

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 43

CHLORDECONE

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 the 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.

IBN 92 4 154183 0

©World Health Organization 1984

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

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

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

PRINTED IN FINLAND
84:6276 - VAMMALA 5500

CONTENTS

	<u>Page</u>
ENVIRONMENTAL HEALTH CRITERIA FOR CHLORDECONE	
1. SUMMARY AND RECOMMENDATIONS	9
1.1 Summary	9
1.1.1 Properties and analytical methods	9
1.1.2 Uses and sources of exposure	9
1.1.3 Environmental concentrations and exposures	9
1.1.4 Kinetics and metabolism	9
1.1.5 Studies on experimental animals	10
1.1.6 Effects in man	10
1.2 Recommendations	10
2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, AND ANALYTICAL METHODS	11
2.1 Identity	11
2.2 Physical and chemical properties	11
2.3 Analytical methods	12
3. SOURCES IN THE ENVIRONMENT, ENVIRONMENTAL TRANSPORT AND DISTRIBUTION	15
3.1 Production and uses	15
3.2 Transport and distribution	15
3.2.1 Air	15
3.2.2 Water	16
3.2.3 Soil	16
3.2.4 Abiotic degradation	17
4. ENVIRONMENTAL LEVELS AND EXPOSURES	18
4.1 General population exposure	18
4.2 Occupational exposure	19
4.3 Wildlife	20
5. KINETICS AND METABOLISM	21
5.1 Animal studies	21
5.2 Human studies	21
6. STUDIES ON EXPERIMENTAL ANIMALS	23

	<u>Page</u>
6.1 Single exposures	23
6.2 Short-term exposures	23
6.2.1 Dermal toxicity	23
6.3 Long-term exposures and carcinogenicity studies	23
6.4 Reproduction and teratology studies	23
6.5 Mutagenicity	27
6.6 Behavioural studies	28
6.7 Neurotoxicity	28
6.8 Other studies	28
7. EFFECTS ON MAN	30
7.1 Poisoning incidents in the general population	30
7.2 Occupational exposure	30
7.3 Treatment of poisoning in man	30
8. EFFECTS ON ORGANISMS IN THE ENVIRONMENT	31
8.1 Aquatic organisms	31
8.2 Terrestrial organisms	34
8.3 Microorganisms	37
8.4 Bioaccumulation and biomagnification	38
8.5 Population and community effects	41
8.6 Effects on the abiotic environment	41
8.7 Appraisal	41
9. PREVIOUS EVALUATIONS OF CHLORDECONE BY INTERNATIONAL BODIES	43
10. EVALUATION OF HEALTH RISKS FOR MAN AND EFFECTS ON THE ENVIRONMENT	44
10.1 Chlordecone toxicity	44
10.2 Exposure to chlordecone	44
10.3 Effects on the environment	44
10.4 Conclusions	45
REFERENCES	46

TASK GROUP MEETING ON ENVIRONMENTAL HEALTH CRITERIA FOR
ORGANOCHLORINE PESTICIDES OTHER THAN DDT (CHLORDANE,
HEPTACHLOR, MIREX, CHLORDECONE, KELEVAN, CAMPHECHLOR)

Members

- Dr Z. Adamis, National Institute of Occupational Health,
Budapest, Hungary
- Dr D.A. Akintonwa, Department of Biochemistry, Faculty of
Medicine, University of Calabar, Calabar, Nigeria^a
- Dr R. Goulding, Chairman of the Scientific Sub-committee, UK
Pesticides Safety Precautions Scheme, Ministry of
Agriculture, Fisheries & Food, London, England (Chairman)
- Dr S.K. Kashyap, National Institute of Occupational Health
(Indian Council of Medical Research), Meghaninager,
Ahmedabad, India
- Dr D.C. Villeneuve, Environmental Contaminants Section,
Environmental Health Centre, Tunney's Pasture, Ottawa,
Ontario, Canada (Rapporteur)
- Dr D. Wassermann, Department of Occupational Health, The
Hebrew University, Haddassah Medical School, Jerusalem,
Israel (Vice-Chairman)

Representatives of Other Organizations

- Dr C.J. Calo, European Chemical Industry Ecology and
Toxicology Centre (ECETOC), Brussels, Belgium
- Mrs M.Th. van der Venne, Commission of the European
Communities, Health and Safety Directorate, Luxembourg
- Dr D.M. Whitacre, International Group of National Associations
of Agrochemical Manufacturers (GIFAP), Brussels, Belgium

Secretariat

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

^a Unable to attend.

Secretariat (contd).

Mrs B. Goelzer, Division of Noncommunicable Diseases, Office
of Occupational Health, World Health Organization, Geneva,
Switzerland

Dr Y. Hasegawa, Division of Environmental Health,
Environmental Hazards and Food Protection, World Health
Organization, Geneva, Switzerland

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

Mr B. Labarthe, International Register for Potentially Toxic
Chemicals, United Nations Environment Programme, Geneva,
Switzerland

Dr I.M. Lindquist, International Labour Organisation, Geneva,
Switzerland

Dr M. Vandekar, Division of Vector Biology and Control,
Pesticides Development and Safe Use Unit, World Health
Organization, Geneva, Switzerland

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 CHLORDECONE

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 Assembly 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 met in Geneva from 28 November to 2 December, 1983. Dr K.W. Jager opened the meeting on behalf of the Director-General. The Task Group reviewed and revised the draft criteria document and made an evaluation of the health risks of exposure to chlordecone.

This document is a combination of drafts 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 Properties and analytical methods

Chlordecone (Kepone) is a tan- to white-coloured solid.

Gas chromatography with electron capture detection is the method most widely used for the determination of chlordecone.

1.1.2 Uses and sources of exposure

Chlordecone was used as an insecticide and as a base material in the manufacture of the insecticide kelevan. Its production in the USA was discontinued in 1976; information about its production elsewhere is lacking.

Exposure of the general population through its normal use can be regarded as minimal and is mainly related to residues in food. Poisoning amongst workers and severe contamination of the surrounding area and rivers have occurred where manufacture and formulation were carried out in a careless and unhygienic manner. The exposure of people living near these plants must have been considerable.

Small children may be exposed through playing with insect traps containing chlordecone.

1.1.3 Environmental concentrations and exposures

Chlordecone presents a major hazard for aquatic ecosystems because of its stability and persistence in sediments, its bioaccumulation in food chains, and its acute and chronic toxicity. Low concentrations cause reductions in both algal growth and invertebrate populations, thereby affecting productivity at other trophic levels. The few data available on terrestrial ecosystems indicate low acute toxicity but some long-term effects on vertebrate reproduction.

1.1.4 Kinetics and metabolism

Chlordecone is readily absorbed following ingestion by animals and human beings. It is also absorbed following inhalation and dermal exposure. It is widely distributed in the body; accumulation occurs mainly in the liver. The half-life in the body is of the order of several months and excretion is slow, mainly via the faeces.

1.1.5 Studies on experimental animals

Chlordecone is moderately toxic with single exposures. Acute toxic symptoms in all species tested included severe tremors. It can cause skin irritation. In long-term studies, lower doses caused tremors and other neurological symptoms, liver hypertrophy with induction of mixed function oxidases, hepatobiliary dysfunction, and centrilobular hepatocellular necrosis.

Chlordecone interferes with reproduction, and it is fetotoxic in experimental animals.

It is not generally active in short-term tests for genetic activity. Chlordecone is carcinogenic in both sexes of mice and rats producing hepatocellular carcinomas.

1.1.6 Effects in man

No accidental poisonings have been reported.

A large number of cases of occupational poisoning were reported in a manufacturing plant where work hygiene and safety precautions were insufficient. Neurological symptoms, especially nervousness and tremors, together with oligospermia and joint pains were reported.

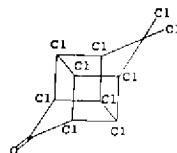
1.2 Recommendations

1. Careful surveillance should be maintained over the future production of chlordecone and the nature and extent of its use.
2. The levels in the environment should continue to be monitored.
3. It is desirable that a long-term follow-up study should be conducted on workers whose health has been affected by chlordecone.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES,
AND ANALYTICAL METHODS

2.1 Identity

Chemical structure:



Molecular formula:	C ₁₀ Cl ₁₀ O
CAS chemical name:	1,1a,3,3a,4,5,5,5a,5b,6-decachloro-octahydro-1,3,4-metheno-2H-cyclobuta[cd]pentalen-2-one
Synonyms:	decachloro-pentacyclo[5,2,1,0 ^{2,6} ,0 ^{3,9} ,0 ^{5,8}]decan-4-one, decachloro-octahydro-1,3,4-metheno-2H,5H-cyclobuta[cd]pentalen-2-one
Trade names:	GC 1189, Kepone, Merex
CAS registry number:	143-50-0
Relative molecular mass:	490.6

2.2 Physical and Chemical Properties

Chlordecone is a tan- to white-coloured solid that sublimes with some decomposition at 350 °C (IARC, 1979). Its vapour pressure is less than $3 \cdot 10^{-7}$ at 25 °C.

In the anhydrous form, chlordecone is soluble in organic solvents such as benzene and hexane. The hydrated compound is less soluble in apolar solvents. Oxygenated solvents such as alcohols and ketones are recommended for the hydrated form (Blanke et al., 1977). Chlordecone is also soluble in light petroleum and may be recrystallized from 85 - 90% aqueous ethanol (Information Canada, 1973). It is readily soluble in acetone (IARC, 1979).

Early reports did not include any evidence of chlordecone degradation in the natural environment (Dawson, 1978; Geer, 1978), but, in a more recent study, microbial action has been shown to transform chlordecone into monohydro- and possibly dihydro-chlordecone (Orndorff & Colwell, 1980a).

Technical grade chlordecone contains from 88.6% to 99.4% chlordecone (Blanke et al., 1977), 3.5 - 6.0% water (Dawson, 1978) and 0.1% hexachlorocyclopentadiene. It has been formulated as a wettable powder (50% chlordecone), emulsifiable concentrates, granules, and dust (Information Canada, 1973).

2.3 Analytical Methods

Various methods for the determination of chlordecone are summarized in Table 1.

Table 1. Methods for the determination of chlordescone

Sample type or medium	Sampling method extraction/clean-up	Analytical method	Limit of detection	Reference
general		gas chromatography electron capture detection (GC/ECD)	0.005 - 0.01 µg	Moseman et al. (1978)
formulations, concentrations, wettable powders	extract (acetone), decant, evaporate to dryness, dissolve (decane), boil, cool	infrared (IR) (c = o band)	-	Allied Chemicals Corporation (1966)
technical grade	extract (acetone-decane), heat to remove acetone, boil, cool	infrared (IR) (c = o band)	-	Allied Chemicals Corporation (1966)
air	trap on filter and back up impinger containing sodium hydroxide solution, extract filter (benzene-methanol), acidify extract (benzene), bulk extracts	gas chromatography electron capture detection (GC/ECD)	0.1 µg/m ³	NIOSH (1977)
food: apples	extract (benzene), decant, filter	gas chromatography electron capture detection (GC/ECD)	80 µg/kg	Brewerton & Slade (1964)

Table 1 (contd).

Sample type or medium	Sampling method extraction/clean-up	Analytical method	Limit of detection	Reference
potatoes	extract (methylene chloride), column chromatography (CC)	thin-layer chromatography (TLC) (revelation: silver nitrate/ultra-violet) gas chromatography electron capture detection (GC/ECD)	200 µg/kg	Proszynska (1977)
bananas	extract (isopropanol-benzene), evaporate to dryness, dissolve (hexane), liquid/liquid partition, extract (benzene)	gas chromatography (GC)/micro coulometric detection	3 µg/kg	Allied Chemicals Corporation (1963)
water	add XAD-2 resin to water, extract (toluene ethyl acetate), column chromatography (CC)	gas chromatography electron capture detection (GC/ECD)	0.015 µg/kg	Harris et al. (1980)
soil and sediment	extract (50% methanol in benzene), column chromatography (CC)	gas chromatography electron capture detection (GC/ECD)	10 - 20 µg/kg	Blanke et al. (1977); Moseman et al. (1977); Saleh & Lee (1978); Grudorff & Colwell (1980b)
biological tissues	extract (toluene in ethyl acetate), column chromatography (CC)	gas chromatography electron capture detection (GC/ECD)	10 µg/kg	Magy et al. (1979)

3. SOURCES IN THE ENVIRONMENT, ENVIRONMENTAL TRANSPORT AND DISTRIBUTION

3.1 Production and Uses

The synthesis of chlordane was first reported in 1952 by Gilbert & Giolito (1952). Commercial production in the USA started in 1966 (IARC, 1979).

Chlordane is manufactured by the condensation of 2 molecules of hexachlorocyclopentadiene in the presence of sulfur trioxide, followed by hydrolysis to the ketone. It is also produced during the synthesis of mirex and is a contaminant of technical grade mirex. From the 1950s until 1975, some 1 600 000 kg of chlordane were produced in the USA, of which between 90% (Sterrett & Boss, 1977) and 99.2% (US EPA, 1976b) was exported to Africa, Europe, and Latin America. The bulk of the remainder, 12 000 - 70 000 kg (US EPA, 1976b) was used in ant and cockroach traps in the USA or, after 1978, stored until it could be disposed of safely. It has been reported that most of the chlordane exported was used in the manufacture of kelevan (Cannon et al., 1978).

Chlordane has been used extensively in the tropics for the control of banana root borer (Anonymous, 1978a; Langford, 1978). It is regarded as an effective insecticide against leaf-cutting insects, but less effective against sucking insects (Information Canada, 1973). It can be used as a fly larvicide, as a fungicide against apple scab and powdery mildew (Information Canada, 1973), and to control the Colorado potato beetle (Motl, 1977), rust mite on non-bearing citrus, and potato and tobacco wireworm on gladioli and other plants (Suta, 1978).

Life Science Products in Hopewell, Virginia, produced up to 2700 kg of chlordane a day between April, 1974 and June, 1975, when the plant was closed (Lewis & Lee, 1976). Chlordane production was discontinued in the USA in 1976. However, a year later it was reported that a French company was considering the establishment of production facilities in France (Anonymous, 1978b), but no further information on this proposal is available.

3.2 Transport and Distribution

3.2.1 Air

Laboratory and field observations indicate that chlordane does not volatilize to any significant extent (Dawson, 1978). However, in the past, the release of copious quantities of chlordane dust from production facilities has

represented a major source of environmental and human contamination. It has been suggested that chlordecone emissions from the Hopewell plant "were of a fine particle size having a long residence time in the atmosphere" (Lewis & Lee, 1976).

3.2.2 Water

The solubility of chlordecone in water is low (1 - 2 mg/litre) and, as in the case of mirex, contamination is more likely to be associated with the particulate matter in the water than with the water itself (Orndorff & Colwell, 1980b). With the exception of contamination in the James River system, very little information is available on chlordecone residues in water. Sampling after the closure of the Life Science Plant revealed chlordecone levels of 1 - 4 µg/litre in Bailey Creek, 0.1 µg/litre in the Appomattox River, and 0.3 µg/litre in the James River and at the mouth of Bailey Creek (Smith, 1976).^a Chlordecone was not detected (limit of determination 0.01 mg/kg) in samples taken from the James River several months after the plant was shut down (Huggett et al., 1977). However, it was detected periodically in the water table of Hopewell at levels as high as 3.4 µg/litre but typically 0.1 µg/litre (Dawson, 1978) and was also detected in the New York water supply of the Great Lakes Basin by Suta (1978).

Residues as high as 0.21 µg chlordecone/litre have been reported in runoff from a banana plantation in Guadeloupe (Snegaroff, 1977).

3.2.3 Soil

Chlordecone has a high affinity for soils and sediments such that, at equilibrium in the environment, residue levels in particulate matter will be 10^4 - 10^5 times that in any surrounding water (Dawson, 1978). Consequently, sediments act as sinks for chlordecone-contaminated water and soils provide a sink for most atmospheric contamination. Again, most of the residue data result from work in and around Hopewell and the James River system. Sediment levels were as high as 10 mg/kg in Bailey Bay, and it has been estimated that as much as 47 000 kg of chlordecone lie on the bottom of the James River (Chigges, unpublished data, 1977).

^a Smith, W.C. (1976) Kepone discharges from Allied Chemical Corporation, Hopewell, Virginia, Denver, Colorado, US EPA, National Field Center (Internal EPA Memorandum).

Soil residue levels in Hopewell ranged from as high as 10 000 - 20 000 mg/kg near the plant to 2 - 6 mg/kg at a distance of 1 km (US EPA, 1976a) and it was estimated (Anonymous, 1978) that 1000 kg of chlordane lay within a 1 km radius of the plant. Most of the soils tested in Hopewell contained detectable levels of chlordane with concentrations generally decreasing with increasing distance from the plant (Dawson, 1978). Chlordane residues may be expected in sediments of waterways in the vicinity of other production-formulation facilities, but no data are available on this.

The US EPA (Anonymous, 1978a) estimated that a field that had been treated with chlordane (4.2 kg active ingredient/ha) should have a residue level of 100 mg/kg in the top 3 cm of soil, after application. Reports of actual determinations in soil are scarce, but the United Fruit Company (Anonymous, 1978a) described a residue level of 15 - 25 mg/kg, 6 months after an application of 6.73 kg active ingredient/ha. Snegaroff (1977) reported soil residue levels of 9.5 mg/kg and a level of 0.135 mg/kg in sediments in streams neighbouring on a banana plantation in Guadeloupe.

3.2.4 Abiotic degradation

Chlordane is an extremely stable compound and, as mentioned in section 2, it is not expected to be degraded in the environment to any significant extent. However, there have been reports of trace amounts of monohydro-chlordane being found (Carver et al., 1978, Orndorff & Colwell, 1980b), but the mechanism of its formation is not clear. Solar irradiation of chlordane in the presence of ethylenediamine will result in 78% degradation after 10 days, but no study of the degradation products or their toxicity has been undertaken (Dawson, 1978).

4. ENVIRONMENTAL LEVELS AND EXPOSURES

4.1 General Population Exposure

Precise information on general population exposure to chlordecone is not available. However, a summary of the daily exposure from several sources in different regions in the USA has been compiled (Suta, 1978).

(a) Air

Airborne chlordecone has been known to spread 60 miles from a point source (Feldmann, 1976), and the potential exists for further dispersion of fine particles (Lewis & Lee, 1976).

(b) Water

At present, exposure via drinking-water does not present a health hazard with the possible exception of that in the Hopewell area. Values quoted for the lower James River ranged from 0.1 to 10 µg/litre (Suta, 1978).

(c) Food

The USA action levels for chlordecone residues in foods are 0.3 mg/kg for shellfish, 0.3 mg/kg for finfish, 0.4 mg/kg for crabs, and 0.01 mg/kg for banana peels (Suta, 1978). While the majority of shellfish taken from the polluted James river in 1976 contained less than the 0.3 mg/kg action level of chlordecone, oyster and clam samples in certain areas contained 0.21 - 0.81 mg/kg, crab samples contained 0.45 - 3.44 mg/kg, and finfish samples 0.02 - 14.4 mg/kg. These data prompted a fishing ban on the James River (Shanholtz, 1976).

In 1978, samples of spot, flounder, mullet, trout, and croakers from the James River contained chlordecone but in concentrations below the 0.3 mg/kg action level (Suta, 1978). In bluefish, one sample was above 0.1 mg/kg (0.2 mg/kg) (US FDA, 1977). The shellfish sampled in the same area contained chlordecone, but at levels that could not be reliably determined (Reuber, 1977). All crabs in the area contained chlordecone, but all levels were below the action level.

In 1976, samples from the polluted Chesapeake Bay contained levels of 0.037 mg/kg for 75 finfish samples and 0.61 mg/kg for 11 crab samples, and levels in 3 samples of oysters and one sample of clams were non-detectable (US EPA, 1979).

Residues in Atlantic coast bluefish (66 samples) ranged from 0.01 to 0.06 mg/kg, with the higher concentrations found

off the Virginia coast (Peeler, 1976). South Atlantic coastal fish were relatively free of chlordane as only 1 out of 132 samples contained detectable levels (Reuber, 1977).

Residues of chlordane in edible plants have only been reported in New Zealand (Brewerton & Slade, 1964). No data are available in the literature for chlordane residue levels in bananas (Suta, 1978).

Chlordane has been found in 9 out of 298 samples of human milk, but the detection limit was relatively high (1 µg/kg) (Suta, 1978). Samples were taken in the southern USA, and chlordane residues were only found in areas that had received bait treatment for fire ants.

(d) Exposure in infants

Two major sources of chlordane exposure for infants are insect traps and human milk. The USDA (1977)^a has reported that, of 56 cases of non-occupational exposure to chlordane, 52 were children under the age of 5, and all but 9 of these had come into contact with insect traps. This is understandable as children of this age group are fairly inquisitive and their activity areas are likely to overlap target areas for ant and cockroach traps. The same study also cited exposure of 2 adults and 2 persons of unspecified age.

To date, chlordane contamination of human milk has only been reported in 9 samples (Suta, 1978) in the southeastern USA. However, relatively few samples have been tested for chlordane.

(e) Miscellaneous

Since tobacco plants were treated with chlordane, this may have also represented an exposure route, but again no residue data are available.

4.2 Occupational Exposure

Chlordane received its notoriety when severe and widespread industrial poisoning was discovered at the Life Science Plant (LSP) in Hopewell in 1975. From March 1974 to June 1975, the LSP recorded output of chlordane was 769 390 kg (Dawson, 1978). The total production was certainly above this figure, but massive amounts of chlordane found their way into

^a Comments of the Secretary of Agriculture in response to the Notice of Intent to cancel pesticide products containing chlordane, trade name "Kepone". Washington DC vs. USDA, January 11, 1977.

the soil, water, and air surrounding the plant. The workers in the plant and the families in the area were exposed to extremely high concentrations of chlordecone dust. High volume air samplers (Pate & Tabor, 1962), 200 m from the plant, recorded chlordecone levels as high as 54.8 mg/m³, which constituted 50% of the total particulate load. Lower concentrations of chlordecone were detected in the air 25 km away from the plant. Concentrations of chlordecone dust within the plant were not monitored, but levels reaching 11.8 mg/litre were found in blood samples of workers from the LSP (Heath, 1978). Illness was found in 76 of the 133 current and former workers of the plant examined. Families of the LSP workers were also examined, as well as Allied Chemical Corporation people working in the area of the plant, workers from the sewage treatment plant that received chlordecone sludge, and residents of Hopewell. It was found that the blood levels of workers who were ill averaged 2.53 mg/litre, whereas the average level in workers not reporting ill was 0.60 mg/litre (Heath, 1978).

4.3 Wildlife

Residue levels for phytoplankton in the James River were found to average 1.3 mg/kg (Huggett et al., 1977).

Chlordecone residues were also found in several species of birds that inhabit the southeastern USA coast, such as the blue heron, mallard duck, coot, black duck, wood duck, herring gull, Canada goose, hooded mersanger, and the bald eagle (Dawson, 1978). Residue levels were as high as 13.23 mg/kg (Dawson, 1978), but typically between 0.02 and 2 mg/kg. Eggs from the bald eagles and the osprey in Virginia were also examined and were found to contain residue levels ranging from 0.14 to 0.19 mg/kg, and 0.06 to 1.5 mg/kg, respectively (Dawson, 1978).

Studies on marsh plants in the James River Basin indicated that there was no translocation of chlordecone from root to aerial plant tissue (Lunz, 1978).

5. KINETICS AND METABOLISM

Only limited information is available on the absorption, distribution, metabolism, and excretion of chlordecone in human beings and animals. These aspects of the chemical are therefore discussed together, rather than in separate sections.

5.1 Animal Studies

The results of earlier studies by Huber (1965) indicated that, after dietary exposure, chlordecone was accumulated mainly in the liver of mice. The brain, fat, and kidneys also contained some residues. Chlordecone was well absorbed and distributed throughout the body of rats after oral administration. Following a single oral dose at 40 mg/kg body weight, the highest concentrations were found in the adrenal glands and liver, followed by the fat and lung (Egle et al., 1978). The compound had a long biological half-life and disappeared more slowly from the liver than from other tissues. Excretion occurred mainly in the faeces, a total of 66% of the dose being removed in the faeces and 2% in the urine in the 84 days following administration. Faecal excretion of chlordecone in rats was increased by the administration of an ionic exchange resin, cholestyramine (Boylan et al., 1977). Excretion of chlordecone by the gastrointestinal tract, in addition to the biliary route, occurs in rats as well as human beings (Boylan et al., 1979). A small amount of chlordecone alcohol was found in rat faeces suggesting that chlordecone underwent reductive biotransformation in the rat (Blanke et al., 1978).

5.2 Human Studies

A number of studies were conducted to investigate the kinetics of chlordecone in workers who were exposed to this chemical. Chlordecone was present in high concentrations in the liver (mean and range) (75.9 mg/kg; 13.3 - 173 mg/kg), whole blood (5.8 mg/litre, 0.6 - 32 mg/litre), and subcutaneous fat (21.5 mg/kg, 2.2 - 62 mg/kg) of 32 male workers (Cohn et al., 1976). Adir et al. (1978) reported that, in occupationally-exposed workers, serum chlordecone concentrations ranged from 120 to 2109 µg/litre. Six to 7 months later, the concentration dropped to 37 - 486 µg/litre. The half-life was estimated to be 63 - 148 days. Chlordecone was eliminated, primarily in the faeces, at a mean daily rate of 0.075% of the estimated total store in the body (Cohn et al., 1976). Cholestyramine was found to increase the faecal excretion of chlordecone by a factor of

6 - 7, presumably by interfering with reabsorption from the intestine. Chlordecone underwent extensive biliary excretion and enterohepatic circulation. Elimination by the gastrointestinal tract also played an important role (Boylan et al., 1979). Chlordecone alcohol was identified in human faeces (Blanke et al., 1978).

6. STUDIES ON EXPERIMENTAL ANIMALS

6.1 Single Exposures

Toxicity data resulting from single exposures to chlordecone in several animal species are summarized in Table 2. Toxic symptoms included severe tremors in all species tested. These tremors usually reached a maximum within 2 - 3 days, then gradually subsided. Tremors were exacerbated by excitement.

In dermal studies on rats and rabbits, no skin irritation was observed when chlordecone was administered in oil, but in aqueous solution it produced marked irritation, oedema, and scab formation (Epstein, 1978).

6.2 Short-Term Exposures

The effects of chlordecone following short-term exposures are summarized in Table 3. In general, they include nervous symptoms, liver hypertrophy, induction of mixed-function oxidases (EC 1.14.14.1), and structural and ultrastructural changes in the liver, thyroid, adrenals, and testes. Death sometimes followed.

6.2.1 Dermal toxicity

A study has been reported (Epstein, 1978) in which chlordecone concentrations equivalent to 5 and 10 mg/kg body weight were tested on groups of 6 male albino rats for 3 weeks, totalling 15 applications; the animals were killed 2 weeks after termination of exposure. Two out of 6 animals in the low-dose group and 1 out of 6 in the high-dose group showed testicular atrophy. Otherwise, there were no consistent or significant pathological changes.

6.3 Long-Term Exposures and Carcinogenicity Studies

The long-term and carcinogenic effects of chlordecone are summarized in Table 4. Effects in these studies were similar to those reported following short-term exposures. The data indicate that chlordecone is carcinogenic in mice and rats. These studies were reviewed by IARC (1979) and it was concluded that chlordecone produced hepatocellular carcinomas in both sexes of mice and rats.

6.4 Reproduction and Teratology Studies

The reproductive performance of mice fed 0, 10, 30, or 37.5 mg chlordecone/kg diet was impaired in terms of offspring

Table 2. Acute toxicity of chlordecone

Species	Sex	Route of administration	LD ₅₀ (mg/kg body weight)	Reference
dog	M & F	oral	250	Larson et al. (1979b)
rabbit	?	oral	65	NIOSH (1978)
chicken	?	oral	480	NIOSH (1978)
rat	?	oral	95	NIOSH (1978)
rabbit	?	dermal	345	NIOSH (1978)
rat	M	oral (oil)	132	Larson et al. (1979b)
rat	F	oral (oil)	126	Larson et al. (1979b)
rat	M	oral (aqueous)	96	Epstein (1978)
rabbit	M	oral (oil)	71	Larson et al. (1979b)
rabbit	M	oral (aqueous)	65	Epstein (1978)
rabbit	M	dermal (oil)	410	Epstein (1978)
rabbit	M	dermal (aqueous)	435	Epstein (1978)
pig	M	oral (approx.)	250	Epstein (1978)
rat	M	oral (aqueous)	9.6 ^a	Epstein (1978)
rat	M	oral (peanut oil)	125	Gaines (1969)
rat	F	oral (peanut oil)	125	Gaines (1969)
rat	M	dermal (xylene)	2000	Gaines (1969)
rat	F	dermal (xylene)	2000	Gaines (1969)

^a These animals were dosed for 20 consecutive days excluding Sundays.

and litter size (Huber, 1965). No litters were produced by females fed 40 mg/kg, but litter production did resume within 7 weeks following withdrawal of the chlordecone, although litters were still smaller than those of untreated controls. Histological examination of the testes showed they were normal, but corpora lutea were virtually absent from the ovaries. The authors concluded that reproductive failure was largely due to an effect in females characterized by prolonged FSH and estrogen stimulation, inducing constant estrus, large follicles and absence of corpora lutea but with levels of LH subminimal for ovulation.

Table 3. Summary of short-term studies with chlordane

Species	Sex	Duration	Dose	Effects	Reference
mouse	M	14 days	1, 10, or 50 mg/kg diet	induction of hepatic mixed-function oxidases at 2 highest levels	Fabacher & Hodgson (1976)
rat	M	8 days	200 mg/kg diet	ultrastructural changes in the liver and adrenal medulla, decreased adrenal catecholamines, and increased P-450 values	Baggett et al. (1977, 1980)
rat	F	15 days	50, 100, or 150 mg/kg diet	decreased body weight gain and induction of mixed-function oxidases at all 3 levels of treatment	Mehendale et al. (1978)
rat	M	15 days	10, 50, or 150 mg/kg diet	decreased biliary excretion at 10 mg/kg and higher; body weight gain affected at 50 mg/kg and higher; liver enlargement at all 3 levels of treatment	Mehendale et al. (1978)
rat	M & F	3 months followed by "clean" diets for 4.5 months	25 mg/kg diet	tremors after 4 weeks; liver hypertrophy; liver and adrenals both showed histological changes; after recovery period, liver still showed histological abnormalities	Cannon & Kimbrough (1979)
rat		14 days	1 mg/kg diet	induction of hepatic mixed-function oxidases	Baker et al. (1972)

Table 4. Summary of long-term and carcinogenicity studies with chlordecone

Species	Duration	Dose	Effects	Reference
rat	2 years	5, 10, 25, 50, or 80 mg/kg diet	all rats on 2 highest doses died during first 6 months; depressed growth occurred at 10 mg/kg and higher; liver hypertrophy occurred at levels of 10 mg/kg and higher; histopathological findings in liver, kidneys, and testes at 25 mg/kg; haematological changes at 25 mg/kg	Larson et al. (1979b)
dog	127 weeks	1, 5, or 25 mg/kg diet	weight gain reduced at 25 mg/kg; no treatment-related histological abnormalities observed	Larson et al. (1979b)
mouse	90 weeks	20 - 40 mg/kg diet	survival reduced at high-dose level in males; hepatocellular carcinomas induced in both males and females	Anonymous (1976)
rat	up to 24 months	1 - 80 mg/kg diet	hepatocellular carcinomas observed in some intermediate dose groups, but not all	Larson et al. (1979b)
mouse	12 months	0 - 100 mg/kg diet	tremors observed after 4 weeks in all mice fed 30 or more mg/kg; deaths observed at 2 highest doses; liver enlargement observed at 40 mg/kg and higher; microscopic and electron microscopic changes observed in dose-dependent manner	Huber (1965)
rat	exposure for 80 weeks followed by 16 weeks of observation	8 - 26 mg/kg diet	increased incidence of hepatocellular carcinomas observed in high-dose females	Anonymous (1976)
rat	up to 2 years	1 mg/kg diet	increased incidence of malignant tumours in male and female rats	Reuber (1978, 1979)

In a study reported by Good et al. (1965), male and female mice fed chlordecone in the diet at levels ranging from 10 to 375 mg/kg for 1 month, were randomly paired with animals at the same feeding level and then maintained on the same diet for 4 months. The results indicated that chlordecone caused a dose-dependent effect on reproduction, even at 10 mg/kg.

Similar effects on reproduction were noted by Hammond et al. (1978) in rats fed 30 mg/kg; the estrogenic properties of this chemical were also noted (Couch et al., 1977; Bulger et al., 1979; Hammond et al., 1979). In female rats fed 25 mg chlordecone/kg diet for 3 months, followed by a control diet for 4.5 months, reproduction was completely inhibited during the treatment period. Two months after exposure was discontinued, reproduction was only partially restored (Cannon & Kimbrough, 1979). Chlordecone has also been shown to interfere with egg production in both quails (McFarland & Lacy, 1969) and hens (Naber & Ware, 1965).

Chlordecone was administered by gastric intubation in doses of 2, 6, and 10 mg/kg body weight per day to rats and 2, 4, 8, and 12 mg/kg body weight per day to mice on days 7 - 16 of gestation (Chernoff & Rogers, 1976). In rats, the highest dose caused 19% maternal mortality and fetuses exhibited reduced weight, reduced degree of ossification, oedema, undescended testes, enlarged renal pelvis, and enlarged cerebral ventricles. Lower dose levels induced reductions in fetal weight and degree of ossification. Male rats born to treated dams did not show any reproductive impairment. In the mouse, fetotoxicity was observed only at the highest dose level and consisted of increased fetal mortality and clubfoot.

In a study by Rosenstein et al. (1977), rats were administered chlordecone by gavage from day 2 of gestation at levels of 1, 2, or 4 mg/kg body weight per day. At parturition, all control pups and those from mothers receiving 1 mg/kg body weight were normal. Two-thirds of the females receiving 2 mg/kg and all females receiving 4 mg/kg aborted or had still births.

Chlordecone was administered to female rats at concentrations of 2.5 mg/kg body weight per day and to mice at 6.0 - 24 mg/kg body weight per day on days 7 - 16 of gestation and also postpartum (Chernoff et al., 1979a). Although there were toxic manifestations in the mother (death) and fetuses (litter mortality, decreased litter weight), ophthalmological studies did not reveal cataracts or outlined lenses.

6.5 Mutagenicity

Chlordecone was found to be negative at dose levels of 3.6 or 11.4 mg/kg body weight per day for 5 days in a dominant lethal study on rats (Simon et al., 1978). Chlordane gave

negative results when tested for enhancement of unscheduled DNA synthesis in primary cultures of adult rat hepatocytes (Williams, 1980; Probst et al., 1981) and was not mutagenic in Salmonella typhimurium (Probst et al., 1981).

6.6 Behavioural Studies

In studies on rats administered 40 - 80 mg chlordecone/kg diet, behavioural changes including hyperactivity, decreased ambulation in an open field, and delayed emergence from the home cage were seen at both dose levels within one week (Reiter et al., 1977; Reiter & Kidd, 1978; Tilson et al., 1979). Chlordecone was given intragastrically, 5 - 6 days per week, at dosages of 1, 5, and 10 mg/kg body weight for 4 - 76 days to male and female Zivic-Miller rats. A dose of 1 mg/kg body weight disrupted the multiple-fixed-ratio test and the fixed-interval test after 3 injections and a dose of 5 mg/kg decreased the spaced-responding test after 9 - 10 injections. Gradual recovery occurred after discontinuation of treatment (Dietz & McMillan, 1978).

6.7 Neurotoxicity

Chickens (Naber & Ware, 1965), quail (McFarland & Lacy, 1969), fish (Couch et al., 1977), hamsters (Martinez et al., 1976), mice (End et al., 1979), rats (Epstein, 1978), and man (Martinez et al., 1978) have all displayed neurotoxic symptoms on exposure to chlordecone. Biochemically, chlordecone has been shown to inhibit Mg-ATPases in fish brain (IARC, 1979) and rat liver (Desai et al., 1977) and also to cause disruption of rat brain synaptosomal membranes (End et al., 1979).

6.8 Other Studies

Chlordecone has been shown to inhibit several enzymes (in vitro) including maleate dehydrogenase (Anderson et al., 1977), lactate dehydrogenase (EC 1.1.1.27) (Anderson & Noble, 1977; Anderson et al., 1978), and succinic acid dehydrogenase (Kawatski & Hecker, 1979).

Chlordecone has been demonstrated to enhance the hepatotoxic effects of both chloroform and carbon tetrachloride (Cianflone et al., 1980), but had no similar effect on the response of the rat liver to polyhalogenated biphenyls (Chu et al., 1980). It was able to increase the detoxification of lindane in weanling rats (Chadwick et al., 1979). Pretreatment of rats with low non-toxic levels of dietary chlordecone (10 mg/kg, 15 days) potentiated the hepatotoxicity (Curtis et al., 1979) and lethality of carbon

tetrachloride (Klingensmith & Mehendale, 1982a) about 70-fold in male rats and 25-fold in female rats (Agarwal & Mehendale, 1982a). Comparative doses of other inducers of microsomal enzymes such as mirex, photomirex, and phenobarbital did not potentiate carbon tetrachloride toxicity to such an extent (Curtis & Mehendale, 1980; Klingensmith & Mehendale, 1982b). Hepatobiliary dysfunction, elevation of hepatic enzymes in serum, and centrilobular hepatocellular necrosis were the characteristic features for the rat. The hepatotoxicity and lethality of bromotrichloromethane were also potentiated about 5-fold by chlordane (Agarwal & Mehendale, 1982b).

Like mirex, chlordane has been shown to modify hepatobiliary function (Mehendale, 1979), possibly due to interference with energy production and utilization.

In an inhalation study reported in a review (Epstein, 1978), male rats were exposed to test and control dusts for 2 h per day for 10 days and killed 2 weeks later. Air flow was maintained at 10 - 12 litre/min, and the effective chlordane concentrations were 3.7 and 15.4 µg/litre. The reviewer concluded, contrary to the authors of the actual study, that chlordane at both dose levels induced toxic effects, including hepatomegaly and histopathological changes in the liver and lungs.

7. EFFECTS ON MAN

7.1 Poisoning Incidents in the General Population

No information is available concerning such incidents.

7.2 Occupational Exposure

Life Sciences Products Co. (LSPC) was formed in November 1973 and went out of production in July 1975. In a study carried out by the Center for Disease Control (Cannon et al., 1978), 133 employees, including 33 currently employed, were interviewed, examined, had blood samples taken, and completed a standard questionnaire. Of the 133 examined, 76 (57%) had developed clinical illness described as nervousness, tremor, weight loss, opsoclonus, pleuritic and joint pain, and oligospermia. Illness rates were higher for production workers than non-production workers, and the mean blood-chlordecone level for workers with illness was 2.53 mg/litre compared with a level of 0.60 mg/litre in workers without disease. Laboratory findings from the above study showed an increase in serum alkaline phosphatase (EC 3.1.3.1) activity in several patients (Taylor et al., 1978) and morphological changes in peripheral nervous tissue (Martinez et al., 1978).

7.3 Treatment of Poisoning in Man

The treatment is symptomatic.

Administration of cholestyramine will increase the excretion of chlordecone, and so reduce the body burden of the chemical (Cohn et al., 1976, 1978; Anonymous, 1977).

8. EFFECTS ON ORGANISMS IN THE THE ENVIRONMENT

8.1 Aquatic Organisms

The results of studies on the toxicity of chlordecone for a variety of algae are given in Table 5.

Acute and short-term toxicity values for invertebrate species are also tabulated (Table 6). A more comprehensive table listing different conditions and exposure times is available on request from the IRPTC, Geneva. A life cycle study is available for mysid shrimps, Mysidopsis bahia (Nimmo et al., 1977). This test was long enough to cover the production of several broods. The average number of young produced by each female was reduced from the control level of 15.3 to 8.9 on exposure to 0.39 µg chlordecone/litre. Juveniles produced grew more slowly than controls. Young females exposed to as little as 0.072 µg chlordecone/litre for 14 days were shorter than controls. The authors pointed out that reproductive success was related to body size, the number of eggs produced being greater in bigger females. In a life cycle study of a copepod, Eurytemora affinis, a dominant zooplankter, the intrinsic rate of natural increase was reduced by all concentrations of chlordecone greater than 5µg/litre (Allan & Daniels, 1982). This was due to a combination of a reduced rate of survival, delayed onset of reproduction, and reduced fecundity.

The toxicity of chlordecone for fish varies with species (Table 6). Juvenile fish are generally less susceptible to chlordecone than adults. Symptoms of chlordecone poisoning (Hansen et al., 1976) progressed from scoliosis (darkening of the posterior third of the body) through haemorrhaging near the brain and anterior point of darkening, oedema, fin rot, incoordinated swimming, and cessation of feeding. Symptoms increased in severity before death, which occurred between 5 and 8 days after initial exposure. Juveniles showed reduced growth at 0.08 µg chlordecone/litre with some showing scoliosis during a 36-day test. Embryo survival was reduced when adults were exposed to chlordecone. When adults were exposed to 1.9 µg/litre, their embryos developed abnormally or died, even when incubated in chlordecone-free water. Fry from embryos exposed to 6.6 or 33 µg chlordecone/litre were visibly affected within 24 h of hatching. Symptoms of poisoning in fry less than 1 week old included diminished activity, loss of equilibrium, cessation of feeding, and emaciation. Fry more than 1 week old had symptoms identical to those in adult fish, except for haemorrhaging and oedema. Sixty percent of juvenile fish that had survived 36 days' exposure to 0.08 µg chlordecone/litre had scoliosis and

Table 5. Toxicity of chlordecone for algae

Alga	Flow/ stat	Temp (°C)	Salinity ‰/oo	End point	Parameter	Concentration (µg/litre)	Reference
<u>Chlorococum</u> sp.	stat	20±0.5	30	growth retardation	7-day EC50	0.35	Walsh et al. (1977)
<u>Dunaliella</u> <u>fertii</u>	stat	20±0.5	30	growth retardation	7-day EC50	0.58	Walsh et al. (1977)
<u>Nitzschia</u> sp.	stat	20±0.5	30	growth retardation	7-day EC50	0.60	Walsh et al. (1977)
<u>Thalassiosira</u> <u>pseudonana</u>	stat	20±0.5	30	growth retardation	7-day EC50	0.60	Walsh et al. (1977)

Table 6. Toxicity of chlordane for aquatic organisms

Organism	Flow/ stat	Temp (°C)	Salinity ‰/∞	End point	Parameter	Concentration (µg/litre)	Reference
grass shrimp (<i>Palaemonetes pugio</i>)	flow	25-28	10-20		96-h LC50 19-day LC50	121 1.4	Schimmel & Wilson (1977) Nimmo et al. (1977)
blue crab (<i>Callinectes sapidus</i>)	flow				96-h LC50 48-h LC50	>210 1000 ^a	Schimmel & Wilson (1977) Butler (1963)
eastern oyster (<i>Crassostrea virginica</i>)	flow	14		inhibition shell deposition	96-h EC50	57 ^a	Butler (1963)
American eel (<i>Anguilla rostrata</i>) juvenile stage VIA	flow	19	flesh		96-h LC50	35	Roberts & Bendl (1982)
sheepshead minnow (<i>Cyprinodon variegatus</i>)	flow				96-h LC50	69.5	Schimmel & Wilson (1977)
spot (<i>Leiostomus xanthurus</i>)	flow				96-h LC50	6.6	Schimmel & Wilson (1977)
bluegill sunfish, juv (<i>Lepomis macrochirus</i>)	flow	19-21			96-h LC50	50	Roberts & Bendl (1982)
channel catfish, juv (<i>Ictalurus punctatus</i>)	flow	20-23			96-h LC50	514	Roberts & Bendl (1982)

^a Nominal concentration, not measured.

blackened tails. In clean water, symptoms persisted for more than ten days (Hansen et al., 1976).

Estimation of the long-term effects of chlordecone on juvenile fish from the results of acute tests can result in severe underestimation. When juvenile spot were fed sublethal doses of chlordecone (0.3 and 0.7 mg/kg diet per day) for 56 days, they developed bone damage including fracturing and thickening of vertebrae (Stehlik & Merriner, 1983).

Desaiah & Koch (1975) conducted in vitro studies on brain ATPase activity in channel catfish (Ictalurus punctatus) and demonstrated a significant inhibition of oligomycin-sensitive (mitochondrial) Mg^{2+} , oligomycin-insensitive Mg^{2+} , and Na^+-K^+ ATPases with increasing concentrations of chlordecone. Inhibition was 25.7% and 36.7% at chlordecone concentrations of 1.25 and 2.5 μM , respectively. The authors noted that the resulting reduction in energy supply could have physiological consequences. Winkelhake et al. (1983) showed the inducement of an acute phase (C-reactive) protein in the serum of rainbow trout after administration of chlordecone at 5 mg/kg. The formation of these proteins is the initial reaction to bacteria or response to foreign proteins.

8.2 Terrestrial Organisms

(a) Plants

Little work on the effects of chlordecone on plants has been reported. In one experiment, chlordecone increased both the quality and quantity of the cotton yield (Gawaad et al., 1976). Residues in seeds were always <1 mg/kg, despite different application rates.

(b) Insects

In a study on bees, Atkins & Anderson (1962) reported an LT_{50} value for a 200 mg dose of chlordecone of 68 h. They tested chlordecone in 1961 on bee colonies that had shown a progressive resistance to DDT over a 5-year period. They obtained an LT_{50} value of 45 h for chlordecone, in 1952, when tested on a different strain of DDT-susceptible bees. The authors implied that DDT resistance carries over to other organochlorine insecticides; but, though lower susceptibility to chlordecone was shown by DDT-resistant bees, the results do not directly demonstrate this. The results of later studies by Atkins et al. (1973) suggest that chlordecone would have to be used at 5 times the recommended application rate to kill 50% of bee populations. At the recommended usage rate of 2.25 kg/ha, chlordecone was not harmful to 3 out of 4 predatory insect species and arthropods, monitored in an apple orchard.

There is no information on the effects of chlordane on amphibians or reptiles.

(c) Birds

Chlordane was shown not to be very toxic when fed to either young or adult birds (Table 7). Species tested were not very representative. Birds fed lethal doses of the insecticide developed characteristic whole-body tremor, prior to death (DeWitt et al., 1962; Naber & Ware, 1965; McFarland & Lacy, 1969). Japanese quail injected daily with 0.5 mg chlordane/bird showed liver damage (damage to hepatic parenchymal cells, including disruption of mitochondria, with cellular debris in the bile and bile ducts), with increased numbers of phagocytic Kupffer cells lining the liver sinusoids (US EPA, 1979).

Sublethal effects of chlordane on birds are pronounced despite the compound's low acute toxicity. A sublethal dose of 200 mg chlordane/kg diet administered to Japanese quail caused structural changes in the liver, adrenals, and gonads (Eroschenko & Wilson, 1975). Many sublethal effects of the compound are attributable to its estrogenic effects. Dosing with chlordane caused oviduct maturation in sexually immature females held on non-stimulatory daylengths, but mature females were not affected (Eroschenko & Wilson, 1975). Ovaries from chlordane-treated females contained more primary oocytes and smaller follicles than those from controls. A central effect on follicle-stimulating hormone production was postulated by McFarland & Lacy (1969), but direct hormone measurement does not seem to have been carried out. Estrogen-like stimulation of secondary sexual characteristics caused male pheasants to develop female plumage at dietary doses of 50, 100, and 150 mg chlordane/kg (DeWitt et al., 1962). Males also showed malformed sperm and reduced reproductive success. Eroschenko & Wilson (1975) reported effects on the testicles in both immature and adult quail; seminiferous tubules were distended with watery fluid that caused a significant weight increase in the testes, germinal epithelium and spermatozoa were reduced, and abundant intraluminal cellular debris was common.

Both egg laying and chick survival were reduced in domestic hens fed 75 or 150 mg chlordane/kg diet for 12 weeks. Only 56% of chicks hatched from hens treated with 75 mg/kg survived for 20 days, no chicks or hens treated with 100 mg/kg survived. Residues were still detectable in eggs laid 3 weeks after treatment ceased (Naber & Ware, 1965). Eggshell deposition was affected by chlordane. A peculiarly thick spongy layer developed leading to blockage of shell pores and suffocation of the embryo (Erben, 1972). Changes in

Table 7. Toxicity of chlordane for birds

Species	Age	Route	Parameter	Concentration (mg/kg)	Reference
mallard duck	young	diet	LC50	400	Dewitt et al. (1962)
bobwhite quail	young	diet	LD50	600	Dewitt et al. (1962)
bobwhite quail	adult	diet	LC50	530	Dewitt et al. (1962)
ringnecked pheasant	young	diet	LD50	600	Dewitt et al. (1962)
ringnecked pheasant	adult	diet	LD50	115	Dewitt et al. (1962)

shell structure occurred in Japanese quail fed 225 mg chlordecone/kg diet (US EPA, 1979).

There is no information on the toxicity of chlordecone for non-laboratory mammals.

8.3 Microorganisms

Effects of chlordecone on soil microorganisms were investigated by Gawaad et al. (1972a). Application of chlordecone to 3 soil types in the Nile Delta altered fungal, actinomycete, and other bacterial populations for as long as 45 days, compared with controls (Gawaad et al., 1972a). Unfortunately, chlordecone was applied at a very high rate (22.0 kg/ha) and therefore the results are difficult to interpret in terms of likely effects on crops. The magnitude and duration of effects on populations differed with soil type, but the general pattern was a fall in numbers in the first week followed by an increase in the second week with numbers eventually returning to normal levels. In a second experiment in which effects on nitrogen transformation in treated soils were studied, chlordecone was shown to affect fungi and bacteria responsible for ammonification, and Nitrobacter, which is responsible for changing nitrite to nitrate, but not Nitrosomonas, which is responsible for changing ammonia to nitrite (Gawaad et al., 1972b).

Similar effects on microbial populations were found by Meyers et al. (1982), when chlordecone at 0.5 mg/litre was applied to static carbon metabolism microcosms; no significant total treatment variation was seen in either bacterial or fungal populations after 10 days incubation. Similar results were obtained in response to continuous application of chlordecone. Chlordecone is probably highly toxic for sludge microorganisms, since massive amounts of beneficial bacteria in a sludge digester were killed after chlordecone wastes were discharged into the sewage system (Bray, 1975). Portier & Meyers (1982) stated that microcosms (simulated aquatic microenvironmental systems) were "sensitive" to chlordecone "under a variety of regimes". Among response criteria used were microbial diversity, enzymatic activity, ATP, and material turnover.

The toxicity of chlordecone for mixed populations of microorganisms was determined by standard plate assays on Zobell marine medium containing 0.02, 0.2, or 2 mg chlordecone/litre (Mahaffey et al., 1982). All these concentrations of chlordecone reduced the number of colony-forming aerobes but did not affect anaerobes. Gram-positive organisms were more sensitive to chlordecone than gram-negative organisms. Oxygen uptake by gram-negative isolates was reduced by 25 - 100% by chlordecone at 20 mg/litre. A

significant reduction in the specific activities of NADH oxidase and succinoxidase by the addition of chlordecone at 0.49 mg/litre indicated that chlordecone can inhibit electron transport.

8.4 Bioaccumulation and Biomagnification

Data on the bioconcentration of chlordecone are given in Table 8. It should be noted that none of the exposures were representative of realistic environmental levels. Bioaccumulation in detritus, such as decomposing Spartina cyanosuroides, was demonstrated by Odum & Drifmeyer (1978). As detritus is a major energy source in aquatic environments, this could represent an important entrance for chlordecone into aquatic food webs. Both aquatic invertebrates and fish bioaccumulate chlordecone to very high levels. Depuration is slow in fish, thus residues tend to be high. Levels of chlordecone accumulated in edible fillets were almost the same as the whole body concentrations in sheepshead minnows and spot; therefore one of the largest residue reserves in contaminated fish is in the edible portion (Bahner et al., 1977).

Residues were higher in female sheepshead minnows than in males (Bahner et al., 1977), and residues in juveniles tended to increase with increasing concentrations of chlordecone in the water (Hansen et al., 1976). When chlordecone was fed to juvenile spot for 28 days, the body burden of chlordecone increased additively and equilibrium was not attained (Stehlik & Merriner, 1983). Chlordecone accumulation in an estuarine food chain (composed of green algae, oysters, mysids, grass shrimps, sheepshead minnows, and spot) occurred at concentrations as low as 0.023 µg/litre (Bahner et al., 1977). All species had equilibrated tissue concentrations of chlordecone 8 - 17 days after the beginning of the exposure. Clearance of chlordecone from oysters was rapid; levels were non-detectable, 7 - 20 days after exposure ceased. Clearance was slow in shrimp and fish, with tissue levels of chlordecone decreasing by 30 - 50% in 24 - 28 days. When oysters were fed chlordecone-contaminated algae, the maximum overall accumulation and transfer of chlordecone (or "food-chain potential") from water to algae and then to oysters was 2.1 (Bahner et al., 1977). However, the transfer potential (transfer from one trophic level to the next) from algae to oysters was only 0.007; therefore, transfer of chlordecone from algae to oyster and retention in oyster were inefficient. When spot were fed mysids that had eaten chlordecone-contaminated brine shrimp, the food-chain potential from water to brine shrimp to mysids and finally to fish ranged from 3.9 to 10.5. The transfer potential from shrimp to mysids was 0.53

Table 8. Bioaccumulation of chlordane

Organism	Temp (°C)	Salinity ‰/oo	Flow/ stat	Bioconc. factor (BCF)	Exposure concentration (µg/litre)	Time	Reference
algae, unicellular	19.5- 20.5	30	stat	230-800	100	24 h	Walsh et al. (1977)
oyster (<u>Crassostrea virginica</u>)				9354	0.03	19 d	Bahner et al. (1977)
				9278	0.39	21 day	
grass shrimp (<u>Palaemonetes pugio</u>)				698	12-121	96 h	Schimmel & Wilson (1977)
				(425-933)			
				5127	0.023	28 day	Bahner et al. (1977)
spot (<u>Leiostomus xanthurus</u>)				11425	0.4	28 day	Bahner et al. (1977)
				3217	0.029	30 day	Bahner et al. (1977)
spot (<u>Leiostomus xanthurus</u>)				1120	1.5	96 h	Bahner et al. (1977)
fathead minnow (<u>Pimephales promelas</u>)			flow	16600	0.004	56 day	Huckins et al. (1982)

Table 8 (contd).

Organism	Temp (°C)	Salinity ‰	Flow/ stat	Bioconc. factor (BCF)	Exposure concentration (µg/litre)	Time	Reference
sheepshead minnow, juv. 21- day (<u>Cyprinodon variegatus</u>)	28-32	11-31	flow	1800	0.041	life cycle test	Goodman et al. (1982)
sheepshead minnow, juv. 42- day (<u>Cyprinodon variegatus</u>)	28-32	11-31	flow	2400	0.041	life cycle test	Goodman et al. (1982)
sheepshead minnow adult male (<u>Cyprinodon variegatus</u>)	28-32	11-31	flow	3900	0.041	life cycle test	Goodman et al. (1982)
sheepshead minnow adult female (<u>Cyprinodon variegatus</u>)	28-32	11-31	flow	3700	0.041	life cycle test	Goodman et al. (1982)
sheepshead minnow, embryos (<u>Cyprinodon variegatus</u>)	28-32	11-31	flow	2900	0.041	life cycle test	Goodman et al. (1982)
sheepshead minnow, juvenile progeny (<u>Cyprinodon variegatus</u>)	28-32	11-31	flow	2400	0.041	life cycle test	Goodman et al. (1982)

1

and from mysids to spot, 0.85. This indicated that much of the chlordecone was being transferred through the trophic levels.

No data are available on the bioconcentration of chlordecone by terrestrial organisms.

8.5 Population and Community Effects

— Chlordecone is strongly adsorbed on sediment. Effects on aquatic organisms are therefore partly from material in the water and partly from material obtained from sediment. D'Asaro & Wilkes (1982) examined the effects of sediments, previously exposed to chlordecone at a known concentration, and of James River sediments contaminated with chlordecone, on an estuarine community established in aquaria supplied with non-filtered sea water. Mysid shrimps showed a dose-related mortality rate, when exposed to sediments previously equilibrated at 0.1, 1.0, or 10 µg chlordecone/litre. Mysids were not affected by James River sediment. Oysters showed dose-dependent reduced shell growth, when exposed to chlordecone-equilibrated sediments, and also responded adversely to river sediment. Lugworms Arenicola cristata disappeared from aquaria after 28 days of treatment with sediment exposed to 10 µg chlordecone/litre, though numbers were not affected by lower doses. Both lugworms and oysters concentrated chlordecone from the sediment.

8.6 Effects on the Abiotic Environment

No data are available on the effects of chlordecone on the abiotic environment.

8.7 Appraisal

As actual levels of chlordecone in natural waters are extremely low, because most of the chlordecone is transferred rapidly to sediments, bioconcentration and toxicity test levels are often unrealistically high. However, bearing in mind the potential for bioaccumulation, data suggest that chlordecone is both acutely and chronically toxic for aquatic organisms. A major omission in the aquatic toxicity data is the toxicity of chlordecone for detritus feeders that will be exposed to significant concentrations in contaminated sediments. Exposure of the lowest level of the aquatic food chain to concentrations of chlordecone above a threshold of 0.35 - 1 mg/litre will cause disturbance or destruction, sufficient to affect productivity at other levels of the food chain. Few data are available on the sublethal effects of chlordecone on aquatic organisms. In fish, such effects include: retardation of growth, which will ultimately affect

fecundity, scoliosis, inhibition of ATPase, and stimulation of some immune response. Juvenile fish appear to be less sensitive to chlordecone than adults.

Chlordecone appears to have little effect on soil microorganisms at concentrations that would result from agricultural use. However, discharges directly into sewage systems are highly toxic for sludge microbes. Agricultural application rates cause little acute toxicity to non-target invertebrates or birds, but chlordecone at higher dosages can have pronounced effects on many reproductive variables in birds. No data are available on effects on amphibia, reptiles, or non-laboratory mammals.

9. PREVIOUS EVALUATIONS OF CHLORDEZONE BY INTERNATIONAL BODIES

IARC (1979) evaluated the carcinogenic hazard resulting from exposure to chlordane and concluded that "there is sufficient evidence for its carcinogenicity in rats and mice. In the absence of adequate data in humans, it is reasonable for practical purposes to regard chlordane as if it presented a carcinogenic risk to humans".

No acceptable daily intake (ADI) for chlordane has been proposed by FAO/WHO.

In recent years, official registrations for a number of uses of chlordane have been withdrawn in certain countries for various reasons (IRPTC, 1983).

Regulatory standards established by national bodies in 12 different countries (Argentina, Brazil, Czechoslovakia, the 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 International Register of Potentially Toxic Chemicals Legal File (IRPTC, 1983).

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

10.1 Chlordecone Toxicity

Chlordecone is moderately toxic in acute studies on rats, i.e. the oral LD₅₀ values range from 95 to 132 mg/kg body weight. It can enter the body via ingestion, inhalation, and via the skin. It is not metabolized to any significant extent. It bioaccumulates mainly in the liver, and it is excreted very slowly via the faeces.

Toxic effects include neurological symptoms, especially tremors, liver hypertrophy with enzyme induction, centrilobular hepatocellular necrosis, and hepatobiliary dysfunction. It can impair reproduction (mouse, 10 mg/kg diet or 0.5 mg/kg body weight per day) and is fetotoxic (rat, 2 mg/kg body weight per day).

Chlordecone was not generally active in short-term tests for genetic activity. There is sufficient evidence of its carcinogenicity for mice and rats.

Careless occupational handling in a manufacturing plant caused a series of poisonings with neurological symptoms, especially nervousness and tremors, oligospermia, and joint pains.

10.2 Exposure to Chlordecone

Exposure of the general population through the normal use of chlordecone can be regarded as minimal and is mainly related to residues in food.

Small children may be exposed when playing with insect traps.

10.3 Effects on the Environment

The environmental hazard posed by chlordecone is associated with its stability and persistence in sediments, which provide a long-term source of contamination, in conjunction with its massive bioaccumulation in aquatic food chains. One of the largest reserves of chlordecone in food is in the edible portion of contaminated fish. Although chlordecone has a low solubility in water, between 0.35 and 1 mg/litre is sufficient to reduce algal growth, thereby affecting productivity at other trophic levels. Chlordecone is acutely and chronically toxic for aquatic invertebrates and causes loss of equilibrium, reduction in reproductive success, and decreased shell growth at sublethal concentrations. Reduction in mysid populations due to low-level chlordecone

contamination has important consequences for fish productivity. Symptoms of exposure range from diminished activity and emaciation to abnormal development and death.

The few data available indicate that chlordecone is not acutely toxic for terrestrial invertebrates. Subacute doses of chlordecone induce significant toxic effects in birds including tremors, liver damage, and reproductive failure.

Excretion of chlordecone is extremely slow.

10.4 Conclusions

1. Serious illness has been suffered by workers occupationally over-exposed to chlordecone.
2. Based on the findings in mice and rats, this chemical should be considered, for practical purposes, as being potentially carcinogenic for human beings.
3. For the above reason, reservations must remain about the occurrence of residues of chlordecone in food.
4. Adverse effects on the organisms studied, as well as persistence, suggest that chlordecone presents a long-term hazard for the environment.
5. Taking into account these considerations, it is felt that the use of this chemical should be discouraged, except where there is no adequate alternative.

REFERENCES

- ADIR, J., CAPLAN, Y.H., & THOMPSON, B.C. (1978) Kepone serum half-life in humans. Life Sci., 22: 699-702.
- AGARWAL, A.K. & MEHENDELE, H.M. (1982a) Potentiation of CCl₄ hepatotoxicity and lethality by chlordecone in female rats. Toxicology, 26: 231-242.
- AGARWAL, A.K. & MEHENDELE, H.M. (1982b) Potentiation of bromotrichloromethane hepatotoxicity and lethality by chlordecone pre-exposure in the rat. Fundam. appl. Toxicol., 2: 161-167.
- ALLAN, J.D. & DANIELS, R.E. (1982) Life table evaluation of chronic exposure of Eurytemora affinis (Copepoda) to Kepone. Mar. Biol. (Berlin), 66: 179-184.
- ALLIED CHEMICAL CORPORATION (1963) Determination of kepone (GC-1189). Residues in crops, 26 June, Morristown, New Jersey, Allied Chemical Corporation.
- ALLIED CHEMICAL CORPORATION (1966) Assay method for kepone, 8 March, Morristown, New Jersey, Allied Chemical Corporation.
- ALLIED CHEMICAL CORPORATION (1977) Summary of basic information - Kepone insecticide, Morristown, New Jersey, Allied Chemical Corporation (Product Information Technical Data Sheet 1189-01-1012. Source 120).
- ANDERSON, B.M. & NOBLE, C., Jr (1977) In vitro inhibition of lactate dehydrogenases by Kepone. J. agric. food Chem., 25: 28-31.
- ANDERSON, B.M., NOBLE, C., Jr, & GREGORY, E.M. (1977) Kepone inhibition of malate dehydrogenases. J. agric. food Chem., 25: 485-489.
- ANDERSON, B.M., KOHLER, S.T., & YOUNG, R.W. (1978) Interactions of Kepone with rabbit muscle lactate dehydrogenase. J. agric. food Chem., 26: 130-133.
- ANONYMOUS (1976) Report on (NCI) carcinogenesis bioassay of technical grade chlordecone (Kepone). Am. Ind. Hyg. Assoc. J., 37: 680-681.

ANONYMOUS (1977) Getting Kepone out of the body. Med. World News, 18: 32.

ANONYMOUS (1978a) Kepone/mirex/hexachlorocyclopentadiene - an environmental assessment, Washington DC, US NRC, US Department of Commerce (US NTIS, PB 280-289).

ANONYMOUS (1978b) UK prohibits burning of Kepone. Chem. Aust., 45: 142.

ATKINS, E.L. & ANDERSON, L.D. (1962) DDT resistance in honey bees. J. econ. Entomol., 55: 791-792.

ATKINS, E.L. Jr, GRAYWOOD, E.A., & MACDONALD, R.L. (1973) Toxicity of pesticides and other agricultural chemicals to honey bees, California, 38 pp (Laboratory Studies, Calif. Agric., Extension M-16).

BAGGETT, J.McC., KLEIN, R.L., MEHENDALE, H.M., & THURESON-KLEIN, A.K. (1977) Acute Kepone treatment of rats: a biochemical and ultrastructural study. Pharmacologist, 19: 199-205.

BAGGETT, J.McC., THURESON-KLEIN, A., & KLEIN, R.L. (1980) Effects of chlordane on the adrenal medulla of the rat. Toxicol. appl. Pharmacol., 52: 313-322.

BAHNER, L.H., WILSON, A.J., Jr, SHEPPARD, J.M., PATRICK, J.M., Jr, GOODMAN, L.R., & WALSH, G.E. (1977) Kepone bioconcentration, accumulation, loss, and transfer through estuarine food chains. Chesapeake Sci., 18: 299-308.

BAKER, R.C., COONS, L.B., MAILMAN, R.B., & HODGSON, E. (1972) Induction of hepatic mixed function oxidases by the insecticide mirex. Environ. Res., 5: 418-424.

BENTLEY, R.E. (1975) Acute toxicity of kepone to Bluegill Lepomis macrochirus and Rainbow Trout Salmo gairdneri, 7pp (Toxicity Report submitted to Allied Chemical Corporation, Morristown, New Jersey, EG & G Environmental Consultants, Bionomics, Wareham, Massachusetts).

BLANKE, R.V., FARISS, M.W., GRIFFITH, F.D., Jr, & GUZELIAN, P.S. (1977) Analysis of chlordane (Kepone) in biological specimens. J. anal. Toxicol., 1: 57-62.

BLANKE, R.V., FARISS, M.W., GUZELIAN, P.S., PATERSON, A.R., & SMITH, D.E. (1978) Identification of a reduced form of

chlordecone (Kepone) in human stool. Bull. environ. Contam. Toxicol., 20: 782-785.

BOYLAN, J.J., EGLE, J.L., & GUZELIAN, P.S. (1977) Stimulation of chlordecone (Kepone) excretion by cholestyramine in rats. Pharmacologist, 19: 210.

BOYLAN, J.J., COHN, W.J., EGLE, J.L., BLANKE, R.V., & GUZELIAN, P.S. (1979) Excretion of chlordecone by the gastrointestinal tract: evidence for a non-biliary mechanism. Clin. Pharmacol. Ther., 25: 579-585.

BRAY, T.J. (1975) Health hazard. Chemical firm's story underscores problems of cleaning up plants. Wall Street J., December 2.

BREWERTON, H.V. & SLADE, D.A. (1964) Kepone residues on apples. N.Z. J. agric. Res., 7: 647-653.

BUCKLER, D.R., WITT, A., MAYER, F.L., & HUCKINS, J.N. (1981) Acute and chronic effects of Kepone and mirex on the fathead minnow. Trans. Am. Fish. Soc., 110: 270-280.

BULGER, W.J., MUCCITELLI, R.M., & KUPFER, D. (1979) Studies on the estrogenic activity of chlordecone (Kepone) in the rat: effects on uterine estrogen receptor. Mol. Pharmacol., 15: 515-524.

BUTLER, P.A. (1963) A review of fish and wildlife service investigations during 1961 and 1962. In: George, J.C., ed. Commercial Fisheries Investigations, Pesticide-Wildlife Series, US Department of the Interior, Fish and Wildlife Services, Vol. 167, pp. 11-25.

CANNON, S.B. & KIMBROUGH, R.D. (1979) Short-term chlordecone toxicity in rats including effects on reproduction, pathological organ changes and their reversibility. Toxicol. appl. Pharmacol., 47: 469-476.

CANNON, S.B., VEAZEY, J.M., Jr, JACKSON, R.S., BURSE, V.W., HAYES, C., STRAUB, W.E., LANDRIGAN, P.J., & LIDDLE, J.A. (1978) Epidemic Kepone poisoning in chemical workers. Am. J. Epidemiol., 107: 529-537.

CARVER, R.A., BORSETTI, A.P., & KAMPS, L.R. (1978) Gas-liquid chromatographic determination of Kepone residues in finfish, shellfish, and crustaceans. J. Assoc. Off. Anal. Chem., 61: 877-883.

- CHADWICK, R.W., COPELAND, M.F., & ROSENSTEIN, L. (1979) Effect of Kepone exposure during gestation and lactation on the metabolism of lindane by weanling rats. Toxicology Lett., 4: 247-252.
- CHERNOFF, N. & ROGERS, E.H. (1976) Fetal toxicity of Kepone in rats and mice. Toxicol. appl. Pharmacol., 38: 189-194.
- CHERNOFF, N., LINDER, R.E., SCOTTI, T.M., ROGERS, E.H., CARVER, B.D., & KAVLOCK, R.J. (1979a) Fetotoxicity and cataractogenicity of mirex in rats and mice with notes on Kepone. Environ. Res., 18: 257-269.
- CHU, I., VILLENEUVE, D.C., VALLI, V.E., & REYNOLDS, L.M. (1980) Short-term study of the combined effects of mirex, photomirex, and Kepone to halogenated biphenyls in the rat. J. Toxicol. environ. Health, 6: 421-432.
- CIANFLONE, D.J., HEWITT, W.R., VILLENEUVE, D.C., & PLAA, G.L. (1980) Role of biotransformation of the alterations of chloroform hepatotoxicity produced by Kepone and mirex. Toxicol. appl. Pharmacol., 53: 140-149.
- COHN, W.J., BLANKE, R.V., GRIFFITH, F.D., Jr, & GUZELIAN, P.S. (1976) Distribution and excretion of Kepone in humans. Gastroenterology, 71: A8-901.
- COHN, W.J., BOYLAN, J.J., BLANKE, R.V., FARISS, M.W., HOWELL, J.R., & GUZELIAN, P.S. (1978) Treatment of chlordecone (Kepone) toxicity with cholestyramine. Results of a controlled clinical trial. N. Engl. J. Med., 298: 243-248.
- COUCH, J.A., WINSTEAD, J.T., & GOODMAN, L.R. (1977) Kepone-induced scoliosis and its histological consequences in fish. Science, 197: 585-587.
- CURTIS, L.R. & MEHENDELE, H.M. (1979) The effects of Kepone pretreatment on biliary excretion of xenobiotics in the male rat. Toxicol. appl. Pharmacol., 47: 295-303.
- CURTIS, L.R. & MEHENDELE, H.M. (1980) Specificity of chlordecone-induced potentiation of carbon tetrachloride hepatotoxicity. Drug Metab. Dispos., 8: 23-27.
- CURTIS, L.R., WILLIAMS, W.L., & MEHENDELE, H.M. (1979) Potentiation of the hepatotoxicity of carbon tetrachloride following pre-exposure to chlordecone (Kepone) in the male rat. Toxicol. appl. Pharmacol., 51: 283-293.

D'ASARO, C.N. & WILKES, F.G. (1982) Cycling of xenobiotics through marine and estuarine sediments, 51 pp (US EPA Report No. 600/3-82-074; PB82-239252).

DAWSON, G.W. (1978) Kepone mitigation feasibility report: Appendix A: The feasibility of mitigating kepone contamination in the James River Basin (US NTIS PB Report, PB 286 085).

DESAIAH, D. & KOCH, R.B. (1975) Inhibition of ATPases activity in channel catfish brain by Kepone and its reduction product. Bull. environ. Contam. Toxicol., 13: 153-158.

DESAIAH, D., HO, I.K., & MEHENDALE, H.M. (1977) Effects of Kepone and mirex on mitochondrial magnesium ion-dependent ATPase activity in rat liver. Toxicol. appl. Pharmacol., 39: 219-228.

DEWITT, J.B., CRABTREE, D.G., FINLEY, R.B. & GEORGE, J.L. (1962) Effects of pesticides on fish and wildlife: a review of investigations during 1960, Washington DC, US Department of the Interior, Bureau of Fish and Wildlife Services, pp 4-15, 31-33, 49-52 (Circular No. 143).

DIETZ, D.D. & McMILLAN, D.E. (1978) Effects of mirex and Kepone on schedule controlled responding. Pharmacologist, 20: 225.

EGLE, J.L., Jr, FERNANDEZ, S.B., GUZELIAN, P.S., & BORZELLECA, J.F. (1978) Distribution and excretion of chlordecone (Kepone) in the rat. Drug Metab. Dispos., 6: 91-95.

END, D.W., CARCHMAN, R.A., & DEWEY, W.L. (1979) Disruption of rat brain synaptosomal membranes by the neurotoxic insecticide Kepone. Fed. Proc., 38: 845.

EPSTEIN, S.S. (1978) Kepone-hazard evaluation. Sci. total Environ., 9: 1-62.

ERBEN, H.K. (1972) [Ultrastructure and wall thickness of pathological eggshells.] Abkhandl. Math. Naturwissensch., Lichen Klasse, 6: 192-216 (in German, Pestic. Abstr., 7: 74-0598-602).

EROSCHENKO, V.P. & WILSON, W.O. (1975) Cellular changes in the gonads, livers and adrenal glands of Japanese quail as affected by the insecticide Kepone. Toxicol. appl. Pharmacol., 31: 491-504.

FABACHER, D.L. & HODGSON, E. (1976) Induction of hepatic mixed-function oxidase enzymes in adult and neonatal mice by Kepone and mirex. Toxicol. appl. Pharmacol., 38: 71-77,

FELDMANN, E.C. (1976) The lesson from Kepone. J. pharmacol. Sci., 65: 1.

GAINES, T.B. (1969) Acute toxicity of pesticides. Toxicol. appl. Pharmacol., 14: 5-534.

GAWAAD, A.A.A., HAMMAD, M.H., & EL-GAYAR, F.H. (1972a) Studies on soil insecticides. X. Effect of some soil insecticides on soil microorganisms. Zentr. Bakteriol. Parasitenk. Infect and Hygien. Abt 2, 127: 290-295.

GAWAAD, A.A.A., HAMMAD, M.H., & EL-GAYAR, F.H. (1972b) Studies on soil insecticides. XI. Effect of some soil insecticides on the nitrogen transformation in treated soils. Zentr. Bakteriol. Parasitenk. Infect and Hygien. Abt 2, 127: 296-300.

GAWAAD, A.A.A., EL-GAYAR, F.H., & KHADR, A.A. (1976) Effect of certain soil insecticides on the germination of cotton seeds, growth, dry weight, cotton yield and the quality of yield. Biol. Abstr., 61: 5840.

GEER, R.D. (1978) Predicting the anaerobic degradation of organic chemical pollutants in waste water treatment plants from their electrochemical reduction behavior, Bozeman, Montana, Montana University Joint Water Resources Research Center (US NTIS Report No. ISS-MUJWRRRC-95 MTIS PB-289224).

GILBERT, E.E. & CIOLITO, S.L. (1952) US Patent 2.616.825 and US Patent 2.616.928, 4 November, to Allied Chemical and Dye Corporation.

GOOD, E.E., WARE, G.W., & MILLER, D.F. (1965) Effects of insecticides on reproduction in the laboratory mouse. I. Kepone. J. Econom. Entomol., 58: 754-757.

GOODMAN, L.R., HANSEN, D.J., MANNING, C.S., & FAAS, L.F. (1982) Effects of Kepone on the sheepshead minnow in an entire lifecycle toxicity test. Arch. environ. Contam. Toxicol., 11: 335-342.

HAMMOND, B., BAHR, J., DIAL, O., MCCONNEL, J., & METCALF, R. (1978) Reproductive toxicology of mirex and Kepone. Fed. Prod. Fed. Am. Soc. Exp. Biol., 37: 501.

HAMMOND, B., KATZENELLENBOGEN, B.S., KRAUTHAMMER, N., & MCCONNELL, J. (1979) Estrogenic activity of the insecticide chlordecone (Kepone) and interaction with uterine estrogen receptors. Proc. Natl Acad. Sci., 76: 6641-6645.

HANSEN, D.J., GOODMAN, L.R., & WILSON, A.J., Jr (1976) Kepone: Chronic effects on embryo, fry, juvenile and adult sheepshead minnow Cyprinodon variegatus. In Hansen, D.J., ed. Prepublications of kepone in the marine environment, Gulf Breeze, Florida, US EPA Office of Research and Development, Environmental Research Laboratory, 28 pp.

HARRIS, R.L., HUGGETT, R.J., & SLONE, H.D. (1980) Determination of dissolved Kepone by direct addition of XAD-2 resin to water. Anal. Chem., 52: 779-780.

HEATH, C.W., Jr (1978) Industrial toxins and the community, Washington DC, US Department of Health, Education and Welfare, pp. 259-261 (US DHEW (NIOSH) Publication No. 78-169).

HEITMULLER, T. (1975) Acute toxicity of kepone to fiddler crabs (Uca pugilator), 5 pp (Toxicity Test Report, submitted to Allied Chemical Corporation, Morristown, New Jersey, EG & G, Inc., Bionomics, Marine Research Laboratory, Pensacola, Florida).

HUBER, J.J. (1965) Some physiological effects of the insecticide Kepone in the laboratory mouse. Toxicol. appl. Pharmacol., 1: 516-524.

HUCKINS, J.N., STALLING, D.L., PETTY, J.D., BUCKLER, D.R., & JOHNSON, B.T. (1982) Fate of Kepone and mirex in the aquatic environment. J. agric. food Chem., 30: 1020-1027.

HUGGETT, R.D., HAVEN, D., & NICHOLS, M. (1977) Kepone sediment relationships in James River (Abstract) (Report to US EPA Gulf Breeze Laboratory).

IARC (1979) Some halogenated hydrocarbons, Lyons, International Agency for Research on Cancer (Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Vol. 20).

INFORMATION CANADA (1973) Guide to chemicals used in crop protection, Vol. 6, p. 96.

IRPTC (1983) Legal file, Vols 1 & 2, Geneva, International Register of Potentially Toxic Chemicals, United Nations Environment Programme.

- KAWATSKI, J.A. & HECKER, R.J. (1979) Kepone inhibition of succinic acid dehydrogenase in mouse liver mitochondrial preparations. Proc. N. D. Acad. Sci., 33: 24.
- KLINGENSMITH, J.S. & MEHENDEALE, H.M. (1982a) Chlordecone-induced mobilization of body fat and lipolysis in the male rat. J. Toxicol. environ. Health, 10: 121-129.
- KLINGENSMITH, J.S. & MEHENDEALE, H.M. (1982b) Potentiation of CCl₄ lethality by chlordecone. Toxicol. Lett., 11: 149-154.
- LANGFORD, H.D. (1978) Kepone, mirex pesticide residues persist, full effects unknown. News Rep., 28: 1, 4-5.
- LARSON, P.S., EGLE, J.L., Jr, HENNIGAR, G.R., LANE, R.W., & BORZELLECA, J.F. (1979b) Acute, subchronic, and chronic toxicity of chlordecone. Toxicol. appl. Pharmacol., 48: 29-41.
- LEWIS, R.G. & LEE, R.E. (1976) Air pollution from pesticides: sources, occurrence and dispersion. In: Air pollution from pesticides and agricultural processes, Boca, Florida, CRC Press Inc.
- MADY, N., SMITH, D., SMITH, J., & WEZWICK, C. (1979) Analysis of Kepone in biological samples. NBS (US) Spec. Publ., 519: 341-343.
- MAHAFFEY, W.R., PRITCHARD, P.H., & BOURQUIN, A.W. (1982) Effects of Kepone on growth and respiration of several estuarine bacteria. Appl. environ. Microbiol., 43: 1419-1424.
- MARTINEZ, A.J., TAYLOR, J.R., ISAACS, E., DYCK, P.J., & HOUFF, S.A. (1976) Kepone poisoning ultrastructure of nerves and skeletal muscles. J. Neuropathol. exp. Neurol., 35: 323.
- MARTINEZ, A.J., TAYLOR, J.R., DYCK, P.J., HOUFF, S.A., & ISAACS, E. (1978) Chlordecone intoxication in man: II. ultrastructure of peripheral nerves and skeletal muscle. Neurology, 28: 631-635.
- McFARLAND, L.Z. & LACY, P.B. (1969) Physiologic and endocrinologic effects of the insecticide Kepone in the Japanese quail. Toxicol. appl. Pharmacol., 15: 441-450.
- MEHENDEALE, H.M. (1979) Modification of hepatobiliary function by toxic chemicals. Fed. Proc. Fed. Am. Soc. Exp. Biol., 38: 2240-2245.

MEHENDALE, H.M., TAKANAKA, A., DESAIAH, D., & HO, I.K. (1978) Effect of pre-exposure to Kepone on hepatic mixed-function oxidases in the female rat. Toxicol. appl. Pharmacol., 44: 171-180.

MEYERS, S.P., GAMBRELL, & DAY, (1982) Determination of environmental impact of several substitute chemicals in agricultural affected wetlands, Washington DC, US Environmental Protection Agency, 150 pp (US EPA Report No. EPA-600/4-82-052; PB82-242017).

MOSEMAN, R.F., CRIST, H.L., EDGERTON, T.R., & WARD, M.K. (1977) Electron capture gas chromatographic determination of Kepone residues in environmental samples. Arch. environ. Contam. Toxicol., 6: 221-231.

MOSEMAN, R.F., WARD, M.K., CRIST, H.L., & ZEHR, R.D. (1978) A micro derivatization technique for the confirmation of trace quantities of Kepone. J. agric. food Chem., 26: 965-968.

MOTL, M.L. (1977) EPA develops process to destroy Kepone. Environ. Manage., 1: 491-493.

NABER, E.C. & WARE, G.W. (1965) Effect of Kepone and mirex on reproductive performance in the laying hen. Poult. Sci., 44: 875-880.

NIMMO, D.R., BAHNER, L.H., RIGBY, R.A., SHEPPARD, J.M., & WILSON, A.J., Jr (1977) Mysidopsis bahia: An estuarine species suitable for life cycle bioassays to determine sublethal effects of a pollutant. In: Prepublications of kepone in the marine environment, Gulf Breeze, Florida, US EPA Office of Research and Development, Environmental Research Laboratory.

NIOSH (1977) NIOSH manual of analytical methods, Part 1, NIOSH monitoring methods, Vol. 1, 2nd ed., Washington DC, National Institute for Occupational Safety and Health, pp 225-1-256-6 (Method No. P Cam 225, US DHEW (NIOSH) Publication No. 77-157B).

NIOSH (1978) Registry of toxic effects of chemical substances, Washington DC, US Department of Health, Education and Welfare, p. 751.

ODUM, W.E. & DRIFMEYER, J.E. (1978) Sorption of pollutants by plant detritus: a review. Environ. health Perspect., 27: 133-137.

- ORNDORFF, S.A. & COLWELL, R.R. (1980a) Microbial transformation of Kepone. Appl. environ. Microbiol., 39: 398-406.
- ORNDORFF, S.A. & COLWELL, R.R. (1980b) Distribution and characterization of Kepone-resistant bacteria in the aquatic environment. Appl. environ. Microbiol., 39: 611-622.
- PATE, J.B. & TABOR, E.C. (1962) Analytical aspects of the use of glass fiber filters for the collection and analysis of atmospheric particulate matter. Am. Ind. Hyg. Assoc. J., 23: 145-156.
- PORTIER, R.J. & MEYERS, S.P. (1982) Microbial responses to sequential and differential application of a xenobiotic in aquatic microcosms. Abst. Annu. Meet. Am. Soc. Microbiol., 82: Abstract Q63.
- PROHST, G.S., McMAHON, R.E., HILL, L.E., THOMPSON, C.Z., EPP, J.K., & NEALS S.B. (1981) Chemically-induced unscheduled DNA synthesis in primary rat hepatocyte cultures. A comparison with bacterial mutagenicity using 218 compounds. Environ. Mutat., 3: 11-32.
- PROSZYNSKA, B. (1977) [Method for determining despirol residues in potatoes.] Roozn. Panstw. Zakl. Hig., 28: 201-207 (in Polish).
- REITER, L. & KIDD, K. (1978) The behavioral effects of subacute exposure to Kepone or mirex on the weanling rat. Toxicol. appl. Pharmacol., 45: 357.
- REITER, L., KIDD, K., LEDBETTER, G., CHERNOFF, N., & GRAY, L.E., Jr (1977) Comparative behavioural toxicology of mirex and Kepone in the rat. Toxicol. appl. Pharmacol., 41: 143.
- REUBER, M.D. (1977) Kepone carcinogenicity affirmed by Reuber. Pest. Toxic Chem. News, 5: 6-7.
- REUBER, M.D. (1978) Carcinogenicity of Kepone. J. Toxicol. environ. Health, 4: 895-911.
- REUBER, M.D. (1979) The carcinogenicity of Kepone. J. environ. Path. Toxicol., 2: 671-686.
- ROBERTS, M.H., Jr & BENDL., R.E. (1982) Acute toxicity of Kepone to selected freshwater fish. Estuaries, 5: 158-164.

ROSENSTEIN, L., BRICE, A., ROGERS, N., & LAWRENCE, S. (1977) Neurotoxicity of Kepone in perinatal rats following in utero exposure. Toxicol. appl. Pharmacol., 41: 142-143 (Abstract 28).

SALEH, F.Y. & LEE, G.F. (1978) Analytical methodology for Kepone in water and sediment. Environ. Sci. Technol., 12: 297-301.

SALEH, F.Y., LEE, G.F., & BUTLER, J.S. (1978) Kepone and other selected chlorinated hydrocarbon pesticides and PCEs behavior during hydraulic dredging of the James River near Hopewell, Virginia. J. environ. Sci. Health, Part A, A13: 261-294.

SCHIMMEL, S.C. & WILSON, A.J. Jr (1977) Acute toxicity of Kepone to four estuarine animals. Chesapeake Sci., 18: 224-227.

SHANHOLTZ, M.I. (1976) Emergency rule, Virginia State Board of Health. Prohibiting the taking of crabs from the James River and its tributaries and the taking of fish for human consumption, Richmond, Virginia, Virginia Department of Health, 3 pp.

SIMON, G.S., KIPPS, B.R., TARDIFF, R.G., & BORZELLECA, J.F. (1978) Failure of Kepone and hexachlorobenzene to induce dominant lethal mutations in the rat. Toxicol. appl. Pharmacol., 45: 330-331.

SNEGAROFF, J. (1977) Organochlorine insecticidal residues in the soil and rivers of banana-growing region of Guadeloupe. Phytiatr. Phytopharm., 26: 251-267.

STEHLIK, L.L. & MERRINER, J.V. (1983) Effects of accumulated dietary Kepone on spot (Leiostomus xanthurus). Aq. Toxicol., 3: 345-358.

STERRETT, F.S. & BOSS, C.A. (1977) Careless Kepone. Environment, 19: 30-37.

SUTA, B.E. (1978) Human population exposures to mirex and kepone, Springfield, Virginia, US Department of Commerce (US NTIS PB REP., PB-285, 430).

TAYLOR, J.R., SELHORST, J.B., HOUFF, S.A., & MARTINEZ, A.J. (1978) Chlordecone intoxication in man. I. Clinical observations. Neurology, 28: 626-630.

TILSON, H.A., BYRD, M., & RILEY, M. (1979) Neurobehavioral effects of exposing rats to Kepone via the diet. Environ. Health Perspec., 33: 321.

US EPA (1976a) Preliminary report on Kepone levels found in environmental samples from the Hopewell, Virginia area, Research Triangle Park, North Carolina, US Environmental Protection Agency, Health Effects Research Laboratory.

US EPA (1976b) Review of the Chesapeake Bay Program. Seminar on kepone held at Virginia Institute of Marine Sciences, 12-13 October, 1976, Research Triangle Park, North Carolina, US Environmental Protection Agency.

US EPA (1979) Reviews of the environmental effects of pollutants. 1. Mirex and Kepone, Washington DC, US Environmental Protection Agency (EPA Report No. EPA-600/1-78-013; PB80-12595).

US FDA (1977) Compliance program evaluation-FY77 Kepone and mirex contamination, Washington DC, US Department of Health, Education and Welfare.

WALSH, G.E., AINSWORTH, K., & WILSON, A.J., Jr (1977) Toxicity and uptake of Kepone in marine unicellular algae. Chesapeake Sci., 18: 222-223.

WILLIAMS, G.M. (1980) Classification of genotoxic and epigenetic hepatocarcinogens using liver culture assays. Ann. N.Y. Acad. Sci., 349: 273-282.

WINKELHAKE, J.L., VODICNIK, M.J., & TAYLOR, J.L. (1983) Induction in rainbow trout of an acute phase (C-reactive) protein by chemicals of environmental concern. Comp. Biochem. Physiol. C., 74: 55-58.