.S. (1982) Toxicity and metabolism of endosulfan in 3 freshwater catfishes. Environ. Pollut., 27: 223-231.

RAO, D.M.R., DEVI, A.P., & MURTY, A.S. (1980) Relative toxicity of endosulfan, its isomers, and formulated products to the freshwater fish Labeo rohita. J. Toxicol. environ. Health, 6: 825-834.

RAO, D.M.R., DEVI, A.P., & MURTY, A.S. (1981) Toxicity and metabolism of endosulfan and its effect on oxygen consumption and total nitrogen excretion of the fish, Macrognathus aculeatum. Pestic. Biochem. Physiol., 15: 282-287.

ROBERTS, D. (1972) The assimilation and chronic effects of sub-lethal concentrations of endosulfan on condition and spawning in the common mussel (Mytilus edulis). Mar. Biol., 16: 118-125.

ROSALES, M.T.L., BOTELLO, A.V., BRAVO, H., & MANDELLI, E.F. (1979) PCBs and organochlorine insecticides in oysters from

coastal lagoons of the Gulf of Mexico. Bull. environ. Contam. Toxicol., 21: 652-656.

SANDERS, H.O. (1969) Toxicity of pesticides to the crustacean Gammarus lacustri, US Department of the Interior, Fish and Wildlife Service, Bureau of Sport, Fish and Wildlife p. 18 (Technical Paper No. 25).

SANDERS, H.O. & COPE, O.B. (1968) The relative toxicity of several pesticides to naiads of three species of stoneflies. Limnol. Oceanogr., 13: 112-117.

SANNA, M., PELOSI, N., CAROCCI, C., & DE VINCENZI, S. (1979) Soil pollution: situation of some agricultural and seaboard urban zone in the province of Rome. Boll. Chim. Unione Ital. Lab. Prov., 5: 260-270.

SASTRY, K.V. & SIDDIQUI, A.A. (1982) Effect of endosulfan and quinalphos on intestinal absorption of glucose in the freshwater murrel, Channa punctatus. Toxicol. Lett., 12: 289-293.

SCHOETTGER, R.A. (1970) Toxicology of thiodan in several fish and aquatic invertebrates, US Department of the Interior, Bureau of Sport, Fish and Wildlife, Investigations in Fish Control, Vol. 35, pp. 1-31.

SCHUMACHER, H.G., KLEIN, W., & KORTE, F. (1971) [Contributions to ecological chemistry. XXXII. Photochemical reactions of endosulfan in solution.] Tetrahedron Lett., 24: 2229-2232 (in German).

SCHUMACHER, H.G., PARLAR, H., KLEIN, W., KORTE, F. (1973) Photochemical reactions of endosulfan. Chemosphere, 2: 65-68.

SCHUPHAN, I., BALLSCHMITER, K., & TOELG, G. (1968) [On the metabolism of endosulfan in rats and mice.] Z. Naturforsch., 23: 701-706 (in German).

SCHUPHAN, I., SAJKO, B., & BALLSCHMITER, K.Z. (1972) [On chemical and photochemical breakdown of the cyclodien-insecticides, aldrin, dieldrin, endosulfan and other hexachlorobicyclo-(2.2.2)-hepten-derivatives.] Z. Naturforsch., 276: 147-156 (in German).

SHUTTLEWORTH, J.M. (1971) Determination of endosulfan and endosulfan sulfate residues in sugar beetroot and sugar beet pulp. Project No. 015, Middleport, New York, Niagara Chemical

Division, FMC Corporation Research & Development (Project Report No. M-2866).

SIEVERS, J.F., AURAND, K., HERZEL, F., KOPPE, P., & NIEMITZ, W. (1972) Studies on the endosulfan content of the Rhine and main rivers and of Silverbank filtrates. Environ. Qual. Saf., 1: 239-243.

SINGH, B.B. & NARAIN, A.S. (1982) Acute toxicity of thiodan to catfish (Heteropneustes fossilis). Bull. environ. Contam. Toxicol., 28: 122-127.

SINGH, N.N. & SRIVASTAVA, A.K. (1981) Effects of endosulfan on fish carbohydrate metabolism. Ecotoxicol. environ. Saf., 5: 412-417.

SRIVASTAVA, V. & MISRA, P.C. (1981) Effect of endosulfan on plasma membrane function of the yeast Rhodotorula gracilis. Toxicol. Lett., 7: 475-480.

STEVENSON, J.H., NEEDHAM, P.H., & WALKER, J. (1978) Poisoning of honeybees by pesticides: investigations of the changing pattern in Britain over 20 years. Rep. Rothamsted Exp. Stn, 2: 55-72.

STEWARD, D.K.R. & CAIRNS, K.G. (1974) Endosulfan persistence in soil and uptake by potato tubers. J. agric. food Chem., 22(6): 984-986.

STRACHAN, W.M.J., HUNEAULT, H., SCHERTZER, W.M., & ELDER, F.C. (1980) Organochlorines in precipitation in the Great Lakes Region. In: Afghan, B.K., & McKay, D., ed. Hydrocarbons and halogenated hydrocarbons in the aquatic environment, New York, London, Plenum Press, pp. 387-396.

TARAR, J.L. & SALPEKAR, C.R. (1980) Relative tolerance of soil algae to some selected insecticides. Sci. Cult., 46: 105-107.

TERZIEV, G., DIMITROVA, N., & RUSEV, P. (1974) Forensic medical and forensic chemical study of acute lethal poisonings with thiodan. Folia Med., 16: 325-329.

TIBERIN, P., KRISTAL, N., & ISRAELI, R. (1970) EEG findings in poisoning by endosulfan. Electroencephalogr. clin. Neurophysiol., 28: 642-648.

TRUHAUT, R., GAK, J.C., & GRAILLOT, C. (1974) Study of the modalities and action mechanisms of organochlorine

insecticides. I. Comparative study of the acute toxicity in hamster and rat. J. eur. Toxicol., 7: 159-166.

TUCKER, R.K. & CRABTREE, D.G. (1970) Handbook of toxicity of pesticides to wildlife, Gulf Breeze, Florida, US Department of the Interior, Fish and Wildlife Service, Bureau Sport Fish and Wildlife, pp. 131 (Resource Publication 84).

VERMA, S.R., RANI, S., BANSAL, S.K., & DALELA, R.C. (1980) Effects of the pesticides thiotox, dichlorvos, and carbofuran on the test fish Mystus vittatus. Water Air Soil Pollut., 13: 229-234.

VERMA, S.R., RANI, S., BANSAL, S.K., & DALELA, R.C. (1981) Evaluation of the comparative toxicity of thiotox, dichlorvos, and carbofuran to two freshwater teleosts Ophiocephalus punctatus and Mystus vittatus. Acta. hydrochim. hydrobiol., 9: 119-129.

VERMA, S.R., BANSAL, S.K., GUPTA, A.K., PAL, N., TYAGI, A.K., BHATNAGAR, M.C., KUMAR, V., & DALELA, R.C. (1982a) Bioassay trials with 23 pesticides to a freshwater teleost, Saccobranchus fossilus. Water Res., 16: 525-529.

VERMA, S.R., TONK, I.P., & DALELA, R.C. (1982b) Effects of a few xenobiots on three phosphatases of Saccobranchus fossilis and the role of ascorbic acid in their toxicity. Toxicol. Lett., 10: 287-292.

VERMA, S.R., RANI, S., TONK, I.P., & DALELA, R.C. (1983) Pesticide-induced dysfunction in carbohydrate metabolism in three freshwater fishes. Environ. Res., 32: 127-133.

WEGMAN, R.C.C. & GREVE, P.A. (1978) Organochlorine, cholinesterase inhibitors and aromatic amines in Dutch water samples, Sept. 1969-Dec. 1975. Pestic. Monit. J., 12: 149-162.

WEGMAN, R.C.C. & GREVE, P.A. (1980) Halogenated hydrocarbons in Dutch water samples over the years. In: Afghan, B.K. & McKay, D., ed. Hydrocarbons and halogenated hydrocarbons in the aquatic environment, New York, London, Plenum Press, pp. 405-415.

WHO (1984) The WHO recommended classification of pesticides by hazard. Guidelines to classification 1984-1985, Geneva, World Health Organization (Unpublished report VBC/84.2).

WOLFE, H.R. (1976) Field exposure to airborne pesticides. In: Lee, R.E., ed. Air pollution from pesticides and agricultural processes, Florida, CRC Press, pp. 137-161.

WONG, H.F. & DONNELLY, J.P. (1968) A preliminary pesticide survey in the Bay of Quinte and international section of the St. Lawrence River, August-October 1968, Department of National Health and Welfare, Division of Public Engineering (Manuscript Report KR-68-4).

WORTHING, C.R. (1979) The pesticide manual, 6th ed., Croydon, British Crop Protection Council (BCPC Publications).

YADAV, A.S., VASHISHAT, R.K., & KAKAR, S.N. (1982) Testing of endosulfan and fenitrothion for genotoxicity in Saccharomyces cerevisiae. Mutat. Res., 105, 403-407.

ZANINI, E., BARBERIS, E., & RONCO, C. (1980) Gas chromatographic determination of vinclozolin and endosulfan in strawberries. J. agric. food Chem., 28: 464-466.

ZIMMERLI, B., ZIMMERMANN, H., & MAREK, B. (1979) [Transfer of biocidal materials from paint into the gas phase: endosulfan.] Chemosphere, 8(7): 465-472 (in German).