IPCS International Programme on Chemical Safety

Environmental Health Criteria 91

Aldrin and Dieldrin

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

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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.

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NOTE TO READERS OF THE CRITERIA DOCUMENTS

Every effort has been made to present information in the criteria documents as accurately as possible without unduly delaying their publication. In the interest of all users of the environmental health criteria documents, readers are kindly requested to communicate any errors that may have occurred 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.

* * *

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. 7988400 - 7985850).

* * *

The proprietary information contained in this document cannot replace documentation for registration purposes because the latter has to be closely linked to the source, the manufacturing route, and the purity/impurities of the substance to be registered. The data should be used in accordance with paragraphs 82-84 and recommendations paragraph 90 of the Second FAO Government Consultation (FAO, 1982).

ENVIRONMENTAL HEALTH CRITERIA FOR ALDRIN AND DIELDRIN

A WHO Task Group on Environmental Health Criteria for Aldrin and Dieldrin met in Geneva from 13 to 17 July 1987. Dr K.W. Jager, IPCS, opened the meeting and welcomed the participants on behalf of the heads of the three IPCS cooperating organizations (UNEP/ILO/WHO). The group reviewed and revised the draft criteria document and made an evaluation of the risks for human health and the environment from exposure to aldrin and dieldrin.

The first draft of this document was prepared by Dr G.J. VAN ESCH of the Netherlands on the basis of a review of all studies on aldrin and dieldrin including the proprietary information, made available to the IPCS by Shell International Chemical Company Limited, London, United Kingdom.

The second draft was also prepared by Dr van Esch, incorporating comments received following the circulation of the first draft to the IPCS contact points for Environmental Health Criteria documents.

Dr K.W. Jager and Dr P.G. Jenkins, both members of the IPCS Central Unit, were responsible for the technical development and editing, respectively, of this monograph.

The assistance of Shell in making available to the IPCS and the Task Group its toxicological proprietary information on aldrin and dieldrin is gratefully acknowledged. This allowed the Task Group to make its evaluation on a more complete data base.

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. The United Kingdom Department of Health and Social Security generously supported the cost of printing.

INTRODUCTION

Aldrin and dieldrin are the common names of insecticides containing 95% HHDN and 85% HEOD, respectively.

Throughout this monograph the names aldrin and dieldrin are used, although concentrations determined in the different matrices are actually those of the active molecules HHDN and HEOD.

Aldrin is readily metabolized to dieldrin (HEOD) in plants and animals. Only rarely are aldrin residues present in food or in the great majority of animals, and then only in very small amounts. Therefore, national and international regulatory bodies have considered these two closely related insecticides together. The practicality of considering them jointly is further emphasized by the lack of significant difference in their acute and chronic toxicity and by their common mode of action.

1. SUMMARY

1.1 General

Aldrin and dieldrin, both organochlorine pesticides and manufactured commercially since 1950, were used throughout the world up to the early 1970s. Both compounds were used as insecticides in agriculture for the control of many soil pests and in the treatment of seed. Insects controlled by these compounds include termites, grasshoppers, wood borers, beetles, and textile pests. Dieldrin has also been used in public health for the control of tsetse flies and other vectors of debilitating tropical diseases. Both aldrin and dieldrin act as a contact and stomach poison for insects.

Since the early 1970s, both compounds have been severely restricted or banned, in a number of countries, from use, especially in agriculture. Nevertheless, the use for termite control continues in other countries. Global production, which was estimated to be 13 000 tonnes/year in 1972, decreased to less than 2500 tonnes/year in 1984.

The purity of technical grade aldrin and dieldrin is 90% and > 95%, respectively. Impurities for aldrin include octachlorocyclopentene, hexachlorobutadiene, and polymerization products, and for dieldrin polychloroepoxyoctahydrodimethanonaphthalenes.

Both compounds are practically insoluble in water and moderately to highly soluble in most paraffinic, aromatic, and halogenated hydrocarbons, and in esters, ketones, and alcohols. The vapour pressure of aldrin is 6.5×10^{-5} mmHg at 25 °C and that of dieldrin is 3.2×10^{-6} mmHg at 25 °C.

Analytical methods for the determination of aldrin and dieldrin in food, feed, and the environment are described in section 2.

1.2 Environmental Transport, Distribution, and Transformation

A major use of aldrin is as a soil insecticide. Hence, aldrin-treated soil is an important source of aldrin and its reaction product dieldrin in the environment.

Aldrin has a low propensity for movement away from treated areas, either through volatilization or by leaching. It is mainly and rapidly adsorbed on soils with a high organic matter content, but only moderately adsorbed by clay soils. Aldrin and dieldrin rarely penetrate more than 20 cm beneath the top treated layer of soil. Aldrin adheres to soil particles to such an extent that only traces can be removed by water. For this reason, contamination of ground water does not generally occur.

The disappearance of aldrin from soil resembles a first-order reaction. Immediately after application, there is a short period of rapid loss due to volatilization and thereafter a second longer exponential period of decline, mainly due to conversion to dieldrin,

which is slower to dissipate. However, there is the possibility of migration by way of soil erosion, as wind drift, sediment transport, and surface run-off. From data on residues of aldrin in the environment, it appears that it is mainly retained in the soil and that 97% of the primary residue is not the parent compound but its epoxide, dieldrin.

Photodieldrin is a photodegradation product of dieldrin and does not occur widely in the environment.

Aldrin applied to soils is lost slowly in temperate areas, three-quarters of the applied aldrin being lost during the first year in a typical case. The rate of loss slows later as aldrin is converted to dieldrin. There is some evidence that the rate of loss is greater under the anaerobic conditions of rice paddies than under aerobic conditions. Dieldrin is lost from the soil very rapidly in tropical areas, up to 90% disappearing within 1 month, whereas the half-life of dieldrin in temperate soils is approximately 5 years. Volatilization appears to be the principal route of loss from the soil, though atmospheric levels of dieldrin and aldrin are generally low. Some dieldrin is washed from the atmosphere by rain, but levels in ground water are very low because of strong adsorption to soil particles. Dieldrin has been detected, in small amounts, in surface water contaminated by run-off from agricultural land.

1.3 Environmental Levels and Human Exposure

Aldrin and dieldrin have been found in the atmosphere, in the vapour phase, adsorbed on dust particles, or in rainwater at variable levels according to the situation. They have been detected mainly in agricultural areas, where the mean level in the air has been of the order of 1-2 ng/m^3, with maximum levels of about 40 ng/m^3. In rainwater, concentrations of the order of 10-20 ng/litre, or occasionally higher, have been found.

Concentrations found in the air in houses treated for the control of termites were much higher, ranging from 0.04 to 7 μg/m^3, depending on the time of sampling (i.e., the number of days of after application) and the type of house. Within 8 weeks, the concentrations decreased rapidly. Treatment of internal wood in houses resulted in dieldrin concentrations in the air ranging from 0.01 to 0.5 μg/m^3. Aldrin and dieldrin migrated into food from treated laminated timber and plywood, and by direct contact and/or sorption from the atmosphere.

The occurrence of dieldrin in the aquatic environment has been reported. However, the concentrations were very low, mainly less than 5 ng/litre. Higher levels have been generally attributed to industrial effluents or soil erosion during agricultural usage. River sediments may contain much higher concentrations (up to 1 mg/kg).

Aldrin is found only rarely in food, but dieldrin is more common, especially in dairy products, meat products, fish, oils and fats, potatoes, and certain other vegetables (especially the root veg-

etables). Maximum residue limits (MRLs) in the range of 0.02 to 0.2 mg/kg product have been recommended over the years by the FAO/WHO Joint Meetings on Pesticide Residues. Recent studies in different countries have shown that the actual concentrations of dieldrin in these food commodities are generally lower. Studies from the United Kingdom indicate this decrease clearly. In 1966-67, the mean level of dieldrin residues in a total diet study was 0.004 mg/kg food, whereas in the period 1975-77 it was 0.0015 mg/kg, and in 1981, 0.0005 mg/kg. This downward trend has been confirmed in other countries, for instance in the USA. This may be due to the restriction or banning of the use of these compounds.

A large number of investigations has been reported in which the adipose tissue, organs, blood, or other tissues of the general population have been examined for the presence of dieldrin. Over the last 25 years, surveys have been carried out in many countries all over the world. Most of the mean values for adipose tissue have been in the range of 0.1-0.4 mg/kg. Surveys in the Netherlands, the United Kingdom, and the USA have indicated a decline in concentrations in adipose tissue, since the mid-1970s. Blood concentrations range from 1 to 2 μg/litre. Levels in the liver are below 0.4 mg/kg, while those in other tissues, including the kidneys, brain, and gonads, are below 0.1 mg/kg tissue.

As a result of transplacental exposure, dieldrin is present in the blood, adipose tissue, and other tissues of the fetus and newborn infants. The concentrations are one tenth to one half of those of their mothers. There is no difference between infants and adults in the brain/liver/fat ratio of dieldrin concentrations. Dieldrin is also excreted in mother's milk. Over the last 15 years, samples of mother's milk have been analysed for the presence of organochlorine pesticides, including dieldrin, in various countries. In most countries, the dieldrin concentration in milk amounts to 6 μg/litre, though higher levels have occasionally been found.

1.4 Kinetics and Metabolism

In both animals and human beings, aldrin and dieldrin are readily absorbed into the circulating blood from the gastrointestinal tract, through the skin, or through the lungs following inhalation of the vapour. A study on human volunteers showed that absorption through the intact skin amounts to 7-8% of the applied dose. Inhalation studies with human volunteers suggested that up to 50% of inhaled aldrin vapour is absorbed and retained in the human body. After absorption, it is rapidly distributed throughout the organs and tissues of the body and a continuous exchange between the blood and other tissues takes place. In the meantime, aldrin is readily converted to dieldrin, mainly in the liver but also to a much lesser extent in some other tissues, such as the lungs. This conversion proceeds very rapidly.

When 1-day-old rats were given oral doses of 10 mg aldrin/kg body weight, their livers contained dieldrin 2 h after treatment. Over the

course of the next few hours, dieldrin concentrated to a greater extent in the lipid tissues.

Numerous studies carried out with ^{14}C-labelled aldrin and dieldrin have shown that part of the ingested material is passed unabsorbed through the intestinal tract and eliminated from the body, part is excreted unchanged from the liver into the bile, part is stored in the various organs and tissues particularly in the adipose tissue, and part is metabolized in the liver to more polar and hydrophilic metabolites. In human beings and most animals, the metabolites are excreted primarily via the bile in the faeces. It has also been shown that both aldrin and dieldrin are biodegraded into the same metabolites.

Most of the currently available information on the biodegradation metabolism in mammals is based on studies on dieldrin in the mouse, rat, rabbit, sheep, dog, monkey, chimpanzee, and in human beings. The overall picture shows only quantitative variations between species, and the mechanisms in rats seem to be similar to those in primates.

The major metabolite, except in the case of the rabbit, is the 9-hydroxy derivative. This metabolite is found in the faeces and in a free or conjugated form in the urine. Small amounts of three other metabolites have been found and identified in experimental animals. These are the *trans*-6,7-dihydroxy derivative, dicarboxylic acid derived from the dihydroxy compound, and the bridged pentachloroketone.

Only the 9-hydroxy compound has been demonstrated in the faeces of human beings and neither this nor the other metabolites have been found in human blood or other tissues. Dieldrin was found to be present in the faeces of occupationally exposed workers, whereas the concentrations in the samples from the general population were below the limits of detection. Examination of the urine of five workers indicated that urinary excretion of dieldrin and its four metabolites was minor compared to the elimination of the 9-hydroxy metabolite via the faeces.

The conversion of aldrin to dieldrin by mixed-function monooxygenases (aldrin-epoxidase) in the liver and the distribution and the subsequent deposition of dieldrin (mainly in lipid-containing tissues, such as adipose tissue, liver, kidneys, heart, and brain) proceed much more rapidly than the biodegradation and ultimate elimination of unchanged dieldrin and its metabolites from the body. Thus, at a given average daily intake of aldrin and/or dieldrin, dieldrin slowly accumulates in the body. However, this accumulation does not continue indefinitely. As dosing continues, a "steady state" is eventually reached at which the rates of excretion and intake are equal. The upper limit of storage is related to the daily intake. This has been demonstrated in rats, dogs, and human beings.

When the intake of aldrin/dieldrin ceases or decreases, the body burden decreases. The biological half-life in man is approximately 9-12 months. Significant relationships have been found between the concentrations of dieldrin in the blood and those in other tissues in rats, dogs, and human beings.

Numerous investigations of the concentrations of dieldrin in the blood, adipose tissue, and other tissues of members of the general population and from special groups, carried out in several different countries, have shown that at equilibrium the ratio of dieldrin concentrations in the adipose tissue, liver, brain, and blood is about 150:15:3:1.

Dieldrin is transported via the placenta and reaches the fetus. Accumulation takes place in the same organs and tissues as in the adult, but to a much lower level. There seems to be an equilibrium between the levels in the mother and the fetus.

Photodieldrin is also metabolized into bridged pentachloroketone in the rat and dog. Both compounds were found in the adipose tissue, liver, and kidneys when animals were administered high levels of photodieldrin. No residues of these compounds could be detected in human adipose tissue, kidneys, or breast milk. The accumulation of photodieldrin in the adipose tissue of experimental animals was much less than that of dieldrin.

1.5 Effects on Organisms in the Environment

1.5.1 Accumulation

Most residues in organisms are of dieldrin, since aldrin is readily converted to dieldrin in all organisms.

The uptake of dieldrin from medium into fungi, streptomycetes, and bacteria over 4 h has yielded concentration factors ranging from 0.3 to >100. Protozoa take up more dieldrin than algae. Algae take up dieldrin from the culture medium very rapidly, maxima often being reached within a few hours.

Many species of aquatic invertebrates concentrate dieldrin from very low water concentrations, yielding high concentration factors. A steady state is reached within a few days. On transfer to clean water, the loss of dieldrin is rapid, the half-life being 60-120 h.

Bioconcentration factors for whole fish are greater than 10 000. The half-life for loss of accumulated dieldrin was found to be 16 days for one species of fish.

The bioconcentration of dieldrin in aquatic organisms is principally from the water rather than by ingestion of food.

Earthworms take up dieldrin from the soil and concentrate it to a maximum of about 170 times. There is little correlation between levels in earthworms and levels in most types of soil.

Many investigations have been carried out to estimate the occurrence of dieldrin in the tissues or eggs of non-target species. The concentrations found cover a wide range from 0.001 mg/kg up to 100 mg/kg tissue, but most are below 1 mg/kg tissue.

Both the body tissues and eggs of birds accumulate dieldrin readily. Similarly, various mammal species have been shown to accumulate dieldrin, particularly in the fatty tissues.

1.5.2 Toxicity for microorganisms

The effects of dieldrin on unicellular algae are very variable, some species being markedly affected by 10 μg/litre and others unaffected even by 1000 μg/litre. Aldrin and dieldrin have only minor effects on soil bacteria, even at levels far exceeding those normally encountered. Most studies have shown no effects at exposure levels of 2000 mg/kg soil. Effects on photosynthesis have been reported in several different species of algae, with aldrin showing a more marked effect than dieldrin at the same concentration. However, these slight effects on the biochemical processes of soil algae were only transitory.

1.5.3 Toxicity for aquatic organisms

Aldrin and dieldrin are highly toxic for aquatic crustaceans, most 96-h LC_{50} values being below 50 μg/litre. However, a few reported results of up to 4300 μg/litre illustrate species variability. Daphnids are less sensitive to dieldrin than aldrin, with 48-h tests yielding LC_{50} values of 23-32 μg/litre for aldrin and 190-330 μg/litre for dieldrin. Molluscs are significantly more resistant, with 48 h values ranging up to >10 000 μg/litre. The results of studies over several weeks have confirmed the relative resistance of daphnids and molluscs. The most susceptible aquatic invertebrates are the larval stages of insects with 96-h values of 0.5-39 μg/litre for dieldrin and 1.3-180 μg/litre for aldrin.

Both aldrin and dieldrin were highly toxic in acute tests on fish. Values for 96-h LC_{50}s in various fish species varied from 2.2 to 53 μg/litre for aldrin, and from 1.1 to 41 μg/litre for dieldrin. Several studies have revealed that toxicity increases with increasing temperature. In a long-term study on *Poecilia latipinna*, there was 100% mortality at dieldrin concentrations of 3 μg/litre or more. Dieldrin administered in the food of rainbow trout at up to 430 μg/kg body weight per day did not have any effects on mortality, but enzymic changes were reported. Morphological changes in liver mitochondria were seen using the electron microscope. The ammonia-detoxifying mechanism of fish is sensitive to dieldrin, the no-observed-adverse-effect level being less than 14 μg/kg body weight per day. Different life stages of fish have been found to have different susceptibilities to dieldrin. Eggs were resistant and juvenile stages were less susceptible than adults.

The acute toxicity of both aldrin and dieldrin is high for larval amphibia with 96-h LC_{50}s of the order of 100 μg/litre.

1.5.4 Toxicity for terrestrial organisms

The toxicity of dieldrin for higher plants is low, crops only being affected at application rates greater than 22 kg/ha. Aldrin is more phytotoxic, to tomatoes and cucumbers particularly, but only at appli-

cation rates many times greater than those recommended. Cabbage is the most sensitive crop to aldrin.

Oral LD_{50}s for honey bees ranging from 0.24 to 0.45 μg/bee for aldrin and from 0.15 to 0.32 μg/bee for dieldrin have been reported. Contact toxicity ranged from 0.15 to 0.80 μg/bee for aldrin and from 0.15 to 0.41 μg/bee for dieldrin. Two studies have indicated that dieldrin is relatively non-toxic for predatory insects eating pest species.

In laboratory studies, earthworms tolerated aldrin at a level of 13 mg/kg of artificial soil with <1% mortality. The 6-week LC_{50} was 60 mg aldrin/kg soil.

The acute toxicities of aldrin and dieldrin have been found to vary by more than an order of magnitude for 13 species of birds, ranging from 6.6 to 520 mg/kg body weight for aldrin and from 6.9 and 381 mg/kg body weight for dieldrin. In four bird species, subacute oral toxicity varied between 34 and 155 mg/kg for aldrin and 37 and 169 mg/kg for dieldrin. Repeated testing over a period of time did not indicate the development of resistance in these species. Reproductive studies on several species of domestic birds have indicated that levels of dieldrin in the diet of more than 10 mg/kg cause some adult mortality. There are no reproductive effects on egg production, fertility, hatchability, or chick survival at levels of dietary dieldrin not causing maternal toxicity. Eggshell thickness is not directly affected by dieldrin. However, reduced food consumption is a symptom of dieldrin poisoning, and eggshell thickness can be reduced by decreased food intake.

Among non-laboratory mammals, the response to dieldrin varies from species to species. Four vole species showed acute LD_{50}s ranging from 100 to 210 mg/kg body weight, making them less susceptible to dieldrin than laboratory species. Shrews survived a diet containing 50 mg dieldrin/kg but died with a dietary level of 200 mg/kg. Blesbuck (antelope) survived for 90 days at 5 and 15 mg/kg diet but all died within 24 days at levels of 25 mg/kg or more. All blesbuck in an area sprayed with dieldrin at 0.16 kg/ha died, the calculated dietary intake being 1.82 mg/kg per day. Thirty percent of springbok survived the spray with no after-effects. Toxicological signs of dieldrin poisoning were similar to those of laboratory mammals.

1.5.5 Population and ecosystem effects

It has been suggested that some mammal populations have been affected by dieldrin. Small mammals were probably killed by eating dieldrin-dressed seed, but populations were replenished by immigration. Bats have been killed by dieldrin in wood preservatives.

Residues of dieldrin have been reported in many species of birds. Throughout the world, the highest residues have been found in birds of prey at the top of foodchains. The dieldrin content of bird tissues and eggs has paralleled usage patterns and decreased with restrictions in the use of aldrin and dieldrin. It is not easy to identify the effects

of dieldrin, because residues occur together with residues of other organochlorines. Dieldrin is more toxic to birds than DDT and probably has been responsible for more adult deaths that DDT. However, the reproductive effects of dieldrin in the field are more difficult to prove. There are seasonal changes in the contents of dieldrin in bird tissues. Furthermore, effects can occur long after exposure to the source of the pollutant.

1.6 Effects on Experimental Animals and *In Vitro* Test Systems

Aldrin and dieldrin are of a high order of toxicity; the oral LD_{50}s for both compounds in the mouse and rat range from 40 to 70 mg/kg body weight. The dermal toxicity is in the range of 40-150 mg/kg body weight, depending on the animal species and the solvent used. Technical aldrin and dieldrin were found to produce slight to severe irritation in the rabbit skin, but this effect was mainly caused by the solvent. In the Magnusson & Kligman guinea-pig maximization test, aldrin produced a sensitization effect. However, during 20 years of manufacture and formulation, no cases of skin sensitization occurred in a group of over 1000 workers.

The vapour pressures of both aldrin and dieldrin are low and acute inhalation effects do not normally arise. The effects observed in acute toxicity studies by all routes involve the central nervous system and include hyperexcitability, tremors, and convulsions.

Short- and long-term oral studies have been carried out with aldrin and dieldrin on the mouse, rat, dog, hamster, and monkey. The liver is the major target organ in the rat and mouse, with an increased liver/body weight ratio and hypertrophy of the centrilobular hepatocytes occuring, which in the early stages may be reversible. Microscopically these changes include increased cytoplasmatic oxyphilia and peripheral migration of basophilic granules. These changes were not found in the liver of the hamster and the monkey. In the dog, mild liver changes (fatty changes and slight hepatic cell atrophy) were accompanied by kidney changes consisting of vacuolization in the epithelia of distal renal tubules and tubular degeneration. In the rat, the overall no-observed-adverse-effect level from the available short-term and long-term studies is 0.5 mg/kg diet, equivalent to 0.025 mg/kg body weight. With feeding levels equivalent to 0.05 mg/kg body weight or more, an increasing dose-related hepatomegaly and histological changes occurred. In the dog, no-effect levels of 0.04-0.2 mg/kg body weight were found.

A number of long-term carcinogenicity studies on mice of different strains were carried out with aldrin or dieldrin. In all studies, benign and/or malignant liver cell tumours were found. Females seemed to be less sensitive than males. No other types of tumours were induced.

Long-term studies on the other animal species (rat, hamster) did not show any increase in tumour incidence. Photodieldrin, fed at concentrations up to 7.5 mg/kg diet, did not induce tumours.

In addition, a number of special studies have been published that have so far failed to elucidate the mechanism of the induction of the liver tumours in mice.

In most of the reproduction studies (over 1-6 generations) carried out with aldrin or dieldrin on mice and rats, the major effect was an increased mortality rate in pre-weaning pups. Reproductive performance was only affected at doses causing maternal intoxication. Studies on dogs were too limited to draw firm conclusions, apart from a consistent increase in pre-weaning pup mortality.

It can be concluded from the results of these reproduction studies that 2 mg dieldrin/kg in the rat diet and 3 mg dieldrin/kg in the mouse diet, equivalent to 0.1 and 0.4 mg/kg body weight per day, respectively, are no-observed-adverse-effect levels for reproduction.

No evidence of teratogenic potential was found in studies on the mouse, rat, or rabbit using oral doses of aldrin and dieldrin of up to 6 mg/kg body weight. Single doses of aldrin and dieldrin, equal to about half the LD_{50}, caused severe fetotoxicity and an increased incidence of teratogenic abnormalities in the mouse and hamster. The significance of these findings in the presence of likely maternal toxicity is doubtful.

Many *in vivo* and *in vitro* mutagenicity studies have been carried out, but the results of nearly all these studies were negative.

The acute oral toxicity of photodieldrin is higher than that of dieldrin in the mouse, rat, and guinea-pig. In acute and short-term toxicity studies, the symptoms of intoxication and the effects on target organs are quantitatively and qualitatively similar to those of dieldrin. Photodieldrin did not induce tumours in mice and rats.

Like most other chemical substances, aldrin and dieldrin do not have a single mechanism of toxicity. The target organs are the central nervous system and the liver. In human beings and other vertebrates, intoxication following acute or long-term overexposure is characterized by involuntary muscle movements and epileptiform convulsions. Survivors recover completely after a short period of time of residual signs and symptoms. In the liver there is an increased activity of microsomal biotransformation enzymes, particularly of the monooxygenase system with cytochrome P-450. This induction of the microsomal enzymes is reversible and, if it exceeds a certain level, it appears to be linked to cytoplasmic changes and hepatomegaly in the liver of rodents.

All the available information on aldrin and dieldrin taken together, including studies on human beings, supports the view that for practical purposes these chemicals make very little contribution, if any, to the incidence of cancer in man.

1.7 Effects on Man

Aldrin and dieldrin are highly toxic for human beings. Severe cases of both accidental and occupational poisoning have occurred but only rarely have fatalities been reported. The lowest dose with a

fatal outcome has been estimated to be 10 mg/kg body weight. Survivors of acute or subacute intoxications recovered completely. Irreversible effects or residual pathology have not been reported.

Adverse effects from aldrin and dieldrin are related to the level of dieldrin in the blood. Determination of the level of dieldrin in the blood provides a specific diagnostic test of aldrin/dieldrin exposure. The level of dieldrin in the blood of male workers below which adverse effects do not occur, (the threshold no-observed-adverse-effect level) is 105 μg/litre blood. This corresponds to a daily intake of 0.02 mg dieldrin/kg bodyweight per day.

Environmental exposure (mainly dietary though also, to a small extent, respiratory) leads to the presence of dieldrin at very low levels in organs, adipose tissue, blood, and mother's milk. As far as can be judged from the extensive clinical and epidemiological studies, there is no reason to believe that these prevailing body burdens constitute a health hazard for the general population. In a continuing study lasting more than 20 years, involving more than 1000 industrial workers in an aldrin/dieldrin insecticide-manufacturing plant, no increase in cancer incidence occurred among workers who had been exposed to high levels of aldrin and dieldrin. More significantly, there were no signs of any premonitory change in liver function in these workers.

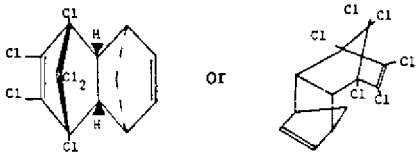
An epidemiological mortality study was carried out at a manufacturing plant in the USA on a cohort of 870 workers exposed to aldrin, dieldrin, and endrin. With almost 25 000 man-years of observation, no specific cancer risk associated with employment at this plant could be identified.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

2.1.1 Primary constituent: aldrin[a]

Chemical structure



Chemical formula: $C_{12}H_8Cl_6$

Relative molecular mass: 364.9

IUPAC chemical name[b]: (1*R*,4*S*,4a*S*,5*S*,8*R*,8Ra*R*)-1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-dimethanonaphthalene or 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-*exo*-1,4-*endo*-5,8-dimethanonaphthalene

Common synonyms and trade names: ENT 15 949 (compound 118), HHDN, Octalene, OMS 194

CAS registry number: 309-00-2

RTECS registry number: IO2100000

Technical product

Common trade name: Aldrin. This is the common name of an insecticide containing 95% of HHDN.

Purity: The minimum content of aldrin (as defined above) in technical aldrin is 90%.

Impurities: octachlorocyclopentene (0.4%), hexachlorobutadiene (0.5%), toluene (0.6%), a complex mixture of compounds formed by polymerization during the aldrin reaction (3.7%) and carbonyl compounds (2%) (FAO/WHO, 1968b

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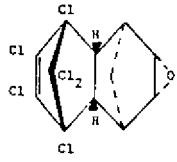
[a] From: Worthing & Walker (1983).

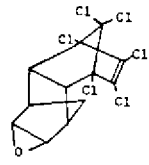
[b] Other chemical names are given in Appendix I.

2.1.2 Primary constituent: dieldrin[a]

Chemical structure:



or



Chemical formula:	$C_{12}H_8OCl_6$
Relative molecular mass:	380.9
IUPAC chemical name[b]:	(1*R*,4*S*,4a*S*,5*R*,6*R*,7*S*,8*S*,8a*R*)-1,2,3,4,10,10-hexachloro-1,4,4a,5,6,7,8,8a-octahydro-6,7-epoxy-1,4:5,8-dimethanonaphthalene or 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-*endo*-1,4-*exo*-5,8,-dimethanonaphthalene
Common synonyms and trade names:	ENT 16 225 (compound 497), HEOD, Alvit, Octalox, OMS 18, Quintox
CAS registry number:	60-57-1
RTECS registry number:	IO1750000
Technical product	
Common trade name	Dieldrin. This is the common name of an insecticide containing 85% of HEOD.
Purity:	Technical dieldrin contains not less than 95% of dieldrin, as defined above.
Impurities:	other polychloroepoxyoctahydrodimethanonaphthalenes, endrin 3.5% (FAO/WHO, 1968b)

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[a] From: Worthing & Walker (1983).
[b] Other chemical names are given in Annex I.

2.2 Physical and Chemical Properties

2.2.1 Aldrin

Pure aldrin is a colourless crystalline solid. It has a melting point of 104-104.5 °C.

Technical aldrin (90%) is a tan to dark brown solid with a melting point of 49-60 °C. Its vapour pressure is 8.6 mPa at 20 °C (6.5×10^{-5} mmHg at 25 °C). Its density is 1.54 g/ml at 20 °C. Its solubility in water is 27 µg/litre at 27 °C (practically insoluble). and in acetone, benzene, and xylene is > 600 g/litre. Aldrin is stable at < 200 °C and at pH 4-8, but oxidizing agents and concentrated acids attack the unchlorinated ring. Aldrin is non-corrosive or slightly corrosive to metals because of the slow formation of hydrogen chloride on storage (Shell, 1976, 1984; Worthing & Walker, 1983).

2.2.2 Dieldrin

Technical dieldrin (95%) consists of buff to light tan flakes (setting point > 95 °C) with a mild odour. Its melting point is 175-176 °C. Its vapour pressure is 0.4 mPa at 20 °C (3.2×10^{-6} mmHg at 25 °C). Its density is 1.62 g/ml at 20 °C. Its solubility in water is 186 µg/litre at 20 °C (practically insoluble), but it is moderately soluble in most paraffinic and aromatic hydrocarbons, halogenated hydrocarbons, ethers, esters, ketones, and alcohols. Dieldrin is stable to alkali, mild acids, and to light. It reacts with concentrated mineral acids, acid catalysts, acid oxidizing agents, and active metals (iron, copper). It is non-corrosive or slightly corrosive to metals in the same way as aldrin (Shell, 1976; Worthing & Walker, 1983).

2.3 Analytical Methods

2.3.1 Sampling methods

Methods of sampling and storage have been reviewed by Beynon & Elgar 1966. Sample collection is broadly divisible into two types: adventitious sampling (particularly of wildlife) and systematic sampling (soil, total diet surveys) in which samples are collected in accordance with the principles of statistical design. Surveys of dieldrin in human blood and adipose tissue are a partial combination of these two classes of sample collection. The sampling methods for total diet surveys were reviewed by Cummings (1966), and the sampling of air for pesticide residues has been discussed in detail by Lewis (1976).

2.3.2 Analytical methods

Since the introduction of the method of gas-liquid chromatography with electron capture detection (GLC/EC) (Goodwin et al., 1961), old methods, based on, for instance, total organic chlorine or the

colorimetric phenyl azide procedure, have been abandoned. The great majority of analytical data relating to the occurrence of residues of aldrin or dieldrin since that time have been based on GLC/EC procedures. There has been considerable evolution of various aspects (especially extraction and clean up procedures) of the methodology. The many publications on specific procedures are reviewed in the Codex Publication "Recommendations for methods of analysis of pesticide residues", CAC/PR 8-1986, (FAO/WHO, 1986b). This review lists 22 individual publications, four of which refer to simplified methods. It also lists the following compendia of methods which may also be consulted.

- Official methods of analysis of the Association of Official Analytical Chemists, 14th Edition 1984.
- Pesticide analytical manual, Food & Drug Administration, Washington DC, USA.
- Manual on Analytical methods for pesticide residues in foods, Health Protection Branch, Health and Welfare, Ottawa, Canada, 1985.
- Methodensammlung zur Rueckstandsanalytik von Pflanzenschutzmitteln (Methods for analysing residues of plant protective agents) 1984 Verlag Chemie GmbH, Weinheim, Federal Republic of Germany.
- Chemistry Laboratory Guidebook, USDA.

Whatever procedure is adopted should be carried out within the requirements of the CAC publication "Codex Guidelines on Good Laboratory Practice in Pesticide Residue Analysis", CAC/PR 7-1984, (FAO/WHO, 1984).

It is important to recognize that the electron capture detector is not specific for aldrin and dieldrin and in the analysis of samples without a precise history of treatment, confirmation of the identity of the residue is an essential part of the analysis. Reports of the occurrence of aldrin in environmental samples in the past, are now thought, in many cases, to have been instances of misidentification. The occurrence of PCBs in the same sample has been a particularly troublesome source of interference. Many procedures for the confirmation of identity are available and include comparison of the position of the peak on different chromatographic columns, thin-layer chromatography, and derivatization. The most definitive method, however, involves the uses of mass spectrography as the detector. With this procedure, much of the uncertainty with regard to the identification of the residue has been eliminated. The mass spectrography procedure described by Hargesheimer (1984) is effective for the determination of chlorinated hydrocarbon residues in the presence of PCBs. The limit of determination of individual methods depends to a considerable extent on the amount of effort the analyst devotes to extraction and clean-up procedures. With samples of food and feeds, for example, a limit of determination of 0.01 mg/kg is normally regarded as acceptable, but in water and air far lower levels are achievable, depending on the care and effort taken.

It should be recognized that there is considerable variation in the results that can be obtained on the same sample by different analysts and in different laboratories and variations of 100% are by no means uncommon at the lower end of the scale. A valuable account of the variation found among 120 laboratories for a sample of butterfat containing known amounts of 11 different chlorinated hydrocarbon insecticides was given by Elgar (1979).

3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

3.1 Natural Occurrence

Aldrin and dieldrin are not known to occur as natural products.

3.2 Man-Made Sources

3.2.1 Production levels and processes; uses

3.2.1.1 World production figures

The first laboratory synthesis of aldrin and dieldrin was in 1948 by J. Hyman & Co. (Thompson, 1976). The method was licensed to Shell and manufacture began in 1950, first in the USA and later on in the Netherlands (IARC, 1974).

Production has decreased since the early 1960s. The production capacity was 20 000 tonnes in 1971, and the estimated 1972 production was 13 000 tonnes. In 1984, less than 2500 tonnes of aldrin and dieldrin were manufactured, approximately one third of which was used in Australia, the United Kingdom, and the USA (Van Duursen, 1985).

Up to the late 1960s and early 1970s, aldrin and dieldrin were used throughout the world. Since then, many countries have severely restricted or banned their use, especially in agriculture, because of their persistent character in the environment (IARC, 1974). The main remaining uses are in the control of disease vectors and termites and industrial applications.

3.2.1.2 Manufacturing processes

Aldrin is synthesized by the Diels-Alder reaction of hexachlorocyclopentadiene with an excess of bicycloheptadiene at 100 °C. The yield is more than 80%, calculated on the hexachlorocyclopentadiene (Melnikov, 1971).

Commercial production of dieldrin is believed to be through epoxidation of aldrin with a peracid (e.g., peracetic or perbenzoic acid), but an alternate synthetic route involves the condensation of hexachlorocyclopentadiene with the epoxide of bicycloheptadiene (Galley, 1970).

3.2.1.3 Release into the environment during normal production

Loss of aldrin and dieldrin, together with isobenzan, in waste water from a manufacturing plant in the Botlek area of the Netherlands caused deaths among sandwich terns *(Sterna sandvicentis)*, eider ducks *(Somateria mollissima)*, and, to a lesser extent, some other bird species, feeding on marine organisms containing high levels of these insecticides in the Wadden Sea during 1962-65. Following improvement

of the waste-water purification of the plant, the residue levels in the marine organisms decreased during subsequent years (Koeman, 1971).

3.2.2 Uses

3.2.2.1 Aldrin

Aldrin is a highly effective broad-spectrum soil insecticide. It kills insects by contact and ingestion, and possesses slight fumigant action within the soil, which ensures distribution in the top soil where the pests are found.

It is used to control soil insects, including termites, corn rootworms, seed corn beetle, seed corn maggot, wireworms, rice water weevil, grasshoppers, and Japanese beetles, etc. Crops protected by aldrin soil treatment include corn and potatoes; it is used as a seed dressing on rice. Aldrin is also used for the protection of wooden structures against termite attack. It is supplied mainly as an emulsifiable concentrate or wettable powder.

3.2.2.2 Dieldrin

Dieldrin is used mainly for the protection of wood and structures against attack by insects and termites and in industry against termites, wood borers, and textile pests (moth-proofing). It acts as a contact and stomach poison.

Dieldrin is no longer used in agriculture. It has been used as a residual spray and as a larvacide for the control of several insect vectors of disease. Such uses are no longer permitted in a number of countries.

It is available as an emulsifiable concentrate or wettable powder.

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

4.1 Transport and Distribution Between Media

4.1.1. Leaching of aldrin and dieldrin

As would be expected from their very low water solubility, hydrophobic character, and strong adsorption by soil, aldrin and dieldrin are very resistant to downward leaching through the soil profile.

Since one of the major uses of aldrin is as a soil insecticide, aldrin-treated soil is an important source of aldrin in the environment.

Bowman et al. (1965) studied the leaching of aldrin through six different types of soil, by passing water through them. In five out of six soil types, only traces were recovered in the leachates. However, 16% of applied aldrin was found in the leachate from a sandy soil type. Other studies indicate that leaching of aldrin through soil is minimal (Harris, 1969; Herzel, 1971; El Beit et al., 1981a,b).

A study was carried out to determine the possible involvement of aldrin applied for the control of termites around house foundations. Seven types of soil collected from different geographical areas in the USA were investigated by placing the soils (adjusted to 0, 5, 10, or 15% water content) in glass columns. The soil columns were separated into five layers of 5 cm by filter paper support cloth. An emulsion of aldrin was placed on the top of the column, equivalent to 0.365 kg aldrin/m^2. The layers of soil were removed approximately 24 h after application of the emulsion and the concentration of aldrin determined. Penetration below 20 cm did not occur in any soil at any of the water contents. In certain soils, penetration only took place in the first 5 cm and, in others, in the third layer (10-15 cm). Water content also plays a role in the penetration. In another study, layers of 4 cm were used, with comparable results (Carter & Stringer, 1970).

Several field studies on the leaching of aldrin through different types of soil have been carried out. In these studies, aldrin was applied to the surface or tilled to a depth of about 15 cm at dose levels of 1.8-20.7 kg/ha. From the results, it is clear that, even up to 5 years after application, aldrin and dieldrin were still present in the treated layer, with little penetration to layers immediately below the treated layer. From these studies, it appears that there is little movement (Lichtenstein et al., 1962; Daniels, 1966; Park & McKone, 1966). However, Wiese & Basson (1966) found some movement, even in clay soil.

In studies by Powell et al. (1979), sandy soil in which tomato plants were growing was sprayed with an aldrin emulsion (2.2 kg/ha) on six occasions at intervals of 1-2 weeks. Approximately one year after the final treatment, soil core samples were taken and the concentrations of aldrin and dieldrin in the 0-5, 5-10, 10-15, 15-22.5 cm

layers were determined. About 73% of the total residue in the 0-22.5 cm layer was in the 0-15 cm layer. The ratio of aldrin to dieldrin in the four strata was similar. The remark should be made that in this study there were a number of confounding factors (e.g., the field was ploughed).

Stewart & Fox (1971) applied aldrin as a spray to four turf plots at doses of 3.3, 4.4, or 6.6 kg/ha. Loam and silt soil core samples were taken to a depth of 30 cm 9-13 years after treatment. Aldrin was not detected; 93-100% of the total dieldrin in the 30 cm core was in the top 15 cm layer of soil.

In studies by Lichtenstein et al. (1971), aldrin was applied to a silt loam at a rate of 4.4 kg/ha and rototilled to a depth of 10-12.5 cm. After 10 years, the percentage of the applied aldrin in the 0-22.5 cm layer was 0.18% as aldrin and 5.2% as dieldrin. The ratios of concentrations in the 0-15 cm layer relative to the 15-22.5 cm layer were: aldrin, 2.5; dieldrin, 4.9.

^{14}C-Aldrin was incorporated to a depth of 15 cm in experimental plots in which potatoes were grown in the Federal Republic of Germany (sandy loam; equivalent to 2.9 kg/ha) and England (sandy clay loam; equivalent to 3.2 kg/ha). After 6 months, the concentrations of aldrin in both cases were as follows: at 0-10 cm, 0.58 and 0.59 mg/kg; at 10-20 cm, 0.23 mg/kg and < 0.01 mg/kg; at 20-40 cm 0.02 and < 0.01 mg/kg and at 40-60 cm, < 0.01 mg/kg (in both locations) (Klein et al., 1973). In a parallel study, the ^{14}C activity in leach water collected at a depth of 60 cm was determined over a 3-year period; the cumulative rainfall during this period was 160 cm. About 10% of the ^{14}C activity, applied initially to a depth of 15 cm, was found in the leachate over a period of 3 years. Almost all the ^{14}C activity was present as dihydrochlordene dicarboxylic acid (Moza et al., 1972).

In studies by Stewart & Gaul (1977), aldrin (5.6 and 11.2 kg/ha) was incorporated to a depth of 15 cm into a sandy loam soil for three successive years. Various crops were grown and soil samples were collected for 14 years. Residues of aldrin and dieldrin below 15 cm were negligible in the tenth year after the initial application, whereas the residues of aldrin plus dieldrin in the 0-15 cm layer were 0.2 and 1.7 mg/kg, respectively, at the two different treatments levels.

The results of these leaching studies indicate the almost quantitative adsorption of aldrin by organic matter and clay minerals. Water molecules compete with aldrin for the adsorption sites in clay minerals, and it has been found that aldrin is bound to a greater extent in dry soil (Baluja et al., 1975; Kushwaha et al., 1978b). The adsorption and desorption of aldrin has been studied by Tejedor et al. (1974) in whole soil and in the clay and organic (humic) fractions. It was concluded that the organic fraction was mainly involved in the adsorptive uptake of aldrin and that the clay fraction was the major factor affecting the retention of aldrin. There does not appear to be a simple relationship between water solubility and leaching, presumably because of the variations in the adsorptive capacity of clay minerals

in various types of soil (Yaron et al., 1967). A chromatographic model of the movement of pesticides through soils has been proposed (King & McCarty, 1968; Oddson et al., 1970).

In the laboratory, the investigations by Eye (1968) and Harris (1969) of the transport of dieldrin by water through soil are particularly relevant and are consistent with the chromatographic model for chemicals in soil of King & McCarty (1968). The elution of dieldrin from soil by 1600 ml water was investigated in a study of six types of soil placed in chromatographic columns. The dieldrin content of the total eluate, as a proportion of the applied dieldrin, varied from 1% (loam soil) to 65% (soil containing 93% sand) (Bowman et al., 1965).

The leaching of dieldrin through soil columns (30 cm diameter) was studied by Thompson et al. (1970). A dieldrin emulsion was applied to the surface (equivalent to 31 kg dieldrin/ha) of soil columns 35 cm deep, and water was added to the surface until about 30 litres (equivalent to about 6 months rainfall) had passed down the columns in 120 h. It was concluded that dieldrin did not readily leach from the three types of soil investigated into drainage water, and that cracks and crevices caused by drying or by earthworms and other animals favour the leaching of dieldrin. The results of an investigation using sloping troughs gave results consistent with the soil column study.

4.1.2 Surface run off

Run off from treated land caused by soil erosion is a potential source of dieldrin residues in surface waters in areas where erosion is not controlled by good farming practice. Sediments bearing aldrin and dieldrin can result in low concentrations in aqueous solution, although these are limited due to adsorption onto the sediments. Thus, rainwater run off (without sediment) does not appear to be a major contributor.

Richard et al. (1975) and Sparr et al. (1966) sampled various surface waters in the USA and reported levels of dieldrin ranging from < 1 to 42 ng/litre and of aldrin in the region of 0.05 μg/litre.

To gain data on the erosion of treated land, Caro & Taylor (1971) and Caro et al. (1976) incorporated dieldrin into the soils of two small watersheds in Ohio, USA, and studied run-off losses over a three-year period. In the first case, there was practically no surface soil erosion and the total loss of dieldrin was confined to run-off water. The area was 1.07 ha and the loss over the period was less than 0.5 g dieldrin, the highest level in the water being 4 μg/litre. In the second study, there was a substantial loss of soil by erosion and the amount of dieldrin lost in the solid sediment was 77 g in only 8 months. The loss in the water itself was just under 2.5 g and the highest water concentration was 20 μg/litre. It should, however, be borne in mind that in this case the soil had been mechanically compacted to aggravate the effects of erosion, so that it is questionable whether the results bear much relation to normal agricultural practice. The authors commented that there was only a poor correlation between rainfall events and the amounts of dieldrin lost.

Sediment-bearing residues of aldrin or dieldrin will yield some of their burden to true solution in the water which they enters. Sharom et al. (1980) showed that the ratio of dieldrin concentration in soil to that in water (in equilibrium with the soil) was between 100 and 500 for mineral soils, whilst that same ratio for aldrin was likely to be around 5-6 times higher. Thus, with 1 mg dieldrin/kg sediment, one could expect a water concentration of about 10 μg/litre.

The movement of aldrin and dieldrin by run off and soil erosion was studied by Haan (1971). Each pesticide was applied at 1.65 kg/ha to the surface of small plots, mainly consisting of silt loam (slope, 1-2%), in a greenhouse. Water was applied and the run-off water, sediment, and surface soil (0.6 cm deep) were analysed. It was estimated that 94.8% and 95.4%, respectively, of the applied aldrin and dieldrin remained in the surface soil (0.6 cm depth). It was concluded that there was no difference in the potential for loss from soil by rainfall, whether the rainfall occurred shortly after aldrin application or several days later.

4.1.3 Loss of aldrin and dieldrin from soils - volatilization

Most authors consider that the principal loss of aldrin and dieldrin from soils is by volatilization. There is widespread evidence for this, although other mechanisms (sections 4.4.1 and 4.4.2) may also play an important role.

Volatilization from soils was first demonstrated when it was shown that mosquitoes were killed by vapour emanating from treated soil blocks (Barlow & Hadaway, 1955, 1956; Gerolt, 1961).

When aldrin is incorporated into the soil, it is most readily lost from the surface layer. Subsequently, material from deeper layers has to rise to the surface to replenish what was lost. The position is somewhat complicated by its gradual conversion to the less volatile dieldrin, although this, too, behaves in a qualitatively similar manner.

There are two routes to the surface: transport in ascending capillary water - analogous to the process of salinization - and vapour diffusion through the soil pores. Both of these processes are strongly affected by hydrophobic adsorption, a phenomenon common to many hydrophobic pesticides of low water solubility. Adsorption by the soil has the effect, at practical rates of application, of reducing the vapour pressure and hence the saturation vapour density in the soil atmosphere. It also reduces the maximum concentration in the soil solution.

There is a very extensive literature on soil adsorption, especially of dieldrin and the following general situation is now well established.

Adsorption, as measured by reduced vapour density, takes place in all soils but is greatest at low moisture levels; that is to say soils in equilibrium with air of relative humidity below around 95%. (Barlow & Hadaway, 1955, 1956; Gerolt, 1961; Harris, 1964, 1972; Igue et al., 1972).

In dry soils, mineral components play the most important part, whereas in moist soils it is organic matter that dominates (Harris & Lichtenstein, 1961; Harris et al., 1966; Harris & Sans, 1967; Harris, 1972). In fact, Harris demonstrated a linear relation between organic matter and adsorption in moist soils. On the other hand, in a dry mineral soil with predominantly montmorillonitic clay and very low organic matter, practically no dieldrin volatilized until the relative humidity of the air in equilibrium with soil reached saturation. At this point volatilization readily resumed.

In moist soils, Spencer et al. (1969) found that adsorption, expressed as a reduction in vapour density, became less marked as the dieldrin level increased. At 20 °C, 10% moisture in the soil, and 1 mg dieldrin/kg soil, the dieldrin vapour density was only 2 ng/litre, compared with 52 ng/litre when the dieldrin level in the soil was increased to 25 mg/kg. This level is close to the figure for free dieldrin. Similar results were reported at 30 °C and 40 °C by Spencer & Cliath (1973).

In dry soils, however, adsorption is far stronger. At 100 mg dieldrin/kg moist soil (Spencer et al., 1969), the depression in vapour pressure was negligible. However, as the moisture content of the soil fell to a critical level of 2.1%, there was a dramatic decrease in vapour density, so that below 2% moisture the vapour density was practically zero. The same authors showed that the level of water in their soil needed to provide a monomolecular layer was 2.8%. They concluded that the critical point at which adsorption increased was when the monomolecular layer started to be lost, leaving adsorption sites available for occupation by dieldrin. Restoration of the moisture status of the soil, however, restored the vapour density to its original level.

Whilst most of these studies were carried out on one soil, Gila silt loam, and whilst the figures would be different for other soils, the qualitative conclusions are largely valid for all soils. Adsorption is expected to be least on sandy soils of low organic matter content.

Adsorption by soils can also be determined by measuring the reduction in the saturation concentration of the soil solution (Eye, 1968; Tejedor et al., 1974; Baluja et al., 1975). As in the case of reduced vapour pressure caused by adsorption by moist soils, the organic matter content of the soil was the principal soil characteristic affecting adsorption from solution. Eye (1968) also demonstrated the dominating influence of organic matter, whereas clay content, surface area, and cationic exchange capacity showed very little correlation. These findings are compatible with those of Yaron et al. (1967).

In studies involving the percolation of dieldrin, dissolved in water, through columns of soils with differing contents of organic matter, Sharom et al. (1980) also showed that the soil capacity for adsorption was largely determined by its content of organic matter. Moreover, adsorption followed the Freundlich adsorption equation. They

reported Freundlich adsorption constants for a range of soils and pesticides, including dieldrin, and showed that, for a given pesticide, adsorption was strongly dependent on the organic matter content of the soil. Moreover, the strength of adsorption by a given soil depended mainly on the water solubility of the pesticide, so that dieldrin, with its low water solubility, was more strongly adsorbed than, for instance, the much more water-soluble lindane. Although aldrin was not studied, it may be inferred from these data that aldrin would be adsorbed correspondingly more strongly, owing to a much lower water solubility than that of dieldrin.

4.1.3.1 Movement within the soil profile - mass flow

Spencer & Cliath (1973) concluded from laboratory studies that dieldrin could ascend the soil profile by mass flow in capillary water moving up to the surface through a moisture gradient, and that this mechanism could account for 3-30% of the total upward movement. However, with low solubility products such as dieldrin, Jury et al. (1983) pointed out that volatilization decreases with time, because ascent to the surface is rate limiting. With high solubility compounds, however, the reverse is true as more material reaches the surface, dissolved in capillary water, to become available for evaporation. However, it is not only water solubility that determines the behaviour, but the value of Henry's constant for the partition of the compound between air and water. These authors considered the critical value to be 2.7×10^{-5}; above this value mass flow is progressively less important. The value of Henry's constant for dieldrin (6.7×10^{-4}) is substantially higher (Jury et al., 1983) and that for aldrin higher still, so that on this basis it is doubtful whether mass flow ever does play a significant role in the transport of aldrin or dieldrin up the soil profile.

In support of the view that transport by mass flow is not appreciable, the mathematical models that have been proposed to describe the loss of aldrin and dieldrin from soils (Farmer & Letey, 1974; Mayer et al., 1974; Jury et al., 1983) tend to demonstrate, in comparisons with laboratory data, that ascent to the surface is predominantly by vapour diffusion rather than mass flow.

4.1.3.2 Movement within the soil profile - diffusion

Diffusion is regarded as the main route by which aldrin and dieldrin ascend the soil profile to reach the surface. Diffusion increases with soil temperature, concentration, decreasing adsorption capacity (usually the same as decreasing organic matter), maintenance of moisture content above the wilting point, and the "tortuosity" of the soil pore system (a measure of the openness of the soil). With regard to moisture content, Farmer & Jensen (1970) found that diffusion coefficients of dieldrin in three soils in equilibrium with air of 94% relative humidity were 9.7, 4.4, and 3.8, but at 75% relative humidity

the values were 0.6, 0.4, and 0.4, respectively. According to Farmer & Letey (1974), the critical moisture level is probably the "fifteen atmosphere percentage", usually considered to be a reasonable measure of the water content at the wilting point.

Tortuosity increases as soils are compacted. Working with moist soils of differing bulk densities, Farmer et al. (1973), showed that diffusion of dieldrin was about twice as fast in a soil with a density of 0.75 g/cm^3 as when it was compressed to a bulk density of 1.5 g/cm^3.

4.1.3.3 Actual volatilization losses - laboratory studies

Lichtenstein & Schulz (1970) reported that aldrin was lost by volatilization from a silt loam soil about 20 times faster than dieldrin. Helene et al. (1981) reported a 31% loss of aldrin from a highly humic soil after 120 days but 62% from a soil of low organic matter content.

In studies of moist soils in volatilization chambers, Farmer et al. (1972) and Igue et al. (1972) found that the rate of loss by volatilization gradually decreased with time. However, if translated into terms of the open field, this could still represent a loss of between 0.2 and 1.4 kg/ha per year, depending on the depth of incorporation.

With a surface application of dieldrin in a microagroecosystem chamber, Nash (1983) reported loss of dieldrin at the rate of 1-4 g/day, but this rate fell to about a half of its initial value within 6-7 h. Incorporation of the dieldrin had the effect of greatly slowing this loss rate (Nash, 1983).

4.1.3.4 Actual volatilization losses - field studies

The data on volatilization losses in the field are limited and refer only to dieldrin. Caro & Taylor (1971) reported loss by volatilization from an incorporated dieldrin application (5.6 kg/ha) of 2.8% of that applied (after 18 weeks). Spencer et al. (1973) cited unpublished studies by Caro & Taylor (1971) where a surface application was lost at the rate of 3% per hour. In a later study, Caro & Taylor (1976) found that 4.5% of a dieldrin application was lost by volatilization in the first year after treatment. By the autumn, the loss rate was only 0.2 g/ha per day, although this increased to 0.9 g/ha per day immediately after the land was cultivated, due, presumably, to the exposure of fresh soil.

Taylor et al. (1972, 1976) estimated a loss of dieldrin of 0.2 kg/ha from an incorporated application of dieldrin. However, only 6% remained from a surface application after 16 weeks, although in this case a small amount was recovered as photodieldrin (Turner et al., 1977).

Willis et al. (1972) demonstrated an 18% loss from a very high application (22 kg/ha) of dieldrin after 5 months where the soil was kept moist by irrigation. However, losses were substantially less when

the soil was not irrigated or when maintained under flood conditions. The maximum rate of loss by volatilization was 0.2 kg/ha per day.

4.1.4 Losses of residues following treatment of soil with aldrin

One of the earliest systematic studies of the decline of aldrin and dieldrin residues in soils, arising from the application of aldrin to the soil, was by Decker et al. (1965), who sampled a wide range of soils of known treatment history from Illinois, USA. They demonstrated the transformation of aldrin to dieldrin and considered that the loss of residues was a two-stage process. There was a comparatively rapid loss in the first year after treatment, a typical loss being 75% of the applied dose. Thereafter, residues declined with a half-life of 2-4 years, the reduced rate being apparently due to the greater proportion of dieldrin in the residues. Elgar (1966) incorporated 2.2 kg aldrin/ha into soils in the United Kingdom and reported somewhat similar results for the decline of residues, although there were indications that the rate of decline slowed in later years as the level in the soil fell to around 0.3 mg/kg. Further studies of this kind have been reported by Lichtenstein et al. (1970), Onsager et al. (1970), and Korschgen (1971). Although the rates of decline were very variable, they were not inconsistent with the data of Decker et al. (1965), bearing in mind the inherent variability of soil data.

There are indications that loss rates are higher in tropical soils than in temperate climates. Whilst Agnihotri et al. (1977) found that epoxidation was faster in tropical than temperate soils, leading to the possibility of slower decline because of higher dieldrin levels, Gupta & Kavadia (1979) found in India that declines were often much faster. In one case, half of the aldrin applied had been lost in only 38 days. Wiese & Basson (1966) also reported comparatively high loss rates in South Africa. Using three rates of treatment and three soils, they found that half of the original application was lost between 1 and 2 months.

Elgar (1975) conducted a series of studies in temperate, warm temperate, and tropical soils and reported rates of decline that were compatible with those of Decker et al. (1965). Again, losses from the tropical sites occurred more rapidly than from the temperate sites. He deduced the following empirical expression to describe loss rates, expressed as the sum of aldrin and dieldrin residues surviving n years after a single application.

$$C(n) = fC(o)\,(1-p)^{n-1}$$

In this expression, C(o) is the initial residue level, C(n) is the level after n years, f is the proportion remaining after the first year, and p is the proportion lost in each of the succeeding years. In Elgar's studies, the mean estimate of these latter two parameters was f = 0.25 and p = 0.44, but in the Decker work, the value of p was somewhat less. It is also possible to derive an equation that

describes the accumulation of residues in a soil subject to a regular routine of annual applications. The implications of this equation are that residue levels do not continue to increase indefinitely, but reach a plateau. In the case of Elgar's data, the plateau level, one year after the last of n applications, would be around 60% of the level observed immediately after the first application. This prediction is well borne out by the soil monitoring data presented in Table 1.

Studies of the decline of residues arising from aldrin applied for the control of termites (Bess & Hylin 1970; Carter & Stringer, 1970) reveal slower rates of decline than would be expected, considering the deep application.

Separate studies have been carried out on dieldrin residue losses. These show considerably slower rates of decline than in the case of aldrin, but there is a very wide range in the data reported. Thus, Edwards (1966) reported that the average time for the disappearance of 95% of the residues was 8 years, but Wiese & Basson (1966) found much faster rates. Intermediate rates were reported by Stewart & Fox (1971) and Beyer & Gish (1980). It seems probable that the rate of decline of dieldrin in the soil is reasonably well reflected by Elgar's equation for the years that succeed the first year of aldrin application.

4.1.5 Losses of residues from water

The partition of dieldrin between the vapour phase and water was determined by a dynamic gas-flow method using ^{14}C-dieldrin (Atkins & Eggleton, 1970). The partition coefficient at 20 °C (expressed on a weight/volume basis for air and water) was constant at 540, up to a concentration of 0.033 mg dieldrin/litre water. At higher concentrations, there was a rapid increase in the partition coefficient, which was attributed to the aqueous solution becoming saturated at 0.033 mg/litre. Using the values for vapour pressure (3.47×10^{-4} Pa) and water solubility found in this study, the wash-out ratio for the removal of dieldrin vapour from atmospheric air by rain was 0.65. It was suggested that the concentration of dieldrin in the rainfall in London (Abbott et al., 1965) (Table 6) may indicate the presence of dieldrin in particulate matter in the atmosphere rather than in the vapour phase.

The rate of dry deposition of dieldrin (vapour phase) on grass, calculated from the results of wind tunnel studies, was 4×10^{-2} cm/second. The average lifetime of dieldrin in the atmosphere, assuming loss by wash-out and dry deposition only, was estimated to be 28 weeks (Atkins & Eggleton, 1970).

The rate of transfer of dieldrin from water to air and vice versa has been determined (Slater & Spedding, 1981). The transfer velocity from water, measured in a wind tunnel, increased as the air speed (measured at 6 cm above the water surface) increased. When there was no air movement, the transfer velocity was 2.6×10^{-5} cm/second compared to 15×10^{-5} cm/second at an air velocity of 31.1 km/h. The transfer velocity from air to water was measured by passing air through

Table 1. Concentrations of aldrin and dieldrin in soil[a]

Location	Year	Use	Number of sites	Mean concentration in mg/kg (maximum value in brackets)		Comments	Reference
				aldrin	dieldrin		
United Kingdom		aldrin: potatoes	21	0.02 (0.12)	0.09 (0.41)	LD < 0.03 mg/kg	Wheatley et al. (1962)
	1965	aldrin: potatoes; dieldrin: seed-dressing, carrots, and wheat; cumulative applications during 5 years prior to sampling (0.14-3.4 kg/ha)	10	0.15 (0.7)	0.48 (0.7)	LD not reported; apparently < 0.02 mg/kg; various soil types; residues in soil microfauna also determined	Davis (1968)
Canada							
S.W. Ontario	1964-65	aldrin: various crops; known usage	13	0.19 (0.8)	0.57 (1.3)	LD < 0.1 mg/kg; soil of various types (sand-muck); aldrin used to a considerable extent (1954-60) on 27 sites	Harris et al. (1966)
		no reported use 1961-64	14	0.18 (2.1)	0.25 (1.6)		
		none used 1954-64	5	LD	LD		
Atlantic provinces	1965	aldrin: 1-5 applications during 15 years prior to sampling; cumulative application 0.5-45 kg/ha; root crops	18	0.46 (1.5)	0.41 (1.45)	LD 0.01 mg/kg; no detectable residues of aldrin or dieldrin in orchard soils to which aldrin/dieldrin had not been applied	Duffy & Wong (1967)

Table 1 (contd).

Location	Year	Use	Number of sites	Mean concentration in mg/kg (maximum value in brackets) aldrin	dieldrin	Comments	Reference
Canada (contd).							
		vegetables	17	0.66 (2.5)	0.36 (1.35)		
Southern Ontario	1971	aldrin: tobacco	4 (50 samples)	ND	0.16 (0.19)	LD 0.001 mg/kg; woodlots were adjacent to treated areas, but not directly sprayed	Frank et al. (1974)
		cereals	4 (60 samples)	ND	0.16 (0.19)		
		woodlots	12 samples	ND	trace		
Saskatchewan	1970	soil from 21 vegetable farms	41 samples	0.03 (0.28)	0.06 (0.77)	LD 0.005 mg/kg; aldrin found in 25% of samples dieldrin found in 55% of samples	Saha & Sumner (1971)
Southern Ontario	1972-75	soil samples from orchards				LD < 0.0004 mg/kg dieldrin had been used (1955-65) at recommended rates of 0.8-1.3 kg/ha	Frank et al. (1976)
		apple: 0-15 cm	31	ND	0.03 (0.38)		
		15-30 cm		ND	0.001 (0.03)		
Southern Ontario	1972-75	sweet cherry: 0-15 cm	16	ND	0.001 (0.01)		Frank et al. (1976)
		15-30 cm		ND	LD		

Table 1 (contd).

Canada (contd).							
		sour cherry:	12				
		0-15 cm		ND	0.005 (0.04)		
		15-30		ND	0.003 (0.02)		
		peach:	11				
		0-15 cm		ND	0.04 (0.11)		
		15-30 cm		ND	0.02 (0.07)		
		vineyards:	16				
		0-15 cm		ND	0.009 (0.035)		
		15-30 cm		ND	0.004 (0.023)		
USA							
Seven eastern states	1965	aldrin and dieldrin in 3 crops:				LD 0.05 mg/kg; proportions of soil samples with measurable residues: potatoes, 76%; carrots, 21%; peanuts, 100%	Seal et al. (1967)
		peanuts:	5	ND	0.15 (0.20)		
		carrots:	19	ND	0.19 (0.26)		
		potatoes:	25	ND	0.10 (0.20)		
	1965-67	aldrin and dieldrin used regularly	17 (278 samples)	0.02 (0.47)	0.21 (2.84)	LD 0.01 mg/kg; aldrin detected in 15% of samples and dieldrin in 67% of samples from areas of regular use	Stevens et al. (1970)
		limited use	16	LD	0.001 (0.001)		
		no known use	18	LD	LD		

Table 1 (contd).

Location	Year	Use	Number of sites	Mean concentration in mg/kg (maximum value in brackets)		Comments	Reference
				aldrin	dieldrin		
USA (contd).							
Colorado	1967	aldrin: various soil types (1-4.3% organic matter); nominal concentrations in soil at time of application: 0.06-6.75 mg/kg	11	0.16 (0.61)	0.19 (0.44)	LD < 0.02 mg/kg; some fields had been treated annually for 9 years; time of last treatment prior to sampling varied from 0-9 years	Mullins et al. (1971)
		dieldrin: nominal concentrations in soil at time of application: (0.13-0.63 mg/kg	9	ND	0.05 (0.30)		
Arizona	1968	3 types of soil (organic matter 0.5-6.6%) from area downwind of an area of insecticide use	13	LD	0.0003 (0.0013)	LD not defined; appears to be about 0.0001 mg/kg; no relationship between concentration of dieldrin and distance from area of application	Laubscher et al. (1971)
10 major areas of onion growing	1969	samples of soil	71	0.02 (0.96)	0.79 (16.72)	LD 0.01 mg/kg; aldrin in 4.2% of samples and dieldrin in 73% of samples	Wiersma et al. (1972)

Table 1 (contd).

USA (contd).							
9 areas growing sweet potatoes	1969	samples of soil	92	0.01 (0.11)	0.17 (2.18)	LD 0.01 mg/kg; aldrin in 3.3% and dieldrin in 60.9% of samples	Sand et al. (1972)
Rice-growing areas	1972	samples of soil	99	0.01 (0.25)	0.04 (0.27)	LD 0.01 mg/kg; aldrin in 39% and dieldrin in 85% of samples	Carey et al. (1980)
USA National Monitoring Program (35 states)	1970	samples of soil	1506	0.02 (4.25)	0.04 (1.85)	LD 0.01 mg/kg; aldrin in 13% and dieldrin in 31% of samples	Crockett et al. (1974)
12 states in the cornbelt region	1970	average application of dieldrin was 1.3 kg/ha	12 (389 samples)	0.05 (2.98)	0.07 (2.04)	LD < 0.01 mg/kg; dieldrin residues attributed primarily to the use of aldrin; aldrin had been used in one or more years from 1954	Carey et al. (1973)
14 cities	1970	soil from urban areas sampled to a depth of 7.6 cm	356	LD	0.1 (12.8)	LD < 0.03 mg/kg; aldrin not detected in any samples; dieldrin in in samples from 22 sites (6.5%) in 6 cities	Carey et al. (1976)
Japan, S.W.							
Kyushu district			99 samples	0.07 (1.01)	0.29 (1.73)	LD 0.001 mg/kg	Suzuki et al. (1973)

[a] LD = limit of detection; ND = not determined.

a column of downward-flowing water, and was found to increase as the interfacial velocity increased from 0.9×10^{-2} cm/second (at 10 km/h) to 5.2×10^{-2} cm/second (at 34.2 km/h). It was suggested that the exchange of dieldrin between water and air was controlled by diffusive processes either in the air boundary or water boundary layers. The Henry's law constant (ratio of the concentrations in air and aqueous phases at equilibrium) for dieldrin was 1.3×10^{-3} at 20 °C. It was concluded that the resistances to transfer of dieldrin from water to air and vice versa were similar.

The physical and thermodynamic principles of exchanges of chemicals between water and air have been discussed (Mackay & Wolkoff, 1973; Liss & Slater, 1974; Mackay & Leinonen, 1975; Mackay et al., 1979; Smith et al., 1981). An estimate of the half-life of the evaporation of dieldrin at 25 °C from a column of water of 1 m depth was derived by Mackay & Leinonen (1975). Although this estimate (539 days) is not based on the most recent and reliable values for the vapour pressure and water solubility of dieldrin, it is probably of the right order.

4.1.6 Aldrin and dieldrin in the atmosphere

Small amounts of dieldrin have been detected in the atmosphere (Table 6). Baldwin et al. (1977) conducted a study at Bantry Bay on the west coast of Ireland, well away from point sources of emission. They found concentrations of dieldrin between 0.06 and 1.6 ng/kg, with an average of 0.36 ng/kg, but no aldrin, photodieldrin, or photoaldrin. No dieldrin was detected on solid matter trapped on filter pads; the limit of determination ranged from 1.1 to 7.2 pg/kg (parts per thousand trillion of air).

The reason for the very low level of occurrence of dieldrin in the global atmosphere, if, as seems probable, a major part of the aldrin used in agriculture escapes from the soil by evaporation, has been the subject of considerable speculation. It appears unlikely that direct photochemical reactions are involved, since there have been no reports of photodieldrin being detected. Washout by rain may be an important factor. Indeed, Baldwin et al. (1977) cited literature figures for Hawaii of 1-97 ng/litre, and Abbott et al. (1965) reported 1-95 ng/litre in rainfall in London and other locations in the United Kingdom. MacCuaig (1975), on the other hand, working in the vicinity of a dieldrin application in Ethiopia, reported 100 µg/litre in rainwater. These results support the suggestion of Atkins & Eggleton (1970) that, though washout of the atmosphere by rain would be inefficient in the case of dieldrin, it could lead to substantial losses. If this were so, dieldrin deposits would be expected on soil adjacent to treated areas, but the fact that large areas of soil in the cornbelt of the USA (Carey et al., 1973) have no detectable levels of aldrin or dieldrin seems to cast doubt on the extent to which rain acts to disperse aldrin and dieldrin onto untreated land near to treated areas.

It would appear possible, therefore, that there are losses of aldrin and dieldrin in the atmosphere. Glotfelty (1978) mentioned the high reactivity of free radical species in the atmosphere, in particular hydroxyl radicals. These could presumably play an important role in the degradation of molecules occurring as vapour.

4.1.7 Aldrin and dieldrin in water

The data regarding the occurrence of aldrin and dieldrin in both ground and surface waters are summarized in Table 7 (section 5.1.3). As would be expected from the extreme resistance of dieldrin and, especially, aldrin to leaching from soil, the occurrence of either compound in groundwater is rare. Spalding et al. (1980) took a series of groundwater samples in Nebraska, USA, where aldrin had been used extensively for the control of corn rootworm and could not detect it in any of the samples. Their limit of determination was between 5 and 10 ng/litre. Junk et al. (1980) reported somewhat similar results from Nebraska. Richard et al. (1975), in a wide-ranging study, examined the water supplied to a series of cities in Iowa, USA, from boreholes. Again, no aldrin or dieldrin was reported; their limit of determination appears to have been 0.5 ng/litre.

Surface waters, by contrast, have often been reported to contain small amounts of dieldrin. In a programme of sampling various surface waters in Iowa, Richard et al. (1975) reported levels of dieldrin ranging from 3 to 75 ng/litre in rivers and streams and levels in reservoirs from 3 to 18 ng/litre. In rivers in Iowa and Louisiana, levels ranged from < 1 to 42 ng/litre. During the period 1976-80, dieldrin was found in 2.4% of samples from national surface waters in the USA, (maximum concentration of 0.61 µg/litre) and in 21.7% of national surface water sediments (maximum concentration of 5300 µg/kg) (Carey & Kutz, 1985).

The dieldrin in surface water probably comes from run-off from treated land. Sparr et al. (1966) sampled drainage ditches and a river in a maize growing area in northwest Indiana, USA. Levels reached 0.6 µg/litre in the river but, in the ditches from fields treated with aldrin at up to 5.6 kg/ha, levels seldom exceeded the limit of determination (0.05 µg/litre). Water draining from rice paddies that had been planted with aldrin-treated seed also contained small amounts of dieldrin (1 µg/litre after seeding and falling by the 14th week to 0.07 µg/litre). The authors calculated that about 1 g of aldrin had been lost from the rice paddy surface water during the whole 14-week period.

Hindin et al. (1964) reported aldrin in irrigation water up to 2.3 µg/litre, but no dieldrin. However, in view of the readiness with which aldrin is epoxidized to dieldrin in surface waters, there must be some doubt as to the identity of the residue they actually measured.

It does appear that dieldrin can occur in surface waters draining from agricultural areas, but the amounts are usually so small that they could not be expected to represent a major proportion of the product

applied to the soil. The ultimate fate of these small levels of dieldrin in water is not known. It is probably that adsorption onto particulate matter, volatilization, and various degradation mechanisms all play a role.

4.2 Translocation From Soil Into Plants

The uptake of aldrin and dieldrin by plants is much higher in root crops than in grain crops. It is influenced by the levels in soils, the strength of adsorption, and the depth of application.

In grain crops, it is rare for residues to reach detectable levels in the grain (FAO/WHO, 1970a; Gupta & Kavadia, 1979). Root crops are much more prone to take up residues from treated soils, as observed by Harris & Sans (1967) who found that carrots, radishes, and turnips had the highest residues. Onions, lettuce, and celery were intermediate and cole crops showed no detectable uptake at all (Lichtenstein, 1959).

The level of aldrin and dieldrin in the soil influences the degree of uptake as shown by Lichtenstein et al. (1970) and Edwards (1973a,b), who both reported on ratios of the concentrations in plants to those in the soil. Further work by Onsager et al. (1970), Voerman & Besemer (1975), Bruce & Decker (1966), and Saha et al. (1971) provided compatible results.

The availability of aldrin and dieldrin for uptake by plants depends on the strength of adsorption by the soil and especially the organic matter fraction. Harris & Sans (1967), Beall & Nash (1969), Beestman et al. (1969), and Nash et al. (1970) demonstrated that crops tend to take up more residues from soil of low than of high organic matter. Adding activated charcoal to soil reduced dieldrin uptake by 70% or more in carrots and potatoes (Lichtenstein et al., 1971).

Deep application of dieldrin greatly reduces the uptake (Beall & Nash, 1972). Residues in the plants from a deep (31-32 cm) application were only 1% of those from superficial application. The authors commented that a possible treatment for reducing the uptake of old soil residues by crops would be simply to plough them under.

The mechanism of uptake by crops is not entirely clear and appears to vary considerably from species to species. Beall & Nash (1971), in work with soyabeans grown on soil treated with ^{14}C-labelled dieldrin, found that residues were taken up both by absorption through the roots and by absorption of vapour through the leaves. In the case of cereals, it seems unlikely that root uptake occurs to any great extent (Powell et al., 1970; Gutenmann et al., 1972; Gupta et al., 1979). This probably accounts for the very low levels found in cereal grains from treated crops. On the other hand, it would seem almost certain that it is root uptake which accounts for the residues found in root crops.

4.3 Models of the Behaviour of Water and Chemicals in Soil

Various models for the movement of water and chemicals in porous media have been developed, based on physical variables such as vapour pressure, diffusibility, and adsorption, etc. (Keller & Alfaro, 1966; Bresler & Hanks, 1969; Lindstrom et al., 1971; Davidson & McDougal, 1973; Pionke & Chester, 1973; Van Genuchten et al., 1974). Models for run-off from soil have also been proposed (Crawford & Donigian, 1973; Bailey et al., 1974; Bruce et al., 1975). These models may be useful as a means of defining more precisely the behaviour of aldrin and dieldrin in soil.

4.4 Biodegradation of Aldrin and Dieldrin

When used to protect crops from soil insects, aldrin is usually incorporated into the soil in which the plants are grown. For this reason, most of the work on the biodegradation of aldrin in agriculture has been concerned with the soil system.

4.4.1 Epoxidation of aldrin

The most important transformation of aldrin in the soil is its conversion by epoxidation to dieldrin (Fig. 2, section 6.3.1.1). Epoxidation, essentially biological in nature (Lichtenstein & Schulz, 1960), occurs in all aerobic and biologically active soils, and about 50-70% of the residues remaining in a soil at the end of the season in which the application was made consist of dieldrin. Lichtenstein & Schulz (1959) reported that epoxidation was slower on peat than on mineral soils and was inhibited at low soil temperatures; very little conversion occurred at 7 °C. Subsequently, many authors have demonstrated that a large number of microorganisms are capable of promoting epoxidation, and these were reviewed by Tu & Miles (1976).

Aldrin is also epoxidized by plants, as demonstrated by Gannon & Decker (1958), while Yu et al. (1971) have showed that root homogenates are very effective promoters of aldrin-to-dieldrin epoxidation.

Aldrin is not epoxidized under anaerobic conditions. In their studies on the degradation of aldrin in anaerobic cultures of sewage sludge, Hill & McCarty (1967) found no dieldrin, although aldrin was completely decomposed within 60 days. Sethunathan (1973) reported that epoxidation of aldrin was arrested in flooded soils.

4.4.2 Other metabolic pathways of aldrin

The transformation of aldrin in the soil to aldrin dicarboxylic acid (V, Fig. 2) appears to be well established (Klein et al., 1973; Kohli et al., 1973b; Weisgerber et al., 1974). The occurrence of photodieldrin (III, Fig. 2) as a metabolite derived from aldrin soil treatment is less well established either in soil (Lichtenstein et al., 1970) or in the leaves of wheat grown in aldrin-treated soils (Weisgerber et al., 1974).

4.4.3 Biotransformation of dieldrin

Dieldrin is much more resistant to biodegradation than aldrin, and microbial degradation is probably a minor route of loss from soils, even under anaerobic conditions (Sethunathan, 1973; El Beit, 1981). Kohli et al. (1973b) added ^{14}C-labelled dieldrin to a soil and detected very little degradation, though he did report trace quantities of photodieldrin. Similarly, small amounts of photodieldrin were detected after dieldrin had been applied to onion seed (Kohli et al., 1972).

In the search for organisms that would degrade dieldrin, Matsumura & Boush (1967) found that only a few soil samples produced detectable transformation of dieldrin, although, in some, up to 6% of the dieldrin added was transformed to water-soluble metabolites. Separation of the organisms responsible revealed that *Pseudomonas*, *Bacillus*, and *Trichoderma* species were able to attack the dieldrin molecule. Tu & Miles (1976) list organisms that have been reported to attack dieldrin; these include bacteria, fungi, and one actinomycete.

In spite of the large number of studies on this topic, it is difficult to estimate the extent to which photodieldrin is evolved in soils treated with aldrin. It is perhaps significant that the microorganisms capable of producing photodieldrin in the laboratory have been isolated mainly from anaerobic environments, so that their activity would be very limited in a well-managed agricultural soil. This is borne out by the study of Suzuki et al. (1974) who sampled 52 soils with a history of aldrin treatment in Japan. Photodieldrin levels were very low compared with dieldrin levels and ranged from < 0.001 to 0.035 mg/kg soil (section 4.4.2.1).

The further fate of photodieldrin in soils has received little attention, but Weisgerber et al. (1975) considered it to be less persistent in the soil than dieldrin itself. They also identified two breakdown products, the bridged equivalent of aldrin dihydrochlordene dicarboxylic acid (XII, Fig. 2) and the bridged equivalent of the transdiol (XI, Fig. 2), though these were only present in very small amounts.

4.4.4 Conclusions

Although many studies have been carried out on the biodegradation of aldrin and dieldrin, it seems improbable that this is a major source of loss from soil. On the other hand, it does seem as if transformation of aldrin to aldrin acid in aldrin-treated soils can be a significant pathway, although there is little evidence in the literature that aldrin acid occurs widely as an environmental residue.

4.5 Abiotic Degradation

Abiotic processes play a limited role in the degradation of aldrin and dieldrin in the environment. Of these abiotic processes, the

greatest amount of research has been carried out on photochemically induced changes.

4.5.1 Photochemistry

Aldrin and dieldrin are susceptible to chemical change as a result of irradiation. Robinson et al. (1966b) assigned structure III (Fig. 2) to the transformation product generally referred to as "photodieldrin".

Rosen & Carey (1968) demonstrated the formation of the unepoxidized analogue from aldrin (photoaldrin) (XIII, Fig. 2) when aldrin was irradiated by sunlight or UV light in abiotic conditions, but the major reaction product under these conditions was an unbridged product where a single chlorine atom had been lost at the 3 position. The addition of benzophenone greatly enhanced yields of photoaldrin from aldrin and also photodieldrin from dieldrin. Fischler & Korte (1969) showed that other ketones also increased the formation of photodieldrin.

4.5.1.1 Photochemistry of aldrin and dieldrin in water

Henderson & Crosby (1968) demonstrated that saturated aqueous solutions of dieldrin exposed outdoors to sunlight produced photodieldrin. However, Ross & Crosby (1974, 1975) found that when oxygenated aqueous solutions of aldrin were irradiated with UV light there was little effect in the absence of sensitizers. The addition of acetone or acetaldehyde led to epoxidation; no caged products were formed. Aldrin in rice paddy water was epoxidized but not in the absence of irradiation. Ross & Crosby (1985) showed that a series of amino acids present in natural waters and even humic acids were capable of initiating photooxidation of aldrin to dieldrin in natural sunlight.

Further evidence for the role of oxidants in the phototransformation of aldrin was reported by Draper & Crosby (1984).

4.5.1.2 Photochemistry of aldrin and dieldrin in air

As noted by Miller & Zepp (1983), data on the atmospheric photodegradation of aldrin and dieldrin are sparse. Turner et al. (1977) reported small levels of photodieldrin above a field of grass that had been treated with dieldrin, but considered that it had arisen from volatilization of the photodieldrin from the foliage rather than from formation in the air itself.

In their studies on the occurrence of dieldrin and its photoisomer in the atmosphere on a global scale, Baldwin et al. (1977) reported detectable levels of dieldrin (0.35 ng/m^3) but were unable to detect any photodieldrin (limit of determination of approximately 0.1 ng/m^3) and considered, therefore, that photodieldrin does not accumulate in the atmosphere.

4.5.1.3 Photochemistry of aldrin and dieldrin on plant surfaces

MacCuaig (1975) reported substantial conversion of dieldrin to photodieldrin on the leaves of plants growing in areas of Africa sprayed for locust control. In a more detailed study, Turner et al. (1977) reported the formation of photodieldrin on grass that had been sprayed with dieldrin. They also found that it was lost fairly readily from the foliage but were uncertain whether evaporation was the sole cause.

Harrison et al. (1967) demonstrated the rapid epoxidation of aldrin to dieldrin on apple leaves. Ivie & Casida (1970) showed that rotenone had a very marked effect on the rate of transformation of leaf deposits to photodieldrin and found its activity as a sensitizer to be some 100 times that of benzophenone.

4.5.1.4 Photochemistry of aldrin and dieldrin in soils

Lotz et al. (1983) studied the irradiation of aldrin on a series of mineral substrates. The substrate had a marked influence on the rate of aldrin loss, river sand showing the greatest effect. El Beit et al. (1983) irradiated dieldrin in contact with various substrates and found that degradation was less in the case of a clay soil than a glass surface. However, the relevance of some of the laboratory studies to the practical situation is questionable because of the frequent use of very hard UV as the radiation source.

It appears that photodieldrin does not occur in large amounts in aldrin-treated soil. Lichtenstein et al. (1970) treated a field soil with very high levels of aldrin and found that 98-99% of the surviving residues 6 or 10 years after the last treatment were in the form of dieldrin. Photodieldrin formed 1.6% of the dieldrin residue. Suzuki et al. (1974) sampled 52 soils with a history of aldrin treatment in Japan and measured dieldrin levels ranging from 0.002 to 1.73 mg/kg and photodieldrin levels ranging from < 0.001 to 0.035 mg/kg.

4.5.1.5 Conclusions

The photochemistry of aldrin and dieldrin has been intensively studied and it seems that the use of dieldrin for certain disease vector control operations could lead to photodieldrin formation, although its persistence seems uncertain. Current uses would seem unlikely to represent a significant source, and it is doubtful whether photodieldrin occurs widely in the environment.

4.5.2 Other abiotic processes

4.5.2.1 Reaction with ozone

Ross et al. (1976) reported that ozonization of water contaminated with dieldrin led to substantial reductions in dieldrin levels and

suggested that this process could be used commercially to help clean-up contaminated water.

4.5.2.2 Clay-catalysed decomposition

Fowkes et al. (1960) showed that clay diluents in the dust formulations of many pesticides caused decomposition. In the case of aldrin and dieldrin, the most pronounced reactions occurred with kaolinite and attapulgite, especially when they were acidic. In the case of kaolinite at 65 °C, the half-life of dieldrin was 400 min, which was reduced to only 30 min when the kaolinite had been acidified. Although, these effects were observed at relatively high temperatures, it is possible that this type of decomposition could be significant in the soil environment, though evidence for this has not been reported.

4.6 Bioaccumulation

The relationship between the bioaccumulation factor and the partition coefficient (K_{ow}) of a chemical between octanol and water has been investigated intensively for a number of compounds. The partition coefficient has been shown to be a useful preliminary indicator of the tendency for a chemical to accumulate in organisms, particularly aquatic ones. The partition coefficient of hydrophobic compounds is usually given as its logarithm ($\log_{10} K_{ow}$). The values reported for aldrin and dieldrin (Briggs, 1981) are 7.4 and 6.2, respectively.

Estimates of the bioaccumulation factors for aquatic organisms, determined under controlled laboratory conditions, are given in Table 2.

Aldrin bioaccumulates and biomagnifies mainly in the form of its conversion products. In one model ecosystem study (Metcalf et al., 1973), conversion to dieldrin occurred rapidly and nearly quantitatively. Only 0.5% of the original radioactive aldrin was stored as aldrin in the mosquitofish *(Gambusia affinis)*, which was the organism at the top of this model food chain.

The uptake of dieldrin from water (0.1-1 mg/litre), after 4 h, by three species each of fungi, streptomycetes, and bacteria gave ratios for the concentration of dieldrin in cells or mycelia to that in the supernatant ranging from 0.3 to more than 100. The rate of uptake of dieldrin by mycelia of *Streptomyces venezuelae* and *Trichoderma viride* was very rapid, reaching equilibrium after about 15 min (Chacko & Lockwood, 1967).

The uptake of ^{14}C-dieldrin by *Chlorella pyrenoidosa* or by six species of marine algae *(Skeletonema costatum, Tetraselmis chuii, Isochrysis galbana, Olisthodiscus luteus, cyclotella nana, Amphidinium carteri)* has been studied. In *Chlorella pyrenoidosa*, rapid penetration of algal cells occurred and a maximum radioactivity was reached after 6-24 h, whereas in the six marine algae, it was reached within 1 h. From the study on *Chlorella*, it was concluded that the

Table 2. Bioaccumulation of dieldrin

Species	Concentration in water (µg/litre) or food (mg/kg)	Duration of exposure	Bioaccumulation factor	Reference
Guppy *(Poecilia reticulata)*	0.8, 2.3, or 4.2	32 days	whole fish: 12 500	Reinert (1972)
Sailfin molly *(Poecilia latipinna)*	0.075	34 weeks	muscle: 3900 gill: 50 100	Lane & Livingston (1970)
	1.5	34 weeks	muscle: 4900 gill: 36 400	Lane & Livingston (1970)
Channel catfish *(Ictalurus punctatus)*	0.013 0.027 0.049	70 days 70 days 70 days	dorsal muscle: 2400 1800 3300	Shannon (1977a)
small large small large	0.075 0.075 2 mg/kg food 2 mg/kg food	28 days 28 days 28 days 28 days	dorsal muscle: 2300 3600 0.27 0.62	Shannon (1977b)
Sculpins *(Cottus perplexus)*	0.017, 0.17, or 0.86	32 days	whole fish: 13 300	Chadwick & Brocksen (1969)
Alga *(Scenedesmus obliquus)*	1, 5, or 20	14 days	1300 (based on dry weight of alga)	Reinert (1972)

Table 2 (contd).

Waterflea *(Daphnia magna)*	2.1, 4.5, or 12.8	6 days	14 000 (dry weight)	Reinert (1972)
Common frog *(Rana temporaria)*	0.8	2 days	whole body 387.5	Cooke (1972)
Common toad *(Bufo bufo)*	20	2 days	whole body 280	Cooke (1972)
Barn owl *(Tyto alba)*	0.5 mg/kg food	2 years	carcass: 18.8	Mendenhall et al. (1983)
Short-tailed shrew *(Blerina brevicauda)*	50 mg/kg food	17 days	carcass: 1.6	Blus (1978)
Mink *(Mustela vision)*	2.5 mg/kg food	4-10 weeks	fat: 8.4	Aulerich et al. (1972)

movement of dieldrin into subcellular organelles occurs within 72 h, and that algae are scavengers of dieldrin. The study on the six marine algae showed that there was no correlation between the dieldrin accumulation in the different algae and the number of cells per ml culture. However, the amount accumulated was related to the concentration of dieldrin in the culture (range, 1-1000 µg/litre), and, for each algal species, to the number of cells per culture. No metabolites were detected (Wheeler, 1970; Rice & Sikka, 1973).

In studies by Jefferies & Davis (1968), medium size worms *(Lumbricus terrestris)* were placed in containers, and water and dieldrin-treated compost were added to give a final concentration of 25 mg dieldrin (nominal)/kg moist compost. The containers were kept at 10 °C for 20 days, and the worms were then collected. The average concentration of dieldrin in six batches of worms ranged from 18.4-24.9 mg/kg live weight of worms.

When two species of earthworms *(Lumbricus terrestris* and *Allolobophora caliginosa)* were placed in containers with compost containing 17 mg dieldrin/kg for 4 weeks at 10 °C, the mean concentration of dieldrin in *Lumbricus terrestris* (two studies) was 13.3 mg/kg live weight. The gut content of *L. terrestris* was determined using worms kept in compost (32 mg dieldrin/kg) for 20 days. The mean concentration of dieldrin in whole worms was 13.8 mg/kg live weight, the air-dried gut contents constituted 11.3% of the total live weight, and the mean dieldrin concentration in the tissues of the dissected worms was 10.8 mg/kg tissue. The uptake of dieldrin by *L. terrestris* was compared with that by *A. caliginosa*; after 4 weeks, the concentration of dieldrin in *A. caliginosa* (27.3 mg/kg) was more than twice that in *L. terrestris*. The concentrations of dieldrin in *A. caliginosa* placed in five different soils for 4 weeks are given in Table 3 (Davis, 1971).

Table 3. The concentration of dieldrin in *A. caliginosa* placed in five different soils for 4 weeks[a]

Soil type	Estimated concentration of dieldrin (mg/kg air-dried soil)	Organic matter (% w/v)	Mean concentration of dieldrin in *A. caliginosa* (mg/kg)
Peaty loam	3.1	30.1	0.23
Organic loam	2.7	6.6	0.78
Loamy sand	1.7	1.3	2.99
Silty loam	2.2	2.8	3.56
Clay loam	2.0	1.7	4.55

[a] From: Davis (1971).

A number of field studies have been carried out in which the concentrations of aldrin and dieldrin in earthworms from fields treated with aldrin were determined. Six species of earthworms were collected from a field to which excessive applications of aldrin had been made for 8 years, and two species from experimental plots to which dieldrin had been applied (single treatment). Samples of soil and earthworms from the aldrin-treated fields were analysed for aldrin and dieldrin, and the mean concentrations in the worms are given in Table 4. The overall mean geometric concentrations in soil (dry weight) were 0.72 mg/kg (aldrin) and 0.64 mg/kg (dieldrin). It was suggested that residual soil in the gut may have contributed appreciably to the residues of aldrin in the earthworms. The low residues in *L. terrestris*, relative to the other species, were attributed to the deeper burrowing behaviour of this species, which enable it to live in non-treated layers of soil for part of its life. The concentrations of dieldrin in the soil and earthworms from the experimental plots 6 months after treatment with dieldrin are given in Table 5. The relationship between the concentration of dieldrin in the two species of earthworms and the concentration in the soil was thought to be given by the function, $W = aS^b$, where W is the concentration of dieldrin in the earthworm and S the concentration in the soil. The fact that the estimated value of b (0.794) was significantly less than unity indicates that residues tend to be relatively greater in worms when the concentrations in the soil are low than when higher concentrations are present (Wheatley & Hardman, 1968).

Table 4. Mean concentrations of aldrin and dieldrin in six species of earthworms from aldrin-treated fields

Species	Geometric mean concentration (mg/kg wet weight)	
	Aldrin	Dieldrin
L. terrestris	0.053	1.6
A. longa	0.28	2.2
A. caliginosa	0.52	3.8
A. chlorotica	0.98	4.6
A. rosea	0.64	3.9
O. cyaneum[a]	0.84	2.4

[a] One sample only.

Beyer & Gish (1980) measured the concentrations of dieldrin in four species of earthworms collected from a depth of 0-50 cm in plots that had received a single surface application of a dieldrin wettable powder (0.6, 2.2, or 9 kg dieldrin/ha). Samples of earthworms were collected over a period of 11 years, and the following relationship was derived between the concentration of dieldrin in the worms and the time interval between dieldrin application and worm collection:

Table 5. Concentrations of dieldrin in the soil and earthworms from experimental plots 6 months after treatment with aldrin

Applied dieldrin (kg/ha) (nominal)	Concentrations of dieldrin[a] (mg/kg)		
	Soil[b] (dry weight)	*A. longa*[c]	*A. chlorotica*[c]
0	0.003	0.033	0.028
0.50	0.50	0.70	1.8
0.75	0.85	1.0	2.0
1.0	1.1	1.3	2.9
1.25	1.2	1.3	2.1

[a] Geometric means.
[b] Soil samples taken 6 weeks before earthworm samples.
[c] Wet weight.

$$C(n) = aE^{bn}$$

where C(n) is the concentration in the earthworms n years after soil treatment, and a and b are constants calculated from the data. The mean values of a and b were as follows:

Application rate (kg dieldrin/ha)	a	b
0.6	7.8	-0.41
2.2	21	-0.32
9.0	53.5	-0.16

The average time required for the initial residues of dieldrin in soil to be reduced by 50% was 5.1 years, and the corresponding time for dieldrin in earthworms was 2.6 years (Beyer & Gish, 1980).

In studies by Gish & Hughes (1982), small experimental pasture plots were sprayed with a suspension of a dieldrin wettable powder at application rates of 0.56, 2.24, or 8.97 kg dieldrin/ha. Samples of soil and earthworms were collected on 12 occasions over a period of 2 years, the soil being sampled to a depth of 2.5 cm. The concentration of dieldrin in the soil did not decline during the 2-year period, but that in the earthworms from the two plots treated at the two lower rates declined significantly. The maximum concentration of dieldrin in the earthworms occurred 4 months after treatment. The ratios of dieldrin concentration in earthworms to that in the soil were examined. Residues in earthworms averaged 166 times those in soil in the sampling period 4 months after application when earthworm residues reached a maximum. The effects of several variables on the concentration of dieldrin in earthworms was investigated, and a multiple regression relationship, incorporating five variables, accounted for about 77.2% of the variability of the residues in earthworms.

The accumulation of dieldrin in live fish-food organisms, tubificid worms, and midge larvae (Chironomidae) was investigated by Chadwick & Brocksen (1969), in *Daphnia magna* by Johnston et al. (1971) and Reinert (1972), in crab *(Leptodius floridanus)* and *Artemia salina* nauplii by Epifanio (1973), in mollusc *(Rangia cuneata)* and blue crab *(Callinectes sapidus)* by Petrocelli et al. (1973, 1975), in oyster *(Crassostrea virginica)* by Mason & Rowe (1976) and Emanuelsen et al. (1978), and in an ostracod *(Chlamydotheca arcuata)* by Kawatski & Schmulbach (1972). These studies were carried out at concentrations (in fresh water or sea water) of 0.5-100 µg/litre or by feeding feed or organism containing aldrin or dieldrin. The duration of the studies was a few days up to 43 days. In all organisms, there was a rapid increase of dieldrin concentration in organs and tissues. A steady state was reached after 3-4 and 2 days, respectively, in *Daphnia magna* and *Cassostrea virginica*. In all organisms tested, the elimination was slow and the half-life of dieldrin for tubificed worms and *Crassostrea virginica* was approximately 16 days and 75 h, respectively.

The rate of insecticide accumulation is partly dependent on the concentration in the water, the duration of exposure, and the activity of the animals. The concurrent feeding of aldrin- or dieldrin-containing feed did not have a significant effect on dieldrin accumulation. It can be concluded that water is the principle source of dieldrin accumulation (Kawatski & Schmulbach 1972; Reinert, 1972; Epifanio, 1973).

A number of studies on different species have been carried out by Gakstatter (1968) *(Carassius auratus)*, Chadwick & Brocksen (1969) *(Cottus perplexus)*, Lane & Livingston (1970) *(Poecilia latipinna)*, Hogan & Roelofs (1971) *(Lepomis cyanellus)*, Ludke et al. (1972) *(Notemigonus chrysoleucas, Gambusia affinis, Lepomis cyanellus, L. macrochirus, Ictalurus natalis)*, Reinert (1972) *(Poecilia reticulata)*, Wells et al. (1973) *(Gambusia affinis)*, Wells & Yarbrough (1973) *(Gambusia affinis)*, Addision et al. (1976), *(Salmo salar)*, and Shannon (1977a,b) *(Ictalurus punctatus)*. In these studies, dieldrin was added to the water at different concentrations, and in a few of the studies the dieldrin was radiolabelled. Distribution and accumulation were examined in various organs and tissues (section 6.3.1.3).

Chadwick & Brocksen (1969) found that the accumulation of dieldrin in whole fish (sculpins) was related to the concentration in the water (0.017-8.6 µg/litre) and appeared to reach a steady state by day 32. Reinert (1972) found such a state after only 17 days in *Poecilia reticulata*. Shannon (1977a) studied this aspect in channel catfish *(Ictalurus punctatus)* (length 15 cm) exposed continuously to 0.013, 0.027, or 0.049 µg dieldrin/litre. The concentration of dieldrin in dorsal muscle increased in a curvilinear fashion. Little change occurred within 56 days in the two lower exposure groups, but a significant increase occurred in the 0.049 µg/litre group. Steady-state concentrations appear to have been established in the dorsal muscle of the fish exposed to the two lower concentrations (but not in those exposed to 0.049 µg/litre) after 56-70 days.

Feeding studies using dieldrin-contaminated tubificid worms (25-350 mg/kg) as food source showed that the retention of dieldrin by sculpins was inversely related to the amount of dieldrin they consumed. However, sculpins fed worms containing 0.4-26 mg dieldrin/kg did not show this relationship. It was suggested that the metabolism and excretion of dieldrin was stimulated at the higher concentrations. The findings showed that a maximum of 16% of the dieldrin accumulated would have come from the contaminated food. Thus dieldrin is accumulated in fish far more readily from water than from food (Chadwick & Brocksen, 1969; Reinert, 1972).

In studies on sailfin molly *(Poecilia latipinna)*, exposed to concentrations of 0.75 and 1.5 µg/litre for 34 weeks (flow-through system), Lane & Livingston (1970) found that the ratio of the concentration of dieldrin in the tissues to that in water in the steady state was about 10 000.

From a study on green sunfish *(Lepomis cyanelles)* that were exposed to dieldrin at 6 µg/litre for 124-139 h, it was concluded that the lethal concentrations of dieldrin in blood and brain were approximately 6 and 9 mg/kg tissue, respectively (Hogan & Roelofs, 1971).

Shannon (1977b) exposed channel catfish to 0.075 µg dieldrin/litre water and/or 2 mg dieldrin/kg food for 28 days. Small (15-22.5 cm) and larger fish (3-40 cm) were used and dorsal muscle of the fish was analysed. After 28 days, fish exposed to 0.075 µg/litre had a mean concentration of dieldrin in muscle of 0.175 (small fish) and 0.274 (large fish) mg/kg tissue, fish fed 2 mg dieldrin/kg contained 0.544 (small fish) and 1.243 (large fish) mg/kg tissue, and those given the combined treatment contained 0.898 (small fish) and 2.418 (large fish) mg/kg tissue. The elimination of dieldrin from the dorsal muscle in clean water showed that when fish were exposed to dieldrin in water only, a 50% decrease took place in 8 days. For fish exposed to dietary or combined exposure, it required 20 days.

In a study with different early-life stages of rainbow trout, the bioconcentration factor in the different stages was determined using ^{14}C-dieldrin. It increased during embryonic development from 120, reached a maximum at the sac fry stage of 12 000 and fell again at the early fry stage to 1500. The clearance rate constant sharply increased at the early fry stage. Almost all the dieldrin was recovered from the yolk (Van Leeuwen, 1986).

The yolks of eggs from chickens fed aldrin or dieldrin (1 mg/kg) or 10 mg dieldrin/kg for 2 years contained dieldrin concentrations of 6-25 mg/kg (Brown et al., 1965). Several other studies on the accumulation of dieldrin into avian eggs have been made, details of these being given in Tables 17 and 18 (section 5.1.6).

Clark (1975) fed red-winged blackbirds *(Agelaius phoeniceus)* a diet containing 10 mg aldrin/kg, some of the birds being artificially stressed. The mean number of days that the birds survived was 29.9 for unstressed and 22 for stressed birds. The mean values of brain residue levels at death were 19.8 mg dieldrin/kg for unstressed birds and 22.2 mg dieldrin/kg for stressed birds. Three unstressed birds, sacri-

ficed after 76 days, had dieldrin levels of 6.7, 7.28, and 7.4 mg/kg. The carcass levels of dieldrin increased linearly with time and showed no tendency to level off, as occurred in the brains of unstressed birds. The three unstressed birds sacrificed had the highest carcass dieldrin levels (70.3, 82.8, and 147 mg/kg).

Stickel et al. (1969) fed Japanese quail *(Coturnix coturnix japonica)* diets containing 2, 10, 50, or 250 mg/kg dieldrin for up to 158 days. The mean dieldrin levels in the brain of dead and sacrificed birds were 18.25 mg/kg and 3.35 mg/kg (wet weight), respectively, while the mean liver residues were 19.7 mg/kg (wet weight) and 28.8 mg/kg (wet weight), respectively.

Mendenhall et al. (1983) fed captive barn owls *(Tyto alba)* with diets containing 0.5 mg/kg dieldrin for 2 years. The mean carcass residues were 9.4 mg/kg (wet weight) after 2 years, and the mean dieldrin levels in eggs were 3.6 mg/kg in the first year and 8.1 mg/kg in the second.

Enderson & Berger (1970) fed each of three captive female prairie falcons *(Falco mexicanus)* with 11 starlings, one per day. The starlings had been treated for 14 days with 10 mg/kg dieldrin in their diet. One bird died and showed levels of dieldrin in brain, liver, and muscle of 11, 29, and 4.6 mg/kg (wet weight), respectively. The other two were sampled and found to have mean adipose tissue and brain levels of 532 and 5.84 mg/kg, respectively. The authors also fed wild falcons for 6 weeks prior to egg laying. The analysis of one egg from each clutch showed a mean egg dieldrin content of 41.5 mg/kg, and the mean adipose tissue level of dieldrin in dosed adult falcon, was 83 mg/kg dieldrin.

Turtles *(Pseudemys scripta elegans)* were given intraperitoneal injections of dieldrin (20 mg/kg body weight) and the accumulation in organs and tissues was determined over a period of 70 days. The turtles were fasted during the study. The rate of absorption of dieldrin into the tissues was slow, and there were no clear indications of an approach to steady-state concentrations by day 70. The highest levels of dieldrin were found in body fat and liver, and the levels in plasma and brain were also high (Pearson et al., 1973).

Cooke (1972) studied the effect of dieldrin at nominal concentrations of 0.0008, 0.02, or 0.5 mg/litre on groups of 40 common frog *(Rana temporaria)* tadpoles with hindlimb paddles or hind legs. The exposure lasted 24 or 48 h in amphibian saline. At the highest dose level the mean dieldrin content after 48 h exposure was 42.9 mg/kg tissue. At the dose levels of 0.0008 and 0.02 mg/litre, there were 0.31 and 6.1 mg/kg dieldrin in tissues, respectively. Toad *(Bufo bufo)* tadpoles exposed to 0.02 or 0.5 mg/litre contained 138 mg dieldrin/kg tissue at the higher dose level, after 48 h, and 5.6 mg/kg at the lower.

A laboratory study was undertaken concerning the lethal brain levels for dieldrin in adult and juvenile brown bats *(Myotis lucifugus)*, using 47 female bats collected from a church attic in Maryland, USA. Meal worms containing an average of 0.38 mg dieldrin/kg

(wet weight) were fed to the bats for 52 days, and then untreated worms were administered for another 22 days. The amount of dieldrin in bats increased during dosing and decreased afterwards. These changes did not appear as changes in average dieldrin concentrations in the fat because the amounts were highly variable. During the exposure period a continuous build up of the concentration in fat was seen, but an equilibrium was not reached. The initial half-life for dieldrin loss was estimated to be 24 days. Measurable dieldrin was found in the brains of only 6 out of 47 bats. The levels measured (0.5 to 0.9 mg/kg tissue) were all far below lethal levels. The highest dieldrin level determined in the carcass of 37 bats was 110 mg/kg tissue (lipid weight) (Clark & Prouty, 1984).

Short-tailed shrews *(Blerina brevicauda)* were fed diets containing dieldrin (nominal concentrations of 50, 100, or 200 mg/kg diet) for up to 14 days. All of the animals fed 50 mg/kg survived, but all those fed 200 mg/kg died. The mean dieldrin concentration in the brains of 14 shrews that died was 6.8 mg/kg (range, 3.7-12.6). Some animals sacrificed after 17 days of feeding the 50 mg/kg diet contained mean residues in the brain of 1.8 mg/kg and in the carcass of 58 mg/kg. After 14 days on an untreated diet, the concentrations in the carcass declined by 76% in both sexes, and in the brain by 59% and 84% in males and females, respectively. The half-life of dieldrin was estimated to be less than 14 days (Blus, 1978).

Male mink (3 months old) were fed a diet containing dieldrin (nominal concentrations of 0 and 2.5 mg/kg diet) for 10 weeks, and samples of abdominal fat were taken by biopsy at two-weekly intervals. The mean concentration of dieldrin after 2 weeks was 12.5 mg/kg body fat. For weeks 4-10, an average concentration of 21 mg was found, a steady state being reached after approximately 4 weeks (Aulerich et al., 1972).

4.7 The Fate of Aldrin and Dieldrin in the Environment

On the basis of the current uses of aldrin in agriculture, the first point at which aldrin and dieldrin enter the environment is the soil, dieldrin being derived from aldrin by biological epoxidation. Understanding the fate of aldrin and dieldrin in the environment, therefore, depends firstly on an understanding of its behaviour in the soil.

4.7.1 Aldrin and dieldrin in soils

It was concluded in section 4.1.4 that the regular application of aldrin to soils for the control of soil pests does not lead to an indefinite accumulation in the soil. The results of a considerable number of soil monitoring studies, summarized in Table 1, support this conclusion. Some of the individual monitoring studies are discussed at greater length in this section.

Carey et al. (1973) monitored residues of aldrin and dieldrin over a very wide area of the corn belt in the USA in 1970, when the use of aldrin on maize was probably close to its maximum and the levels were representative of residues in a situation of continuing use. Average values for aldrin plus dieldrin, recalculated for samples that contained positive residues, ranged from 0.05 to 0.87 mg/kg for each of the twelve states. The maximum levels for the whole study were 2.98 mg aldrin/kg and 2.04 mg dieldrin/kg (these values were not both derived from the same sample). In many cases the residues had come from relatively recent applications, as may be judged from the comparatively high proportion of aldrin still remaining. The average was greater than 50% of the combined residues in four of the twelve states, so that many of the samples were probably taken from soils in the same year in which they were treated.

Carey et al. (1980) carried out a further study on rice soils in the USA during the year 1972. At that time, aldrin was used extensively as a rice seed dressing and, according to the data presented by Sparr et al. (1966), overall application rates of aldrin would have been between 0.2 and 0.4 kg/ha. Between 50% and 100% (depending on the state) of the land sampled had received aldrin-dressed seed. As in the case of the maize data, figures for aldrin and dieldrin were presented separately and not paired, so that total residue levels are difficult to deduce. The average level for aldrin was only about 0.02 mg/kg soil and for dieldrin was 0.05 mg/kg, although there were occasional samples that reached 0.25 mg/kg for either aldrin or dieldrin. According to the information presented earlier, degradation of aldrin occurs more readily in the anaerobic conditions of a rice paddy than in fully aerobic soils, and this may have contributed to the much lower level of residues surviving in rice compared with maize. However, it should also be remembered that the initial rates of application were substantially lower in rice than in maize.

In Canada, Harris et al. (1966) reported a series of data for soils in S.W. Ontario and there was limited information on the treatment history of the soils sampled. About a half of the soils showed residues, and these ranged from < 0.01 to 1.5 mg/kg for aldrin plus dieldrin residues. One high figure of 3.5 mg/kg seems anomalous in that it was reported from land that had no treatment history with aldrin or dieldrin. With the exception of this anomalous sample, there was no evidence for accumulation. Fairly similar results were reported by Duffy & Wong (1967), who sampled a series of vegetable-growing areas in Canada in 1965. In cases where it was reported that aldrin or dieldrin had been used (sometimes over a period of several years) residues were mostly below 2 mg/kg.

None of these studies mentioned the occurrence of any dieldrin degradation products, in particular photodieldrin, and yet this would presumably have been detected had it been present. This, taken in conjunction with the work of Suzuki et al. (1974) (section 4.4.2), would seem to be useful evidence that photodieldrin does not, to any appreciable extent, represent a terminal metabolite of aldrin in the soil.

4.7.2 Aldrin and dieldrin in the atmosphere

The relative contributions of the various mechanisms for the loss of aldrin and dieldrin from the soil have not been estimated (as far as can be judged from the literature) but, as mentioned in section 4.1.3, volatilization is usually considered to be the major loss route. Consequently, the occurrence of aldrin or dieldrin vapour in the atmosphere has been the subject of considerable study.

Spencer & Cliath (1975) considered that many pesticides enter the atmosphere after application. This occurs by volatilization during spraying, from treated crops or soils, or from dust from treated soil surfaces blown up by the wind. These routes are difficult to quantify, and only sparse data are available, though a few relating to dieldrin have been cited in section 4.1.3.

Small amounts of dieldrin have been detected in the atmosphere, particularly in agricultural areas and, in one case, close to a formulating plant (section 5.1.1.2). Aldrin has also been detected, though relatively less often (section 5.1.1.1). There is further information on the levels in the atmosphere of aldrin and dieldrin in section 4.1.6.

4.7.3 Conclusion

In spite of the slow rate at which aldrin and dieldrin are lost from soils when applied to them for insect control, there is no evidence for their indefinite accumulation in the environment, either in the soil itself, in water, or in the atmosphere. The evidence suggests that photodegradation products do not accumulate either.

Although there is evidence that a considerable proportion of the aldrin and dieldrin used in agriculture reaches the atmosphere, it seems probable that the degradation processes in the atmosphere described by Glotfelty (1978) for pesticides in general operate to prevent accumulation of aldrin and dieldrin.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 Environmental Levels

5.1.1 Air and rainwater

5.1.1.1 Aldrin

Residues of aldrin in the general atmosphere, either in the vapour phase, adsorbed by dust particles, or in rainwater, have been reported less frequently than for other organochlorine insecticides. Concentrations in the range 0.1-4 ng/m^3 have been found in the air of agricultural communities (Tabor, 1966). In a pilot survey in 1967-1968, out of nine localities in the USA, only one sample from a total of 880 contained aldrin (8 ng/m^3) (Stanley et al., 1971). Aldrin was detected in 13.5% of 2479 air samples collected from 16 states in the USA in the 3-year period 1970-1972. The mean value in these positive samples was 1.6 ng/m^3 and the maximum was 24.6 ng/m^3 (Kutz et al., 1976).

Aldrin was found at a level of 0.9 ng/m^3 in 16 out of 66 air samples taken within 800 m of two formulation plants in 1970 (Lewis & Lee, 1976). One year later, 6 out of 60 samples were found to contain a level of 1.5 ng/m^3, and in 1972 no aldrin could be detected.

5.1.1.2 Dieldrin

In a pilot survey in 1967-1968 in the USA, dieldrin was found in 6% of the 880 samples analysed. The maximum level was 29.7 ng/m^3 (Stanley et al., 1971).

In a survey mentioned above (Kutz et al., 1976), dieldrin was detected in 94% of the 2479 samples. The mean value in these positive samples was [illegible] ng/m^3 and the maximum was 23.9 ng/m^3.

A summary of the concentrations of dieldrin in air and rainwater (washout from the air) is given in Table 6.

5.1.2 Concentrations in houses

5.1.2.1 Aldrin used for subterranean termite control

Aldrin EC (480 g/litre) was applied in a 0.5% solution as a termiticide to typical slab and crawl-space type houses in California [illegible]. Samples of air were taken in the [illegible] and crawl-space at intervals up to 1 year after [illegible] [illegible]

Table 6. Concentration of dieldrin in air, rainwater, and dust

Location	Year	Number of samples	Medium	Analytical[a] procedure	Mean concentration (range)	Comments	Reference
Netherlands							
Delft	1979-81	55	air	glass fibre filter; GC/EC	0.073 ng/m^3 (maximum, 370 ng/m^3) aldrin: 0.039 ng/m^3; maximum, 640 ng/m^3)	24-h samples	Guicherit & Schulting (1985)
United Kingdom							
Wellesbourne	1964-65	11	rainwater	TLC, followed by GLC/EC	24 ng/litre (10-36)	samples of monthly rainfall	Wheatley & Hardman (1965)
	1965	5			9 ng/litre (3-16)	samples collected during periods of prolonged rainfall	
London	1965	11	rainwater	GLC/EC	42 ng/litre (10-95)	samples of monthly rainfall; 2 sampling sites; limit of determination: 10 ng/litre	Abbott et al. (1965)
London	1965	1	air	TLC followed by GLC/EC	20 ng/kg		Abbott et al. (1966)
United Kingdom	1966-67	28	rainwater	alumina column chromatography and TLC followed by GLC/EC	8 ng/litre (1-35)	samples from 7 locations during 12 months; limit of determination: 1 ng/litre	Tarrant & Tatton (1968)

Table 6 (contd).

USA							
Cincinnati	1965	1	dust washed out by gentle rain	florisil column chromatography followed by GLC/EC	3 ng/g dust	source of the dust was the Southern High Plains, approximately 1500 km southwest of Cincinnati	Cohen & Pinkerton (1966)
16 states	1970-72	2479	air	florisil column chromatography followed by GLC/EC	1.7 ng/m^3 (1-23.9)	limit of determination: 1-10 ng/m^3	Kutz et al. (1976)
Hawaii	1970-71	5	rain-water	GLC/EC	5 ng/litre (1-27)		Bevenue et al. (1972a)
	1971-72	14			12 ng/litre (1-97)		Bevenue et al. (1972b)
West Indies							
Barbados	1965-66	15	dust	TLC followed by GLC/EC	2.2 ng/g dust (1-8.1)	samples of dust collected in nylon screens; limit of determination: 1 ng/g (?)	Risebrough et al. (1968)
Barbados	July 1970	12	air-borne dust	silicic acid column chromatography followed by GLC/EC	49 ng/m^3 air (1-190)	source of dust in air probably North Africa	Prospero & Seba (1972)

Table 6 (contd).

Location	Year	Number of samples	Medium	Analytical[a] procedure	Mean concentration (range)	Comments	Reference
Ireland							
Rentry Bay	1973	17	air	florisil column chromatography followed by GLC/EC	0.36 ng/m^3 (0.06-1.6)	aldrin and photodieldrin less than limits of detection (0.1 ng/kg); origin of air samples either westerly from Atlantic Ocean (13 occasions) or easterly from continental Europe (4 occasions)	Baldwin et al. (1977)

[a] TLC = thin-layer chromatography; GC/EC = gas chromatography/electron capture detection; GLC/EC = gas-liquid chromatography/electron capture detection.

houses were < 0.04-0.09 $\mu g/m^3$ at day 28 and were < 0.05 $\mu g/m^3$ at day 56, whereas those in crawl-space houses were 0.06-1.5 $\mu g/m^3$ at day 7, 0.04-0.36 $\mu g/m^3$ at day 28, and 0.06-0.55 $\mu g/m^3$ at day 56. One year after application the air concentration of aldrin was 0.08 $\mu g/m^3$ or less, whereas dieldrin was not detected in any of the samples of air. The concentrations of aldrin in surface wipes from kitchens showed transient peaks 7 days after treatment, the concentrations being higher in wipes from crawl-space houses (0.09 $\mu g/m^2$) than from slab houses (0.012 $\mu g/m^2$). Between day 28 and day 56 the concentrations remained at about 0.04 $\mu g/m^2$ in crawl-space houses and 0.002 $\mu g/m^2$ in slab houses. One year after application, aldrin and dieldrin were not detectable in the kitchen wipe samples from the slab houses, while in the samples from the crawl-space houses the concentration of aldrin amounted to 0.04 $\mu g/m^2$ and that of dieldrin to 0.018 $\mu g/m^2$ (Marlow et al., 1982; Marlow & Wallace, 1983).

5.1.2.2 Aldrin and dieldrin used for remedial treatment of wood

One to ten years after the remedial treatment of inside wood in houses with dieldrin, its concentration in the air was measured. Forty samples from 16 houses in the United Kingdom, covering a wide range of construction type, size, and occupational pattern, were analysed. The concentrations of dieldrin in the air in all interior areas other than roof-voids were between 0.01 and 0.51 $\mu g/m^3$, and in roof-voids, they were between 0.03 and 2.7 $\mu g/m^3$ (Dobbs & Williams, 1983).

Paton et al. (1984) observed that aldrin and dieldrin migrated from treated laminated timber and plywood, used as structural components of commercial containers, into flour in polyethylene bags or metal tubes that were stored in the containers for up to 40 days. The migration was thought to occur through contact with the floor or sorption from the atmosphere. The residues in the flour varied widely depending on temperature, type of packaging material, and location of the flour in the container.

5.1.3. Aquatic environment

Dieldrin occurs more commonly in the aquatic environment than does aldrin, albeit at very low concentrations. The major sources of contamination of rivers, etc., by aldrin and dieldrin are industrial effluents (manufacturing, formulation, and moth-proofing in the textile industry) and soil erosion during agricultural usage (Ichtertstein et al., 1962; Park & McKone, 1966; Epstein & Grant, 1968; Eye, 1968; Croll, 1969; Lowden et al., 1969; Rowe et al., 1971; Burns et al., 1975; Brown et al., 1979). Local use appears to contribute to the presence of dieldrin in sediments in urban areas (Marriaw, 1975). In the USA, the Environmental Protection Agency found that between 118 kg and 14.2 tonnes of dieldrin was carried in the Mississippi River past St Louis each year. Although this is certainly not the case today, it does illustrate the contribution of run-off to the pesticide load in

river systems. This is of special concern with dieldrin because of its stability in water (Eichelberger & Lichtenberg, 1971).

Dieldrin has been detected in the northern Atlantic Ocean at a mean concentration of 5.8 ng/litre (Jonas & Pfaender, 1976), and it is of interest that the dieldrin concentration was apparently unrelated to depth or distance from shore. It was suggested that this may be the result of adsorption to particulate matter. The identification of the component measured as dieldrin was based on gas-liquid chromatographic behaviour (three different stationary phases), but was not rigorously confirmed. Other investigators (Harvey et al., 1973, 1974; Bidleman & Olney, 1974) did not report the presence of dieldrin in the northern Atlantic Ocean, although the analytical methods were appropriate for the detection of aldrin and dieldrin.

Dieldrin residues (0.01-0.3 ng/litre) have also been reported off the coast of Ireland, in the English Channel, and in the North Sea (Dawson & Riley, 1977).

Low levels of dieldrin have been reported in surface waters from several countries. The results of several surveys are summarized in Table 7.

5.1.4 Soil

Aldrin is applied more frequently to the soil (directly or indirectly) than dieldrin. However, as a result of the relatively rapid conversion of aldrin to dieldrin, residues of dieldrin are usually found more frequently in soil and at higher concentrations, except shortly after the application of aldrin to soil. Sediment residue levels tend to lie between those of soil and water, with values up to 140 µg/kg) (Dawson & Riley, 1977). Dieldrin has been reported in the sediments of Lake Ontario and Lake Superior (Frank et al., 1974; Frank et al., 1981), rivers of the USA (Ryckman et al., 1972), bays (Sheets et al., 1970), and off the coasts of Ireland (Dawson & Riley, 1977). A summary of some of the results of monitoring surveys was given in Table 1 (section 4.1.4). This is not a comprehensive review of residues, but it indicates the variations of the concentrations that occur in practice. These results also illustrate the potential for absorption into root crops, and for uptake by soil organisms.

5.1.5 Drinking-water

Studies on drinking-water in the USA have indicated dieldrin residue values up to 8 µg/litre (Kraybill, 1977; Sandhu et al., 1978). In a comprehensive study in the USA, dieldrin residues were found in less than 17% of the samples with 78% of these positive results lying within the range 4-10 ng/litre. The highest residue level found in this study was 110 ng/litre. Dieldrin has also been found in drinking-water in Canada (0.1-4 ng/litre) (Williams et al., 1978) and in the Virgin Islands (average concentration 0.19 µg/litre (Lenon et al., 1972).

Table 7. Concentrations of aldrin and dieldrin in the aquatic environment

Location	Year	Type of water	Number of sites	Mean concentration (ng/litre) (maximum)[a] aldrin	dieldrin	Comments	Reference
Argentina							
Santa Fe and Parana	1981	surface water (20 cm depth)	4	4 (29)	LD	LD not defined; samples collected twice monthly (March-December)	Lenardon et al. (1984)
		suspended solids	4	150 ng/g (1625)	LD	occasional high residues of aldrin attributable to local source of application (1966-68)	
Canada							
Ontario	1971	agricultural and urban rivers	2	1 (7)	11 (41)	LD less than 1 ng/litre	Miles & Harris (1973)
		resort rivers	1	1	4 (11)		
		bottom mud	2	LD	0.9 (dry weight) (4.5)	LD less than 1 ng/g mud	
			1	LD	0.9 (dry weight) (1.4)		
Nova Scotia	1972-73	river	7 (23 samples)	77 (670)	979 (11 800)	LD not defined; water, probably less than 10 ng/litre; sediment, probably less than 1 ng/g	Burns et al. (1975)
		artesian wells	4	LD	10 (10)		

Type of water	Number of sites	Mean concentration (ng/litre (maximum))[a] aldrin	dieldrin	Comments	Reference
[illegible]	[illegible]	47 ([illegible])	100 (200)		
Natural drainage	2 (4 samples)	90 (330)	17.5 (50)	National drainage ditch in a tobacco-growing area	
[illegible]	25	37 ([illegible])	4.9 (86)	High residues in water and sediments attributable to soil erosion, particularly during and after prolonged heavy showers	
Sediment from natural drainage ditch	[illegible]	1088 (2226)	670 (13 750)		
Filtered lake water	34	LD	0.5 (0.5)	LD: filtered water, less than 0.5 ng/litre; sediment, less than 1 ng/g; dieldrin detected (0.5 ng/litre) in one sample of filtered water and in 5 samples of sediment (0.1 ng/g)	Glooschenko et al. (1976)
Sediment	34	LD	0.1 mg/kg dry weight (0.1)		
[illegible]	10	53	0.52 (1.1)		Fytianos et al. (1985)

Table 7 (contd).

United Kingdom							
Kent and Essex	1965-66	rivers	9 (224 samples collected at 2-weekly intervals)	ID (4)	ID (59)	ID less than 3 ng/litre; aldrin found in one sample only	Croll (1969)
Great Britain	1965-66	rivers	11 (75 samples collected at 2-monthly intervals	ID	24.3 (423)	high residues of dieldrin attributable to effluent from moth-proofing plants using dieldrin	Croll (1969)
	1965-67	rivers	15	ID	292 (2840)	high residues of dieldrin attributable to effluent from moth-proofing plants using dieldrin	Croll (1969)
[illegible]	1965-66	underground water	31	ID	ID		Croll (1969)
Hertfordshire	1966	River Lee	6	ID	ID	ID less than 2 ng/litre	Lowden et al. (1969)
[illegible]	1966-68	rivers	14 (30 samples)	ID	114 (650)		
[illegible]	1967	sewage effluent	24	ID	132 (1900)	high concentrations of dieldrin attributable to industrial effluent from moth-proofing plants	Lowden et al. (1969)

Table 7 (contd).

Location	Year	Type of water	Number of sites	Mean concentration (ng/litre) (maximum)[a] aldrin	dieldrin	Comments	Reference
United Kingdom (contd).							
Yorkshire	1976-77	rivers	7 (18 samples)	LD	902 (4900)	LD less than 1 ng/litre; high concentrations of dieldrin in individual rivers (and sewage effluent) attributable to the use of dieldrin for moth-proofing of wool	Brown et al. (1979)
		sewage effluent	1 sample	LD	6240		
		river sediments	10	LD	124 ng/g (dry weight) (432)		
Netherlands	1969-75	raw water	11 (120 samples)	LD	LD (50)	unfiltered water to be used for drinking-water preparation	Greve (1972); Wegman & Greve (1978)
		surface water (depth about 1 m)	26 (1246 samples)	LD	10 (140)	aldrin was detected occasionally at low concentrations; limit of detection about 10 ng/litre	Wegman & Greve (1978) Greve (1972)
Federal Republic of Germany	1970-71	unfiltered surface water	28 (119 samples)	LD	LD (45)	dieldrin reported in only one sample of water	Herzel (1972)
		suspended solids	26	LD	LD	LD not given (appears to be approximately 10 ng/litre)	

Table 7 (contd).

USA							
Major river basins	1965	surface water	99	LD	1 (100)	LD 1 ng/litre; aldrin not detected in any sample; dieldrin detected in 42% of samples	Breidenbach et al. (1967)
Western USA	1965, 1966	rivers	11	0.2 (5)	2.3 (15)	lower LD 5 ng/litre	Brown & Nishioka (1967)
	1966-68	rivers	20	LD (40)	LD (70)	LD not defined; presumed to be about 10 ng/litre	Manigold & Schulze (1969)
Major river basins	1964-68	surface water	about 100 stations	LD	range: 4-407	LD 2 ng/litre; in 37% of the samples dieldrin was present	Lichtenberg et al. (1970)
Iowa	1968 1969 1970	rivers	6 10 10	LD LD LD	2 (10) 8.5 (63) 9 (65)	LD about 1 ng/litre; dieldrin found in 40% of samples (179) analysed	Johnson & Morris (1971)
Western USA	1968-71	rivers	20	LD (10)	LD (30)	LD 5 ng/litre; aldrin detected in only 1 sample (total 716); dieldrin detected in 5% of samples	Schulze et al. (1973)
Hawaii	1970-71	non-potable	10	LD	4.8 (18.6)	LD about 0.2 ng/litre	Bevenue et al. (1972a)
		canals	3	LD	11.9 (18.6)		
		sewage discharge	1	LD	198		

[illegible]	[illegible]	[illegible] water	[illegible]	[illegible] aldrin	[illegible] dieldrin	[illegible]	[illegible]
[illegible]	[illegible]	Canal water	[illegible]		97 (4.6) [?]	Drainage water from a rice field-marshland ecosystem; samples [illegible] collected for 12 weeks [?] after aldrin-treated rice [illegible] had been [illegible]; one sample out of 7 contained [illegible] (275 ng/litre)	Ginn & Fisher (1974)
[illegible] Mississippi River		[illegible] water	[illegible] per [illegible] taken monthly)	LD	[illegible]	LD not defined	Brodtmann (1976)
Iowa	[illegible]	Surface water (streams [?], rivers, and reservoirs	15 (124 samples)	Not reported	17 (76)	LD less than 0.5 ng/litre	Richard et al. (1975)
[illegible] North Atlantic	[illegible]	Ocean surface	[illegible]	[illegible] (0.4)	[illegible] (15.4)	Lower LD: aldrin, less than 0.2 ng/litre; dieldrin, less than 0.4 ng/litre; concentrations of aldrin below LD in 29 samples; one surface sample contained a component with the same retention time of aldrin, corresponding to 0.2 ng/litre	Jonas & Pfaender (1976)
		[illegible] m depth [?]	[illegible]	LD [?]	[illegible] (7.5) [?]		
		[illegible] m depth	[illegible]	LD [?]	[illegible] (11.7) [?]		
		1000 m depth [?]	[illegible]	LD [?]	7 (1.3) [?]		
[illegible]	1979-80 [?]	Rivers [?]		LD [?]	6.0	Occurrence of dieldrin in 7.4% of samples	Carey & Kutz (1985)

[illegible] data [illegible] both water [?], sediments, and suspended solids (ng/kg); LD = limit of detection; ND = not determined.
[illegible]

5.1.6 *Food and feed*

Aldrin is rarely found in plants and animals, since it is readily converted to dieldrin (IARC, 1974). A total-diet study of [illegible] pensioners in Sweden did not detect any aldrin (Abdulla et al., [illegible]). Similarly, a market-basket study in the USA in 1974-1975 (Johnson & Manske, 1977) found aldrin in only one composite out of [illegible] with a value of 7 µg/kg. Traces or low levels of aldrin have been found in vegetable products and meat products (Bilayannis, 1974; Saschenbrecker, 1976; Chaudry et al., 1978; Wessels, 1978). In all cases, dieldrin residues were greater than those of aldrin, even when aldrin was the only compound applied. Aldrin is rarely found in milk or milk fat or in the body fat of cows fed aldrin (Frank et al., 1985; Fremlin & Poortvliet, 1982). In one study where aldrin was found in dairy products, milk samples contained 0.04 mg/litre, butter samples 0.02 mg/kg, and cheese samples 0.02 mg/kg (Heeschen, 1972). For the occurrence of residues in breastmilk, see section 5.2.2.

The analytical procedures used in [illegible] conducted dietary studies are capable of detecting all of the commonly used organochlorine pesticides, so that if aldrin did occur in a dietary sample it would be detected. The lack of mention of aldrin, therefore, can usually be taken as an indication that it was not detected.

Dieldrin residues in food and feed, resulting from the application of aldrin and dieldrin in normal use as well as from field studies, have been reviewed by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) at its meetings in 1963, 1965, 1966, 1967, 1968, 1969, [illegible], 1975, 1975, and 1977 (FAO/WHO, 1964, 1965a,b, 1967a,b, [illegible], 1967a,b, 1970a,b, 1971a,b, 1975a,b, 1977a,b, [illegible]).

Australia, Canada, Japan, the Netherlands, the United Kingdom, and the USA have all reported daily intakes below the ADI (Duggan & Lipscomb, 1969; Iyeta et al., 1971; Duggan & Corneliussen, 1972; FAO, 1971; Smith, 1978; de Vos et al., 1984).

In Australia, Canada, Italy, Japan, the United Kingdom, and the USA, analyses of total diets revealed dieldrin residues (Cummings, 1965, Duggan et al., 1967; Abbott et al., 1969; Corneliussen, [illegible]; Duggan & Corneliussen, 1972; Johnson & Manske, 1977; Hsu et al., [illegible]; Smith, 1978) ranging from 0.006 mg/kg (Cummings, 1966; Corneliussen, [illegible]) to 0.2 mg/kg (Duggan et al., [illegible]; Corneliussen, [illegible]). In 1983-1985, dieldrin was determined in [illegible] typically composed, prepared daily meals in Switzerland, and was detected in 15 of the meals. It was calculated from these results that the average daily intake of the Swiss consumer was 0.9 µg/day. [illegible] 1971-1972 were [illegible] (Wüthrich et al., 1985). Residue levels of [illegible] to [illegible] mg/kg in Canadian pork (Saschenbrecker, [illegible]) [illegible] mg/kg in [illegible] (Stalling et al., 1979) have been reported.

In a market basket survey in the USA, dieldrin was present in only [illegible] food groups, with maximum residues of 5 µg/kg in [illegible], 15 µg/kg in meat, [illegible], and [illegible] (Johnson & Manske, [illegible]).

The JMPR meeting in 1970 summarized data concerning dieldrin residues from the feeding of dieldrin to cattle and poultry. The average ratio of dieldrin levels in fat to levels in feed was 2.43 : 1 in milking cows and 3.95 : 1 in steers (Gannon et al., 1959a). At intake rates of less than 1 mg/kg, the average ratio of dieldrin levels in milk to levels in feed was about 0.1 : 1 after 12 weeks (Gannon et al., 1959b; Williams et al., 1964). In Denmark, the average concentration of dieldrin in butter fat declined from 0.05 mg/kg in 1964 to 0.03 mg/kg in 1966 and to 0.02 mg/kg in 1968 (Bro-Rasmussen et al., 1968). Similar residue levels and decreases were found in Australia, Ireland, New Zealand, Norway, and the United Kingdom. In Canada and the USA, residues in milk fat of 0.011-0.09 mg dieldrin/kg have been measured (Duggan et al., 1967; Wedberg et al., 1978; Frank et al., 1985).

Dieldrin losses resulting from cooking or processing food can be quite substantial, as demonstrated with trout and soybean (Chaudry et al., 1978; Zabik et al., 1979).

More recent information on the occurrence of dieldrin residues in foods is relatively scarce. However, a number of reviews exist.

5.1.6.1 Joint FAO/WHO Food Contamination Monitoring Programme

Information on dietary intakes of aldrin and dieldrin were collected from seven collaborating centres participating in the Joint FAO/WHO Food Contamination Monitoring Programme. The data cover the period from 1971-1983, and the countries involved were Australia, Canada, Guatemala, Japan, New Zealand, the United Kingdom, and the USA. The mean daily intake during this period varied from 0.007 to 0.056 μg/kg body weight (the 90th percentile varied from 0.016 to 0.105 μg/kg body weight). During the later years of this period, the mean values ranged from 7% to 56% of the acceptable daily intake (ADI). A decrease in the dietary intake of aldrin and dieldrin residues was noted during this period in some of the countries. Possibly this decrease was the result of restricting or banning the use of aldrin and dieldrin (Gorchev & Jelinek, 1985).

5.1.6.2 Information summarized by GIFAP (1984)

Australia, 1980: Twenty-four samples of each of 50 different foods were analysed for a range of organochlorine pesticides. In the case of dieldrin, the limit of determination was 0.01 mg/kg. Dieldrin occurred above this level in only 0.04% of the samples, and the maximum level was 0.05 mg/kg.

Canada, 1976-1978: The results of analyses of food commodities were expressed in terms of estimated intakes for the population. The average daily dietary intake of dieldrin for this period was 0.002 μg/kg body weight.

Italy, 1982: Apples were sampled from a variety of locations representing 70% of the country's apple production. There were 300 samples and 80% or 90% were below the limit of determination for aldrin and dieldrin, respectively.

Netherlands, 1977-1978: During the period 1977-1978, residues of organochlorine pesticides were determined in a wide range of market baskets composed of items considered to be representative of the diet of 16-18-year-old boys. Although dieldrin was not specifically mentioned, the studies revealed that none of the organochlorine pesticides contributed residues in excess of the Maximum Residue Limit (MRLs).

5.1.6.3 *United Kingdom (UK MAFF, 1982-1985)*

Residues of dieldrin found in a range of dietary components in 1981 are listed in Table 8.

Table 8. Dieldrin residues in individual food groups of the total-diet study (24 sets of total diet samples, January - December 1981)[a]

Food group	Range of residues (μg/kg)	Average residues (μg/kg)
Bread	ND	ND
Other cereal products	ND	ND
Carcass meat	ND - 40	3.5
Offals	ND - 5	0.5
Meat products	ND	ND
Poultry	ND - 4	1
Fish	ND - 8	2
Oils and fats	ND - 15	1
Eggs	ND - 4	0.5
Green vegetables	ND	ND
Potatoes	ND - 1	< 0.5
Other vegetables	ND - 10	1
Fresh fruit	ND	ND
Milk	ND - 2	0.5
Dairy products	ND - 150	4

[a] The limit of detection in these studies varied with the food group but was sometimes as low as 1 μg/kg.
ND = not detectable.

On the basis of these data, it was estimated that the mean level of dieldrin residues in the total diet in 1981 in the United Kingdom was 0.5 μg/kg. This figure compares with 1.5 μg/kg for the period 1975-1977 and 4 μg/kg for the period 1966-1967. The computed daily intake derived from the 1981 figure was < 0.8 μg/person or < 0.01 μg/kg body weight.

Further data on certain individual products were also reported.

Maize. Two samples of imported maize, representing 3% of the total number of samples taken in a survey conducted in 1981, contained detectable levels of dieldrin, the highest concentration being 0.04 mg/kg. The rest of the samples did not contain dieldrin residues above the limit of determination of 0.01 mg/kg.

Pulses. Separate surveys of residues in pulses obtained from retail outlets were carried out in 1982 and 1983. In 1982, 42 samples involving 12 different kinds of pulses were analysed. In this case, aldrin was found in one sample of haricot beans (0.04 mg/kg) but was below the limit of determination (< 0.01 mg/kg) in all the others. Dieldrin was found in a limited number of mung beans (0.05 mg/kg) but was below the limit of determination (<0.01 mg/kg) in all of the others. Thus, neither aldrin nor dieldrin were detected in the majority of pulses sampled in 1982.

In 1983, 40 samples were analysed and there were no residues reported for aldrin or dieldrin above the level of determination, with the exception of limited samples of mung beans containing dieldrin (maximum, 0.04 mg/kg; mean, < 0.01 mg/kg).

Fruit and vegetables, 1981-1984: A large-scale monitoring project of fruit and vegetables was undertaken in the United Kingdom during the period 1981-1984. Some 40 commodities were sampled during that period, 1649 samples being obtained from retail outlets and analysed. The data were not individually reported but, although most of the commodities were analysed for organochlorine pesticide residues, there were no reports of any sample containing residues of dieldrin exceeding either Codex or EEC maximum residue limits. Information on the incidence of detectable residues of dieldrin was not presented in this case. It is of interest to note that 648 of the samples were grown in the United Kingdom and 1001 were imported.

Lamb meat: Sampling of kidney fat from home-grown lamb destined for export began in October 1984 and data for 928 samples were reported. None contained dieldrin residues above the limit of determination of 0.02 mg/kg.

Fish. The information in Table 5 was obtained from fish caught in areas around the English and Welsh coast where the levels of chemical contamination were known to be high.

Residues of dieldrin in processed fish imported into the United Kingdom were determined in 155 samples of different products obtained from retail outlets in 1985. The data are summarized in Table 6. In a further study, dieldrin residues were determined in a limited number of fish products obtained through retail outlets [illegible]

Table 9. Mean residue levels of dieldrin (mg/kg) in the liver and muscle of marine fish from England and Wales, 1982

Fish	Muscle	Number of samples	Liver	Number of samples
Cod	0.003	43	0.26	73
Dab	0.003	50	0.12	50
Flounder	0.003	49	0.027	49
Mackerel	0.007	29	0.053	23
Plaice	0.004	43	0.040	68
Sole	0.003	50	0.031	50
Whiting	0.009	62	0.26	62

Table 10. Residues of dieldrin (mg/kg) in processed imported fish and shellfish in 1983

Fish	Range[a]	Average	Number of samples
Fillets	≤ 0.005	0.002	21
Plaice	≤ 0.006	0.002	19
Salmon	≤ 0.02	0.004	26
Sardines	≤ 0.004	0.001	11
Tuna	ND	ND	15
Cockles and mussels	≤ 0.01	0.004	2
Crab	ND	ND	15
Prawns	≤ 0.003	≤ 0.001	17
Shrimps	≤ 0.004	0.001	16

[a] ND = not detectable.

Table 11. Residues of dieldrin (mg/kg) in fish oil products, 1983

Product	Range	Mean	Number of samples
Cod liver oil			
Mixtures	0.01-0.02	0.02	8
Capsules	0.04-0.20	0.12	4
Halibut liver oil			
Capsules	0.07-0.1	0.09	4
Fish liver oil			
Capsules	0.1	0.1	1

5.1.6.4 USA

Surveys were carried out in the USA, during the period 1980-1982, covering the diets of infants (aged 6 months), toddlers (aged 2 years) (Gartrell et al., 1986a), and adults (youths aged 16-19 years) (Gartrell et al., 1986b). In each case, the samples were taken from a number of locations (13 in the case of infants and toddlers and 27 in the case of youths). They were selected as being representative of the composition of diets for the three population groups studied. Individual foods were bulked together in food groups and the bulked samples analysed. The lower level of determination was not precisely stated, since it varied according to the food group concerned, but from the data presented it would appear to have been either 1 or 2 μg/kg food item. Results that were below these limits (and hence unquantifiable), but where the identity of the residue could be confirmed, were reported as "T". The analysts' estimate of the value of "T" was used to estimate the average level of residues in the whole food group. Data for dieldrin residues are given in Tables 12, 13, and 14.

Table 12. Dieldrin residues (μg/kg) in infant dietary components[a]

Food group	Range of residues	Average level
Drinking-water	0	0
Whole milk	T	0.1
Other dairy products	T - 1	0.3
Meat, fish, poultry	T - 2	0.5
Grain and cereals	0	0
Potatoes	T - 2	0.2
Vegetables	T - 1	0.1
Fruit and fruit juices	0	0
Oils and fats	0	0
Sugar and adjuncts	0	0
Beverages	0	0

[a] For breast milk, see section 5.2.2.

5.1.6.5 Appraisal of intake studies

The above data demonstrate that in the United Kingdom and the USA the intake of dieldrin residues in food is well below the ADI of 0.1 μg/kg body weight. Moreover, taking into account the rather high dietary intake estimated for adults in the USA, the agreement between estimates for the United Kingdom and the USA is striking, notwithstanding the widely differing origins of the basic food commodities, especially the relatively high proportion of imports in the case of the United Kingdom. The estimated levels of intake in Canada were even lower. The residues in Australia, though very low, were not expressed in terms of intakes.

Table 13. Dieldrin residues (μg/kg) in toddler nietary components

Food group	Range of residues	Average level
Drinking-water	0	0
Whole milk	T	0.1
Other dairy products	T - 3	1.2
Meat, fish, poultry	T - 3	0.8
Grain and cereals	0	0
Potatoes	T - 3	0.3
Vegetables	T - 2	0.5
Fruit and fruit juices	0	0
Oils and fats	2	0.3
Sugar and adjuncts	0	0
Beverages	0	0

Table 14. Dieldrin residues (μg/kg) in adult dietary components

Food group	Range of residues	Average level
Dairy products	T - 3	0.6
Meat, fish, poultry	T - 4	1.2
Grain and cereals	4	0.1
Potatoes	T - 2	0.4
Leafy vegetables	T - 2	0.2
Legume vegetables	0	0
Root vegetables	T - 5	0.4
Garden fruits	T - 11	2.1
Fruits	1	0.1
Oils and fats	T - 2	0.3
Sugar and adjuncts	0	0
Beverages	0	0

Dietary levels of dieldrin residues in both the United Kingdom and the USA appear still to be decreasing, though less so than in previous years.

In 1966, the JMPR established an acceptable daily intake (ADI) of 0-0.1 μg/kg body weight (combined total for aldrin + dieldrin).

5.1.7 Concentrations of dieldrin in non-target species

There have been many investigations of the occurrence of dieldrin in the body tissues or eggs of non-target species. The residues range from less than 0.001 mg/kg to about 100 mg/kg, but most reported residues are less than 1 mg/kg. The wide range of concentrations is partly a reflection of the extreme sensitivity of modern analytical techniques, but there are a number of other factors involved, e.g., the

source and magnitude of the exposure; the component analysed (brain, adipose tissue, eggs, etc), and whether the samples are representative of living, apparently healthy populations (specimens collected by capture, shooting, etc., during systemic monitoring surveys) or consist of animals found dead or dying. Interspecies differences in rates of metabolism also contribute to the variability of residues. The highest residues are found in two main groups of organisms. The first group consists of organisms living near the source of release into the environment; thus, high residues may be found in aquatic organisms near the point of release of an industrial effluent, or in seed-eating birds in areas where seed dressed with aldrin or dieldrin is used in agriculture. The second group of organisms consists of predators, particularly those feeding on aquatic organisms or seed-eating birds or mammals.

The results of some analyses of various species from different geographical areas are summarized in Tables 15 and 16.

There have been very extensive surveys of dieldrin residues in biota that are not directly associated with a particular use of aldrin/dieldrin or their waste disposal.

Soil and earthworms (four genera) were collected from 57 fields from eight states in the USA. The geometric mean concentrations of aldrin and dieldrin in soil were 0.014 and 0.023 and, in earthworms, 0.038 and 0.19 mg/kg dry weight, respectively. Correlation coefficients between the concentrations of dieldrin in earthworms and soil were derived for six types of crops, but none were significant. They were also derived from four different soil types; only the concentrations in the earthworms from silt loam soils were significantly related to the concentrations in the soil (Fish, 1970).

Henderson et al. (1969, 1971) studied the occurrence during the period 1967-1969, of dieldrin in various species of fish from 50 monitoring stations located in the Great Lakes and in major river basins in the USA. The mean concentrations of dieldrin in whole fish lay in the range 0.01-0.28 mg/kg, and the maximum value found was 1.94 mg/kg. The concentrations above 1 mg/kg were found in fish from the Atlantic coast streams, Gulf coast streams, and Great Lake drainage.

Koeman et al. (1967, 1971) and Koeman (1971) studied the presence of dieldrin in fish, mussels, zooplankton, and birds in the Wadden area of the Netherlands during the period 1965-1971. The mean concentrations in mussels, marine fish, freshwater fish, and zooplankton were below 0.1 mg/kg (maximum concentration, 0.23 mg/kg), except in three species of marine fish. In these, the mean concentration was 0.2-0.3 mg/kg (maximum concentration, 0.42 mg/kg). The levels in the liver and/or eggs of the sandwich tern (*Sterna sandvicensis*) and grey heron (*Ardea cinerea*) were up to 5.1 mg/kg (maximum concentration, 12 mg/kg). Mortality among sandwich tern (*Sterna sandvicensis*) and tufted duck (*Nyroca fuligula*) and a few other bird species was reported.

Butler (1973) found mean dieldrin concentrations of 0.01-0.528 mg/kg (maximum concentration, 0.21 mg/kg) in crabs

Table 15 Residues of dieldrin in non-target species and their environment

Geographical area/Year	Species	Type of Sample	Number of Samples	Mean (mg/kg)	Range[a] (mg/kg)	Comments[b]	Reference
Antarctica							
Signy Island [illegible]	Chinstrap penguin (Pygoscelis antarctica)	liver	[illegible]	[illegible]	0.001-0.006	LD not defined; presumably <0.001 mg/kg	Tatton & Ruzicka (1967)
	Fish (Notothenia neglecta)	liver	[illegible]	0.00[illegible]	0.001-0.009		
	Skuas and shags	liver	[illegible]	0.001	LD - 0.002		
	Sheathbill (Chionis alba)		[illegible]	0.009	LD - 0.01[illegible]	Sudden deaths of sheathbills of unknown causes had occurred	
Canada							
[illegible]	Fish (two species)	river water bottom mud	[illegible]	[illegible] 0.0000[illegible] [illegible]	LD - 0.0[illegible] LD - [illegible] 0.[illegible]-[illegible].159	LD in water, < 0.0001 mg/litre; LD in bottom mud, <0.001 mg/kg	[illegible] (1971)
Province of Ontario	Fish (various species)	composites or individual dressed specimens	[illegible]	0.[illegible]	LD - [illegible]	LD < 0.005 mg/kg	Reinke et al (1972)

Table 15 (contd).

Geographical area/Year	Species	Type of sample	Number of samples	Mean (mg/kg)	Range[c] (mg/kg)	Comments[c]	Reference
Canada (contd). Four other provinces	Fish (various species) dressed specimen	composites of headless	119	0.01	LD - 0.08	76 composites from these four provinces contained residues; LD <0.005 mg/kg	Reinke et al. (1972)
Eastern Canada 1970-1976	Leach's storm petrel *(Oceanodroma leucorhoa)*	egg	18	0.05	0.03-0.13		Pearce et al. (1979)
	Double-crested cormorant *(Phalacrocorax auritus)*	egg	90	0.13	0.01-0.68		
	Common eider *(Somateria mollissima)*	egg	25	0.02	0.01-0.04		
	Common tern *(Sterna hirundo)*	egg	50	0.04	0.01-0.13		
	Razorbill *(Alca torda)*	egg	13	0.12	0.01-0.52		
	Common guillemot *(Uria aalge)*	egg	4	0.02	0.02-0.03		
	Black guillemot *(Cepphus grylle)*	egg	3	0.02	0.01-0.05		

Table 15 (contd).

	Atlantic puffin *(Fratercula arctica)*	egg	48	0.06	0.03-0.13		
Falkland Islands 1977	Marine, coastal, and freshwater birds	egg	46	0.002	LD - 0.011	LD not defined, but < 0.002 mg/kg	Hoerschelmann et al. (1979)
Greece							
Saronikos Gulf 1975	Striped mullet *(Mullus barbatus)*	muscle	74	0.004	0.0001-0.050	residues attributed to the discharge of domestic waste and industrial effluents	Voutsinou-Taliadouri & Satsmadjis (1982)
Iraq							
Shatt al-Arab river	Cyprinid *(Barbus xanthopetrus)*	muscle	2	0.003	ND - 0.008		Douabul et al. (1987)
	Indian shad *(Tenualosa ilistra)*	muscle	2	0.028	0.016-0.041		Douabul et al. (1987)
Kenya							
Lake Nakuru 1975		water	10	< 0.0001	-		Greichus et al. (1978b)
		bottom sediment	10	< 0.001[b]	-		
	Plankton	composite	1	0.03[b]	-		Greichus et al. (1978b)
	Chironomids	composite	1	< 0.01[b]	-		
	Water boatmen (Coroxidae)	composite	1	< 0.01[b]	-		

Table 5 (contd).

Geographical area/Year	Species	Type of sample	Number of samples	Mean (mg/kg)	Range[a] (mg/kg)	Comments	Reference
Kenya (contd.)							
Lake Nakuru (contd.)	Fish (*Tilapia grahami*)	composite	100/100	0.02[b]	-		
Netherlands 1964	Mussel (*Mytilus edulis*)		22	0.033	0.014-0.084		Koeman (1971)
1965	marine fish (2 species)	whole body	103	0.27	0.16-0.42		Koeman et al. (1967)
1965	marine fish (2 species)	whole body	32	0.07	0.01-0.23	fish species on which sandwich terns feed	Koeman et al. (1967)
1965	Sandwich tern (*Sterna sand. vinceneis*)	liver	10	5.1	1.9-12	found dead or dying	Koeman et al. (1967)
1965,1966	Sandwich tern	liver	14	0.6	0.2-2	killed, shot, or found dead after a storm	Koeman et al. (1967)
1967	Freshwater fish (3 species)		28	0.02	LD - 0.05	LD < 0.01 mg/kg	Koeman (1971)
1969	Mussel (*Mytilus edulis*)		10/23[a] 100/84	0.012 0.013	0.007-0.016 0.007-0.023		Koeman et al. (1971)
1970	Pike (*Esox lucius*)	whole body	10	0.01	LD - 0.022	LD < 0.003 mg/kg	Koeman et al. (1971)
1971	Roach (*Rutilus rutilus*)	whole body	81/64	0.004	LD - 0.013	LD < 0.005 mg/kg	Koeman et al. (1971)

[illegible]	Composite		0.005			Koeman et al. (1971)
[illegible]		50/1[a]	0.009			Koeman et al. (1971)
[illegible]		3/5[a]	0.022	0.006-0.043		Koeman et al. (1971)
[illegible]	Egg	10	0.062	0.031-0.099		Koeman et al. (1971)
[illegible]	Egg	2/4[a]	1.23	0.9-1.9		Koeman et al. (1971)
[illegible]	Liver Breast Muscle	/ /	0.01 0.1	LD = 0.05 0.03-0.26	LD not defined, but < 0.02 mg/kg	Bennington et al. (1975)
	Egg	Approx. 30 [illegible]		0.220-0.268 [illegible]		Barrett et al. (1985)

Table 15 (contd).

Geographical area/Year	Species	Type of sample	Number of samples	Mean (mg/kg)	Range[c] (mg/kg)	Comments[c]	Reference
United Kingdom							
England, Medway estuary 1974-1975	Brown shrimp *(Crangon vulgaris)*	homogenates of 50 specimens	12	0.0055	0.0012-0.020		Van Den Broek (1979)
England, Medway estuary	Sand goby *(Pomatoschistus minutus)*	homogenates of 50 specimens	9	0.047	0.024-0.077		Van Den Broek (1979)
	Sprat *(Sprattus sprattus)*	homogenates of 50 specimens	13	0.084	0.030-0.142		Van Den Broek (1979)
	Eel *(Anguilla anguilla)*	liver	16	0.051	0.0085-0.090		Van Den Broek (1979)
	Whiting *(Merlangius merlangus)*	liver	9	0.57	0.25-1.10		Van Den Broek (1979)
	Flounder *(Platichthys flesus)*	liver	16	0.21	0.043-0.39		Van Den Broek (1979)
	Plaice *(Pleuronectes platessa)*	liver	12	0.12	0.015-0.23		Van Den Broek (1979)

Table 15 (contd).

Scotland, Firth of Clyde 1971-1972	Plankton (various estuarine and marine species)		12	0.072	0.019-0.230		Williams & Holden (1973)
North Atlantic, northeast transect from Mull of Kintyre 1971-1972	Plankton (various estuarine and marine species)		14	0.003	LD - 0.015	LD < 0.001 mg/kg	Williams & Holden (1973)
Firth of Clyde (coastal waters) 1977	Mussel (*Mytilus edulis*)	homogenates of 50-100 specimens	25 80	0.178 0.022	0.012-2.43 0.006-0.216		Cowan (1981)
Shetland Isles (8 other coastal sites) 1977	Mussel (*Mytilus edulis*)		12	0.013	0.006-0.029		Cowan (1981)
Irish Sea and Firth of Clyde 1974	Seabirds (various species)	liver	21	1.23	0.07-5	heavy mortality of seabirds in Irish Sea; continuous winter storms may have been cause of mortality	Lloyd et al. (1974)

Table [illegible] (contd)

Geographical area/year	Species	Type of sample	Number of samples	PCB (mg kg⁻¹)	Range (mg kg⁻¹)	Comments[c]	Reference
[illegible]	[illegible]	[illegible]					
[illegible]	[illegible]	[illegible]				high mortality of guillemot [illegible]; primary cause of [illegible] probably [illegible] [illegible] body weights of [illegible] and dead birds (43 g and 58% respectively; mean liver weights, 43.8 g and 12.5 g, respectively; PCBs may also have been responsible for the [illegible]	[illegible] (1973)
West Britain (1969-70)	Grey heron (*Ardea cinerea*)	egg					
		Wales	135	0.26	0.66-0.66[b]	concentration increased significantly between March and May	Cooke et al. (1982)
		Avon	103	1.19	1.05-1.35[b]		
		Kent	43	3.90	2.64-3.88[b]		
Shetland Isles, Foula (1976)	Great skua (*Catharacta skua*)	egg	12	0.091	0.022-0.15		Furness & Hutton (1979)
USA (5 states; 1965-1972)	Estuarine molluscs (10 species)	composites of meat from 15 or more mature molluscs				LD 0.005 mg/kg	Butler (1973)

Table 15 (contd).

USA (contd).						
North Carolina, Point of Marsh			71	0.01	LD - 0.019	concentrations in 60 samples below 0.005 mg/kg
Mississippi, Biloxi Bay			78	0.01	LD - 0.019	concentrations in 70 samples below 0.005 mg/kg
Texas, Arroyo Colorado			48	0.021	LD - 0.046	
New York, Hemmstead Harbor			74	0.024	LD - 0.132	
Georgia, Lazaretta Creek			64	0.028	LD - 0.230	
Major river basins in the USA:	fish (various species)	composites of whole fish			LD < 0.001 mg/kg	Henderson et al. (1969).
Atlantic coast streams			74j/141[a,d]	0.14	LD - 1.94	
			157/36[a,e]	0.13	LD - 0.55	
Gulf coast streams			204/48[a,d]	0.12	LD - 1.26	
			59/12[a,e]	0.28	LD - 1.59	
Great Lakes drainage			378/63[a,d]	0.05	LD - 0.50	
			81/18[a,e]	0.06	LD - 0.37	
Mississippi River system			657/139[a,d]	0.06	LD - 0.52	
			153/34[a,e]	0.06	0.01-0.49	
Hudson Bay drainage			51/13[a,d]	0.12	0.03-0.37	
			5/2[a,e]	0.01	0.01	
Colorado River system			112/24[a,d]	0.02	LD - 0.10	
			24/6[a,e]	0.01	0.01	
Interior basins			120/25[a,d]	0.01	LD - 0.06	
			30/6[a,e]	0.02	LD - 0.03	
California streams			90/24[a,d]	0.06	LD - 0.31	
			28/6[a,e]	0.10	0.01-0.36	
Columbia River system			246/64[a,d]	0.02	LD - 0.10	
			70/16[a,e]	0.03	LD - 0.09	
Pacific Coast streams			83/20[a,d]	0.06	LD - 0.52	
			29/6[a,e]	0.01	LD - 0.02	
Alaskan streams			305/24[a,d]	0.003	LD - 0.01	
			30/6[a,e]	0.006	LD - 0.01	

Table 15 (contd).

Geographical area/Year	Species	Type of sample	Number of samples	Mean (mg/kg)	Range[c] (mg/kg)	Comments[c]	Reference
USA (contd) Upper continental rise (southeast of Cape Hatteras)	Bathyl-demersal fish *(Antimora rostrata)*	liver	4	0.017	0.011-0.026	fish caught by trawl at a depth of 2500 m	Meith-Avcin et al. (1973)
California 1970	Common egret *(Casmerodius albus)*	brain	5	4.36	0.60-6.76	birds found dead or moribund; dieldrin considered to be a contributory cause of death of 4 birds	Faber et al. (1972)
South Dakota 1965-1967	Pheasant *(Phasianus colchicus)*	adipose tissue	48	0.08	LD - 1.07	LD < 0.01 mg/kg; 13 samples of fat contained < 0.01 mg/kg	Greichus et al. (1968)
	Sharp-tailed grouse *(Pedioecetes phasianellus campestris)*	living birds	46	0.17	LD - 1.71	13 samples of fat contained < 0.01 mg/kg	
South Dakota 1967	Pheasant	egg	67	0.02	LD - 0.12	LD < 0.01 mg/kg; 13 eggs contained 0.01 mg/kg	Linder & Dahlgren (1970)
Maine and Virginia 1977	Common eider and herring gull	egg	88	LD	LD	LD < 0.1 mg/kg	Szaro et al. (1979)
	Great black-backed gull	egg	28	0.12	LD - 0.55	24 of the eggs contained < 0.1 mg/kg	

Table 15 (contd).

USA (contd).							
Texas, Corpus Christi Bay 1976-1977	Wintering shore-birds (7 species)	carcass (shot birds)	56	0.11	LD - 1	LD < 0.1 mg/kg; 2 carcasses contained < 0.1 mg/kg	White et al. (1980)
Lake Michigan 1977-1978	Red-breasted merganser *(Mergus serrator)*	egg	206	0.77	0.2-2.3	LD < 0.1 mg/kg	Haseltine et al. (1981)
	Mallard *(Anas platyrhynchos)*	egg	27	0.07	LD - 0.53	22 of the eggs contained < 0.1 mg/kg	
	Gadwall *(Anas strepera)*	egg	9	0.1	LD - 0.56	5 of the eggs contained < 0.1 mg/kg	
Florida	Brown pelican *(Pelecanus occidentalis)*					LD < 0.05 mg/kg egg	Blus et al. (1974b)
Atlantic coast		egg	22	0.36	LD - 1.52		
Gulf coast		egg	27	0.10	trace - 0.40		
Florida 1969		carcass (shot birds)	16	0.65	LD - 1.60		Blus et al. (1974b)
South Carolina		carcass (shot birds)	5	0.51	LD - 1.50		
South Carolina							
1969	Brown pelican	egg	11	0.94	0.60-1.62		Blus et al. (1974b, 1977 1979b)
1970		egg	10	0.62	0.20-1.30		
1971		egg	65	0.46	0.20-1.02		
1972		egg	72	0.45	LD - 1.76		
1973		egg	104	0.45	0.16-1.65		
1974		egg	116	0.54	0.17-2.89		
1975		egg	102	0.36	LD - 1.04		

[illegible]	Species	Type of Sample	Number of Samples	Mean (mg/kg)	Range[a] (mg/kg)	Comments[b]	Reference
[illegible]							
[illegible]	Brown pelican	egg	3	0.33	0.24-0.54		Blus et al. (1979a)
[illegible]		egg	12	0.45	0.30-0.79		
[illegible]		egg	21	0.64	0.30-1.12		
[illegible]		egg	25	0.84	0.49-1.61		
[illegible]		egg	30	1.08	0.64-2.25		
[illegible]		egg	25	0.94	0.44-3.03		
[illegible]							
[illegible]		water	10	< 0.0001			Gretchus et al. (1978a)
[illegible]		bottom sediment[c]	10	0.004			
	Plankton	composite	1	< 0.01[d]			
	Oligochaete (Branchiura sowerbyi)	composite	1	0.08[d]			
	Fish (5 spp.)	composite	200/15[e]	0.04[d]	0.03-0.07		
	Cormorant (2 spp.)	brain	10	1.4[f]			

[a] [illegible] the number of individuals incorporated into 2y composites; the range corresponds to the composites.
[b] [illegible] expressed on dry weight basis.
[c] [illegible] prepared, for [illegible] detection.
[d] [illegible]
[e] [illegible] in 1978.

Table 16. Concentrations of dieldrin in non-target organisms

Species (component analysed)	Geographical area	Year	Concentration of dieldrin (mg/kg wet weight)			Reference
			Geometric mean	Arithmetic mean	Range (N)[c]	
Fish (3 spp.) (muscle)	Great Britain R. Thames (tidal)	1977-79	-	0.00042[a]	<0.00035-0.0020 (83)	Rickard & Dulley (1983)
Oysters (flesh)	USA: Louisiana	1968-69	-	0.0014[a]	<0.001-0.0034 (113)	Rowe et al. (1971)
Penguin (abdominal fat)	Antarctic	1966-67	-	0.008[a]	<0.006-0.010 (5)	Tatton & Ruzicka (1967)
Fish, invertebrates (various spp.) (whole body)	USA: Virgin Islands, Puerto Rico	1972-74	-	0.005[a]	<0.005-0.021 (141)	Reimold (1975)
Fish (various spp.) (whole body/tissues)	USA: Western Kansas	1967-69	-	0.01[a]	<0.01-0.08 (393)	Klaassen & Kadoum (1973)
Northern fur seals (liver)	USA: Alaska	1968-69	-	0.05[a]	<0.01-0.091 (23)	Anas & Wilson (1970a,b)
Birds (various spp. including birds of prey) (eggs)	Zimbabwe	1973-76	-	0.004[b]	<0.01-0.67 (34) dry weight	Tannock et al. (1983)
Woodcock (breast muscle)	USA: eastern, mid-western	1970-71	-	0.018[a]	<0.01-0.55 (129)	Clark & McLane (1974)

Table 16 (contd).

Species (component analysed)	Geographical area	Year	Concentration of dieldrin (mg/kg wet weight)			Reference
			Geometric mean	Arithmetic mean	Range (N)[c]	
Starlings (carcass)	USA	1967-68	-	0.139[a]	<0.005-1.18 (360)	White (1976)
		1970	-	0.117[a]	<0.005-3.59 (125)	White (1976)
Starlings (carcass)	USA	1972	-	0.098[a]	<0.005-1.56 (130)	White (1976)
		1974	-	0.057[a]	<0.005-1.01 (126)	White (1976)
Migratory birds (various spp.) (breast muscle)	USA: Florida	1964-73	-	0.2[a]	<0.01-1.10 (829)	Johnston (1975)
Bats (3 spp.) (carcass)	USA: Maryland, West Virginia	1973	0.2[a]	-	<0.1-3.2 (110)	Clark & Prouty (1976)
Golden eagle (fat)	USA: western, mid-western states	1964-70	-	0.1	<0.1-12 (69)	Reidinger & Crabtree (1974)
Golden eagle (eggs)	Scotland	1964-74	0.12	-	<0.05-6.9 (100)	Cooke et al. (1982)
Tawny owl (liver)	Great Britain	1963-65	0.15	-	<0.05-12.7 (55)	Cooke et al. (1982)

Table 16 (contd).

Peregrine falcon (eggs)	Great Britain	1964-77	0.20	-	<0.05-7.6 (145)	Cooke et al. (1982)
Bald eagle (brain)	USA	1971-72	0.6[b]	-	<0.05-7.8 (37)	Cromartie et al. (1975)
Barn owl (liver)	Great Britain	1963-75	1.21[b]	-	<0.05-70.2 (251)	Cooke et al. (1982)
Hawks, falcons, owls (liver)	Netherlands	1968-69	-	10.8	0.45-31 (19)	Koeman et al. (1969)

[a] Indicates living organisms collected by capture, shooting, etc.
[b] Indicates organisms found dead or dying.
[c] Number in parentheses is the number of specimens.

molluscs collected from 15 coastal states in the USA during the period 1965-1972.

Fish sampled in Canada, in 1970, were found to have a mean concentration of 0.071 mg dieldrin/kg (maximum concentration, 0.189 mg/kg). The concentrations in the water and bottom mud were of the order of 0.005 μg/litre and 0.002 mg/kg, respectively (Miles & Harris, 1971). In another study, fish from five provinces (78 locations) in Canada showed mean concentrations of 0.1-1 mg/kg (maximum concentration, 0.56 mg/kg) (Reinke et al., 1972).

In coastal waters around England, Scotland, and Ireland, a number of studies were carried out to determine dieldrin levels in plankton, mussels, shrimp, and various other marine species (1971-1975). The mean concentrations ranged from 0.003 to 0.178 mg/kg (maximum level, 2.43 mg/kg). Mussels showed the highest levels (Williams & Holden, 1973; Lloyd et al., 1974; Van Den Broek, 1979; Cowan, 1981).

The presence of dieldrin in water, bottom sediment, and living organisms has been studied in Africa (Kenya, Zimbabwe), Signy Island (Antartica), New Zealand, and sub-antartic islands. The concentrations of dieldrin in water were very low (< 0.01 μg/litre), those in bottom sediment were up to 0.004 mg/kg, and those in water organisms (mainly plankton and invertebrates) were 0.01-0.03 mg/kg (dry weight basis). Penguin abdominal fat contained 0.008 mg/kg and liver 0.002 mg/kg. The levels in fish were < 0.1 mg/kg (dry weight) (Tatton & Ruzicka, 1967; Bennington et al., 1975; Greichus et al., 1978 a,b).

In the different areas where water, invertebrates, and fish were analysed, birds and eggs were also studied for the presence of dieldrin. In the eggs of a number of bird species from the Falkland Islands, Hoerschelmann et al. (1979) found an average of about 0.005 mg/kg dieldrin in 17 of the 46 eggs. In eggs of coastal birds in the Federal Republic of Germany, the average concentration (in 27 eggs) was higher (average, 0.031 mg/kg; range, 0.004-0.187 mg/kg).

Parslow & Jefferies (1973) found mean concentrations of up to 0.48 mg/kg in the liver of guillemots *(Uria aalge)* in the Irish Sea. In eggs of the great skua *(Catharacta skua)*, collected on the Shetland Islands, Furness & Hutton (1979) measured a concentration of 0.091 mg/kg (maximum concentration, 0.15 mg/kg). In South Dakota, USA (1965-1967), Greichus et al. (1968) and Linder & Dahlgren (1970) determined concentrations of up to 0.08 mg/kg in the adipose tissue of pheasants and 0.02 mg/kg in eggs. In adipose tissue of grouse, a mean concentration of 0.17 mg/kg was found.

When a number of eggs of several bird species was analysed in eastern Canada (1970-1976), the mean concentrations were 0.06 mg/kg (maximum level, 0.68 mg/kg) (Szaro et al., 1979). In different species of birds (and eggs) in the north and south of the USA, White et al. (1980) found average concentrations in the carcass of 0.13-0.47 mg/kg and Haseltine et al. (1981) found in eggs of mergansers *(Mergus serrator)* a geometric mean concentration of 0.78 mg/kg.

It is of interest that very low residues are found in the great majority of eggs from areas remote from the regions of major

aldrin/dieldrin use. This is true of samples from the Falkland Islands and Antartica and it is also true of a survey of 440 eggs from 19 species of seabirds collected in 1973-1976 in Alaska showing that residues in 410 eggs were less than 0.05 mg/kg (wet weight). The highest residue found was 0.6 mg/kg (Ohlendorf et al., 1982).

In Florida, Louisiana, and South Carolina, Blus et al. (1974b, 1977, 1979a,b) studied the dieldrin concentrations in the carcass and eggs of the brown pelican *(Pelecanus occidentalis)* during the period 1969-1976. The mean concentration in the carcass was about 0.6 mg/kg (maximum concentration, 1.6 mg/kg) and, in the eggs, about 0.6 mg/kg (maximum concentration, 2.89 mg/kg).

Jefferies (1972) carried out a survey of the residue levels in bats from the East Anglian area, United Kingdom, to provide more information on the situation concerning the British bat population. Four species of bats were studied, *Pipistrellus pipistrellus, Plecotus auritus, Myotis nattereri,* and *Myotis daubentoni.* Thirty specimens were collected during the period 1963-1970. Dieldrin was found in eight liver specimens (range 0.04 to 3.3 mg/kg tissue), in two adipose tissue samples (4.0 and 7.9 mg/kg), and in six total body samples (0.07 to 0.50 mg/kg tissue).

Clark et al (1978) estimated the dieldrin levels in 28 juvenile grey bats *(Myotis grisescens)* taken from three caves in Missouri, USA. The concentrations varied between the individual animals and between the caves. Dieldrin was detected in the brain of 18/28 bats, the range being 0.4-10 mg/kg tissue (wet weight basis), and in the carcass of 22/28 bats (range 1.7-1379 mg/kg carcass; lipid weight). The authors believed that there was a direct link between the field mortality of bats and dieldrin residues acquired through the food chain.

Clark et al. (1980, 1983b) detected dieldrin in the brain and carcass of grey bats found dead in a Missouri cave in 1976 and 1977. In 1976, the geometric mean was 7.5 and 650 mg/kg tissue (respectively for brain on wet weight basis and for carcass on lipid weight basis) and in 1977, 8.6 and 867 mg/kg tissue, respectively. Other chlorinated hydrocarbons were also present such as heptachlor epoxide, DDE, and PCBs.

Clark (1981) studied the brain to carcass lipid relationship for dieldrin and estimated a minimum lethal level for brain tissue of 4.6 mg dieldrin/kg (wet weight) and for carcass of 390 (210-800) mg dieldrin/kg tissue (lipid weight).

In two other caves in Missouri, dead grey bats were found in 1980, and dieldrin and other halogenated insecticides were found in the brain and carcass. Seven animals were studied and dieldrin concentrations ranging from not detectable to 21 mg/kg tissue (wet weight) were found in the brain and 4.1-970 mg/kg in the carcass (lipid weight). The concentrations in brain were of the same order as those found in the other caves in Missouri. Bat mortality in July 1981 occurred simultaneously, in one case, with the death of macroinvertebrates in the outlet stream of the cave (Clarke et al., 1983a).

Dieldrin residues ranging from trace to 3.3 mg/kg have been detected in marine mammals, including whales and seals (Holden, 1975; Rosewell et al., 1979). Other mammals in which dieldrin has been found include the fisher, fox, marten, mink, raccoon, and skunk (Frank et al., 1979), the highest concentrations being found in the predators at the top of the food chain, i.e., mink and marten (9.7 µg/kg wet tissue).

Other studies on the presence of dieldrin in non-target species and their environment are summarized in Tables 15 and 16 (Bugg et al., 1967; Koeman et al., 1967; Rowe et al., 1971; Faber et al., 1972; Meith-Avcin et al., 1973; Voutsinou-Talia-Douri & Satsmadjis, 1982). Most of these results are an indication of adventitious contamination, i.e., there is no close relationship to a particular use of aldrin or dieldrin.

The use of aldrin and dieldrin as seed-dressing agents has undoubtedly resulted in high concentrations of dieldrin in the body tissues of animals found dead. An association between the use of aldrin and dieldrin seed dressings and the deaths of wood-pigeons *(Columba palumbus)* was first noted by Carnaghan & Blaxland (1957) and Turtle et al. (1963, 1965). In wood-pigeon, pheasant, partridge, and corvids found dead, Turtle et al. (1965) found mean concentrations of 10, 2.3, 7.3, and 2 mg/kg liver, respectively, (maximum concentrations of 59.2, 28.8, 46.3, and 14 mg/kg liver). The concentrations in birds that had been shot were much lower.

Table 17 summarizes the residue levels found following the use of dieldrin for the control of the tsetse fly and arising from other uses of aldrin and dieldrin, e.g., as seed-dressing agents. Several other reports on seed-dressing incidents in the United Kingdom have been published, e.g., Murton & Vizoso (1963) and Jefferies et al. (1973).

5.1.7.1 Occurrence of dieldrin in birds of prey and fish-eating birds

Changes in the populations of hawks, falcons, and other raptors have prompted extensive studies of the concentrations of dieldrin in the tissues of birds and eggs. These data are summarized in Table 18.

The concentrations of dieldrin in the tissues of bald eagles *(Haliacetus leucocephalus)* that were found dead during the period 1967-1977 were estimated by Mulhern et al. (1970), Belisle et al. (1972), Cromartie et al. (1975), Prouty et al. (1977), and Kaiser et al. (1980). The concentrations (geometric mean) in the brain were 0.1-2.0 mg/kg tissue, with a maximum of 11 mg/kg. Because the population declines of some birds of prey and some fish-eating birds have been associated with the use of aldrin and dieldrin, the residues in some of these species will be discussed in more detail.

(a) Grey heron (Ardea cinerea)

This is one of the highly contaminated species in the United Kingdom. Relatively high levels of dieldrin have been measured in the

Table 17. Residues in non-target species - concentrations related to particular uses or discharges of aldrin/dieldrin

Species	Component analysed	Geographical area	Year	No. of specimens[a]	Concentration of dieldrin (mg/kg) Mean[b]	Range	Comments	Reference
Woodpigeon *(Columba palumbus)*	liver	Netherlands	1966	20	2.8[b]	0.05-27.1	seed dressing	Fuchs (1967)
				4	79[c]	44.2-136		
Pink-footed goose *(Anser branchyrhynchus)*	liver	United Kingdom	1972-73	6	31[c]	15-48	seed dressing	Stanley & Bunyan (1979)
Pheasant *(Phasianus colchicus)*	egg	USA: Illinois	1966	120	0.3	0.02-2.82	soil insecticide	Greenberg & Edwards (1970)
Birds (various spp.)	liver	Kenya	1968	12	28.2[c]	18-57	tse-tse fly control (dead birds found during 10 days after spray application; live birds collected 2 months later)	Koeman & Pennings (1970)
				21	1.7[b]	0.16-6		
	brain			10	14.3[c]	6-22		
				11	0.2[b]	0.06-0.68		
Insects (various spp.)	whole body	Cameroon	1979	227	0.2[c]	ND[e] - 13.2	tse-tse fly control	Mueller et al. (1981)
Fish *(Aphyosemion bualanum)*	whole body			124	0.09	ND - 214.3		
Birds (various spp.)	liver			40	1.51[b]	ND - 7.24		
Fruit bat (2 spp.)	liver			20	79.2[b]	ND - 174.81		
Rat *(Praomys tullbergi)*	liver			13	0.37	ND - 1.20		Mueller et al. (1981)

Table 17 (contd).

Species	Component analysed	Geographical area	Year	No. of specimens[a]	Concentration of dieldrin (mg/kg) Mean[b]	Range	Comments	Reference
Common gallinule *(Gallinula chloropus)*	egg	USA: Louisiana	1965	4/23[d]	9.6	2.23-13.17	rice fields sown with aldrin-treated seed	Causey et al. (1968)
			1966	14	9.4	1.13-22.12		
Purple gallinule *(Porphyrula martinica)*	egg		1965	2/16[d]	9.7	6.47-12.94		
			1966	56	6.5	0.49-15.35		
Common gallinule	egg	USA: Louisiana	1968	6	17.5	4.69-28.07	rice fields sown with aldrin-treated seed	Fowler et al. (1971)
			1969	12	4.8	1.16-10.7		
Purple gallinule	egg		1968	26	9.4	3.23-16.43		
			1969	33	3.8	1.56-13.62		
Invertebrates	composites of whole body	USA: Texas Gulf coast	1967-71	1208/16	1.1[b] (3.1)	LD[f] - 3.2 (LD - 16.3)	aldrin-treated seed	Flickinger & King (1972)
Crayfish (2 spp.)	whole body			105/8	6.3[c] (2.1)	LD - 17 (LD - 9)		
Cricket frog *(Acris crepitans blanchardi)*	whole body			18/3	0.1[b]	LD - 0.1		
Fish (4 spp.)	whole body			592/4	1.2[b]	0.4-2.8		
Turtles (2 spp.)	whole body			5/2	0.9[b] (2.4)	0.6-1.2 (LD - 4.8)		

Table 17 (contd).

Snakes (3 spp.)	whole body	USA: Texas Gulf coast	1967-71	3/3	2.4[b]	0.1-5.7		Flickinger & King (1972)
Great horned owl	brain			1	6.3[c]	-		
Birds (various spp.)	brain			27	8.5[c] (0.1)	LD - 22 (LD - 0.2)	192 dead birds collected from 1967-71	
Fulvous tree duck *(Dendrocygna bicolor)*	egg			69/14	2.5	<0.1-9.5		
Owls (various spp.)	liver	United Kingdom (London Zoo)	1974-76	22	24[c]	1.7-46	death of many owls due to dieldrin poisoning; sawdust from dieldrin-treated wood the probable source of contamination	Jones et al. (1978)

[a] N_1/N_2: N_1 is the number of incorporated into N_2 composites; the range corresponds to the composites.
[b] Indicates living organisms collected by capture, shooting, etc. Values in parentheses are the concentrations of aldrin.
[c] Indicates organisms found dead or dying. Values in parentheses are the concentrations of aldrin.
[d] Clutches/eggs.
[e] ND - not determined.
[f] LD - limit of detection.

Table 18. Concentrations of dieldrin in tissues and eggs of birds of prey and fish-eating birds found dead

Species	Type of sample	Geographical area	Year	No. of specimens	Concentration of dieldrin (mg/kg) Mean[a]	Range[b]	Reference
Kestrel *(Falco tinnunculus)*	liver	Netherlands	1968-69	7	-	1.1-24	Koeman et al. (1969)
Kestrel *(Falco tinnunculus)*	liver	United Kindgom	1963-65	74	1.09	0.94-1.27	Cooke et al. (1982)
			1966-71	144	1.06	0.91-1.24	
			1972-75	125	1.43	1.19-1.72	
			1977	31	0.31	0.21-0.45	
Sparrow-hawk *(Accipiter nisus)*	liver	Netherlands	1969	3	-	0.9-19	Koeman et al. (1969)
Sparrow-hawk *(Accipiter nisus)*	liver	United Kingdom	1963-65	30	1.20	0.97-1.49	Cooke et al. (1982)
			1966-71	82	0.29	0.22-0.38	
			1972-75	83	0.61	0.48-0.78	
			1977	26	0.22	0.15-0.32	
Sparrow-hawk *(Accipiter nisus)*	egg	United Kingdom	1963-65	24	2.09	1.63-2.67	Cooke et al. (1982)
			1966-71	154	0.69	0.60-0.79	
Buzzard *(Buteo buteo)*	liver	Netherlands	1968-69	5	-	0.45-31	Koeman et al. (1969)
Grey heron *(Ardea cinerea)*	liver	United Kingdom	1963-65	26	1.13	0.66-1.94	Cooke et al. (1982)
			1966-67	69	0.92	0.67-1.26	
			1972-75	57	0.74	0.57-0.96	
			1977	12	0.17	0.08-0.37	

Table 18 (contd).

Kingfisher *(Alcedo atthis)*	liver	United Kingdom	1964-65 1966-71 1972-75	4 37 22	6.83 1.56 1.16	3.95-11.8 1.23-1.98 0.89-1.53	Cooke et al. (1982)
Peregrine falcon *(Falco peregrinus)*	liver	United Kingdom	1963-77	15	1.91	1.35-2.71	Cooke et al. (1982)
Barn owl *(Tyto alba)*	liver	United Kingdom	1963-65 1966-71 1972-75 1977	48 94 114 29	1.31 1.42 1.07 0.26	1.08-1.60 1.19-1.69 0.90-1.28 0.18-0.37	Cooke et al. (1982)
Long-eared owl *(Asio otus)*	liver	United Kingdom	1963-77	30	1.75	1.14-2.70	Cooke et al. (1982)
Bald eagle *(Haliaeetus leucocephalus)*	liver	USA	1964-65	44	0.28	LD - 11.9 (LD <0.05 mg/kg)	Reichel et al. (1969)
Peregrine falcon *(Falco peregrinus)*	egg	United Kingdom	1963-65 1966-71 1972-75 1977	23 76 34 12	0.59 0.14 0.18 0.34	0.49-0.71 0.11-0.17 0.11-0.28 0.25-0.46	Cooke et al. (1982)
Bald eagle *(Haliaeetus leucocephalus)*	egg	USA	1969-70	12	0.08[c]	LD - 0.3 (LD <0.05 mg/kg)	Wiemeyer et al. (1972)
		USA: Alaska, 4 other states		11	0.83[c]	0.15-2.3	

[a] Geometric mean, except for footnote [c] which is arithmetic mean.
[b] Range of value within 1 standard error.
[c] Arithmetic mean.

livers of herons found dead, together with high levels of DDT-type compounds and polychlorinated biphenyls (Cooke et al., 1982). The geometric mean concentrations of dieldrin for various periods within the range 1963-1977 are given in Table 18. The geometric mean concentration of dieldrin in the livers of 143 samples over the period 1963-1975 was 0.9 mg/kg. Of the herons found dead, 50% contained less than 1 mg dieldrin/kg liver, whereas 14% contained 10 mg/kg or more.

(b) Kestrel (Falco tinnunculus)

The geometric mean concentration of dieldrin in the livers of 374 kestrels found dead in the United Kingdom during the period 1963-1977 was 1.2 mg/kg (Cooke et al., 1982). Some 50% of the kestrels found dead contained less than 1 mg dieldrin/kg liver, 18% contained more than 10 mg/kg, and 8% more than 20 mg/kg. Higher levels were found in the Netherlands (Fuchs, 1967; Koeman et al., 1969).

Sierra et al. (1987) studied the presence of residues of aldrin and dieldrin in the liver, muscle, fat, kidneys, and brain of four kestrels from the province of Leon, Spain. The concentrations of aldrin ranged from 0.003 to 0.65 mg/kg tissue (highest in fat and kidneys), whereas those of dieldrin ranged from 0.005 to 0.151 mg/kg tissue (highest in liver; fat not estimated). All values were based on wet weight.

(c) Sparrow-hawk (Accipiter nisus)

The geometric mean concentration of dieldrin in the liver of 195 sparrow-hawks found dead in the United Kingdom over the period 1963-1977 was 0.5 mg/kg (Cooke et al., 1982). About 62% of the dead sparrow-hawks contained less than 1 mg dieldrin/kg liver, and about 7% contained more than 10 mg dieldrin/kg liver.

Three sparrow-hawks found dead or dying in the Netherlands in 1969 contained 0.89, 1.1, and 19 mg dieldrin/kg liver, respectively (Koeman et al., 1969). One dead sparrow-hawk (1966) contained 18.4 mg dieldrin/kg liver (Fuchs, 1967).

Sierra et al. (1987) studied the presence of residues of aldrin and dieldrin in three sparrow-hawks in Leon, Spain. The average concentrations of dieldrin ranged from 0.1 to 0.45 mg dieldrin/kg tissue (liver, kidneys, brain) but in fat an average level of 17.3 mg/kg was found (all values were based on wet weight). Only low levels (< 0.01 mg/kg tissue) of aldrin were found in fat.

(d) Barn owl (Tyto alba)

The geometric mean concentration of dieldrin in the liver of 251 barn owls found dead in the United Kingdom (1963-1977) was 1.2 mg/kg (Cooke et al., 1982). About 49% of the barn owls contained less than 1 mg dieldrin/kg liver, while about 15% contained at least 10 mg dieldrin/kg liver.

The concentration of aldrin and dieldrin in the muscle, liver, fat, brain, and kidneys of 23 barn owls, collected in the province of Leon,

Spain, was determined (91 samples in total). The incidence of aldrin in the tissues ranged from 76 to 83%, and of dieldrin from 4 to 27%. The average concentration in these organs and tissues was 0.03–0.11 mg aldrin/kg and 0.009–0.2 mg dieldrin/kg tissue (wet weight). The highest concentration was in the kidneys for aldrin and in the brain for dieldrin (Sierra & Santiago, 1987).

The concentrations in all four of the above species in the United Kingdom showed seasonal, annual, and regional trends. Residue levels in herons decreased progressively after 1963–1965 until 1977, whereas the main decrease in levels in sparrow-hawks occurred between 1963–1965 and 1966–1971, there being little subsequent change. In kestrels and barn owls, there was no overall trend between 1963 and 1974–1975, but significant declines in levels had occurred by 1977. The residues in the livers of herons, kestrels, and barn owls were significantly higher in areas of eastern England (the main wheat bulb fly infestation areas) than in other regions of the United Kingdom. These differences are probably indicative of the use of aldrin- or dieldrin-dressed grain in eastern England. Few samples of sparrow-hawk's livers were available from eastern England, but the residues showed a similar regional difference.

(e) Bald eagle (Haliaecetus leucocephalus)

A survey of the residues of dieldrin in the carcass, liver, and brain of bald eagles was initiated in 1960 by the Patuxent Wildlife Research Centre, USA. The median concentration (1964–1965) was 0.1 mg dieldrin/kg brain and about 0.3 mg dieldrin/kg liver (Reichel et al., 1969). During the period 1966–1977, mean concentrations ranged from 0.1 to 2 mg dieldrin/kg brain (Mulhern et al., 1970; Belisle et al., 1972; Cromartie et al., 1975; Prouty et al., 1977; Kaiser et al., 1980).

(f) Other birds of prey and fish-eating birds

The surveys of the residues of dieldrin in other raptors have been less extensive than those for the five species discussed above. The geometric mean concentrations in the livers of 12 other species (283 birds) in the United Kingdom (Cooke et al., 1982) in the period 1963–1977 were between 0.02 and 2.35 mg/kg. Those for the golden eagle (14 birds) in the USA during the period 1964–1965 were between trace levels and 0.4 mg/kg (Reichel et al., 1969).

5.2 General Population Exposure

5.2.1 Adults

5.2.1.1 Aldrin

In the great majority of investigations into the presence of organochlorine compounds in human blood and other tissues, the level of

aldrin was below the limits of detection. However, there are a few reports of aldrin being present in human blood, placenta, adipose tissue, and other tissues (Radomski & Fiserova-Bergerova, 1965; Kanitz & Castello, 1966; Selby et al., 1969a,b; Herrera Marteache et al., 1978; Fernicola & Azevedo, 1982; Mossing et al., 1985). These findings are unusual. The report that aldrin was present in eight samples of blood, when none was found in the matched adipose tissue samples, also seems anomalous (Selby et al., 1969b). Fernicola & Azevedo (1982) suggested that some other compounds with the same retention time as aldrin had perhaps led to false results. None of these investigators established the identity of the component, reported as "aldrin".

5.2.1.2 Concentrations of dieldrin in adipose tissue

Following the introduction of gas-liquid chromatography, there have been numerous investigations of the concentration of dieldrin in the adipose tissue of members of the general population who have had no know occupational exposure to aldrin or dieldrin. Surveys have been made in more than 20 countries, but in some surveys the number of samples of fat analysed was small. In the USA and the United Kingdom, there have been several surveys during the period 1961-1977. The results are summarized in Table 19, using two statistics to define the samples: arithmetic mean (or geometric mean in some American surveys) and maximum value as an indication of the upper limit of variability (upper confidence limit in a few surveys). The distribution tends to be skewed to the right, i.e., there is a greater number of high values than would be expected if the samples had a normal distribution (Hunter et al., 1963; Morgan & Roan, 1970). The maximum values in some surveys are so large that they may correspond to individuals with an occupational exposure. The results for stillborns and young babies and children are discussed in section 5.2.2.

Most of the mean values are in the range 0.1-0.3 mg dieldrin kg body fat and are usually smaller than those of total DDT by at least a factor of 10. Surveys in the USA, United Kingdom, and Netherlands indicate that there has been a decline of about 50% in the concentration of dieldrin in the body fat since the mid 1970s (Abbott et al., 1981; Ministry of Welfare, Health and Culture, The Netherlands, 1983).

5.2.1.3 Concentrations of dieldrin in blood

The concentrations of dieldrin in whole blood or serum of members of the general population have been determined in a few countries and are summarized in Table 20. The concentrations are very low (μg/litre) and it is essential that the sensitivity of the analytical method is at least 0.1 μg/litre. Two analytical procedures have been used (Dale et al., 1966; Richardson et al., 1967a), which give significantly different results: the acetone extraction procedure (method II in Table 20) gives results that are about 50% higher than the hexane extraction procedure (method I in Table 20) and showed a better repro-

Table 19. Concentrations of dieldrin in the body fat of the general population

Country	Year	No. of samples[a]	Method of clean-up[b]	Dieldrin Mean (mg/kg fat)	Dieldrin Maximum (mg/kg fat)	Reference
North America						
Canada	1966	47 (N)	I	0.22	0.53	Brown (1967)
	1967-68	51 (N)	II	0.12	0.83	Kadis et al. (1970)
	1969	221 (N)	II	0.12	0.46	Ritcey et al. (1973)
	1969	5 (-)	-	0.08	-	Mastromatteo (1971)
	1970	3 (-)	-	0.22	-	Mastromatteo (1971)
	1972	168 (N)	II	0.069	0.35	Mes et al. (1977)
	1969-74	448 (N)	-	0.12	0.88	Holdrinet et al. (1977)
	1976	99 (N)		0.049	0.211	Mes et al. (1982)
	1979-81	175 (N)	II	0.04	0.13	Williams et al. (1984)
	1980	29 (N)		0.046		Mes et al. (1985)
USA	1961-62	28 (B)	II	0.15	0.36	Dale & Quinby (1963)
	1962-66	221 (N)	II	0.14	1.39	Hoffman et al. (1967)
	1964	25 (N)	II	0.29	1.15	Hayes et al. (1965)
	1964	64 (N)	-	0.31	2.82	Zavon et al. (1965)
	1964-67	42 (N)	none	0.21	0.70	Radomski et al. (1968)
	1965-67	146 (N)	none	0.22	0.77	Edmundson et al. (1968)
	1966-68	70 (N)	II	0.14	-	Morgan & Roan (1970)
	1967	30 (N)	II	0.03[f]	-	Casarett et al. (1968)
	1968	48 (N)	II	0.20	-	Warnick (1972)
	1969	15 (N)	II	0.15	-	Warnick (1972)
	1969	26 (B)	II	0.33[f]	0.80[c]	Burns (1974)
	1970	40 (N)	II	0.15	-	Warnick (1972)
	1970	68 (B)	II	0.29[f]	0.73[c]	Burns (1974)
	1970	202 (B)	II	0.2	1.0	Wyllie et al. (1972)
	1970	1412 (N/B)	II	0.18[f]	15.20	Kutz et al. (1979)
	1971	88 (B)	II	0.36[f]	0.78[c]	Burns (1974)
	1971	1615 (N/B)	II	0.22[f]	2.91	Kutz et al. (1979)
	1972	39 (B)	II	0.43[f]	1.00[c]	Burns (1974)
	1972	1913 (N/B)	II	0.18[f]	2.91	Kutz et al. (1979)

Table 19 (contd).

Country	Year	No. of samples[a]	Method of clean-up[b]	Dieldrin Mean (mg/kg fat)	Dieldrin Maximum (mg/kg fat)	Reference
North America (contd).						
USA	1973	1094 (N/B)	II	0.18[f]	5.64	Kutz et al. (1979)
	1974	898 (N/B)	II	0.15[f]	2.21	Kutz et al. (1979)
Louisiana	1980	8 (B)	II	0.15[f]	0.34	Holt et al. (1986)
Louisiana	1984	10 (B)	II	0.10[f]	0.19	Holt et al. (1986)
Central and South America						
Mexico	1975	19 (N)	II	0.06[f]	0.24	Albert et al. (1980)
	1975	9 (B)	II	0.18[f]	0.49	Albert et al. (1980)
	1975	9 (N)	II	0.05[f]	0.12	Albert et al. (1980)
Argentina	-	47 (N)	IV	0.38	0.66[c]	Wassermann et al. (1969)
Brazil	1969-70	17 (N/B)	III	0.02[e]	0.12	Wassermann et al. (1972a)
	1969-70	69 (N/B)	III	0.12[e]	1.62	Wassermann et al. (1972a)
Europe						
Belgium	1968-69	37 (N)	II	0.13	0.50	Wit (1971)
	1975	60 (N)	II	0.26	1.16	Dejonckheere et al. (1977)
	1977	58 (N)	II	0.12	0.69	Van Haver et al. (1978)
Denmark	1965	18 (N)	-	0.20	0.34	Weihe (1966)
	1972-73	70 (N)	II	0.16[f]	0.53	Kraul & Karlog (1976)
France	1971	100 (N)	II	0.45	1.45	Fournier et al. (1972)
Germany, Federal Republic of	1967	15 (B)	I	0.18[f]	0.36	Wuenscher & Acker (1969)
	1973	50 (N)	-	0.14	0.23	Acker & Schulte (1974)

Table 19 (contd).

Europe (contd).						
Greece	-	50 (N/B)	II	0.23	0.87	Panetsos et al. (1975)
Italy	1965	9 (N)	II	0.59	2.77	Kanitz & Castello (1966)
	1966	22 (N/B)	II	0.68[f]	1.55	Del Vecchio & Leoni (1967)
	1965-68	33 (B)	-	0.32	3.15	Paccagnella et al. (1971)
	1965-68	11 (B)	-	1.95	5.70	Paccagnella et al. (1971)
	1965-68	52 (N)	-	0.91	3.55	Paccagnella et al. (1971)
Netherlands	1964	34 (N)	II	0.31[f]	-	Wit (1971)
	1966	11 (N)	II	0.20	0.50	De Vlieger et al. (1968)
	1968-69	34 (N)	II	0.27[f]	1.5	Wit (1971)
	1973-74	102 (N)	-	0.2	-	Greve & Wegman (1985)
	1975	25 (N)	-	0.11	-	Greve & Wegman (1985)
	1976	74 (N)	-	0.09	-	Greve & Wegman (1985)
	1977-78	78 (N)	-	0.11	-	Greve & Wegman (1985)
	1979	25 (B)	-	0.09	-	Greve & Wegman (1985)
	1980	24 (N)	-	0.10	-	Greve & Wegman (1985)
	1981	53 (N)	-	0.07	-	Greve & Wegman (1985)
	1982	54 (N)	-	0.07	-	Greve & Wegman (1985)
	1983	78 (N)	-	0.06	-	Greve & Wegman (1985)
Spain	-	40 (B)	III	0.15	0.49	Herrera Marteache et al. (1978)
Switzerland	1972	13 (B)	II	0.29	0.57	Zimmerli & Marek (1973)
United Kingdom	1961	131 (N)	II	0.21	1.29	Hunter et al. (1963)
	1963-64	66 (N)	II	0.26	0.9	Egan et al. (1965)
	1964	50 (N)	II	0.27	0.85	Robinson et al. (1965)
	1964	50 (B)	II	0.25	0.65	Robinson et al. (1965)

Table 19 (contd).

Country	Year	No. of samples[a]	Method of clean-up[b]	Dieldrin Mean (mg/kg fat)	Dieldrin Maximum (mg/kg fat)	Reference
Europe (contd).						
United Kingdom	1965	101 (N)	II	0.34	1.80	Cassidy et al. (1967)
	1966	53 (B)	II	0.21	0.60	Hunter et al. (1967)
	1965-67	248 (N)	II	0.21	1.0	Abbott et al. (1968)
	1967	18 (B)	II	0.27	0.68	Hunter et al. (1967)
	1969-71	201 (N)	II	0.16	0.68	Abbott et al. (1972)
	1976-77	236 (N)	II	0.11	0.49	Abbott et al. (1981)
	1982-83	187 (N)	-	0.074	0.27	UK-HMSO (1986)
Africa						
Kenya	1969-70	32 (N)	III	0.030[d]	0.18	Wassermann et al. (1972b)
	1969-70	51 (N)	III	0.064[e]	0.28	Wassermann et al. (1972b)
Nigeria	1969	46 (N)	III	0.059[d]	0.73	Wassermann et al. (1972c)
	1969	90 (N)	III	0.13[e]	0.98	Wassermann et al. (1972c)
South Africa	1969	114 (N/B)	IV	0.039	-	Wassermann et al. (1970)
Uganda	1969-70	16 (N)	III	0.023[d]	0.058	Wassermann et al. (1974a)
	1969-70	39 (N)	III	0.031[e]	0.59	Wassermann et al. (1974a)
Asia						
India	1964	35 (N)	II	0.04	0.36	Dale et al. (1965)
Iran	1974-76	170	II	0.049	0.75	Hashemy-Tonkabony & Soleimani-Amiri (1978)

Table 19 (contd).

Asia (contd).						
Israel	1967-69	61 (N)	III	0.10[d]	0.315	Wassermann et al. (1974b)
	1967-69	162 (N)	III	0.14[e]	3.96	Wassermann et al. (1974b)
Japan	Prior to 1973	241 (N)	II	0.13	0.98	Curley et al. (1973)
	1974-75	59 (N)	II	0.09[f]	0.51	Yoshimura et al. (1979)
Thailand	1969-70	8 (N)	III	0.077[d]	0.459	Wassermann et al. (1972d)
	1969-70	27 (N)	III	0.10[e]	1.20	Wassermann et al. (1972d)
	1975-76	9	II	0.322	-	Department of Agriculture Thailand (1976)[g]
Oceania						
Australia	1965	53 (N)	II	0.046	0.43	Bick (1967)
	1965-66	12 (N)	IV	0.67	0.99	Wassermann et al. (1968)
	1969-70	75 (N)	II	0.21	2.60	Brady & Siyali (1972)
New Zealand	Prior to 1967	45 (N)	II	0.28	0.77	Brewerton & McGrath (1967)
	1965	43 (B)	II	0.41	-	Copplestone et al. (1973)
	1966	54 (B)	II	0.30	-	Copplestone et al. (1973)
	1967	68 (B)	II	0.43	-	Copplestone et al. (1973)
	1968	64 (B)	II	0.33	-	Copplestone et al. (1973)
	1969	25 (B)	II	0.27	-	Copplestone et al. (1973)

Table 19 (contd).

Country	Year	No. of samples[a]	Method of clean-up[b]	Dieldrin (mg/kg fat) Mean	Maximum	Reference
Oceania (contd).						
Papua New Guinea	1969-70	38 (N)	II	0.17	0.72	Brady & Siyali (1972)

[a] Samples taken at necropsy (N) or during elective surgery (B).
[b] Method of clean-up:

I Removal of neutral lipids at -70 °C.
II Separation into two or more fractions by eluting from a Florisil column (with prior liquid/liquid partition to reduce neutral lipid content, in most investigations using this clean-up procedure).
III Florisil column clean-up without separation into two or more fractions.
IV Kontes co-distillation.
- Method not reported.

[c] Upper confidence limit ($P = 0.025$) for the set of samples.
[d] Age group 5-24 years.
[e] Age group 25 years and older.
[f] Results expressed in terms of extractable lipid content.
[g] Personal communication to IPCS in 1987.

Table 20. Concentration of dieldrin in the blood of the general population

Country	Year	Number of samples[a]	Analytical method[b]	Dieldrin Mean (µg/litre)	Dieldrin Maximum (µg/litre)	Reference
USA	1965	10 (B)	I	1.4	2.8	Dale et al. (1966)
	1967-68	1000 (S)	I	0.5	25	Watson et al. (1970)
	1967-71	970 (S)	I	0.9	-	Warnick (1972)
	1967-68	37 (H)	III	4	-	Morgan & Roan (1970)
	1970	202 (S)	I	0.9	10	Wyllie et al. (1972)
	Prior to 1981	59 (S)	I	0.6	10.1	Barquet et al. (1981)
	1976-80	6078 (S)	?	~1.4[c]	16	Murphy & Harvey (1985)
Hawaii	1968-70	1107 (S)	I	1.46	11	Klemmer et al. (1973)
Lanai Island	1968-70	484 (S)	I	1.3	26	Klemmer et al. (1973)
Europe						
Netherlands	1978	70 (B)	-	< 0.5	-	Greve & Wegman (1985)
	1980	48 (B)	-	< 0.4	-	Greve & Wegman (1985)
	1981	127 (B)	-	< 0.4	-	Greve & Wegman (1985)
	1982	54 (B)	-	< 0.5	-	Greve & Wegman (1985)

Table 20 (contd).

Country	Year	Number of samples[a]	Analytical method[b]	Dieldrin Mean (µg/litre)	Dieldrin Maximum (µg/litre)	Reference
Europe (contd).						
Switzerland	1972	~100 (S)	I	1.1	-	Zimmerli & Marek (1973)
United Kingdom	1962	20 (B)	II	1.6	10.0	Hunter et al. (1967)
	1964	61 (B)	II	1.4	5.0	Hunter et al. (1967)
	1965	25 (B)	II	1.7	8.7	Hunter et al. (1967)
	1966	55 (B)	II	1.8	4.3	Hunter et al. (1967)
	1968	18 (B)	II	0.9	1.1	Robinson & Roberts (1969)
Oceania						
Australia	-	52 (B)	I^{ust}	2.3	13	Siyali (1972)
	-	47 (B)	I^{ust}	none	-	Siyali (1973)

[a] Samples of whole blood (B), serum (S), whole blood from heart chamber (during autopsy) (H).
[b] Analytical methods (all use gas-liquid chromatography with an electron-capture detector):
I Hexane extraction.
I^{ust} Hexane extraction combined with ultrasonic treatment.
II Acetone extract on silica gel column.
III Solvent extraction and Florisil column clean-up.
[c] In 260 positive samples.

ducibility (Robinson et al., 1967a). An inter-laboratory comparison of the hexane extraction method showed that large variations in results may occur (Thompson, 1976).

5.2.1.4 Concentration of dieldrin in other tissues

A few investigations of the concentrations of dieldrin in other body tissues have been made and some of the results are summarized in Table 21.

5.2.2 Babies, infants, and mother's milk

Dieldrin penetrates the placenta and, as a result of transplacental exposure, may occur in the blood, adipose tissue, and other tissues of the fetus and newborn baby (Table 22). The concentrations are lower by a factor of 2-10 than those of their mothers or other adults (Table 19). There is no difference between infants and adults in the brain/liver/fat ratio of dieldrin concentrations (Fiserova-Bergerova et al., 1967; Casarett et al., 1968). A similar situation exists in animals, e.g., pigs (Uzoukwu & Sleight, 1972).

Dieldrin is also excreted in the milk of human beings and various animal species. Table 23 summarizes the concentrations of dieldrin found in human milk over the last 15 years in various countries, mean concentrations up to 6 μg/litre having been reported. Higher values, occurring occasionally in a few regions, have been associated with house and garden use of aldrin/dieldrin. Thus, in the first several months, a breast-fed infant drinking approximately 150 ml milk/kg body weight per day has a daily intake of 0.15-0.9 μg dieldrin/kg body weight.

Acker et al. (1984) studied the problem of residues in human milk and the importance of breast-feeding for the newborn baby. They concluded that, at least in the early months, the value of breast-feeding outweighed the possible risks from residues of dieldrin, in this case, in human milk. They calculated that the average daily intake of dieldrin by newborn babies was approximately 0.7, 0.75, 0.65, and 0.65 μg/day, respectively, for the 1st, 2nd, 3rd, and 4th months of breast-feeding.

Aldrin has rarely been detected in human milk. It was not detectable in 202 samples of Dutch human milk (Wegman & Greve, 1974; Greve & Wegman, 1985), and in only one (21.8 μg/litre) of 50 Norwegian samples (Bakken & Seip, 1976).

During the first trimester, and usually during the first year, of a baby's life, the concentration of dieldrin in the blood and adipose tissue does not increase and, in most cases, decreases (Astolfi et al., 1974) (Table 22).

The concentration of dieldrin in the blood of breast-fed babies is not higher that that in bottle-fed babies (Eckenhausen et al., 1981), and it is lower than it is in adults.

Table 21. Concentration of dieldrin in various tissues from members of the general population

Tissue	Country	Year	No. of samples	Dieldrin Mean (mg/kg)	Dieldrin Maximum (mg/kg)	Reference
Liver	Canada	1967-68	50	0.25[a]	3.0[a]	Kadis et al. (1970)
	USA	1967	42	0.009	-	Casarett et al. (1968)
	USA	1966	42	0.035	0.22	Fiserova-Bergerova et al. (1967)
	USA	1966-68	35	0.047	-	Morgan & Roan (1970)
	Denmark	1972-73	18	0.29[a]	-	Kraul & Karlog (1976)
	Netherlands	1966	11	0.034	0.081	De Vlieger et al. (1968)
	Japan	1974-75	30	0.39[a]	1.73[a]	Yoshimura et al. (1979)
	Thailand	1975-76	16	0.010	-	Dept. of Agriculture, Thailand (1976)[b]
Kidneys	Canada	1967-68	47	0.10[a]	1.35[a]	Kadis et al. (1970)
	USA	1967	38	0.021	-	Casarett et al. (1968)
	USA	1966	42	0.013	0.04	Fiserova-Bergerova et al. (1967)
	USA	1966-68	35	0.014	-	Morgan & Roan (1970)
	USA	1973	12	0.006	0.009	Anon (1974c)
	Thailand	1975-76	16	0.010	-	Dept. of Agriculture, Thailand (1976)[b]
Brain	Canada	1967-68	30	0.002[a]	-	Kadis et al. (1970)
	USA	1967	32	0.003	-	Casarett et al. (1968)
Brain	USA	1966	42	0.035	0.10	Fiserova-Bergerova et al. (1967)

Table 21 (contd).

Tissue	Country	Year	No. of samples	Dieldrin Mean (mg/kg)	Dieldrin Maximum (mg/kg)	Reference
	USA	1966-68	35	0.007	-	Morgan & Roan (1970)
	Denmark	1972-73	21	0.057[a]	-	Kraul & Karlog (1976)
	Netherlands	1966	28	0.0075	0.021	De Vlieger et al. (1968)
	Thailand	1975-76	16	0.010	-	Dept. of Agriculture, Thailand (1976)[b]
Gonads	Canada	1967-68	39	0.06[a]	0.86[a]	Kadis et al. (1970)
	USA	1967	36	0.008	-	Casarett et al. (1968)
	USA	1966	42	0.035	0.20	Fiserova-Bergerova et al. (1967)

[a] Results expressed in terms of extractable lipid content.
[b] Personal communication to IPCS in 1987.

A study on organochlorine insecticides in the blood of mothers and newborn babies was carried out in an agricultural rural area in the Mississippi Delta (USA). In total, 209 black and 130 white mother-newborn pairs participated. Dieldrin was detected in the blood of 43.5% of black and 51.5% of white mothers and in the blood of 19.1% of black babies and 10% of white babies. The blood concentrations of both mothers and babies were less than 1 μg/litre. Maternal age and birth weight of the baby did not correlate significantly with the prevalence, or with the mean level, of maternal and infant insecticide residues in the blood (d'Ercole et al., 1976).

Data on the occurrence of aldrin and dieldrin in human milk have been submitted by Australia, Guatemala, Japan, and Switzerland, Japan reporting a decline of the concentrations in human milk during the period 1971-1979. Data on dieldrin in human milk have been reported by Canada, the Federal Republic of Germany, Mexico, the Netherlands, Sweden, Switzerland, and the USA, none of the median levels exceeding 3 μg/kg milk. Levels in the USA were below 10 μg/kg milk (limit of detection) (National Food Administration, Uppsala, 1982).

Table 22. Concentration of dieldrin in blood and fat of fetus, newborns, infants, and adults

Country	Year	Age	Number of samples	Dieldrin in blood (µg/litre) Mean	Maximum	Number of samples	Dieldrin in fat (mg/kg fat) Mean	Maximum	Reference
North America									
Canada	1982	mothers during lactation	16	0.1	-				Mes et al. (1984)
USA	1966	fetus, stillborn				6	0.17	0.38	Fiserova-Bergerova et al. (1967)
		0-5 years				12	0.14	0.34	
		6-10 years				6	0.07	0.26	
		31-83 years				12	0.34	0.7	
USA	1968	newborn	26	0.7	1.5	3[a]	0.24	0.35	Curley et al. (1969)
		stillborn	4	ND[b]		7	ND		
South America									
Argentina	1969-70	mothers	13	1.63					Radomski et al. (1971)
		newborn	13	0.59					
		1-5 years	19	0.54					
		5-10 years	18	0.94					
		adults	20	1.43					
	1970	newborn				3	0.12	0.13	Astolfi et al. (1973)
		0-4 months				6	0.02	0.07	
		4-12 months				4	0.05	0.07	
		1-4 years				14	0.06	0.13	
		over 4 years				20	0.07	0.25	

Table 22 (contd).

South America (contd).									
Brazil	1969-70	stillborn				28	0.011	0.174	Wassermann et al. (1972a)
		5-24 years				17	0.023	0.122	
Europe									
Netherlands	1979	newborn	87	0.3	4.6				Eckenhausen et al. (1981)
		2 weeks	22	0.5	-				
		2 months	17	0.4	-				
		3 months	8	0.5	-				
		mothers pre-natal	48	0.8	3.5				
		mothers post-natal	73	0.4	4.1				
Spain (Cordoba)	1982	mothers	10	6	23				Gonzalez-Rodriquez Cordoba et al. (1983)
		babies	10	8	50				
United Kingdom	1969-71	newborn, stillborn				3	0.01	0.02	Abbott et al. (1972)
		1 day-3 months				8	0.03	0.07	
		3 months-4 years				9	0.05	0.10	
		over 4 years				201	0.16	0.68	
United Kingdom	1976-77	newborn				1	0.03	-	Abbott et al. (1981)
		2 months				1	0.02	-	
		3 months				1	0.09	-	
		over 4 years				236	0.11	0.49	

Table 22 (contd).

Country	Year	Age	Number of samples	Dieldrin in blood (µg/litre) Mean	Maximum	Number of samples	Dieldrin in fat (mg/kg fat) Mean	Maximum	Reference
Africa									
Nigeria	1969	stillborn				31	0.002	0.014	Wassermann et al. (1972c)
		0-11 months				47	0.019	0.087	
		1-4 years				54	0.023	0.083	
		adults				90	0.13	0.98	
Asia									
Israel	1968-69	fetus	23	1.3	-	-	-	-	Polishuk et al. (1970)
		pregnant woman	24	1.6	-	16	0.084	-	
		non-pregnant woman	-	-	-	33	0.172	-	
Israel	1967-69	stillborn				44	0.019	0.118	Wassermann et al. (1974b)
		0-11 months				40	0.021	0.125	
		5-24 years				61	0.101	0.315	
		adults				162	0.136	3.96	

[a] Stillborn.
[b] ND = not determined.

Table 23. Concentration of dieldrin in mother's whole milk

Country	Year	No. of samples	Dieldrin Mean (μg/litre)	Dieldrin Maximum (μg/litre)	Reference
North America					
Canada (Ontario)	1969-70	48	0.09[g]	0.25[g]	Holdrinet et al. (1977)
	1971-72	34	0.04[g]	0.17[g]	
	1973-74	24	0.04[g]	0.08[g]	
	1978-79	154	1[a]	26[b]	Dillon et al. (1981)
	1982	~128[c]	~1.3	1.8	Mes et al. (1984)
USA	1972-73	57	< 10	50	Kutz et al. (1979)
	1973-74	57	4	50	Strassman & Kutz (1977)
	1973-75	40	6	42[b]	Barnett et al. (1979)
	1972-75	1436	~5	15	Savage et al. (1981)
Hawaii	1979-80	54	0.04[g]	0.09[g]	Takei et al. (1983)
Central America					
El Salvador	1973-74	40	5	15	De Campos & Olszyna-Marzys (1979)
Guatemala	1971	46	2	10	De Campos & Olszyna-Marzys (1979)
Europe					
Belgium	1968	20	3.4	8	Heyndrickx & Maes (1969)
Denmark	1982	57	0.04[g]	0.47[g]	Anderson & Orbaek (1984)
Germany, Federal Republic of	1981	91	0.05[g]	0.44[g]	Rohwer (1983b)
	1982	132	0.01[g]	0.3[g]	Cetinkaya et al. (1984)
Netherlands	1969	48	3	11	Tuinstra (1971)
	1972	202	5	-	Wegman & Greve (1974)
	1983	278	0.03[g]	0.22[g]	Greve & Wegman (1985)

Table 23 (contd).

Country	Year	No. of samples	Dieldrin Mean (µg/litre)	Dieldrin Maximum (µg/litre)	Reference
Europe (contd).					
Netherlands	1979	69	2.3	-	Eckenhausen et al. (1981)
Norway	1975	50	2.75	3.6	Bakken & Seip (1976)
Portugal	1972	164	11	21	Graca et al. (1974)
Spain	1981	20	3	14	Baluja et al. (1982)
Sweden (Stockholm)	1978	51[d]	22[g]	54[g]	Noren (1983a,b)
	1979	54[d]	20[g]	31[g]	
	1980	36[d]	18[g]	23[g]	
Switzerland	1983	6	0.5	1	Disler et al. (1984)
United Kingdom	1963-64	19	6	13	Egan et al. (1965)
	1979-80	102	2	12	Collins et al. (1982)
	1983-84	40	5	32	UK-HMSO (1986)
Africa					
Kenya	1983-85	292	range:	2.3-98	Kanja et al. (1986)
Asia					
Israel	1975	29	7	-	Polishuk et al. (1977)
Japan	1973-77	116	2.3	-	Yakushiji et al. (1979)
Oceania					
Australia	1970-71	23	5	11	Stacey & Thomas (1975)
	1971-72	40	25	68	Miller & Fox (1973)

Table 23 (contd).

Country	Year	No. of samples	Dieldrin Mean (µg/litre)	Dieldrin Maximum (µg/litre)	Reference
Oceania (contd).					
Australia	1973	45	5	13	Siyali (1973)
	1979-80	267[c]	~8.5	31	Stacey et al. (1985)
	1981	74[e]	13	35	Stacey & Tatum (1985)
New Guinea	1972	74	0.7	13.2	Hornabrook et al. (1972)

[a] The authors stated that they found aldrin. However, they probably meant dieldrin, since, in mother's milk, the presence of aldrin without dieldrin is highly unlikely, whereas the reverse is the rule.
[b] In an area of high pesticide use.
[c] 128 samples from 16 women.
[d] Number of samples included 745, 805, and 973, respectively.
[e] 74 samples from 14 women.
[f] Many of the houses had been treated against termites, but the pesticides used were unknown.
[g] On lipid basis in mg/kg.

6. KINETICS AND METABOLISM

6.1 Absorption

6.1.1 Aldrin

6.1.1.1 Ingestion

Aldrin is readily absorbed from the gastrointestinal tract and through the skin; it is stored as dieldrin, mainly in adipose tissue (section 6.2.1). Aldrin is readily metabolized to dieldrin in plants and animals and is rarely found as such in food or in the great majority of animals.

6.1.1.2 Inhalation

Inhalation studies by Beyermann & Eckrich (1973) on human volunteers suggested that about 50% of inhaled aldrin vapour was absorbed and retained in the human body. However, a study on 10 male volunteers exposed to actual aldrin vapour concentrations of 1.31 $\mu g/m^3$ and some weeks later to 15.5 $\mu g/m^3$ air for a period of 60 min suggested an actual retention in man of 20%.

Physical exertion did not have any significant effect on the retention. Dieldrin could not be detected in the exhaled air. The concentration of dieldrin in the blood of the volunteers was lower than 1 μg/litre before and after exposure (Bragt et al., 1984).

6.1.2 Dieldrin

Studies on rabbits, dogs, monkeys, and human beings have shown that dieldrin is absorbed through the intact skin (Shah & Guthrie, 1976; Sundaram et al., 1978; Fisher et al., 1985). There have been many studies demonstrating the absorption of dieldrin through the gastrointestinal tract (section 6.2).

6.1.3 Photodieldrin (and other metabolites of dieldrin)

Studies demonstrating the absorption of photodieldrin through the gastrointestinal tract are summarized in section 6.2.3.

6.2 Distribution

6.2.1 Aldrin

6.2.1.1 Mouse

In studies by Deichmann et al. (1975), Swiss-Webster mice were fed diets containing 0, 5, or 10 mg aldrin/kg, over seven generations. The

retention of dieldrin following the feeding of aldrin over four generations significantly increased the concentration of dieldrin in abdominal fat and in the lipids of the total carcass. There was also a significantly increased retention of dieldrin in the carcass in the F_1 generation, with some further (but not statistically significant) increase in concentration and total retention of dieldrin in the F_2 and F_3 generation. The dieldrin concentration in the total lipids of mouse carcasses were: for the F_0 generation, 60 mg/kg; for the males in the F_1, F_2, and F_3 generations, a mean of 100 mg/kg; and for the females in the F_1, F_2, and F_3 generations, a mean of 132 mg/kg. The dieldrin concentration was below 1 mg/kg in pups from the F_4 generation, born of parents that carried a considerable load of aldrin or dieldrin (thus exposed *in utero* and via lactation) and fed the control diet from weaning to the age of 260 days. The concentrations of dieldrin in the F_5 and F_6 generations were similar to those in the 2nd-4th generations.

6.2.1.2 Rat

When single oral doses of 10 mg aldrin/kg body weight were given to neonate Sprague Dawley rats, aldrin was detectable up to 6 days after dosing in the stomach and small intestine, but only for 72 h in the kidneys. In the liver, the aldrin concentration increased during the first 6 h, and then declined during the following days. Dieldrin was detected as early as 2 h after dosing and had reached a maximum after 24 h. It then declined. The only metabolic conversion product detected in the liver was dieldrin. The concentration of aldrin was very low relative to that of dieldrin, except in the case of studies in which tissues were analysed within a few hours of dosing with aldrin (Farb et al., 1973).

In studies by Ludwig et al. (1964), two male Wistar rats were given daily oral doses of 4.3 μg ^{14}C-aldrin by stomach tube for 3 months and were killed 24 h after the final dose. The total radioactivity in the body as a proportion of the total cumulative dose was 3.6%, but, after 82 days, the value had fallen to 0.21%. The ratio of dieldrin to aldrin in the carcass was approximately 15 : 1; in abdominal fat, it was about 18 : 1.

6.2.1.3 Dog

Deichmann et al. (1969, 1971), gave beagle dogs oral doses of aldrin in capsules. Three males were given 0.3 mg aldrin/kg body weight and 4 females were given 0.15 or 0.3 mg aldrin/kg body weight, 5 days per week, for 14 months. During the last 10 months of the dosing period, the concentration of dieldrin in the blood of dogs given 0.3 mg aldrin/kg body weight was in the range 42–183 μg/litre, while the concentration in the subcutaneous fat was 37–208 mg/kg. The levels in the animals receiving 0.15 mg aldrin/kg body weight were 40–130 μg/litre

and 12-67 mg/kg in blood and subcutaneous fat, respectively. The apparent partition ratio, subcutaneous fat/blood, was about 1000.

6.2.1.4 Human studies

Little is known about the distribution of aldrin in the human body after transfer from the gastrointestinal tract or skin into the circulating blood. As a result of its relatively rapid conversion to dieldrin, aldrin is rarely detected in human tissues.

6.2.2 Dieldrin

6.2.2.1 Laboratory animals

(a) *Mouse*

Following a preliminary comparison of the distribution of dieldrin and three known animal metabolites in CFE rats and CFI mice (Baldwin et al., 1972), a more detailed comparison was made of male CFE rats and two strains of male mice (CFI and LACG) (Hutson, 1976). The latter study also included a comparison of the effects of a pre-treatment with diets containing dieldrin at 20 mg/kg diet (rats) or 10 mg/kg diet (mice) for 4 weeks. ^{14}C-Dieldrin was administered orally as a single dose of about 3 mg/kg body weight to both the pretreated and non-pretreated groups, and the animals were killed 8 days after dosing. The concentrations of the 6,7-dihydroxy metabolite were below the limits of detection (less than 0.02 mg/kg) in the fat, liver, and kidneys of all the animals. The concentrations of the 9-hydroxy metabolite were very small or below the limits of detection (less than 0.03 mg/kg) in the fat and kidneys; small concentrations (about 0.4 mg/kg) were found in the livers of the two strains of mice. The bridged pentachloroketone (PCK) was present in the liver of CFE rats in small amounts (about 0.04 mg/kg), but quite large concentrations were found in the kidneys: 2.48 (no pre-treatment) and 6.11 mg/kg (4-week pre-treatment). The concentrations in the fat in both groups were small (mean, 0.17 mg/kg). In the two strains of mice, the concentrations of PCK in the liver were very small (about 0.5 mg/kg) except in the pretreated animals. Concentrations in the kidneys of the two strains of mice were below the limits of detection (less than 0.02 mg/kg) in the absence of pre-treatment or small (about 0.15 mg/kg) in pretreated mice. In the fat of the mice (no pre-treatment), the PCK concentrations were below the limits of detection (less than 0.04 mg/kg), but, in the pretreated mice, the concentrations were about 1.3 mg/kg. The concentrations of dieldrin in the fat were much higher than in the other tissues, and those in the mice were about twice those in the rat.

(b) *Rat*

Heath & Vandekar (1964) studied the transport of ^{36}Cl-dieldrin from the gastrointestinal tract by cannulation of the thoracic lymph

duct in rats. They found that only one-seventh of the absorbed dieldrin was recovered from the lymph and most of the dieldrin was absorbed via the portal vein.

Iatropoulos et al. (1975) indicated that the transport of dieldrin from the gastrointestinal tract to the liver of Sprague Dawley rats is mainly through the portal venous system. However, during the subsequent redistribution of dieldrin, the lymphatic system seemed to be a major route.

When female Osborne-Mendel rats were fed a diet containing 50 mg technical dieldrin (87%)/kg for 6 months, the concentrations of dieldrin in the blood, liver, and fat increased rapidly during the first 2 weeks. During the next 26 weeks, the concentrations fluctuated but did not appear to increase significantly. The mean concentrations for the final 4 months were (groups of four to six animals): in blood, 240 µg/litre; in liver, 6.8 mg/kg; and in fat, 159.5 mg/kg tissue. The distribution ratios (blood = 1) for this period were: liver, 28 and fat, 666 (Deichmann et al., 1968).

In the studies by Walker et al. (1969b), groups of 25 male and 25 female Carworth Farm E rats were fed diets containing 0.1, 1, or 10 mg dieldrin (99%)/kg diet. The control group consisted of 45 animals of each sex. Small groups of rats were killed after 26, 52, and 78 weeks and the remaining animals after 104 weeks. The concentration of dieldrin in blood, brain, liver, and fat was estimated. An approximate plateau level was reached during the first 26 weeks. The tissue uptake ratios (concentration of dieldrin in tissues/concentration in diet) for female rats in the three test groups were: in blood, 0.056; in brain, 0.19; in liver, 0.35; and in fat, 8.8. The uptake ratios for male rats were significantly lower than those for females. The partition ratios (concentration in tissues relative to that in blood) for males/females, respectively, were: in brain, 3.3/2.6; in liver, 7.8/5.9; and in fat, 104/137. It was considered that the results were consistent with the use of a compartmental model.

Osborn-Mendel rats (6 male and 6 female) were orally administered approximately 50 µg ^{14}C-dieldrin/kg body weight, dissolved in corn oil, 5 days/week, for 9 weeks. The animals were killed 24 h after the last dose, and the radioactivity in nine tissues was measured. More radioactivity was retained in the tissues by females than by males, except in the case of kidneys (where the female : male ratio was about 0.3 : 1). Adipose tissue was the main storage site for dieldrin. The lowest levels were present in spleen, brain, and heart, while higher levels were found in liver, lung, adrenals, and especially in the kidneys (Dailey et al., 1970).

In a study on Charles River rats, administered ^{14}C-dieldrin in the diet for 8 h, Matthews et al. (1971) found a high level of radioactivity in the kidneys. The same was found in the kidneys of male rats in the study by Iatropoulos et al. (1975).

In studies by Baron & Walton (1971), male Osborn-Mendel rats were fed diets containing 25 mg dieldrin/kg diet for 8 weeks. On the first 4 days of the 9th week, oral doses of ^{14}C-dieldrin were administered,

together with sufficient non-radioactive dieldrin to maintain a 24-h intake equivalent to 25 mg/kg diet. Groups of five rats were killed on days 1-4 of the 9th week. The remaining rats were divided into two groups, one group being fed the diet containing 25 mg dieldrin/kg and the other being given the control diet. An equilibrium level of 50 mg dieldrin/kg adipose tissue was reached by the 8th week. The concentration of dieldrin in the adipose tissue of the animals given the control diet in the 9th week declined rapidly during the subsequent 18 days. The rate of decline corresponded to a half-life of about 4-5 days. It was postulated that an active transport of dieldrin into and out of fat, differing from the mechanism for lipids, may have occurred (Baron & Walton, 1971).

Groups of two male and two female Sprague Dawley rats were administered dietary concentrations of 0.04 mg ^{14}C-dieldrin/kg, 0.04 mg ^{14}C-dieldrin/kg plus 0.16 mg dieldrin/kg, or 0.04 mg ^{14}C-dieldrin/kg plus 1.96 mg dieldrin (99%)/kg, for 39 weeks, and the animals were then killed. The daily intake of food was restricted to 12 and 15 g for female and male animals, respectively. In all three groups, the recovery of ^{14}C activity in whole carcasses, as a proportion of the total administered dose, was significantly higher in female rats (mean 6.9%) than in male rats (mean 2.1%) (Davison, 1973).

When single doses of 10 mg dieldrin/kg body weight (in corn oil) were administered orally to male Sprague Dawley rats, the concentration of dieldrin in the plasma attained a maximum value (500 µg/litre) after about 2 h. Up to 48 h after dosing, it fluctuated between 200 and 500 µg/litre, but then declined quite rapidly to about 10 µg/litre during the next 8 days. In the brain, the highest concentration (about 1 mg/kg) was attained after about 4 h; it remained essentially steady for a further 44 h, and then declined in a similar manner to that in the plasma. The concentration/time relationships for muscle, kidneys, and liver were similar to those for the brain. A slower approach to a maximum value was observed in retroperitoneal fat, the 4 h and 24 h concentrations being about 10 and 40 mg dieldrin/kg fat, respectively. After 48 h, the concentration in fat declined in a similar manner as did those in the plasma and brain (Hayes, 1974).

Moss & Hathway (1964) administered ^{14}C-dieldrin intraperitoneally to rats, and determined the partition of radioactivity between plasma and erythrocytes. The ratio (plasma : erythrocytes) 2 h after dosing was 2.1 : 1; 4 days after dosing, it was 1.6 : 1, though the activities had declined by 49% and 32%, respectively, in plasma and erythrocytes.

(c) *Rat and rabbit* in vitro

The partition of ^{14}C-dieldrin-related activity between the soluble proteins of blood and the cellular components has been studied *in vitro*. The radioactivity was located mainly in the erythrocytes and plasma of rats and rabbits, whereas that in leukocytes, platelets, and erythrocyte membranes was much lower. The activity in the erythrocytes was associated with haemoglobin and an unknown constituent. The radio-

activity in the serum of rats (electrophoresis at pH 8.6) was associated with pre- and post-albumin, whereas that in rabbit serum was associated with albumin and α-globulin. Electrophoresis at pH 4.5 gave a pattern which was similar in rats and rabbits but the patterns at pH 4.5 were different from those at pH 8.6; there were four incompletely separated peaks of radioactivity (Moss & Hathway, 1964).

It has been demonstrated *in vitro* that the transport of dieldrin between rat hepatocytes and the extracellular medium is a much faster process than the metabolic transformation reaction in hepatocytes (Ichinose & Kurihara, 1985).

(d) *Dog*

In studies by Richardson et al. (1967b), three beagle dogs were fed a diet containing dieldrin (equivalent to 0.1 mg/kg body weight) for 128 days, and two animals were used as controls. The concentration of dieldrin in the blood increased in an approximately curvilinear manner up to day 93. There were fluctuations during the next 5 weeks, but any increase was small relative to that during the first 5 weeks of the study (a mean plateau concentration of about 130 μg/litre blood appears to be consistent with the data). One week after the dieldrin diet was discontinued, the dogs were killed and samples of blood, fat, heart, liver, kidneys, pancreas, spleen, lung, and muscle were taken for analysis. The mean concentrations of dieldrin in the organs and tissues were 150 μg/litre in blood, 1090 μg/kg in the heart, 4420 μg/kg in liver, 2330 μg/kg in kidneys, 14 030 μg/kg in pancreas, 710 μg/kg in spleen, 1227 μg/kg in lungs, 25 333 μg/kg in fat, and 566 μg/kg in muscle. The mean partition ratio fat/blood was 161. There was a highly significant linear relationship between the logarithm ($\log_{10}$) of the concentration of dieldrin in the blood and the logarithm ($\log_{10}$) of the length of the dosing period.

Six mongrel dogs (four males, two females) were orally dosed daily with dieldrin dissolved in corn oil for 5 days (1 mg dieldrin/kg body weight) and thereafter at doses of 0.2 mg/kg body weight for a further 54 days. Six control animals were used. Samples of blood were taken twice weekly from day 7 onwards and analysed for dieldrin content. The concentration of dieldrin in the blood of all the animals showed a small but significant increase from day 7 to day 59. Biopsy samples of subcutaneous fat were obtained on days 16 and 50. The fat/blood partition ratio on day 16 was 216 and that on day 50 was 117 (Keane & Zavon, 1969b).

In studies by Walker et al. (1969b), groups of five male and five female beagle dogs were given daily oral doses (by capsule in olive oil) of dieldrin (99%) at 0, 0.005, or 0.05 mg/kg body weight, for 2 years. The concentration of dieldrin in the blood increased in all animals during the first 12 weeks of the study and reached an approximately steady state value from week 18 to about week 76. During the last 6 months, there were significant deviations from the apparent asymptotic value for weeks 18-76. The reasons for this are not under-

stood, but there was also an upward tendency in the concentration of dieldrin in the control animals. There were statistically significant relationships between the concentrations of dieldrin in the diet (calculated from the daily oral dose) and those in the blood, brain, liver, and adipose tissue. The tissue uptake ratios were similar in both males and females, those for males being (concentration of dieldrin in diet = 1): blood, 0.06; brain, 0.22; liver, 4.4; and adipose tissue, 10.0. There were also statistically significant relationships between the concentrations of dieldrin in the blood and those in the other three tissues. The partition ratios (concentration of dieldrin in blood = 1) for the male dogs were: brain, 3.7; liver, 10; and adipose tissue, 169.

(e) *Monkey*

Two female rhesus monkeys were given an intravenous injection of ^{14}C-dieldrin (2.5 mg/kg body weight) in 1,2-propylene glycol and two male rhesus monkeys received, respectively, a single oral dose of ^{14}C-dieldrin at 0.5 or 0.36 mg/kg body weight. The females were killed 75 days after dosing and the males 10 days after dosing. With both routes of administration, the highest radioactivity was found in the adipose tissue, bone marrow, and liver. The activity in the brain was relatively low (about 2% of that in the adipose tissue). Metabolites were not found in the organs, but they were present in the bile (Mueller et al., 1975b).

In studies by Mueller et al. (1979), groups of 1-5 male rhesus monkeys were fed diets containing 0, 0.01, 0.1, 0.5, or 1 mg dieldrin/kg diet for 70-74 months. Two other rhesus monkeys were fed 5 mg dieldrin/kg diet for 4 months, 2.5 mg/kg for the next 5 months, and 1.75 mg/kg for a further 64 months. One rhesus monkey was fed 5 mg/kg for 4 months, 2.5 mg/kg for the next 5 months, and then 1.75 mg/kg diet, this dietary concentration gradually increasing until after 23 months from the onset of the trial it had reached 5 mg/kg (this feeding level being continued for a further 46 months). The mean concentrations of dieldrin in the livers of these monkeys were: in the 0.01 mg/kg group, 1.2 mg/kg; in the 0.1 mg/kg group, 1.3 mg/kg; in the 0.5 mg/kg group, 4.1 mg/kg; in the 1 mg/kg group, 5.5 mg/kg; in the 5.0/2.5/1.75 mg/kg group, 13.6 mg/kg; and in the one animal fed 5, 2.5, 1.75, and 5 mg/kg diet, 23.3 mg/kg. The distribution of dieldrin in liver subcellular fractions was determined by isotope dilution. The highest proportion of dieldrin was present in the microsomal fraction, with about 60% of the total in the subcellular fractions, and about 12.5% of the total in the soluble fraction. The remaining 3 fractions (nuclear, mitochondrial, and lysosomal) contained similar proportions, about 9% in each fraction (Wright et al., 1978). The modes of distribution of dieldrin (and metabolites) in rhesus monkeys were similar to those in rats.

6.2.2.2 Transplacental transport

(a) *Mice*

Pregnant mice were each given 0.4 mg ^{14}C-dieldrin intramuscularly and its distribution was studied by means of whole-body autoradiography. The highest values for ^{14}C activity were found in the fat, liver, intestines, and mammary glands, while moderate activity was found in the ovaries and brain. Moderate levels were also found in fetal liver, fat, and intestines, indicating transfer across the placenta (Baeckstroem et al., 1965).

(b) *Rat*

Transplacental transfer of ^{14}C-dieldrin was found in Sprague Dawley rats that were administered the compound intravenously (tail vein) on days 13, 16, or 21 of gestation. Relatively high levels were present in the fetus 5 min after injection, and they continued to increase for 40-60 min after which they declined by about 60% in 2-3 days. The transfer of ^{14}C activity was greater during late gestation. Phenobarbital pretreatment decreased the amount of radioactivity in the fetus (Eliason & Posner, 1971).

(c) *Rabbit*

The transport of ^{14}C activity from mother to blastocyst and from mother to fetus was demonstrated in pregnant New Zealand white rabbits following intravenous injection of ^{14}C-dieldrin into the ear vein (0.14 mg dieldrin/kg body weight). The ^{14}C activity in blastocysts of rabbits injected on the 6th day of pregnancy was generally low compared with the activity in maternal blood. However, 40-60 min after dosing, the activities were very similar. After 60 min, the ^{14}C activity in blastocysts declined rapidly, relative to that in maternal blood. In rabbits dosed intravenously on the 16th day of pregnancy, the transfer of ^{14}C activity was transplacental, no activity being detected in allantoic or amnionic fluids. The ratio of ^{14}C activity in the whole fetus to that in the maternal blood remained fairly constant up to 100 min after dosing, suggesting an equilibrium between the mother and the fetus. The results for rabbits injected on the 24th day of pregnancy indicated that two-way placental transport of ^{14}C activity was occurring (Hathway et al., 1967).

6.2.2.3 Domestic animals

Studies on domestic animals, in which body tissues, milk, or eggs were analysed, indicate that the pharmacokinetics of aldrin and dieldrin in these species are broadly similar to those in laboratory animals (Gannon et al., 1959a,b; Ivey et al., 1961; Williams et al., 1964; Cummings et al., 1966; Davison, 1970, 1973; Brown et al., 1974).

None of the known metabolites of dieldrin were detected in the body tissues or milk of cows fed ^{14}C-dieldrin in their diet for 41 days (Baldwin, 1972; Potter et al., 1972).

Dieldrin accumulation ratios (concentration in tissues, milk, or eggs relative to the concentration in the diet) are given in Table 24.

Table 24. Accumulation ratios for dieldrin in domestic animals

Animal	Sample analysed	Feeding period (months)	Accumulation ratio	Reference
Cow	renal body fat	3	2.43	Gannon et al. (1959a)
	whole milk	3	0.18	Gannon et al. (1959b)
	milk fat	12	6	Vreman et al. (1980)
Hen	renal body fat	3	43.1	Gannon et al. (1959a)
	body fat	13	10-24	Brown et al. (1974)
	egg	7	1.5	Cummings et al. (1966)
Hog	renal body fat	3	2.9	Gannon et al. (1959a)
Hog (young)	body fat	2 (body weight increase, 290%)	1.14	Dobson & Baugh (1976)
Lamb	renal body fat	3	1.05	Gannon et al. (1959a)
Steer	renal body fat	3	3.95	Gannon et al. (1959a)

6.2.2.4 Human volunteers

A study on volunteers was carried out in which daily oral doses of 0, 10, 50, or 211 µg dieldrin/man (three men per dose group) were given in gelatine capsules for 18 months (Hunter & Robinson, 1967; Hunter et al., 1969). The control group comprised four men. From the 18th month to the 24th month, the volunteers given 50 µg continued to receive dieldrin at this level, whereas all other volunteers, including those in the control group, received 211 µg/day. The concentrations

of dieldrin in the blood of the volunteers given 211 μg dieldrin daily throughout the study had increased 10-fold by the end of 18 months to 15 μg/litre, while that of the group given 50 μg/day had increased 4-fold to 5 μg/litre. The increase in the case of the group given 10 μg/day was slight; after 5 months, a 2-fold increase had occurred to 3 μg/litre, and there was little change during the subsequent 13 months. From 21-24 months, the concentrations of dieldrin in the blood of the groups given 50 or 211 μg/day fluctuated, but there was no indication of a significant continuing increase in either set of samples. The concentrations of dieldrin in adipose tissue after 15 months had increased approximately 3-fold in the group given 10 μg/day (mean: 0.4 mg/kg tissue), approximately 4-fold in the group given 50 μg/day (mean, 0.7 mg/kg tissue), and approximately 11-fold in the group given 211 μg/day (mean, 2 mg/kg tissue). The concentrations of dieldrin in the adipose tissue showed an apparent increase at 24 months relative to those at 18 months, but this may be partly related to the fact that the samples were taken by needle biopsy at 24 months. Overall, it was concluded that the results for the groups given 50 or 211 μg/day indicated an approach to an upper limit (asymptote), the relationship being of the form:

$$\text{concentration of dieldrin in tissues} = A - Be^{-kt}$$

where A is the asymptotic value attained as time (t) approaches infinity, and B and k are empirical constants (k corresponds to the first-order rate constant for the elimination of dieldrin). The mean values of the asymptote (A) for blood were 5.9 μg/litre in the group given 50 μg/day and 20.2 μg/litre in the group given 211 μg/day. Relationships were also derived between the daily intake of dieldrin and the steady-state (asymptotic) values for blood and adipose tissue, respectively:

$$\text{amount of dieldrin ingested } (\mu g/day) = \frac{\text{concentration of dieldrin in blood } (\mu g/litre)}{0.086}$$

$$= \frac{\text{concentration of dieldrin in adipose tissue } (mg/kg)}{0.0185}$$

It is emphasized that these relationships correspond to the condition of a steady state between intake, storage, and elimination of this compound. The distribution ratio (concentration of dieldrin in adipose tissue/concentration in blood) was 136 (Hunter & Robinson, 1967; Hunter et al., 1969).

6.2.2.5 General population

De Vlieger et al. (1968) collected samples of brain tissue, liver, and adipose tissue from 11 routine autopsies in the Netherlands, and found a significant relationship between the dieldrin concentrations in the various tissues. They suggested a tentative scheme for the distribution of dieldrin between the various tissues. This scheme is reproduced in Fig. 1, but the figures have been updated by recalculation conforming to the latest empirical formula of Hunter et al. (1969) (Jager, 1970).

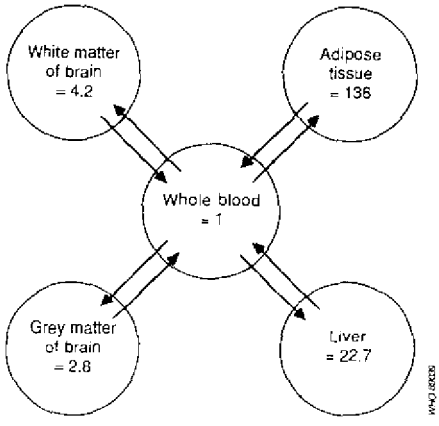

Fig. 1. Distribution of dieldrin between blood and tissues in man. From: Jager (1970), modified from De Vlieger et al. (1968).

6.2.3 Photodieldrin (and major metabolites of dieldrin)

6.2.3.1 Laboratory animals

(a) *Rat*

Brown et al. (1967) fed rats diets containing 3 or 10 mg photodieldrin/kg diet for 26 days, the 10 mg/kg-group then being fed a control diet for a further 2 or 8 days. The half-life of photodieldrin in adipose tissue was calculated to be 1.7 days in male rats and 2.6 days in female rats. The storage ratio in adipose tissue was considerably higher in females (1.3) than in males (0.5).

In studies by Dailey et al. (1970), young rats were given daily oral doses of 5 μg ^{14}C-photodieldrin per rat, orally or intraperitoneally, for 12 weeks. Although there was considerable variation, the radioactivity in the tissues of female rats was 3-10 times greater than in male rats, except in the kidneys, where the ^{14}C activity in males was about 13 times that in females, regardless of the route of administration.

When rats were fed diets containing 0, 0.1, 1, 10, or 30 mg photodieldrin/kg diet for 13 weeks, the concentrations of photodieldrin in the body tissues of female rats receiving up to 10 mg/kg diet were 2-15 times greater than those in males. High concentrations of pentachloroketone (PCK) were found in the kidneys of male rats receiving 30 mg/kg (276 mg PCK/kg kidney weight compared with 29 mg photodieldrin/kg). The corresponding concentrations for females were lower: 13.55 mg PCK and 1.85 mg photodieldrin per kg kidneys (Walker et al., 1971).

In studies by Walton et al. (1971), groups of weanling rats (Charles River strain) were fed photodieldrin at concentrations of 0, 1, 5, or 25 (decreased to 12.5 mg) mg/kg diet for 90 days, while other groups of rats were fed dieldrin at the same concentrations. The concentrations of both photodieldrin and dieldrin in the adipose tissue of female rats were higher than in male rats.

(b) *Dog*

Following the administration of a single oral dose of photodieldrin to one male and one female dog (160 and 120 mg/kg body weight, respectively), the concentrations of photodieldrin in the female dog's tissues, with the exception of the liver, were much higher than those in the male (Brown et al., 1967).

The concentrations of photodieldrin in the liver and adipose tissue of dogs fed photodieldrin at 0, 0.005, 0.05, or 0.2 mg/kg body weight for 3 months were related to the dose rate and similar in males and females. In the kidneys, the concentrations of photodieldrin and its metabolite (PCK) were similar in male and female dogs and much lower (of the order of 0.1-0.2 mg/kg kidneys) than in rats (Walker et al., 1971).

6.2.3.2 Human beings

In samples of human adipose tissue, kidneys, and breast milk, no residues of photodieldrin or the pentachloroketone metabolite were detected (Robinson et al., 1966b; Anon., 1973, 1974a,c).

6.3 Metabolic Transformation

6.3.1 Aldrin and dieldrin

The initial and major step in the biotransformation of aldrin is the formation of the corresponding epoxide dieldrin. There is considerable evidence that this transformation is mediated by mixed-function monooxygenases, sometimes called aldrin-epoxidase, which have been found in a wide variety of organisms, e.g., plant roots (Mehendale et al., 1972), insects (Krieger & Wilkinson, 1969; Terriere & Yu, 1976), fish (Burns, 1976), and various mammals, including man. The endoplasmic reticulum of the liver of vertebrates is an important site of these enzymes.

6.3.1.1 Laboratory animals

(a) *In vitro*

The *in vitro* metabolism of ^{14}C-dieldrin by unwashed microsomes from a male rat pretreated with phenobarbital has been investigated by Hutson (1976). The addition of uridine 5′-diphosphoglucuronic acid (UDPGA) increased the yield of a polar metabolite. The 9-hydroxy derivative was not detected either in the presence or absence of UDPGA, and investigation of the polar metabolite indicated that it was the glucuronide of the 9-hydroxy derivate. The rate of conversion of dieldrin to the glucuronide of 9-hydroxy dieldrin, measured after 30 min incubation, was 0.0028 nmols/min per mg protein. In the absence of UDPGA, the conversion of dieldrin to 9-hydroxy dieldrin could not be detected, and the rate was estimated to be less than 0.0002 nmols/min per mg protein.

A rat hepatocyte culture suspension effectively epoxidized aldrin to dieldrin (Kurihara et al., 1984).

(b) *In vivo*

From the results of a comparative metabolic study on rat and mouse (section 6.2.2.1), it appears that the main differences between the species are a more rapid metabolism of dieldrin in rats, a much greater production of the pentachloroketone by rats, and the production of small amounts of polar urinary metabolites by mice. The two strains of mice (CF1 and LACG) were similar to one another in most, but not all, parameters measured. Thus, the distinguishing features of the metabolism of dieldrin in CF1 mice, unique to this strain and which could account for tumour initiation in mice, have not been found. The hydroxylation of dieldrin in mice is less efficient than in rats, and the formation of the glucuronide of 9-hydroxy dieldrin is the result of the consecutive action of hepatic microsomal monooxygenase and uridine diphosphoglucuronyl transferase. The 9-hydroxy dieldrin formed initially is probably bound to the microsomal membrane, and the availability of UDPGA may be rate-limiting in the overall formation of the glucuronide. The binding of 9-hydroxy dieldrin to the microsomal membrane may inhibit the first oxidative step, unless the concentration of bound metabolite is reduced by conversion to the water-soluble glucuronide (Hutson, 1976).

Of the species studied, rats, mice, rabbits, sheep, rhesus monkey, and chimpanzee (Feil et al., 1970; Mueller et al., 1975a), the major metabolite, except in the case of the rabbit, is the 9-hydroxy derivative (Fig. 2, compound VI). This derivative is found in the faeces and free or conjugated in the urine. Excretion of the glucuronide occurs via the bile duct into the lower intestines, where it is converted to the free 9-hydroxy compound. The initial chemical identification of this metabolite was based on a combination of physical and chemical methods (Richardson et al., 1968; Baldwin et al., 1970; Feil et al.,

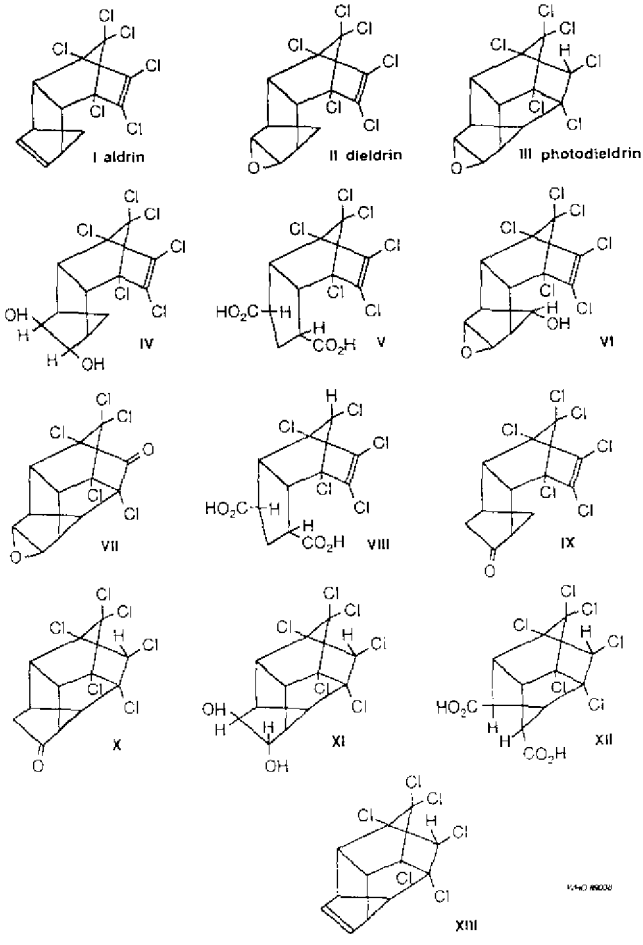

Fig. 2. Chemical structures of aldrin, dieldrin, photodieldrin, and their metabolites. For trivial structures see Appendix 1.

1970), but it was subsequently synthesized and the structure confirmed (Bedford & Harrod, 1972a). The stereochemical configuration of the 9-hydroxy group has been shown to be *syn* oriented with respect to the 6, 7-epoxy group (Baldwin et al., 1973).

The other metabolites, the chemical identities of which have been rigorously established, are detailed below.

(a) The *trans*-6,7-dihydroxy compound (Fig. 2, compound IV) is formed by the hydration (formal) of the epoxide ring of dieldrin (Korte & Arent, 1965). This compound is a major metabolite in rabbit urine, but of relatively minor importance in other species. The formation of the *cis*-diol by rat microsomes has been demonstrated, together with its epimerization to the *trans*-diol (McKinney et al., 1973). Both the *cis*- and *trans*-diols have been synthesized (Korte & Arent, 1965; Chau & Cochrane, 1970b; Bedford & Harrod, 1972b).

(b) The dicarboxylic acid (Fig. 2, compound V) is derived from the dihydroxy metabolite (Baldwin et al., 1972; Oda & Mueller, 1972). This compound has also been synthesized (Buechel et al., 1966), and has been shown to undergo further degradation (formation of two isomers of a monodechlorinated derivative) after intravenous injection into male and female rats (Lay et al., 1975).

(c) The bridged pentachloroketone (PCK) (Fig. 2, compound VII) is mainly found in the urine and kidneys of male rats, but, even in rats, it is a minor metabolite (Damico et al., 1968; Klein et al., 1968; Richardson et al., 1968). In other species, it is a very minor metabolite of dieldrin. It is also a metabolite of photodieldrin (Klein et al., 1970), and has been synthesized (Bedford & Smith, 1978).

The Chemical Abstract or Von Baeyer AG/IUPAC names of aldrin, dieldrin, photodieldrin, and metabolites are given in Appendix 1.

Methods for the quantitative determination of the four metabolites are available. They depend on the availability of authenticated analytical standards (Ludwig & Korte, 1965; Richardson, 1971; Baldwin et al., 1972).

6.3.1.2 Human studies

A metabolite of dieldrin detected in human faeces has been shown to be the 9-hydroxy derivative (Richardson & Robinson, 1971).

6.3.1.3 Non-domestic organisms

The conversion of aldrin to dieldrin was studied in algae (*Chlorella* and diatoms) and protozoa (Dinoflagellates and mixed protozoa) after exposure for 24 h to 0.1 mg aldrin/litre. The amount of dieldrin present in the cultures was of the order of 0.06-0.2 µg/litre). The amounts of dieldrin were greater in the protozoa than in the algae; it was concluded that these planktonic species have enzyme systems that epoxidize aldrin (Khan et al., 1972b).

The conversion of aldrin to dieldrin in 12 species of fresh-water invertebrates has been compared. Ten species were exposed for 2 h to concentrations of 0.1 or 0.25 mg aldrin/litre, and two species of molluscs were exposed to 0.25 mg aldrin/litre for 4 h. The concentrations of dieldrin relative to aldrin in the whole bodies of eight

species from four phyla (Coelenterata, Platyhelminthes, Annelida, and Arthropoda) were in the range 1.03-8.48%. In two species of Insecta (dragon fly nymphs and *Aedes* larvae), the values were 24.9% and 42.4%, respectively. The two species of molluscs had dieldrin concentrations (relative to aldrin) of 17-19% (Khan et al., 1972b).

In a study on an ostracod *(Chlamydotheca arcuata)* exposed to ^{14}C-labelled aldrin (5.5-11.2 µg/litre), aldrin was readily converted to dieldrin, 83% conversion occurring within 24 h. The elimination of aldrin and dieldrin appeared to involve both passive and active processes, and it was concluded that dieldrin was eliminated more rapidly after dieldrin exposure than after aldrin exposure (Kawatski & Schmulbach, 1972).

A number of *in vitro* studies have been carried out concerning the influence of these insecticides on mixed-function oxidase activity. The epoxidation of aldrin to dieldrin by this enzyme system has been demonstrated in crayfish *(Cambarus)* (Khan et al., 1972a,b), in snail *(Lymnea palustris)* and clam (Khan et al., 1972b), and in midge larvae *(Chironomus riparius)* (Estenik & Collins, 1979).

The conversion of aldrin to dieldrin by lobsters *(Homarus americanus)* was reported by Carlson (1974).

The mixed-function oxidase activities in five species of fresh water fish, as measured by the conversion of aldrin to dieldrin, were investigated by Ludke et al. (1972). The fish were exposed to aldrin (50 µg/litre) for 4 h, and the concentrations of aldrin and dieldrin in the liver were determined. Contrary to earlier reports, the conversion by epoxidation of aldrin to dieldrin in fish may be the rule rather than an exception.

The epoxidation of ^{14}C-aldrin to dieldrin in susceptible and resistant mosquitofish *(Gambusia affinis)* has been investigated. The fish were exposed to 5 µg ^{14}C-aldrin/litre for 4 or 8 h and the concentration of aldrin and dieldrin in liver and brain were determined. The concentration of dieldrin (expressed in terms of protein content) was significantly higher in the livers of resistant fish than in susceptible fish). It was concluded that resistant mosquitofish convert aldrin to dieldrin and/or water-soluble compounds at a greater rate than susceptible mosquitofish (Wells et al., 1973).

In studies by Addison et al. (1976), Atlantic salmon fry *(Salmo salar)* were injected intramuscularly with ^{14}C-aldrin, to initial whole-body concentration of 5 mg/kg. The fish were maintained in flowing fresh water, and were removed at five intervals up to 56 days for the measurement of whole-body residues. The time required for 50% epoxidation of aldrin was between 1 and 2 days. Less than 10% of the radioactivity remained in the fish at the end of the exposure. It was concluded that there was rapid elimination either of unchanged aldrin or its epoxide, dieldrin, from the fish.

6.3.2 Photodieldrin (and major metabolites of dieldrin)

6.3.2.1 Rat

Besides unchanged photodieldrin, bridged pentachloroketone (PCK) (Fig. 2, compound VII), a metabolite of photodieldrin, was isolated from the brain, liver, adipose tissue, and blood of rats (Carworth Farm, type E) fed diets containing 10 or 30 mg photodieldrin/kg for 13 weeks (Baldwin & Robinson, 1969).

In studies by Klein et al. (1970), Osborne-Mendel rats were given ^{14}C-photodieldrin, orally or intraperitoneally, 5 days/week, for 12 weeks, and urine was collected quantitatively every day. A metabolite was found in the urine of male rats and shown to be PCK. Small amounts of other (unidentified) more polar urinary metabolites were also present.

6.3.2.2 Monkey

Metabolites were detected in the urine and faeces of a female rhesus monkey given daily oral doses of 0.8 mg ^{14}C-photodieldrin/kg body weight for 175 days. Two metabolites were identified in the urine: the *trans*-diol (Fig. 2, compound XI) and its glucuronide conjugate. A faecal metabolite was tentatively identified as the diol. A third metabolite was present in both urine and faeces, and it was suggested that this might be a monohydroxy derivative of photodieldrin (Nohynek et al., 1979).

6.4 Elimination and Excretion

6.4.1 Aldrin

6.4.1.1 Rat

When male rats were given daily oral doses of 4.3 μg ^{14}C-aldrin (equivalent to about 0.2 mg aldrin/kg diet) for 3 months, the radioactivity in the urine increased from about 2% of the dose of aldrin during the first week to about 10% during the 12th week. In the faeces, the excreted radioactivity increased from about 48% during the first week to about 93% during the 12th week. After about 8 weeks, a saturation level was reached (i.e., there was a balance between the rates of intake of aldrin and excretion of aldrin plus aldrin-related materials). Extracts of urine and faeces were examined by paper chromatography. Because the urine was probably contaminated by faeces in the metabolism cages, only the trend is given. In both faeces and urine, the aldrin content decreased during the 12 weeks. The hydrophilic metabolites increased, reaching 75% (faeces) and 95% (urine) of total radioactivity after 12 weeks. The level of dieldrin was more or less constant (Ludwig et al., 1964).

6.4.2 Dieldrin

6.4.2.1 Laboratory animals

As described in section 6.2.2.1, Hutson (1976) studied the comparative metabolism of dieldrin in CFE rats and two strains of mice after a single oral dose of 3 mg/kg body weight ^{14}C-dieldrin. The excretion of ^{14}C activity in the faeces of the rats was 62.4% of the administered dose in the non-pretreated group and 69% in the dieldrin-pretreated group. In the case of the CF1 mice, the pretreatment period did not have any effect on the faecal excretion (51.5%), whereas, in the LACG mice, the faecal excretion of ^{14}C activity increased from 27.2% for the non-pretreated group to 48.8% for the 4-week pretreated group. The total ^{14}C activity excreted in the urine of the two strains of mice was low (0.42-2.6% of dose) compared with that in the urine of male rats (5.5-6.6%). In both species of rodents, the faeces was the major route of excretion of ^{14}C activity. In the urine of both the male CFE rat and the male CF1 mice, the amount of the dicarboxylic acid metabolite in the urine was small compared with that of pentachloroketone plus dieldrin, while in the male LACG mice, the amount of the acidic metabolite was twice that of pentachloroketone plus dieldrin. Both strains of mice excreted, proportionally, much larger amounts of a polar (unidentified metabolite) in the urine than did the CFE rats. In the faeces of the male CFE rats (no pretreatment), the major component was the 9-hydroxy derivative. This was also found by Matthews et al. (1971). However, in both mouse strains (no pretreatment), this compound was a minor metabolite, but it became the major product in the dieldrin-pretreated group. In isolated liver microsomes, most of the ^{14}C activity appeared to be present as dieldrin, and the 9-hydroxy metabolite was not detected.

A number of other studies on the excretion of dieldrin via urine and/or faeces have been carried out. Dailey et al. (1970) found that male rats excreted higher levels of ^{14}C radioactivity via urine and faeces than females. Davison (1973) confirmed this in a study lasting 39 weeks. Maximal excretion of ^{14}C activity occurred in the 6th week in both sexes, regardless of the amount of dieldrin given. A steady state was reached and maintained from the 6th to the 39th week.

In studies by Robinson et al. (1969), rats were fed a diet containing 10 mg dieldrin/kg diet for 8 weeks. The decline in the concentration of dieldrin in blood, brain, liver, and adipose tissue was studied during the subsequent 12 weeks when a control diet was fed. There was an initial rapid decline in the dieldrin concentration during the first 10 days of the post-exposure period in the blood, liver, and brain, followed by a slower decline. The changes in the concentration of dieldrin in the brain, adipose tissue, blood, and liver corresponded to biological half-lives of 3 to about 10 days.

When male and female rats were administered 3 g of diet containing 10 mg ^{14}C-dieldrin/kg diet, followed by a control diet *ad libitum*, ^{14}C activity in the kidneys of male rats was 10-fold higher than in

the female rats (the animals were killed 9 days after administration of ^{14}C-dieldrin). Most of the activity in the male kidneys was due to pentachloroketone, whereas, in the female kidneys, only dieldrin was detected (Matthews et al., 1971).

The excretion of ^{36}Cl activity by female rats dosed intravenously (680 μg/h for 2.5-5 h; total doses of 8-16 mg/kg body weight) with ^{36}Cl-dieldrin has been studied. The ^{36}Cl activity detected in the faeces was about 7 times that found in the urine, indicating excretion via the bile (Heath & Vandekar, 1964).

Comparable results were found by Cole et al. (1970), who gave male rats a single intravenous dose of 0.25 mg ^{14}C dieldrin/kg body weight. Similar doses of ^{14}C-dieldrin were administered intravenously to male rats with bile fistulas. About 30% of the administered ^{14}C activity was excreted via the bile during the first 24 h after dosing, and after 4 days a total excretion of about 60% had occurred. Isolated perfused rat liver preparations were also investigated; some 20% of the original perfusate dose was collected in the bile over a period of 8 h.

Rapid excretion of ^{14}C-dieldrin (or its metabolites) from isolated perfused rat livers via the bile of rats has also been reported by Klevay (1970), the rate of excretion by male rats being about 3 times as rapid as that by female rats.

In studies by Mueller et al. (1975a), mice, rats, rabbits, rhesus monkeys, and one chimpanzee were given a single oral dose of 0.5 mg/kg body weight ^{14}C-dieldrin, and urine and faeces were collected for 10 days. For all species except the rabbit, the main route of excretion was the faeces. The faecal excretion of unchanged dieldrin was high in the first 48 h and then declined rapidly. The urine samples contained only metabolites of dieldrin. The mean total amount of radioactive material excreted (males and/or females) in faeces and urine within 10 days after dosing (expressed as percentage of administered dose) was 37% in mice, 11% in rats, 2% in rabbits, 20% in rhesus monkeys, and 6% in the chimpanzee. In all five species, 9-hydroxydieldrin and 4,5-aldrin-*trans*-dihydrodiol were the major metabolites. The metabolism in the rat seems to be comparable to that of primates; however, mice and rabbits showed the opening of the epoxide to diol as the predominant reaction.

6.4.2.2 Human studies

The occurrence of a neutral metabolite of dieldrin in human urine in amounts indicative of exposure to aldrin/dieldrin was reported by Cueto & Hayes (1962) and Cueto & Biros (1967).

Quantitative estimates of the amounts of a metabolite of dieldrin, 9-hydroxy-dieldrin, in the faeces of seven workmen occupationally exposed to aldrin/dieldrin and five male members of the general population have been made. The average concentration of the 9-hydroxy derivative in 24-h collections of faeces of the seven workmen was 1.74 mg/kg (range, 0.95-2.80 mg/kg), whereas the average concentration in faeces of the five members of the general population was 0.058 mg/kg

(range, 0.033-0.12 mg/kg). Dieldrin was present in the faeces of the workmen (average concentration, 0.18 mg/kg), but, in samples from the general population, it was below the limit of detection. Examination of the urine of five of the workmen indicated that this route of elimination of dieldrin and four known metabolites was minor. It was concluded that the 9-hydroxy-dieldrin in the faeces represented the major excretory pathway of dieldrin from male human beings. It should be noted, however, that the urine was not examined for glucuronide or other conjugates of the hydroxy metabolites). There was good correlation between the estimated daily intake of dieldrin (calculated from the concentrations of dieldrin in the blood) and excretion in faeces of total equivalent dieldrin (Richardson, 1971). This relationship is based on a number of assumptions, and it is probably more relevant that the concentration of the 9-hydroxy-dieldrin in the faeces (produced by the metabolism of absorbed dieldrin) is significantly related to the concentration of dieldrin in the blood, which is a measure of the body burden arising from absorption of aldrin plus dieldrin.

When ^{14}C-Dieldrin was applied in acetone (4 $\mu g/cm^2$) once to the forearm of volunteers, 7.7% of the applied ^{14}C activity was excreted in the urine over a 5-day period. A single intravenous injection of ^{14}C-dieldrin resulted in 3.3% being excreted in the urine over a 5-day period (Feldman & Maibach, 1974).

6.4.3 Photodieldrin (and major metabolites of dieldrin)

6.4.3.1 Rat

In studies by Dailey et al. (1970), young rats were given daily doses of 5 g ^{14}C-photodieldrin, orally or intraperitoneally, for 12 weeks. Urine and faeces were collected daily and pooled in weekly groups. The excretion of ^{14}C activity via the urine of females was considerably less than that by males, by either method of dosing. The ^{14}C activity in urine after oral and ip administration increased slowly during the 12 weeks (males about 10% and females 5%), the highest levels in urine (up to 33%) being found in males dosed intraperitoneally. Faecal excretion of ^{14}C activity was initially lower in females, but greater during the latter half of the study (of the order of 20-40%). In males, during the whole study, it was about 30%.

6.4.3.2 Monkey

A juvenile female rhesus monkey was given daily oral doses of 2 mg ^{14}C-photodieldrin (equivalent to 0.8 mg/kg body weight), and the treatment was continued until, between days 70 and 76, the daily excretion of ^{14}C activity was in balance with the daily intake. When dosing ceased, the animals had retained about 50% of the cumulative dose of photodieldrin. Collection of excreta was continued for a further 100 days, during which a further 30.1% of the dose, administered during the 76-day period, was excreted. During the period of

dosing, a major part of the faecal ^{14}C excretion consisted of photodieldrin (probably indicating incomplete absorption in the gastrointestinal tract), while 20-50% of the excreted activity was in the urine. After dosing ceased, 60% of the excreted ^{14}C activity appeared in the urine (Nohynek et al., 1979).

In studies by Nohynek et al. (1979), one male and one female juvenile rhesus monkey were given single intravenous doses of 4.5 mg ^{14}C-photodieldrin (2 mg/kg body weight). Urine and faeces were collected separately every 24 h, and the animals were killed after 21 days. Excretion of ^{14}C activity was high during the first 7 days (male, 39%; female, 27.3%, of the given dose). It then decreased rapidly and reached a nearly constant value of 0.2% of the administered dose. Approximately 45% (male) and 34% (female) of the dose had been excreted by day 21.

6.5 Retention and Turnover

6.5.1 Non-domestic organisms

A few studies have been carried out on the uptake and elimination of aldrin and/or dieldrin in invertebrates: marine clams *(Mya arenaria* and *Mercenaria mercenaria)* (Butler, 1971); naiad mollusc *(Amblema plicata)* (Fikes & Tubb, 1972); mussel *(Lampsilis siliquiodea)* (Bedford & Zabik, 1973); crab *(Leptodius floridanus)* (Epifanio, 1973); and ostracod *(Chlamydotheca arcuata)* (Kawatski & Schmulbach, 1972). The concentration of aldrin or dieldrin in organs and tissues increased rapidly during the first 1-2 weeks of exposure, but remained virtually constant thereafter. When the organisms were placed in clean water, the concentration declined in a (semi)-logarithmic manner in relation to time. The estimated half-life for the tested organisms varied, e.g., for *Lampsilis siliquiodea*, it was 4.7 days, whereas for *Amblema plicata*, it was about 3-4 weeks.

The elimination of ^{14}C-dieldrin from bluegills *(Lepomis macrochirus)* and goldfish *(Carassius auratus)* was studied by Gakstatter & Weiss (1967). The fish were exposed to 30 µg ^{14}C-dieldrin/litre (initial concentration) until toxic symptoms appeared (5-8 h), and were then placed in recovery aquaria together with unexposed fish. The water in the recovery aquaria was continuously renewed. Samples of five fish were taken on 10 different occasions during the recovery period. The ^{14}C activity in whole fish of both species, expressed as equivalent dieldrin, declined by about 90% within 16 days, the half-time for elimination being about 4 days. The control bluegills and goldfish accumulated a maximum equivalent dieldrin concentration of 0.29 and 0.22 mg/kg, respectively, on day 4 of the period in the recovery aquaria, indicating transfer of dieldrin or derived material from contaminated to uncontaminated fish.

In another study, the distribution of aldrin and dieldrin in the tissues of *Carassius auratus* was determined following an 8-h exposure to ^{14}C-aldrin (50 µg/litre) in a static study. After the exposure,

fish were placed in a continuously flushed aquarium for 32 days. Dieldrin was found in all tissues examined immediately after the exposure. The percentage of dieldrin in the total residues in the tissue increased with time, reaching about 95% on day 32 (except in visceral fat). During the recovery period, the total concentration of aldrin plus dieldrin in the blood declined from 2.1 mg/litre (as aldrin) to 0.4 mg/litre. The corresponding changes in the brain concentrations were 5.45 mg/kg to 2.3 mg/kg. Total residues in the nerve cord did not show a consistent decline and varied from 4.56 to 21.6 mg/kg throughout the 32-day period; however, these residues were determined by thin-layer chromatography, not by gas-liquid chromatography (Gakstatter, 1968).

The partitioning of ^{14}C activity into particulate fractions of the brain and liver of resistant and susceptible mosquitofish has been studied after exposure of the fish to ^{14}C-aldrin or ^{14}C-dieldrin. The ^{14}C activities in total brain, cell membrane, and five cellular fractions were significantly higher in susceptible fish than in resistant fish for both aldrin and dieldrin. However, this difference was much less marked in the case of the liver. It was suggested that a basic structural change in polarity exists in the myelin of resistant fish, which could provide a membrane barrier (Wells & Yarbrough, 1973).

The fate of dieldrin in the digestive tract of juvenile lake trout *(Salvelinus namaycush)* has been studied. Macerated trout flesh containing an average of 1.05 mg/kg was injected in the stomach. The decline in the dieldrin content of the stomach was parallel to that of the food from the stomach. Little or no dieldrin was found in the intestines (Stewart & Stein, 1974).

In studies by Chadwick & Brocksen (1969), groups of sculpins *(Cottus perplexus)* were exposed to 1.3 µg dieldrin/litre for 12 days, followed by removal to uncontaminated continuously renewed water. The concentration in whole fish declined in a curvilinear fashion from about 2.5 mg/kg fish to about 1 mg/kg fish in 60 days and to about 0.5 mg/kg fish in 90 days.

Sailfin molly *(Poecilia latipinna)* were exposed to 12 µg dieldrin/litre for up to 6 h by Lane et al. (1970). Two products, thought to be metabolites of dieldrin, were detected in the liver and other organs, and it was suggested that they were partially dechlorinated derivatives of dieldrin.

6.5.2 Biological half-life in human beings

The concentration of dieldrin in the blood of volunteers given oral daily doses for 2 years (section 6.2.2.4) was determined over a period of 8 months after termination of the deliberate exposure (Hunter et al., 1969). A small, but statistically significant, decline occurred, corresponding to a mean value of 369 days for the half-life of dieldrin in blood. However, there were significant differences between the rates of decline of the individual volunteers.

The concentration of dieldrin in the blood of 15 workmen was determined for a period of 3 years following termination of occupational exposure to aldrin/dieldrin (Jager, 1970). The mean half-life was 266 days.

When a state of equilibrium has not yet been reached, the *apparent* half-life will be much shorter, due mainly to a redistribution of dieldrin between compartments in the body.

6.5.3 Body burden and (critical) organ burden; indicator media

Whatever the route of exposure, the effect, if any, will be determined by the concentration of the chemical in the target organ or tissue. It has been shown that the distribution between the various tissues of mammals is fairly constant within and between species (Robinson & Hunter, 1966; Hunter & Robinson, 1967; Hunter et al., 1967; Robinson & Roberts, 1969; Walker et al., 1969b). Thus, at a state of equilibrium, the dieldrin level in the blood reflects the concentration of the active compound in the target tissues and therefore represents the best practical parameter for the internal exposure that is associated with a biochemical, clinical, or pathological effect. Since the biological half-life of dieldrin in human blood is known (266 days) (Jager, 1970), a reliable estimation of the blood level at the time of discontinuance of the exposure can be made. This, in turn enables, better than anything else, the evaluation of the likelihood of an observed symptom of disease or indisposition being associated with exposure to dieldrin. Also, the established mathematical relationship between the dieldrin level in the blood and the total daily equivalent oral intake thus enables, on the basis of the concentration of dieldrin in the blood, the evaluation of a current exposure or an exposure of a short time ago *vis-à-vis* the acceptable daily intake established by the FAO/WHO Joint Meeting on Pesticide Residues.

Determination of the dieldrin concentration in blood is the method of choice in monitoring exposed workers or the general population (section 9.2.1.1).

6.6 Appraisal

Aldrin is readily absorbed through the skin, by inhalation of the vapour, or into the circulating blood from the gastrointestinal tract. It has not been possible to determine the percentage of an ingested dose of aldrin or dieldrin that is actually absorbed into the body because of the intestinal hepatic biliary cycle. Work with human volunteers (Feldmann & Maibach, 1974) showed that absorption through the skin amounted to 7-8% of the applied dose. Inhalation studies with human volunteers (Beyermann & Eckrich, 1973; Bragt et al., 1984) suggested that about 50% of inhaled aldrin vapour is absorbed and retained in the human body. After absorption, it is rapidly distributed to the organs and tissues of the body, and a continuous exchange between the blood and other tissues takes place. In the meantime,

aldrin is readily converted to dieldrin, mainly in the liver but, to a much lesser extent, in some other tissues, e.g., the lungs (Mehendale & El-Bassiouni, 1975).

This conversion proceeds very rapidly. The livers of even 24-h-old rats, given oral doses of 10 mg aldrin/kg body weight, contained dieldrin 2 h after treatment (Farb et al., 1973). In the course of the next few hours, dieldrin and what little is left of the aldrin in blood and other tissues, concentrates more in the lipid tissues (Heath & Vandekar, 1964; Hayes, 1974). In human beings, aldrin is found rarely, if at all, in human blood or other tissues, except in cases with acute poisoning by accidental or intentional ingestion of massive doses.

Studies carried out with ^{14}C-labelled aldrin and dieldrin have shown that part of the ingested material is passed unabsorbed through the intestinal tract and eliminated from the body, part is excreted unchanged from the liver into the bile, part is stored unchanged in the various organs and tissues (particularly the adipose tissue), and part is metabolized in the liver to more polar and hydrophilic metabolites. These metabolites, in human beings and most animals, are excreted primarily via the bile in the faeces. It had also been shown that aldrin and dieldrin are both biodegraded into the same metabolites (Damico et al., 1968; Klein et al., 1968). The biodegradation products have been identified in the rat within 15 min after an intravenous injection (Moersdorf et al., 1963). Most of the currently available information on the biodegradation metabolism in mammals is based on studies with dieldrin on the mouse, rat, rabbit, sheep, dog, monkey, chimpanzee, and human beings (Ludwig et al., 1964; Datta et al., 1965; Korte, 1965; Korte & Arent, 1965; Richardson et al., 1967b, 1968; Klein et al., 1968; Matthews & Matsumura, 1969; Baldwin et al., 1970, 1972; Feil et al., 1970; Richardson & Robinson, 1971; Mueller et al., 1975a,b). Although there appear to be differences between species and, in the rat, differences between the sexes, the overall picture shows only quantitative variations between species.

In the species studied (with the exception of the rabbit) the major metabolite is the 9-hydroxy derivative. This is found in the faeces and free or conjugated in the urine. Three other metabolites have been found and identified in experimental animals:

(a) *trans*-6,7-dihydroxy derivative;
(b) dicarboxylic acid derived from the dihydroxy compound; and
(c) the bridged pentachloroketone (PCK).

The latter is also a metabolite of photodieldrin (Klein et al., 1970).

Only the 9-hydroxy compound was found in the faeces of seven occupationally exposed industrial workers (1.74 mg/kg) and five male members of the general population (0.058 mg/kg). Neither the 9-hydroxy compound nor the other metabolites have been found in human blood or other tissues. Dieldrin was present in the faeces of the workmen (average 0.18 mg/kg), whereas the concentrations in the samples from the general population were below the limits of detection. Examination

of the urine of five workmen indicated that urinary excretion of dieldrin and its four metabolites is minor relative to elimination of the 9-hydroxy metabolite via the faeces (Richardson, 1971).

The conversion of aldrin to dieldrin and the distribution and the subsequent deposition of dieldrin (mainly in lipid tissues) proceed much faster than the biodegradation and ultimate elimination of unchanged dieldrin and its metabolites from the body. At a given average intake of aldrin and/or dieldrin, dieldrin slowly accumulates in the body. This accumulation or "storage", however, does not increase indefinitely. As the concentration of dieldrin in the liver cells increases, the metabolizing enzyme activity in the microsomes increases, and so the rate of biodegradation of dieldrin, and hence the elimination from the body, is enhanced. Thus, the accumulation proceeds at an ever slower rate until the concentrations of dieldrin in blood and tissues approach upper limits of storage and an amount of dieldrin equal to the average daily intake is eliminated each day. These upper limits of storage are related to the daily intake. This has been demonstrated in rats and dogs (Walker et al., 1969b) and in human beings (Hunter & Robinson, 1967; Hunter et al., 1969). When the intake of aldrin/dieldrin ceases or decreases, the body burden decreases. The biological half-life in human beings is 9-12 months (Hunter & Robinson, 1967; Hunter et al., 1969; Jager, 1970). Significant relationships exist between the concentrations of dieldrin in the blood and those in other tissues of rats, dogs, and human beings (Hunter & Robinson, 1967; Deichmann et al., 1968; Keane & Zavon, 1969b; Hunter et al., 1969; Walker et al., 1969b).

Numerous investigations of the concentrations of dieldrin in body fat, blood, and other tissues from members of the general population and from special groups have been carried out in several countries. The results are summarized and discussed in section 5.2. The ratio of dieldrin concentrations in fat, liver, brain, blood is about 150 : 15 : 3 : 1.

Dieldrin penetrates the placenta and is present in the blood, fat, or other organs of the fetus, newborn babies, and infants (Table 22). The concentrations are much lower (by 50% or more) than those in adults. The ratio of dieldrin concentrations in blood, brain, liver, and fat in infants is not different from that ratio in adults (Fiserova-Bergerova et al., 1967; Casarett et al., 1968). Dieldrin is excreted in mother's milk, average values being about 3-5 µg/litre mother's milk (Table 23). The ratio of the dieldrin concentration in mother's blood to that in mother's milk is about 1 : 2-3.

7. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

7.1 Microorganisms

Neither aldrin nor dieldrin have significant effects on populations of microorganisms in soil or fresh water at realistic concentrations. Some physiological processes of microorganisms are affected by low concentrations of both aldrin and dieldrin, but these would appear to have little or no environmental significance. Aldrin and dieldrin have only minor deleterious effects on soil bacterial populations, even at concentrations that are much higher than those used in agricultural practice.

The effects of insecticides on soil microbes have been reviewed by Tu & Miles (1976). Of 15 strains tested, aldrin did not have any effect on the growth of 11 bacterial species (single cultures) but caused some growth inhibition in four species. Dieldrin did not have any effect on 13 bacterial species but had some inhibitory effect in two species. Neither aldrin nor dieldrin at 2000 mg/kg soil had effects on bacteria in laboratory studies; soil fungi were also little affected. In pot studies, using aldrin at 4 and 120 mg/kg soil, there were no quantitative changes in bacteria during any part of the vegetative period. Aldrin inhibited the growth of *Rhizoctonia solani* in plate cultures by 20% or more at 6.2 mg/litre and higher concentrations. Dieldrin was less toxic, producing an average inhibition of about 15%, which was not dose related over the range of 1-100 mg/litre. The evolution of carbon dioxide (CO_2) (a measure of soil organisms respiration) was significantly reduced by dieldrin at 1000 mg/kg soil (but not at 100 mg/kg), whereas aldrin produced a significant reduction at concentrations as low as 25 mg/kg soil. Slight effects on nitrification were initially found when aldrin and dieldrin were incorporated at 2000 mg/kg in a sandy loam soil, but nitrification was normal after about 10 weeks. Short-term inhibition of nitrification was also produced by aldrin and dieldrin at 25 mg/kg in a sandy loam soil (aldrin for 1 week, dieldrin for 2 weeks). Decreased sulfur oxidation was observed in soil containing aldrin or dieldrin (2000 mg/kg), the inhibition decreasing considerably after 3 months. Five annual applications of aldrin or dieldrin (5.5-22 kg/ha) to a Ramona sandy loam had no measurable effect on the numbers of soil bacteria or fungi, did not influence the ability of the soil population to decompose plant residue, and did not alter soil aggregation.

The effect of dieldrin on the activities of three soil enzymes was determined at concentrations of 5 or 10 mg dieldrin/kg soil by Tu (1981). The dehydrogenase activity of the dieldrin-treated soil (10 mg/kg) did not differ from controls, whereas at 5 mg dieldrin/kg, the activity was significantly greater than controls after 2 weeks (50% increase). Urease activity at both treatment levels was significantly reduced after a 1-week incubation but significantly increased after 2 weeks. Phosphatase activity was significantly reduced at 5 mg dieldrin/kg, but not at 10 mg/kg.

The 96-h EC_{50} (growth) for algae *(Chlamydomonas* sp., *Phaeodactylum tricornutum, Dunaliella* sp., *Chlorella ovalis,* and *Chlorella pyrenoidosa)* was > 100 µg dieldrin/litre (Adema & Vink, 1981).

The photosynthetic activity of four species of marine phytoplankton in the presence of dieldrin was investigated using ^{14}C-labelled Na_2CO_3. A range of nominal concentrations (0.01-1000 µg/litre) was used, and the plant cultures were exposed for 24 h. The ^{14}C uptake of *Dunaliella tertiolecta* during 7 days post-treatment was unaffected by up to 1000 µg dieldrin/litre. Two other species *(Skeletonema costatum* and *Coccolithus huxleyi)* showed significant reductions in ^{14}C uptake at levels of dieldrin above 10 µg/litre, and the photosynthetic activity of *Cyclotella nana* was reduced at concentrations above 1 µg dieldrin/litre (Menzel et al., 1970).

In studies by Schauberger & Wildman (1977), three species of fresh-water algae *(Anabaena cylindrica, Anacystis nidulans, Nostoc muscorum)* were exposed to aldrin or dieldrin at concentrations of 0-1000 µg/litre. After exposure for 7 days, there was no significant effect on the photosynthetic pigment absorption of the three species at concentrations up to 10 µg (nominal)/litre. However, at 1 mg/litre, aldrin almost completely suppressed the absorption by photosynthetic pigments (chlorophyll and phycocyanin), these being indicators of physiological health and growth. Dieldrin (1 mg/litre) produced a reduction of about 40%.

The growth response of two cyanobacteria (blue-green algae) in the presence of aldrin, dieldrin, or two metabolites of dieldrin, photoaldrin, or photodieldrin was determined at nominal concentrations of 0.2-950 µg/litre (Batterton et al., 1971). None of these compounds had significant effects on the growth rate constants at concentrations of 95 µg/litre or at lower concentrations over periods of 26-30 h. The investigators considered that dieldrin and its derivatives reduced the growth rate constant at 475 and 950 µg/litre, *Agmenellum quadriplicatum* being more sensitive than *Anacystis nidulans.* Aldrin did not have a significant effect on either species, but photoaldrin affected *Agmenellum quadriplicatum* at 950 µg/litre.

In studies by Powers et al. (1977), a marine dinoflagellate *(Exuviella baltica)* was incubated with dieldrin (0.1, 1, or 10 µg (nominal)/litre), and the numbers of cells were counted during a period of 6 days. No adverse effects on optical counts were observed at the two lower concentrations, but there was a marked reduction in the size and number of cells at 10 µg dieldrin/litre.

7.2 Aquatic Organisms

The toxicity of aldrin and dieldrin to aquatic invertebrates is very variable. For some species both compounds are highly toxic, whereas for others there is no effect until the compounds are dissolved to artificially high concentrations, many times their solubility in water. Both aldrin and dieldrin are highly toxic to most species of fish in laboratory tests, with acute LC_{50} values well within the

solubility of the compounds. It should be borne in mind that aldrin and dieldrin are strongly bound to particulate matter in water, which reduces their availability to aquatic organisms and, in consequence, their potential toxicity.

7.2.1 Aquatic invertebrates

7.2.1.1 Acute toxicity

A convenient overview, in graphical format, of the toxicity of aldrin and dieldrin to many aquatic organisms was produced by Craig (1977). The 96-h LC_{50} values of aldrin and dieldrin for crustaceans and molluscs were in the range 0.2-10 000 µg/litre.

Dieldrin is moderately toxic to fresh-water annelids (4000-7000 µg/litre) and molluscs (> 100-640 µg/litre). Insects are the most sensitive group (aldrin, 1-200 µg/litre; dieldrin, 0.2-40 µg/litre). The values for a number of species are given in Table 25.

7.2.1.2 Short-term toxicity, reproduction, and behaviour

(a) *Short-term toxicity*

When naiads of two species of stonefly were exposed for 30 days in a continuous-flow system, the 30-day LC_{50}s for aldrin and dieldrin were, respectively, 2.5 and 2 µg/litre for *Pteronarcys californica*, and 22 and 0.2 µg/litre for *Acroneuria pacifica* (Jensen & Gaufin, 1966).

The LC_{50} for adult molluscs *(Mytilus edulis* and *Dreissena polymorpha)* exposed for 3-4 weeks was 180-200 µg dieldrin/litre (Adema & Vink, 1981).

McLeese et al. (1982) exposed polychaete worms *(Nereis vireus)* to dieldrin in sea water or sediment for 12 days. The LC_{50} in sea water was > 170 µg/litre (in surficial water > 20 µg/litre; in sediment > 13 mg/kg).

Table 26 gives the LC_{50} values for a number of invertebrate species.

(b) *Reproduction*

The effects of dieldrin on the embryonic development of the American oyster (*Crassostrea virginica)* and of aldrin on that of the hard clam *(Mercenaria mercenaria)* were studied by Davis & Hidu (1969). Table 27 gives the concentrations producing approximately 50% reduction in the development of fertilized eggs during 48 h, those producing about 50% reduction in larval survival during 12 days (clams) or 14 days (oysters), and the effects on larval growth during 10 or 12 days of exposure (expressed as a percentage of growth of control larvae).

Table 25. Acute toxicity of aldrin and dieldrin for aquatic invertebrates

Species	Developmental stage, body weight, or length	Vehicle	Temperature (°C)	96-h LC_{50} (static test) (μg/litre)		Reference
				Aldrin	Dieldrin	
Daphnids						
Daphnia magna				(29)[a]	330[a]	Anderson (1959)
Simocephalus serrulatus	first instar	dispersed via acetone	15 21	(23)[a] (32)[a]	(240)[a]	Johnson & Finley (1980)
Daphnia pulex	first instar	dispersed	15	(28)[a]	(190)[a]	Johnson & Finley (1980)
Crustacea						
Seed shrimp (*Cypridopsis vidua*)	mature	dispersed via acetone	21	(18)[a]	-	Johnson & Finley (1980)
Sowbug (*Asellus brevicaudus*)	mature	dispersed via acetone	21	-	5	Johnson & Finley (1980)
Scud (*Gammarus fasciatus*)	mature	dispersed via acetone	21	4300	640	Johnson & Finley (1980)
Sand shrimp (*Crangon septemspinosa*)	0.25 g, 2.6 cm	dispersed via acetone	20	8	7	Eisler (1969)
	2 g	dispersed via hexane	20	-	0.4	McLeese & Metcalfe (1980)
	2 g	dispersed in sediment	10	-	4.1	McLeese & Metcalfe (1980)

Table 25 (contd).

Crustacea (contd).						
Grass shrimp (*Palaemonetes vulgaris*)	0.47 g, 3.1 cm	dispersed via acetone	20	9	50	Eisler (1969)
Grass shrimp (*Palaemonetes kadiakensis*)	mature	dispersed via acetone	21	50	-	Johnson & Finley (1980)
Grayfish (*Orconectes nais*)	mature	dispersed via acetone	21	-	740	Johnson & Finley (1980)
Hermit crab (*Pagurus longicarpus*)	0.28 g, 0.35 cm	dispersed via acetone	20	33	18	Eisler (1969)
Molluscs						
Mercenaria mercenaria	egg	dispersed via acetone	24	(> 10 000)[a]	-	Davis & Hidu (1969)
Crassostrea virginica	egg	dispersed via acetone	24	-	(640)[a]	Davis & Hidu (1969)
Slipper limpet (*Crepidula fornicata*)	veliger	-	-	-	> 100	Adema & Vink (1981)
Pond snail (*Lymnaea stagnalis*)	egg juvenile	-	-	-	> 200	Adema & Vink (1981)
Insects						
Pteronarcys californica	naiad, 3-3.5 cm	dispersed via ethanol	15.5	1.3	0.5	Sanders & Cope (1968); Johnson & Finley (1980)

Table 25 (contd).

Species	Developmental stage, body weight, or length	Vehicle	Temperature (°C)	96-h LC_{50} (static test) (µg/litre)		Reference
				Aldrin	Dieldrin	
Insects (contd).						
Pteronarcella badia	naiad, 1.5-2 cm	dispersed via ethanol	15.5	-	0.5	Sanders & Cope (1968); Johnson & Finley (1980)
Claassenia sabulosa	naiad, 2-2.5 cm	dispersed	15.5	-	0.6	Sanders & Cope (1968); Johnson & Finley (1980)
Pteronarcys californica	naiad, 2-5 cm	dispersed via acetone	12.8	180	39	Jensen & Gaufin (1966)
Acroneuria pacifica	naiad, 2-2.5 cm	dispersed via acetone	12.8	143	24	Jensen & Gaufin (1966)
Damselfly (*Ischnura venticalis*)	juvenile	dispersed via acetone	24	-	12	Johnson & Finley (1980)
Other invertebrates						
Bristle worm (*Ophryotrocha diadema*)	2- 3-day-old larva	dispersed via acetone	21	-	> 100	Hooftman & Vink (1980)
	4-week-old adult worm	dispersed via acetone	21	-	> 100	Hooftman & Vink (1980)

[a] Values in parentheses are the 48-h LC_{50}.

Table 26. Short-term LC_{50}s of dieldrin in invertebrates

Species	Stage	LC_{50} at end of study (μg/litre) (time of exposure)	Reference
Ophryotrocha diadema	larva (2-3 days)	>10 (5-6 weeks)	Hooftman & Vink (1980)
	adult (4 weeks)	60 (5-6 weeks)	Hooftman & Vink (1980)
Daphnia magna	larva	100 (3 weeks)	Adema & Vink (1981)
	adult (0.3 cm)	200 (7 days)	Adema & Vink (1981)
Artemia salina	larva	40 (4 weeks)	Adema & Vink (1981)
	adult (1 cm)	50 (male) (7 days) 110 (female) (7 days)	Adema & Vink (1981)
Chaetogammarus marinus	larva	1.8 (4 weeks)	Adema & Vink (1981)
	adult (1 cm)	3.6 (14 days)	Adema & Vink (1981)
Palaemonetes varians	adult (4 cm)	0.3 (7 days)	Adema & Vink (1981)
Crangon crangon	adult (4 cm)	4 (14 days)	Adema & Vink (1981)

When adult mud snails *(Nassa obsoleta)* were exposed to up to 10 000 μg dieldrin/litre for 96 h, and then transferred to dieldrin-free sea water for 33 days, no mortality occurred throughout the study and the length of the animals was normal after 33 days. There was a significant increase in total egg deposition during the 33-day post-treatment period in the case of snails exposed to 10 μg dieldrin/litre, but there was a significant reduction at 100, 1000, and 10 000 μg dieldrin/litre (Eisler, 1970).

(c) *Behaviour*

In studies by Klein & Lincer (1974), fiddler crabs, *(Uca pugilator)* were fed diets containing 0, 0.1, 1, 10, and 50 mg dieldrin/kg diet for 14 days and observed for another 25 days. Behaviour, measured as righting response, was modified at dose levels of 1 mg/kg or more, and

Table 27. Concentrations producing about 50% reduction in the development of fertilized eggs during 48 h, in larval survival during 12 days (clams) or 14 days (oysters), and effects on larval growth during 10 or 12 days exposure[a] (Davis & Hidu, 1969)

Organism	Effect	Aldrin (μg/litre)	Dieldrin (μg/litre)
Clam	development of	> 10 000	-
Oyster	fertilized eggs	-	640
Clam	larval survival	410	-
Oyster		-	> 10 000
Clam	larval growth	250[b]	-
Oyster		-	500[c]

[a] Expressed as a percentage of growth of control larvae.
[b] 80% reduction.
[c] 50% reduction.

even in the group given 0.1 mg/kg, difficulty in righting was seen after 11 days. With 10 and 50 mg/kg diet, an increase in mortality was observed, but not with 1 mg/kg diet.

7.2.2 Fish

7.2.2.1 Acute toxicity

Both aldrin and dieldrin are highly toxic to fish under laboratory conditions. A summary of reported 96-h LC_{50} values for fresh water and marine species is given in Table 28. In parallel studies, dieldrin was consistently more toxic than aldrin. The 96-h LC_{50}s range from 2.2 to 53 μg aldrin/litre and from 1.1 to 41 μg dieldrin/litre in various fish species. It should be noted that the range for aldrin exceeds the water solubility of the compound.

The results of studies by Macek et al. (1969) indicate that a rise in temperature increases the toxicity of aldrin and dieldrin for bluegills and rainbow trout. However, Johnson & Finley (1980) stated that toxicity was not appreciably (only a factor of 2) changed by variations in temperature or water hardness.

Macek (1975) investigated the effects of simultaneous exposure of bluegills to DDT and dieldrin and concluded that the acute toxicity of dieldrin in the concentration range 5.9-6.6 μg/litre was not increased by the presence of DDT (concentration range, 4.5-5 μg/litre).

Anderson & Weber (1975) found that new-born and juvenile guppies *(Lebistes reticulatus)* were more resistant to dieldrin than adults. A

Table 28. Acute toxicity of aldrin and dieldrin for fish

Species	Weight (g)	Vehicle	Temperature (°C)	96-h LC_{50} (static test) (µg/litre) Aldrin	Dieldrin	Reference
Fresh-water						
Rainbow trout (*Salmo gairdneri*)	0.6	dispersed via acetone	13	2.6	-	Johnson & Finley (1980)
	1.4	dispersed via acetone	13	-	1.2	Johnson & Finley (1980)
	3.2	dispersed via acetone	20	17.7	9.9	Katz (1961)
	0.6-1.5	dispersed via acetone	1.6 7.2 12.7	3.2 3.3 2.2	2.4 1.1 1.4	Macek et al. (1969)
Cutthroat trout (*Salmo clarki*)	1.1	dispersed via acetone	9	-	6[a]	Johnson & Finley (1980)
Chinook salmon (*Oncorhynchus tshawytscha*)	1.45-5	dispersed via acetone	20	7.5	6.1	Katz (1961)
	0.8	dispersed via acetone	15	14.3	-	Johnson & Finley (1980)
Coho salmon (*Oncorhynchus kisutch*)	2.7-4.1	dispersed via acetone	20	45.9	10.8	Katz (1961)
Goldfish (*Carrassius auratus*)	1-2	dispersed via acetone	25	32	41	Henderson et al. (1959)

Table 28 (contd).

Species	Weight (g)	Vehicle	Temperature (°C)	96-h LC_{50} (static test) (µg/litre)		Reference
				Aldrin	Dieldrin	
Freshwater (contd).						
Goldfish (*Carassius auratus*)	1	dispersed via acetone	18	-	1.8	Johnson & Finley (1980)
Carp (*Cyprinus carpio*)	NA	NA	20	4[b]	-	Rehwoldt et al. (1977)
Fathead minnow (*Pimephales promelas*)	0.6	dispersed via acetone	18	8.2	3.8	Johnson & Finley (1980)
	1-2	dispersed via acetone	25	32	18	Henderson et al. (1959)
Guppy (*Lebistes reticulatus*)	0.1-0.2	dispersed via acetone	25	37	25	Henderson et al. (1959)
	NA[d]	NA	20	20[b]	-	Rehwoldt et al. (1977)
	NA (young)	NA	24	-	3.2-7	Adema & Vink (1981)
	NA (adult)	NA	24	-	35[c]	Adema & Vink (1981)
	juvenile	NA	25		10.9	Anderson & Weber (1975)
	newborns	NA			36.7	Anderson & Weber (1975)
Black bullhead (*Ictalurus melas*)	1.5	dispersed via acetone	24	19	-	Johnson & Finley (1980)

Table 28 (contd).

Channel catfish (*Ictalurus punctatus*)	5.2	dispersed via acetone	18	53	-	Johnson & Finley (1980)
	1.4	dispersed via acetone	18	-	4.5	Johnson & Finley (1980)
Bluegill (*Lepomis macrochirus*)	0.7	dispersed via acetone	18	6.2	-	Johnson & Finley (1980)
	1.3	dispersed via acetone	18	-	3.1	Johnson & Finley (1980)
	1-2	dispersed via acetone	25	15	8.8	Henderson et al. (1959)
	0.6-1.5	dispersed via acetone	12.7 18.3 23.8	7.7 5.8 4.6	17 14 8.8	Macek et al. (1969)
Pumpkinseed sunfish (*Lepomis gibbosus*)	NA	NA	20	20[b]	-	Rehwoldt et al. (1977)
Largemouth bass (*Micropterus salmoides*)	2.5	dispersed via acetone	18	5	3.5	Johnson & Finley (1980)
Striped bass (*Marone saxatilis*)	NA	NA	20	10[b]	-	Rehwoldt et al. (1977)
Banded killyfish (*Fundulus diaphanus*)	NA	NA	20	21[b]	-	Rehwoldt et al. (1977)
White perch (*Roccus americanus*)	NA	NA	20	42[b]	-	Rehwoldt et al. (1977)
American eel (*Anguilla rostrata*)	NA	NA	20	16[b]	-	Rehwoldt et al. (1977)

Table 28 (contd).

Species	Weight (g)	Vehicle	Temperature (°C)	96-h LC_{50} (static test) (µg/litre)		Reference
				Aldrin	Dieldrin	
Marine species						
Common goby (*Gobius microps*)	NA (adult)	NA	15	-	3.5	Adema & Vink (1981)
Plaice (*Pleuronectes platessa*)	(length: 2-3 cm)	NA	15	-	1.7	Adema & Vink (1981)
	length: 10 cm	NA	15	-	4	Adema & Vink (1981)
	yolk-sac larva	NA	5-10	-	30	Adema & Vink (1981)
	egg-metam larva	NA	5-10	-	> 32	Adema & Vink (1981)
Threespine stickleback (*Gasterosteus aculeatus*)	0.4-0.8	dispersed via acetone	20	27.4	13.1	Katz (1961)

[a] Hardness = 162 mg $CaCO_3$/litre.
[b] Hardness = 50 mg $CaCO_3$/litre.
[c] 48-h LC_{50}.
[d] NA = not available.

relationship between the LC_{50} and body weight was derived for mature, juvenile, and new-born guppies:

$$LC_{50} = aW^b$$

where W is the body weight. The best fit value for the exponent b was 0.81.

7.2.2.2 Long-term toxicity

Sailfin mollies *(Lebistes latipinna)* were exposed in groups of 20 to 0, 0.75, 1.5, 3, 6, or 12 µg dieldrin/litre using a flow-through system for 34 weeks. The mortality of the 0.75 µg/litre group was similar to that of the control group. At 1.5 µg/litre, there was an increase in mortality, and, at 3 µg/litre or more, 100% mortality occurred. The growth rates and reproduction performances were adversely affected in the surviving fish (Lane & Livingstone, 1970).

Rainbow trout *(Salmo gairdneri)* were fed food containing dieldrin for 240 days, the nominal dietary concentrations corresponding to 14, 43, 143, or 430 µg dieldrin/kg body weight per day. The growth rate was not affected at any of the concentrations throughout the 240 days, and there was no mortality or visible adverse effects. The activities of liver glutamate-pyruvate transaminase (GPT) and glutamate-oxaloacetate transaminase (GOT) were not affected, except, in the case of the latter, at the highest dose level. Liver glutamate dehydrogenase (GDH) activity was increased at all dose levels. Electron micrographs of liver cells demonstrated changes in mitochondrial morphology, the highest dose causing swelling and membrane disruption. Since GDH is an intramitochondrial enzyme, examination by electron microscopy gave further evidence that dieldrin altered mitochondrial metabolism. In the brain, GOT activity was significantly decreased at 43 µg/kg and GTP was decreased at 14 µg/kg or more. At all dose levels, brain GDH was decreased and brain glutamine transferase (GT) was increased. Electron microscopy of the medulla and cerebral hemispheres did not show any effects of dieldrin. The concentrations of 16 free amino acids in the brain were determined. The concentrations of four were not significantly changed, whereas eight were significantly altered at 143 µg dieldrin/kg and 12 at 430 µg/kg. Serum ammonia concentrations were significantly increased at 143 and 430 µg dieldrin/kg, but the concentration of ammonia in the brain was not affected. The increase in brain GT was considered to be a possible reason for this lack of effect on brain ammonia, since it compensated for the decrease in GDH activity. Alternatively, brain ammonia may have been transported via the blood to the liver with consequent effects on the liver. The ammonia-detoxifying mechanism of fish seemed to be very sensitive to dieldrin, the no-effect dose being below 14 µg/kg body weight per day (equivalent to 0.36 mg/kg food) (Mehrle & Bloomfield, 1974).

Several studies have described the influence of aldrin and/or dieldrin on enzymes such as mitochondrial succinic hydrogenase, the

epoxidative activities of liver microsomes and the ATPase activity of microsomes of the gills or brain (Chan et al., 1967; Davis et al., 1972; Moffet & Yarbrough, 1972; Yap et al., 1975). Furthermore, the influence of dieldrin during thermal stress has been studied in darters *(Etheostoma nigrum)* (Silbergeld, 1973).

In studies by Verma & Tonk (1984), *Heteropneustes (Saccobranchus) fossilis* was exposed to aldrin for 30 days at a concentration of 0.03 mg/litre. Respiration, haematological parameters, and the activity of two enzymes in liver, kidneys, and gills were determined. The respiration rate decreased and the blood concentrations of glucose, sodium, and chloride ions showed significant increases. The cholesterol content and clotting time were decreased, and the ATPase activity in the three tissues was significantly reduced.

7.2.2.3 Reproduction

Van Leeuwen (1986) carried out studies with dieldrin to study the susceptibility of early-life stages of rainbow trout. The test was performed with fertilized eggs before and after water hardening, and with early eye point eggs, late eye point eggs, sac fry, and early fry. No mortality was found in the different early-life stages using concentrations greater than aqueous solubility (> 10 mg/litre), except for the early fry where a very low 96-h LC_{50} of 0.003 mg/litre was found.

In studies by Cairns et al. (1967), nine populations of guppies *(Lebistes reticulatus)* were exposed in a semi-static system to nominal concentrations of 0 (three populations), 1.8, 5.6, and 10 µg dieldrin/litre (two populations of each) for 14 months. During the first 2-3 months, the exposed populations in five tanks developed greater numbers of individuals (mature, immature, and fry) than did the controls (except one population at 5.6 µg/litre, which was similar to the controls). The difference between the controls and five treatment groups was attributed to the higher predation and harassment observed in the control groups. The total numbers of individuals in control and treatment groups became similar during the final 6-8 months of the study. The average total monthly body weights of the groups treated with 1.8 µg/litre and 5.6 µg/litre began to increase steadily after about 8 months, whereas the total monthly body weights of the group exposed to 10 µg/litre were similar to the controls throughout the 14 months of the study. The production of fry by one of the groups treated with 10 µg/litre declined markedly after the thirty-second week of the study, no new broods of fry being born after the forty-second week. No such marked decline occurred in the other five treatment groups (including one population exposed to 10 µg/litre).

Chadwick & Shumway (1970), conducted studies lasting 130 days on rainbow trout *(Salmo gairdneri)* to determine survival from time of fertilization through to hatching in continuously cycled water. Embryos, alevins, and fry were exposed to dieldrin concentrations ranging from 0.012 to 52 µg/litre. Eggs (embryos) exposed to up to

52 µg dieldrin/litre from the time of fertilization survived until hatching as well as controls, but the mean weight of newly-hatched alevins (minus yolk material) was reduced by higher concentrations (not specified). Alevins were more susceptible than embryos. Their survival was reduced at all concentrations above 0.39 µg/litre. Trout fry, whose survival was unaffected at dieldrin levels of 0.12 µg or less, quickly succumbed at concentrations of 0.39 µg/litre or more.

Smith & Cole (1973), exposed adult winter flounder *(Pseudopleuronectes americanus)* to 2 µg/litre in aquaria continuously supplied with filtered sea water. When fish became ripe, they were artificially spawned, and approximately 30 000 eggs were collected from each of the 24 spawning pairs and cultured. The remaining eggs were analysed. The percentage fertilization of eggs containing 0.61 mg dieldrin/kg or less was 99% (controls, 97.8%). The percentage fertilization of eggs containing 1.21 mg dieldrin/kg was 12%, and all the eggs containing 1.74 mg/kg were infertile. There was no effect on egg development except in the case of the two groups of eggs containing the higher concentrations of dieldrin. The effects on egg mortality were not due to dieldrin in the gametes, and the milt of exposed male flounders contained no detectable residue of dieldrin.

7.2.3 Amphibia and reptiles

The LC_{50} values for tadpoles of two species of frogs (1 week old) and toads (4-5 weeks old) were determined by Sanders (1970). The 96-h LC_{50} (at 15.5 °C) of dieldrin for Western chorus frog tadpoles *(Pseudacris triseriata)* was 100 µg/litre, whereas that of both aldrin and dieldrin for Fowler's toad tadpoles *(Bufo woodhousii fowleri)* was 150 µg/litre.

Cooke (1972) studied the effect of dieldrin at nominal concentrations of 0.008, 0.02, or 0.5 mg/litre on groups of 40 common frog *(Rana temporaria)* or toad *(Bufo bufo)* tadpoles with hindlimb paddles or hind legs. The exposure was for 24 or 48 h in amphibian saline, and the observation period 5 or 15 days. At the highest dose level, the frogs showed an increased mortality, the mean dieldrin content being 42.9 mg/kg tissue. At the two lower dose levels (0.008 and 0.02), there were 0.31 and 6.1 mg/kg dieldrin in tissues, respectively. When toad tadpoles were exposed to 0.02 or 0.5 mg/litre, the animals with the higher dose level showed clear behavioural and structural abnormalities and a reduced rate of development, but these changes returned to normal a few days after exposure. The mean dieldrin content was 138 mg/kg tissue at a dose level of 0.5 mg/litre.

The *in vitro* exposure of toad embryo tissue *(Bufo arenarum)* to dieldrin (4×10^{-5} mol/litre) produced an inhibition of acetyl and butyryl cholinesterase activity. In *in vivo* studies with open-mouth stage embryos, dieldrin produced acetyl cholinesterase inhibition at 0.5×10^{-6} mol/litre. Furthermore, hyperactivity in swimming larvae was observed (de Llamas et al., 1985).

The *in vitro* activity of ATPase in a number of tissues of the male turtle *(Graptemys geographica)* was determined by Wells et al. (1974). There was no consistent dose relationship for either aldrin or dieldrin, except perhaps in the case of the cloacal bladder in the aldrin treatments. The inhibition of Na/K/Mg ATPase by aldrin and dieldrin was in the range of 4-13%. It was suggested that aldrin and dieldrin may affect the transport of metabolites across the cellular membranes as a result of decreased energy for active transport.

7.3 Terrestrial Organisms

7.3.1 Higher plants

Dieldrin has low phytotoxicity, tomatoes and cucumber, for example, being affected only at application rates greater than 22 kg/ha. Aldrin affects some crops at rates greater than 22 kg/ha, beans and cereals being most sensitive. Tomatoes and cucumbers are sensitive to aldrin but only at unrealistically high application rates (Edwards, 1965).

Studies in greenhouses showed that aldrin, administered weekly as an emulsifiable concentrate at a rate of 16 kg active ingredient/ha to 2-3-week-old seedlings of tomato, cauliflower, and Chinese cabbage, inhibited root development and reduced growth rate of cauliflower and Chinese cabbage seedlings. A ten-fold reduction in the aldrin level failed to produce these effects (Hagley, 1965).

Aldrin and dieldrin at 11 kg active ingredient/ha had no effect on the emergence, growth, yield, or chemical composition of soybeans (Probst & Everly, 1957).

7.3.2 Earthworms

In studies by Cathey (1982), earthworms *(Lumbricus terrestris)* were maintained in an artificial nutritionally complete soil, based on shredded paper containing aldrin. The LC_{50} value (6-week exposure) was 60 mg aldrin/kg bedding, and the tolerance level, producing less than 1% mortality, was 13 mg aldrin/kg bedding.

When aldrin (2.5-4.6 kg/ha) was applied as a spray or dust, respectively, to the surface of soil plots and incorporated into the soil, the numbers of earthworms in treated plots were either similar to or greater than those in control plots (Edwards et al., 1967; Griffiths et al., 1967; Edwards & Lofty, 1977).

7.3.3 Bees and other beneficial insects

In a review of five investigations on the toxicity of aldrin and dieldrin to honey bees (Sanger, 1959), the oral LD_{50} values for aldrin ranged from 0.24 to 0.45 µg/bee, while the values for dieldrin were in the range 0.15-0.32 µg/bee. Contact LC_{50} values were 0.15-0.8 µg/bee for aldrin and 0.15-0.41 µg/bee for dieldrin.

Cowie (1967) reported an oral LD_{50} of 0.3 µg dieldrin/bee (range, 0.13-0.54) and a contact LD_{50} of 0.21 µg/bee.

The toxicity of dieldrin to two important predators of cotton pests was investigated by Burke (1959). The contact LD_{50} value for *Hippodamia convergens* was 1.6 mg/g body weight.

In a review of the effects of pesticides on soil fauna, it was concluded that aldrin (and, by implication, dieldrin) is relatively non-toxic for predatory mites *(Acarina* spp.), and that this may contribute to its success as a soil insecticide (Edwards & Thompson, 1973).

7.3.4 Birds

7.3.4.1 Acute toxicity

Estimates of the LD_{50} values for several species of birds are given in Table 29. The variation in acute oral toxicity of dieldrin among six species of birds tested by Tucker & Haegele (1971) was more than ten fold.

7.3.4.2 Short- and long-term toxicity

Values for the subacute LC_{50}s of aldrin and dieldrin, determined using the procedure developed at the Patuxent Wildlife Centre (Hill et al., 1975), are given in Table 30. The LC_{50} values of aldrin and dieldrin for each of the four species tested were of the same order. The annual variations in the LC_{50} of dieldrin over a period of up to 8 years for these four species have been investigated by Hill et al. (1977) (18 times per species). No time-related changes in LC_{50} values were found for any of the species. However, differences were found between birds of different ages in some species, e.g., Japanese quail and mallards (Hudson et al., 1984). There were also differences between the slopes of the average regression lines for the four species. These authors emphasized the need to evaluate both the LC_{50} and the slope of the regression line. Food consumption was reduced by aldrin or dieldrin in the diet.

Wiese et al. (1969) fed diets containing up to 500 mg technical dieldrin (85%)/kg diet to male and female 6-month-old crowned guinea-fowl *(Numida meleagris).* None of the birds fed 1.5 mg/kg for 21 months died. The median survival time for birds fed 5 mg/kg was 524 days; for birds fed 150 and 500 mg/kg, it was 3 and 1 days, respectively. No differences in susceptibility between males and females were found.

The subacute toxicities of technical dieldrin (85%) to three species of birds are given in Table 31 (Basson, 1971).

7.3.4.3 Reproductive studies

The first experimental studies of the effects of aldrin or dieldrin on avian reproduction showed that these compounds were toxic for quail and pheasants. Quail fed a diet containing aldrin or dieldrin at a toxic dose of 0.5 or 1 mg/kg diet did not show any clear effects on egg production, percentage fertility, or percentage hatchability (the birds

Table 29. Acute oral toxicity of aldrin and dieldrin for avian species[a]

Species	LD_{50}		Reference
	Aldrin (mg/kg body weight)	Dieldrin (mg/kg body weight)	
Fulvous whistling duck (*Dendocygna bicolor*)	male: 29.2	female: 100-200	Tucker & Crabtree (1970)
Mallard duck (*Anas platyrhynchos*)	female: 520	female: 381	Tucker & Crabtree (1970)
Canada goose (*Branta canadensis*)		50-150	Tucker & Crabtree (1970)
Domestic fowl (*Gallus domesticus*)	25.5	43	Sherman & Rosenberg (1953)
Japanese quail (*Coturnix coturnix japonica*)		male: 69.7	Tucker & Crabtree (1970)
Bobwhite quail (*Colinus virginianus*)	female: 6.6		Tucker & Crabtree (1970)
California quail (*Callipepla californica*)		8.7	Hudson et al. (1984)
Gray partridge (*Perdix perdix*)		female: 8.8	Tucker & Crabtree (1970)
Chukar partridge (*Alectoris graeca*)		23.4	Tucker & Crabtree (1970)
Sharp-tailed grouse (*Pedioecetes phasianellus*)		male: 6.9	McEwen & Brown (1966)
Ring-necked pheasant (*Phasianus colchicus*)	female: 16.8	female: 79	Tucker & Crabtree (1970)
Pigeon (*Columba livia*)	55	67	Turtle et al. (1963)
		26.6	Tucker & Crabtree (1970)
House sparrow (*Passer domesticus*)		female: 47.6	Tucker & Crabtree (1970)

[a] Details concerning age and weight of birds are not summarized here but can found in the original publications.

had not been exposed earlier to the compounds) (DeWitt, 1955, 1956). No significant effect was found on the fertility or hatchability of eggs of pheasants fed 25 mg dieldrin/kg diet, but at 50 mg/kg there was a clear effect (Genelly & Rudd, 1956).

Table 30. Subacute dietary toxicity of aldrin and dieldrin for avian species[a]

Species	Age (days)	LC_{50} (95% confidence limits)	
		Aldrin (mg/kg diet)	Dieldrin (mg/kg diet)
Mallard duck (*Anas platyrhynchos*)	5	155 (129-186)	153 (123-196)
	10	-	169
Japanese quail (*Coturnix coturnix japonica*)	14	34 (28-41)	62 (53-71)
Bobwhite quail (*Colinus virginianus*)	14	37 (33-41)	37 (30-46)
Ring-necked pheasant (*Phasianus colchicus*)	10	57 (50-64)	58 (51-67)

[a] Aldrin or dieldrin fed for 5 days followed by 3 days of untreated diet.

Table 31. Subacute toxicity of technical dieldrin for three species of birds

Species	Concentration (mg/kg diet)	Median time till death (days)	Median lethal dose (mg dieldrin/kg body weight)
Guinea fowl (*Numida meleagris*)	20	72	72.4
	150	12	11.2
Laughing dove (*Stigmatopelia senegalensis*)	5	49	15.8
	90	4.7	17.3
Sparrow (*Passer melanurus melanurus*)	5	85.1	> 41
	45	7	43.8

Eggs from chickens fed 1 mg aldrin or dieldrin/kg diet for 2 years showed normal fertility and hatchability, although the concentrations of dieldrin in the yolks of the eggs were in the range of 6 to 25 mg/kg. The fertility and hatchability slightly decreased at 10 mg dieldrin/kg diet (Brown et al., 1965).

Other studies on avian reproduction are summarized in Table 32. This table gives the available information on five criteria relevant to reproduction (parental survival, production, fertility and hatchability of eggs, and chick survival) in relation to oral intake of dieldrin and (where reported), the residues of dieldrin in eggs. These

Table 32. Reproductive success of birds in relation to oral intake of dieldrin and the concentration of HEOD in eggs

Species	Intake of dieldrin (mg/kg diet)	Duration	Mean concentration of dieldrin in eggs (mg/kg) (range)	Survival of parents	Reproductive success relative to controls				Reference
					Eggs/hen	Fertility of eggs	Hatchability of eggs	Chick survival	
Mallard duck *(Anas platyrhinchos)*	4	90 days	-	-	NC[a]	NC	Red.[c]	-	Muller & Lockman (1972)
Japanese quail *(Coturnix coturnix japonica)*	1	16 weeks	-	-	NC	NC	NC	-	Shellenberger & Newell (1965)
	10	16 weeks	-	-	NC	NC	NC	-	
	10	18 weeks	19 (6.9-26.9)	NC	NC	NC	NC	NC	Walker et al. (1969a)
	20	9 weeks	39 (19.8-54.1)	Red.	Red.	DC	NC	Red.	
	30	7 weeks	48 (34.7-63.2)	Red.	Red.	DC	Red.	Red.	
	40	6 weeks	84 (76.9-92.5)	Red.	Red.	-	-	-	
	0.1	multi-generation P; F_1	-	NC	NC	NC	NC	NC	Shellenberger (1978)
	1	F_2, F_3	-	NC	NC	NC	NC	NC	
Bobwhite quail *(Colinus virginianus)*	10	34 weeks	-	Red.	NC	-	-	-	Fergin & Schafer (1977)
	20	34 weeks	-	Red.	Red.	-	-	-	
	40	34 weeks	-	Red.	Red.	-	-	-	

Table 32 (contd).

Pheasant (*Phasianus colchicus*)	2 mg/hen /week[b]	13 weeks	(0.6-26.5) (yolks)	NC	NC	NC[a]	Inc.[c]	NC	Atkins & Linder (1967)
	2 mg/hen per week	13 weeks	-	NC	NC	NC	NC	NC	
	4 mg/hen per week	13 weeks	(5.3-40.1) (yolks)	DR	NC	NC	NC	NC	
	4 mg/hen per week	13 weeks	(7.5-20.6) (yolks)	NC	NC	NC	NC	NC	
	6 mg/hen per week	13 weeks	(13.3-52.4) (yolks)	NC	Red.[a]	NC	NC	NC	
	(0) 6 mg/ hen/week[d]	14 weeks	-	Red.	Inc.[c]	Red.[c]	NC	NC	Baxter et al. (1969)
	(0) 8 mg/ hen/week	14 weeks	-	Red.	Inc.[c]	NC	NC	NC	
	(0) 12 mg/ hen/week	14 weeks	-	Red.	Red.[c]	NC	-	-	
	(4) 0 mg/ hen/week	14 weeks	-	NC	Inc.[c]	Red.[c]	Red.	NC	
	(4) 6 mg/ hen/week	14 weeks	-	Red.	NC	Red.[c]	NC	NC	
	(6) 0 mg/ hen/week	14 weeks	-	NC	Red.[c]	NC	-	-	
	(6) 6 mg/ hen/week	14 weeks	-	Red.	Red.[c]	Red.[c]	-	-	
Gray partridge (*Perdix perdix*)	3		1.5 (1-2)	-	DR	NC	NC	NC	Neill et al. (1971)
Domestic fowl (*Gallus domesticus*)	2	16 weeks	(0.34-1.45)	NC	NC	-	NC	NC	Graves et al. (1969)
	5	16 weeks	(1.2-4.8)	NC	NC	-	NC	NC	
	10	13 months	(7.6-16)	NC	NC	NC	NC	NC	Brown et al. (1974)
	20	13 months	(19.6-35.7)	Red.	Inc.[a]	NC	NC	Red.	

Table 32 (contd).

Species	Intake of dieldrin (mg/kg diet)	Duration	Mean concentration of dieldrin in eggs (mg/kg) (range)	Survival of parents	Reproductive success relative to controls				Reference
					Eggs/hen	Fertility of eggs	Hatchability of eggs	Chick survival	
Crowned guinea-fowl (*Numida meleagris*)	0.5	21 months	1.11/1.17[e]	NC	Inc.[a]	NC	NC	NC	Wiese et al. (1969)
	1.5	21 months	2.38/3.35[e]	NC	Inc.[a]	NC	NC	NC	
	5	21 months	7.18/13.56[e]	PR	Inc.[a]	NC	NC	NC	
	15	21 months	15.79[e]	Red.	Inc.[a]	NC	NC	Red.	
Homing pigeon (free-flying) (Columba livia)	~2 mg/kg body weight /week	2 years	(0.03-13.4)[f] (4.5-16.7)[f]	NC NC	NC NC	NC NC	NC NC	NC NC	Robinson & Crabtree (1969)
Barn owl (*Tyto alba*)	0.5	2 years	3.6 (first year) 8.1 (second year)	NC	NC	NC	NC	NC	Mendenhall et al. (1983)

[a] Significant at a probability of < 0.01.
[b] Doses of 2, 4, or 6 mg dieldrin/hen were administered once per week in capsules.
[c] Significant at a probability of < 0.05.
[d] Second-generation hens; offspring of birds used in study by Atkins & Linder (1967). The doses in parentheses refer to the doses administered to the first-generation hens.
[e] Residues in eggs of successive years.
[f] First and second laying periods, respectively.
[g] The term "no change" (NC) indicates that any differences between controls and treatment groups were within the limits of experimental variation. If any of the results for treatment groups are reported to be increased (Inc.) or reduced (Red.), the statistical significance, if reported, is given. Equivocal results have been described "doubtful reduction" (DR), "probably reduced" (PR), and "doubtful change" (DC).

studies show that, depending on the duration of exposure, dose levels of 5-10 mg dieldrin/kg diet reduce the survival of the parent birds. Egg production was reported to be significantly increased in some studies but reduced in others. In general, egg fertility was not influenced, except in one study. Hatchability was not affected, neither in most cases, was the survival of chicks. There seems to be a trend that overall reduction in reproductive success occurs only if the parent birds are showing signs of being affected by dieldrin, e.g., reduced food intake with consequent loss of weight and poor condition. It should be noted that in these studies (with one exception) the eggs were placed in incubators for hatching. Consequently, one aspect of the reproductive process was not studied, namely, parental behaviour. However, in the study on homing pigeons (Robinson & Crabtree, 1969), the parents (and subsequently, their offspring) were free-flying, they brooded their eggs, and fed their young until they fledged.

A 3-generation study of the effects of dieldrin on pheasants *(Phasianus colchicus)*, has not been included in Table 32 because of the complexity of the experimental design. The doses of dieldrin (hens, 6 or 10 mg dieldrin/bird per week; cocks, 4 or 6 mg dieldrin/bird per week) were sufficient to cause mortality of breeding birds, but the production, fertility, and hatchability of eggs and the viability of chicks at the time of hatching were not affected in a consistent manner in relation to dose or generation. The survival of chicks from hens given 6 or 10 mg dieldrin/week was reduced. Residues of dieldrin in eggs or tissues were not determined in this study (Dahlgren & Linder, 1974).

When seven-week-old Japanese quail were given diets containing 3.1 or 50 mg dieldrin/kg diet for 21 days, a significant reduction in egg production occurred in both groups (Call & Harrell, 1974).

With the exception of the study with the barn owl (Mendenhall et al., 1983) and the homing pigeon (Robinson & Crabtree, 1969), the birds that were tested are precocial species which show no parental feeding of the young. Most birds are not precocial and reproduction involves a period of full dependency of the offspring on parental care. Results should, therefore, be interpreted with care; extrapolation directly from the laboratory to the field is difficult.

7.3.4.4 Eggshell thinning

Ratcliffe (1967a) reported that the ratio of eggshell weight to size in three species of birds of prey in the United Kingdom had declined during the period after 1947 relative to pre-1947. This report has stimulated considerable interest in the relationship between eggshell thickness (or the related eggshell index based on the weight/size ratio) and the breeding success of birds, particularly as eggshell thinning seems to be quite a widespread phenomenon, particularly among birds of prey (Hickey & Anderson, 1968; Ratcliffe, 1970; Anderson & Hickey, 1972). There has been considerable speculation on the causes and mechanism of these changes (Cooke, 1973; Mueller & Leach, 1974).

Experimental studies on the effects of dieldrin on eggshell thickness have given conflicting results. The results are summarized in Table 33.

Eggshell weights of crowned guinea-fowl *(Numida meleagris)* fed diets containing up to 15 mg dieldrin/kg diet for 21 months were not affected by the treatments (Wiese et al., 1969).

American sparrow hawks *(Falco sparverius)* were given diets containing dieldrin and North American prairie falcons *(Falco mexicanus)* were fed starlings contaminated with an average of 29 mg dieldrin/kg body weight, along with DDT and DDE at different levels. The purpose of these studies was to show the influence of these pesticides on shell thickness. The results of the two studies, in relation to the effects of dieldrin, cannot be interpreted, in view of the possible effects of DDE on eggshell thinning (Porter & Wiemeyer, 1969; Enderson & Berger, 1970). It has slowly become accepted that metabolites of DDT, particularly DDE, are the most likely cause of eggshell thinning (Cooke, 1973; Newton, 1979; Bunyan & Stanley, 1982). It is also pertinent that the onset of eggshell thinning in wild birds preceded the use of aldrin/dieldrin. There is evidence that eggshell thinning after exposure to dieldrin is related to reduced food consumption. Untreated Coturnix and Mallard, when fasted for 36 h, laid thin-shelled eggs for a few days during and after fasting (Haegele & Tucker, 1974).

7.3.4.5 Concentrations of dieldrin in tissues of experimentally poisoned birds

Many studies have been carried out to estimate the concentrations of dieldrin in the liver, brain, or other tissues of birds that died following oral intake of aldrin or dieldrin. The intakes were either single acute doses or long-term dietary exposure. In some investigations, the concentrations of dieldrin in the tissues of birds that survived after treatment were also reported. The results of these studies are not comparable, because the dose levels and duration of the studies are different. The concentrations that were found in the different studies ranged from a few mg/kg up to about 100 mg/kg tissue (wet weight) (Turtle et al., 1963; Koeman et al., 1967; Robinson et al., 1967b; Robinson, 1969; Robinson & Crabtree, 1969; Stickel et al., 1969; Enderson & Berger, 1970; Linder et al., 1970; Brown et al., 1974; Clark, 1975; Heinz & Johnson, 1981; Mendenhall et al., 1983) (Table 34).

Attempts to define tissue concentrations that can be used as indicators of death by dieldrin poisoning of wild birds lack precision as a result of the overlap between the lowest concentrations in the tissues of birds dying under experimental conditions and the highest concentrations in survivors. Thus, it has been proposed that concentrations of 5 or 10 mg dieldrin/kg brain (Robinson, 1969; Stickel et al., 1969) are indicative of death from aldrin/dieldrin poisoning. Liver concentrations of 10 or 20 mg/kg (Robinson, 1969; Cooke et al., 1982) have been proposed as levels diagnostic of dieldrin poisoning of birds.

Table 33. Effects of dieldrin on eggshell thickness

Species	Dose of dieldrin (mg/kg diet)	Duration	Difference between egg-shell thickness of treated and control birds (%)	Reference
Mallard duck (*Anas platyrhynchos*)	1.6	16 months	-3.4[a]	Lehner & Egbert (1969)
	4	16 months	-2[a]	Lehner & Egbert (1969)
	10	16 months	-4.3[a]	Lehner & Egbert (1969)
	4	90 days	-4.2	Muller & Lockman (1972)
Japanese quail (*Coturnix coturnix japonica*)	3.1	21 days with changes in photoperiod	-8[a]	Call & Harrell (1974)
	50		-8[a]	Call & Harrell (1974)
Domestic fowl (*Gallus domesticus*)	10	12 weeks	0	Davison & Sell (1972)
	20	12 weeks	+0.3	Davison & Sell (1972)
	10	13 months	0	Brown et al. (1974)
	20	13 months	+9.7	Brown et al. (1974)
Pheasant (*Phasianus colchicus*)	6 mg/hen/week[b]	-	0	Dahlgren & Linder (1970)
	10 mg/hen/week[b]	-	0	Dahlgren & Linder (1970)
	(6) 0 mg/hen/week[c]	-	+4.1	Dahlgren & Linder (1970)
	(6) 6 mg/hen/week[c]	-	+4.1	Dahlgren & Linder (1970)
	(10) 0 mg/hen/week[c]	-	+4.1	Dahlgren & Linder (1970)

[a] Significant at or below 0.05.
[b] Administered in capsules once per week (see footnote[b] Table 32).
[c] See footnote[d] Table 32.

Table 34. Concentrations of dieldrin in the tissues of experimentally poisoned birds and in survivors

Species	Tissue analysed	Concentration of dieldrin (mg/kg wet weight) geometric mean, (range of values)				Reference
		No. of samples	Survivors	No. of samples	Dead birds	
Domestic pigeon (*Columba* sp.)	liver	11	8 (3.1-51.2)	20	45.6 (23-81)	Robinson et al. (1967b)
	brain	11	3.6 (1.6-8.5)	19	20 (13.5-32.5)	
House sparrow (*Passer domesticus*)	liver	-	-	19	44.7 (38.4-52.3)	Robinson (1969)
	brain	-	-	19	20 (17.6-22.7)	
Japanese quail (*Coturnix coturnix japonica*)	liver	-		36	40 (17.7-90.4)	Robinson et al. (1967b)
	brain	12	6.9 (3.1-15)	65	17.4 (8.7-34.6)	
Japanese quail (*Coturnix coturnix japonica*)	liver	8	28.8 (2.7-140.8)	9	19.7 (5.7-51.7)	Stickel et al. (1969)
	brain	20	3.4 (0.25-11.9)	17	17.3 (6.2-32.9)	
Redwinged blackbird (*Agelaius phoeniceus*)	brain	3	7.1 (6.7-7.4)	27	19.8 (1-34.5)	Clark (1975)
				27	22.2 (13.5-29.5)	
Prairie falcon (*Falco mexicanus*)	brain	2	2.9 (2.8-3)	1	11	Enderson & Berger (1970)
Barn owl (*Tyto alba*)	brain	2			10 (5-15)	Mendenhall et al. (1983)
	carcass	19	9.4	-	-	

As a general point, interpretation of residue data must be done with extreme caution. Brain residues of dieldrin are probably a good indicator of lethality. However, most bird carcasses collected in the field cannot be analysed for brain residues, because the brain deteriorates rapidly after death. For this reason, most residue data from the field are for levels in the liver, which remains discrete and usable for much longer. A liver residue level symptomatic of death from dieldrin poisoning is more difficult to define. A large, acutely toxic, dose of dieldrin may leave a low residual level of dieldrin in liver because the bird dies rapidly. A smaller, less acutely toxic, dose of dieldrin usually leads to loss of body weight before death because of a lack of ability or desire to feed. This period of starvation prior to death boosts liver residues considerably as dieldrin is released from mobilized fat and concentrated in the liver as detoxification is attempted.

7.3.5 Mammals

The acute and long-term toxicity of aldrin and dieldrin for laboratory mammals is summarized in section 8.

Values for the acute oral LD_{50} and subacute oral LC_{50} in the diet (30 days) of dieldrin for four species of voles *(Microtus* sp.) are given in Table 35.

Table 35. Acute and subacute toxicity of dieldrin for voles[a]

Species	Acute LD_{50} (mg/kg body weight) Average males/females	Subacute LC_{50} (30 days) (mg/kg body weight) Average males/females
Microtus orchrogaster	210	105
Microtus canicaudus	100	40
Microtus montanus	205	
Microtus pennsylvanicus	175	

[a] From: Cholakis et al. (1981).

The toxicological signs in these studies were similar to those in laboratory animals, and these four microtine rodents appear to be less susceptible than laboratory rodents to dieldrin intoxication (Cholakis et al., 1981). When short-tailed shrews *(Blerina brevicauda)* were fed diets containing 50, 100, or 200 mg dieldrin (nominal)/kg diet for up to 14 days, all the animals fed 50 mg/kg dieldrin survived, whereas all those fed 200 mg/kg diet died (Blus, 1978).

Luckens & Davis (1965) studied the acute oral toxicity in big brown bats *(Eptericus fuscus)* caught in Kentucky, USA. Death occurred at all

dose levels above 20 mg/kg body weight. The approximate LD_{50} seemed to be within the range 20-40 mg/kg body weight.

White-tailed deer *(Odocoileus virginianus)* were fed 0, 5, or 25 mg dieldrin/kg diet for up to 3 years as were their progeny. No signs of intoxication were observed, and the survival of adults was not affected. The growth rate of treated females was decreased. Relative liver weights increased at 25 mg/kg. Fertility and *in utero* mortality were comparable for the three groups. Fawns from treated does were smaller at birth, and greater postpartum mortality occurred. The weight gain of fawns was reduced during 2 of the 3 years. Whole milk from doses fed 25 mg/kg contained residues of 17 mg/litre. Residues in the liver of surviving animals were about 4 mg/kg in the low-dose group and 16 mg/kg (wet weight) in the high-dose group. Highest brain residues (12 mg/kg wet weight) occurred in fawns only a few days before death (Murphy & Korschgen, 1970).

When blesbuck *(Damaliscus dorcas phillipsi)* were fed diets containing 5, 15, 25, 35, or 50 mg dieldrin (nominal)/kg diet, none of the animals fed 5 or 15 mg/kg diet died during the 90 days of the study. However, all the animals given higher dose levels died within 24 days. The concentration of dieldrin in the liver was 3.3 and 8.2 mg/kg for the two lowest dose levels, after 90 days. The concentrations of dieldrin in the livers of the dead animals were 9.4, 15.1, and 18.4, respectively, for the three highest treatment groups (Wiese et al., 1973).

In studies by Wiese et al. (1973), an experimental grazing site (250 ha) with a resident population of 35 blesbuck and 20 springbok *(Antidorcas marsupialis)* was aerially sprayed with dieldrin at a rate corresponding to 0.16 kg/ha. The concentration of dieldrin on the veld declined rapidly from 27.6 mg/kg immediately after treatment to 5.04 mg/kg after 14 days. The decline during the following 106 days was much slower (it was 0.75 mg/kg on the 85th day and 0.23 on the 120th day). Behavioural changes were observed in both antelope species after 3 days. From the 4th day, there were further nervous symptoms, including clonic convulsive attacks, and partial or even complete blindness was also noted. Blesbuck died from the 4th day onwards, and the entire population of 35 animals had died by the 19th day. The median time to death was 7.08 days, and there was no significant difference between adults (male or female) and juveniles. The calculated mean intake of dieldrin was 1.82 mg/kg herbage per day. This estimate was much lower than that derived from the feeding trial (the total intake of animals that died was 9.08 mg/kg). The mean concentration in the livers of six blesbuck that died was 8.3 mg/kg. It was inferred that dieldrin was unlikely to be the cause of death of the blesbuck (further investigations implicated photodieldrin). Springbok were less adversely affected: deaths occurred from the 6th day, and 70% had died by the 13th day. Surviving animals recovered with no after-effects, and two ewes lambed normally in the spring following the winter treatment. The average dieldrin concentration in the livers of three springbok that died was 9.2 mg/kg. The pathological findings were similar to those in the common laboratory species.

Few other mammalian species have been investigated. Reduced reproductive success and some mortality has been reported in raccoons fed 2 mg dieldrin/kg diet (Stickel, 1975).

7.4 Effect on Populations and Ecosystems

In order to show that a chemical has had an effect on populations of organisms in the environment it is necessary to satisfy a combination of several criteria. Ideally the exposure to the chemical in the field should be established to compare exposure with effects produced. Population declines should correlate with usage of the chemical and should be reversed by controls on the use of the chemical. Although it is generally recognized that dieldrin affected populations of some animals when its use was widespread, there are some difficulties in establishing its precise effects on the environment. These difficulties arise because the use of dieldrin coincided with the use of other persistent organochlorines, which themselves affect populations of organisms, and also because poisoning by dieldrin was often secondary (poisoned organisms did not take in dieldrin *directly* but from prey that had concentrated the chemical from the environment).

7.4.1 Exposure to dieldrin

It is difficult to establish the exposure of wildlife to dieldrin unless animals are directly feeding on dressed grain or directly exposed to preserved wood. Even where this occurs, the animal will frequently die some distance from the source of exposure. This is particularly true for birds but less so for small mammals. Since exposure cannot be readily monitored directly, most investigators have estimated exposure from the residue remaining in dead or dying animals. Monitoring programmes in several countries sampled both dead and dying animals and compared them with healthy animals taken from the wild. Eggs of birds were also monitored as a measure of dieldrin contamination of populations. These monitoring programmes had to establish criteria by which it could be *definitively* stated that particular individuals had died from dieldrin poisoning. The criteria were based on residue levels in experimentally poisoned animals and were set at 5-10 mg/kg brain tissue and 10-20 mg/kg liver tissue for birds (Robinson, 1969; Stickel et al., 1969; Cooke et al., 1982). These criteria are probably conservative; 20-30% of dead wood pigeons examined in the UK during the period 1961-1964 were judged, by these criteria, to have died from dieldrin poisoning. During this period many seed-eating birds were killed directly by eating dieldren-dressed grain (Robinson, 1969); the actual percentage of death attributable to dieldrin should probably be higher. A high proportion of dead birds from areas of tsetse fly control contained residues which would be judged lethal by these criteria. The great majority of birds sampled contained non-lethal residues of dieldrin (Tables 15, 16, 17, 18, and 34). It should be remembered that all of these sampled birds contained

residues of other organochlorines, in addition to dieldrin. Although there have been reports of populations with no dieldrin contamination, but contamination with other organochlorines, there have been no reports of populations contaminated by dieldrin alone. Furthermore, residues of dieldrin always correlate well with residues of other organochlorines; birds retaining large quantities of dieldrin also retain large quantities of DDE and often polychlorinated biphenyls (PCB) (Newton, 1979).

The literature reporting the presence of dieldrin in birds and mammals from the wild is very extensive and has been selectively reviewed elsewhere (section 5.1.6). Analysis of a few dead animals serves to indicate the presence of dieldrin in wildlife but is of little use in establishing effects at the population level. Only long-term monitoring programmes, measuring changes in dieldrin residues in the population with time and correlating this to ecological monitoring of the size and reproductive success of the population, can approach an objective assessment of the effects of dieldrin. Such programmes have been reviewed by Newton (1979).

7.4.2 Effects on populations of birds

Populations of birds of prey declined during the period of large scale use of organochlorine insecticides. Major studies of changes in bird populations concentrated on a few species mainly in the United Kingdom and North America, though also to some extent in areas of mainland Europe. The following references are illustrative on this subject of the literature: general references, Anon (1964), Prestt (1965), Prestt & Bell (1966), Parslow (1973), Bijleveld (1974), Cooke et al., (1976, 1982), Havera & Duzan (1986); peregrine falcon *(Falco peregrinu)*, Ratcliffe (1963, 1965, 1967b, 1970, 1972, 1980, 1984), Lockie & Ratcliffe (1964), Cade et al. (1968), Enderson & Berger (1968), Hickey (1969); heron *(Ardea cinerea)*, Reynolds (1974); golden eagle *(Aquila chrysaetos)*, Brown (1969), Lockie et al. (1969); sparrow-hawk *(Accipiter nisus)*, Koeman et al. (1972), Newton (1973a,b, 1974, 1976, 1979), Newton & Bogan (1974, 1978); Newton et al. (1979), Marchant (1980); kestrel *(Falco finnunculus)*, O'Connor (1982).

In most of these studies, population decline correlated with organochlorines residues in adult birds and their eggs. Reduced breeding success was associated with thinning of eggshells, behavioural changes resulting in egg breakage, and aggressive interaction between adults resulting in a reduction of the number of young fledged successfully from the clutches. The death of adult birds was reported at the same time as seed-eating species were dying from dieldrin poisoning.

As reported earlier in this section, dieldrin cannot be held responsible for the eggshell-thinning effect, which has been shown to be attributable to DDE (Cooke, 1973). Embryo deaths in shell correlate best with PCB residues in eggs (Newton, 1979). The contribution of dieldrin to these declines is difficult to determine because the birds were subjected to residues of all organochlorines. It is probable that

dieldrin contributed to population declines in some areas but not others (Newton, 1979; Newton & Haas, 1984).

The studies of Blus et al. (1974a,b, 1975, 1979a,b) and Blus (1982) on the brown pelican *(Pelicanus occidentalis)* conclude that the decline in numbers could be ascribed entirely to DDE. The population size of birds of prey in some of the Eastern states of the USA declined when no dieldrin residues were present, DDE alone being a contaminant in these populations. Newton (1979) pointed out that the decline in populations of birds of prey contaminated by DDE is gradual, a result of progressive effects of failure in breeding. The decline of populations of peregrine falcon and sparrow-hawk in the United Kingdom was more sudden and was associated with the death of breeding adults. This was attributed to dieldrin usage, which correlated well with the decline (Newton, 1979; Newton & Haas, 1984).

7.4.3 Effects on populations of mammals

Some mammal species in addition to birds, have been affected by the use of organochlorine pesticides. There are reports of decreases in the number of badgers *(Meles meles)* in some areas of the United Kingdom (Jefferies, 1969, 1975). Declines in the number of bats have been reported in the United Kingdom and the Netherlands (Jefferies, 1972); furthermore, the grey bat *(Myotis grisescens)* in the USA (Clark et al., 1978) and the otter *(Lutra lutra)* have also been affected (Jefferies et al., 1974; Chanin & Jefferies, 1978).

Declines in bat numbers have been associated with the use of dieldrin and lindane in wood preservatives in the United Kingdom (Jefferies, 1972). In the United States, they appear to be related to a combination of organochlorines. Many species migrate long distances, using fat reserves on the journey, and are susceptible to DDE poisoning en route (Clark & Kroll, 1977). No contribution of dieldrin to declines in bat numbers in the USA has been proven. Other declines have been attributed to dieldrin (Chanin & Jefferies, 1978). Jefferies & Pendlebury (1968) studied the effect of aldrin/dieldrin seed dressings on the populations of stoats, weasels, and hedgehogs in the United Kingdom. None of these species showed a decline during the period 1959 to 1962, and there was no evidence that aldrin/dieldrin had any detrimental effects.

Jefferies et al. (1973) studied the behaviour of small mammals in and adjacent to a field sown with dieldrin-dressed wheat. The field mouse *Apodemus*, which lives on the field margin and the open field, immediately fed on dosed grain. Residues of dieldrin in sampled mice was very high. The bank vole *Clethrionomys*, which lives in field margins, did not take the dosed grain. Residues of dieldrin in these small mammals were monitored regularly after sowing. These very quickly dropped to very low levels. The authors propose that those individuals eating dressed grain died quickly or were taken by predators. Populations were quickly replenished by immigration from surrounding areas.

8. EFFECTS ON EXPERIMENTAL ANIMALS AND *IN VITRO* TEST SYSTEMS

8.1 Single Exposures

8.1.1 Aldrin and dieldrin

8.1.1.1 Oral

The acute oral LD_{50} values for technical aldrin and dieldrin in various animal species are shown in Table 36. Intoxication with cyclodiene insecticides consists of increased irritability and tremor, followed later by tonic-clonic convulsions. In rats, convulsions appear within 1 h following oral dosing at high concentrations; death follows within 6 h, or from 2-7 days later. This depends on factors such as the contents of the rat's gastrointestinal tract, the concentration of aldrin/dieldrin in the solvent, and the type of solvent used (Borgmann et al., 1952b; Heath & Vandekar, 1964). Fox & Virgo (1986) reported that dieldrin induced hyperglycemia.

The minimum toxic and the maximum non-toxic doses of aldrin and dieldrin, administered orally to livestock, are indicated in Table 37.

8.1.1.2 Dermal

The minimum lethal dose of aldrin or dieldrin when applied as a dry powder on the intact skin of female rabbits for 24 h was between 600 and 1250 mg aldrin/kg body weight and between 250 and 360 mg dieldrin/kg body weight. In olive oil, the range for aldrin was the same as for dry powder, and the range for dieldrin was between 360 and 600 mg/kg body weight (Treon et al., 1953).

The acute dermal LD_{50} values for technical aldrin and dieldrin in various animal species are shown in Table 38. The signs of intoxication are similar to those that follow oral administration.

8.1.1.3 Inhalation

The vapour pressures of technical aldrin and dieldrin are sufficiently low that an acute inhalation hazard from aldrin or dieldrin vapour does not normally arise.

8.1.1.4 Parenteral

The acute LD_{50} values for technical dieldrin (in glycerol formal) in the rat via intraperitoneal and intravenous routes are 56 and 8-9 mg/kg body weight, respectively (Heath & Vandekar, 1964).

Table 36. Acute oral LD_{50} values for technical aldrin and dieldrin

Species	Vehicle	LD_{50} (mg/kg body weight)		Reference
		Aldrin	Dieldrin	
Mouse	corn oil	44	38	Borgmann et al. (1952a,b)
Mouse	olive oil		~75	Jolly (1954)
Rat (newborn)	arachis oil		168[a]	Lu et al. (1965)
Rat (pre-weaning)	arachis oil		25	Lu et al. (1965)
Rat (adult)	arachis oil		37	Lu et al. (1965)
Rat	arachis oil		51-64	Heath & Vandekar (1964)
Rat	various	38-67		Lehman (1951); Borgmann et al. (1952a); Treon & Cleveland (1955); Gaines (1960); Worthing & Walker (1983)
Rat	various		37-87	Lehman (1951); Borgmann et al. (1952b); Treon & Cleveland (1955); Gaines (1960); Lu et al. (1965); Worthing & Walker (1983)
Hamster	olive oil	320	330	Gak et al. (1976)
Hamster	corn oil		100	Cabral et al. (1979a,b)
Guinea-pig	corn oil	33	49	Borgmann et al. (1952a,b);
Guinea-pig	olive oil		between 10 and 25	Jolly (1954)
Rabbit	corn oil	50-80	45-50	Borgmann et al. (1952a,b)
Dog	corn oil	65-95	65-80	Borgmann et al. (1952a,b)

[a] Transcutaneous intragastric injection.

Table 37. Acute oral toxicity of aldrin and dieldrin for livestock

Compound	Species	Age	Maximum non-toxic dose tested	Minimum toxic dose found	Reference
			(mg/kg body weight)		
Aldrin	calf	1-2 weeks	2.5	5	Radeleff et al. (1955)
	cattle	1 year	10	25	Radeleff et al. (1955)
	sheep	1-2 years	10	15	Radeleff et al. (1955)
Dieldrin	calf	1-2 weeks	5	10	Radeleff et al. (1960)
	cattle	1 year	10	25	Radeleff et al. (1955)
	horse	-	-	25	Radeleff et al. (1960)
	pig	3 weeks	25	50	Radeleff et al. (1960)
	sheep	1 year	15	25	Radeleff et al. (1960)
	sheep	9-12 months	-	LD_{50} 50-75	Jolly (1954)

Table 38. Dermal LD_{50} values for technical aldrin and dieldrin

Species	Vehicle	LD_{50} Aldrin	LD_{50} Dieldrin	Reference
		(mg/kg body weight)		
Mouse	solvent naphtha	-	40-80[a]	Jolly (1954)
Rat	xylene	~100	60-90	Gaines (1960)
Guinea-pig	solvent naphtha	-	120[a]	Jolly (1954)
Rabbit	dimethyl-phthalate	150	150	Lehman (1952)

[a] With complete immersion of body.

8.1.2 Formulated materials

8.1.2.1 Oral and dermal

The acute toxicity of formulated products, particularly the dermal toxicity, is a more realistic guide than that of the technical product to the acute hazard to the user. The percentage of aldrin or dieldrin in the formulation, the solvent used, and the type of formulation (such as an emulsion, wettable powder, dust, etc.) will determine the acute toxicity of the formulated product. Depending on these factors, the oral and dermal LD_{50}s vary from 100 to 4500 and 500 to 16 000 mg total aldrin formulation/kg body weight, respectively. For dieldrin formulations, these figures are 100-400 mg/kg and 200-2700 mg formulation/kg body weight, respectively (Muir, 1970; Rose, 1982, 1984a,b).

For a dieldrin formulation for termite control (680 g/litre suspension concentrate), the dermal LD_{50} in the male rat was 645 mg formulation/kg body weight and in the female rat 284 mg formulation/kg body weight (Rose, 1984c).

8.1.2.2 Inhalation

The acute inhalation LC_{50} (4-h exposure) in rats for aqueous dilutions of a 48% (w/v) emulsifiable concentrate of aldrin (high aromatic solvent) in the form of a spray was estimated to be equivalent to 3% (w/v) aldrin. The median droplet size was 52 μm, and the animals were exposed "nose only". Deaths occurred up to 6 days after exposure, but most of the animals died on the 2nd day after exposure. Signs of intoxication consisted of a subdued and hunched appearance with piloerection, progressing to hypersensitivity and convulsions in the more seriously affected animals. Surviving animals recovered within 2-3 days after exposure. Oral intake (due to grooming) contributed significantly to the results (MacDonald, 1982).

8.2 Short-Term Exposures

Short-term studies on rodents have shown that aldrin and dieldrin affect the liver. The liver/body weight ratio is increased, and histopathological changes that have become known as "Chlorinated Hydrocarbon Insecticide Rodent Liver" (CHIRL) are observed. Microscopically, these CHIRLs consist of enlarged centrilobular hepatocytes with somewhat increased cytoplasmic oxyphilia and peripheral migration of the basophilic granules (Treon & Cleveland, 1955; Ortega et al., 1957).

The cellular and subcellular changes in the liver of different mammalian species have been studied by Wright et al. (1972, 1977, 1978). These studies have shown that dieldrin produces a generalized enlargement of the liver, which, in rats and dogs, is associated with increased size of liver parenchymal cells but, in mice, is associated

with an increase in both cell size and cell number. The earliest ultrastructural change in the livers of mice, rats, and dogs treated with dieldrin was the proliferation of the smooth endoplasmic reticulum (SER). During the initial phase of the exposure to dieldrin, and also to phenobarbital, the increases in the SER in the liver cells of mice, rats, and dogs were of the vesicular type. These changes were associated with an enhanced microsomal mixed-function oxidase, and intracellular whorls of smooth membranes appeared in the liver cells of rats and dogs but not in those of the mouse. The changes in liver subcellular structure and function were reversible in mouse, rat, and dog. In contrast, no liver enlargement or other ultrastructural changes were observed in the livers of rhesus monkeys. *In vitro* determinations showed that the activity of the liver microsomal monooxygenase system was increased after treatment, and this was the most sensitive effect observed. In all species examined, the biochemical and subcellular structural response of the liver to dieldrin was shown to be similar to that found with a number of other chemicals, such as DDT, heptachlor, and phenobarbital (Jansen, 1979). These chemicals also induce in the mouse a type of liver tumour identical to that found with dieldrin (Stevenson & Walker, 1969; Thorpe & Walker, 1973).

8.2.1 Oral

8.2.1.1 Rat

A number of short-term feeding studies (3-9 months duration) were carried out on rats with aldrin. Dose levels of 0.5-300 mg aldrin/kg diet were tested. The results of these old studies showed that dose levels up to 5 mg/kg diet produced no effects, but that levels of 25 mg/kg or more gave an increased liver/body weight ratio and reversible hypertrophy of centrilobular hepatocytes with cytoplastic changes (CHIRL) (section 8.4.2). Dose levels of 150 mg/kg or more resulted in increased mortality (Treon et al., 1951; Borgmann et al., 1952a).

Five further studies were carried out with dieldrin (3-10 months duration), using dose levels of 1-300 mg/kg diet. No effects were seen up to 5 mg/kg, except that Walton et al. (1971) found an increased liver/body weight ratio in females at 5 mg/kg and Ortega et al. (1957) found occasional liver changes at 2.5 mg/kg diet. These changes, e.g., liver enlargement and induction of CHIRL, were found in the other studies at 10 mg/kg diet or more. At 150 mg/kg or more, there was increased mortality (Treon et al., 1951; Borgmann et al., 1952b; Ortega et al., 1957; Walton et al., 1971).

When groups of male albino rats were fed diets equivalent to 2 mg/kg body weight for 6 months, the alkaline phosphatase, SGPT, SGOT, and LD-hydrogenase activities in the serum were increased after 6 months. The urea content decreased after 3 months, and some other parameters were also changed. The growth of the animals was considerably inhibited (Shakoori et al., 1986).

8.2.1.2 Dog

Dogs appear to be more susceptible to aldrin and dieldrin than rats. Dogs administered aldrin in the diet for 5 or 6 days at dose levels equivalent to 0.9-9.1 mg/kg body weight died within 7 months. However, beagle dogs (two males and two females) survived 15.6 months when given 0.043-0.25 mg aldrin/kg body weight. With dieldrin, dogs survived dose levels up to 0.23 mg/kg body weight for 15.7 months. In aldrin- and dieldrin-treated animals, no effects on growth and no changes in haematology were seen. The dogs with 0.25 mg aldrin/kg showed hepatomegaly, and the females had local hyaline (droplet) degeneration of hepatocytes and vacuolization in the epithelia of distal renal tubules. One of the males of this group showed hepatocyte degeneration, while the other exhibited the renal tubular changes seen in the females. In the group fed 0.09 mg/kg, no effects were seen in the males, while the females (and also one female in the group fed 0.23 mg/kg) showed vacuolization in the epithelia of the distal renal tubules. The liver weights of the dieldrin-treated animals were increased. No other dogs showed gross or microscopic abnormalities in the viscera (Treon & Cleveland, 1955).

Four beagle dogs fed dieldrin at daily oral doses of 0.4-0.8 mg/kg body weight showed blood concentrations of 0.27-1.27 mg/litre blood after eight episodes of convulsions (Brown et al., 1964). When two dogs were given 0.2 mg dieldrin/kg body weight, in gelatin capsules daily for 8 months, no signs of intoxication were observed. The concentration in the blood was 0.11-0.22 mg/litre.

In studies by Fitzhugh et al. (1964), twelve mongrel dogs of various ages received aldrin, 6 days/week for periods up to 25 months, at doses of 0.2, 0.5, 1, 2, or 5 mg/kg body weight. Dieldrin was tested in 14 mongrel dogs at doses of 0.2, 0.5, 1, 2, 5, or 10 mg/kg body weight. In both cases, there were two animals per dose level (one male, one female), with the exception of four animals in the groups given 0.5 mg/kg. In the animals tested with aldrin, the 5 mg/kg dogs and one 2 mg/kg dog died in 3-4 weeks; the remaining male dog in the 2 mg/kg group was killed at 25 weeks because of poor condition. All four dogs showed weight loss and fatty changes in the liver and renal tubules. The bone marrow showed a reduced number of mature granulocytes and erythroid cells. At 1 mg/kg, the two dogs survived for 15 and 49 weeks and, at autopsy, showed the same lesions. In the 0.5 mg/kg group, one dog died after 4 days. The remaining three dogs survived for 2 years, one male among these having convulsions during the last 2 months. At 0.2 mg/kg body weight, there were no effects. In the animals tested with dieldrin, all six dogs on 2, 5, and 10 mg/kg died during weeks 2-5. These dogs showed weight loss, fatty changes and slight hepatic cell atrophy in the liver, and a small amount of atypically distributed fat in the kidneys. The bone marrow showed a reduced number of mature granulocytes and erythroid cells. The reported bone marrow findings, which were not replicated in other studies, cannot be interpreted, because of the inadequacy of clinical details, and no

control dogs were used in this study. The two dogs given 1 mg/kg survived for 12 and 43 weeks and, at autopsy, showed the same lesions. One dog given 0.5 mg/kg was sacrificed after 2 weeks because of anorexia and marked emaciation. Detailed histological examination, including that of the brain, did not show any distinct organ damage. The remaining three dogs in the 0.5 mg/kg group died with terminal convulsions or were sacrificed in poor condition at weeks 29, 43, and 81. Two of the dogs showed weight loss. No effects were observed in the 0.2 mg/kg group.

Repeated daily oral administration of 0.2, 1, or 2 mg dieldrin/kg body weight to groups of six mongrel dogs was carried out until intoxication occurred between the 18th and 85th day. A direct relationship was established between the dieldrin concentration in the blood and the severity of clinical signs of intoxication. On the first day of muscle spasms, the average concentration of dieldrin in the blood was about 0.50 mg/litre and, at the time of the first full-blown convulsion, about 0.90 mg/litre (Keane & Zavon, 1969a).

In studies by Walker et al. (1969b), groups of five beagle dogs of each sex received, by capsule, daily doses of 0.005 or 0.05 mg dieldrin (in olive oil)/kg body weight, for 2 years. Control dogs were given capsules containing olive oil. The health, behaviour, and body weight were unaffected, and EEG recordings did not differ between the dogs fed 0.05 mg/kg and the controls. In females given 0.05 mg/kg, liver/body weight ratio was increased. In both sexes, serum alkaline phosphatase activity was increased. However, urine, haematology, clinical chemistry, bromosulfthalein clearance, and relative organ weight data were not affected. No gross or histopathological anomalies were observed.

Deichmann et al. (1969) gave groups of six beagle dogs (aged 1.5-3.5 years) 0 or 0.6 mg aldrin/kg body weight, 5 days/week for 10 months, and then observed them for an additional 12 months. The treated dogs showed hyperexcitability, tremors, and weight loss. One dog died. After 14-18 months, the dogs with aldrin showed cloudy swelling and fatty degeneration in the liver and hypertrophy of hepatocytes. Renal vascular congestion and tubular degeneration were seen in some of the animals.

8.2.1.3 Domestic animals

A dairy cow given aldrin in soybean oil daily by capsule (2.2 mg/kg body weight) exhibited hyperirritability after 27 days. The animal was in heat and was bred the next day. She died on day 29 with convulsions. Autopsy showed a slightly discoloured, pulpy, congestive liver and one slightly enlarged congested kidney. No mortality occurred among cows given 0.8, 1, or 1.5 mg/kg body weight for 48 days (Ely et al., 1954).

In studies by Gannon et al. (1959b), groups of four dairy cows were fed rations containing 0, 0.1, 0.25, 0.75, or 2.25 mg dieldrin/kg for 12 weeks (average total intake, 0, 0.293, 0.75, 2.17, or 6.55 mg dieldrin/kg body weight). No signs of illness and no abnormalities were found when the cows were slaughtered at the end of the test

feeding period or after an additional 6-week period on dieldrin-free rations.

Ivey et al. (1961) fed groups of 2-3 steers, sheep, and hogs rations containing 0, 0.25, 0.75, or 10 mg aldrin/kg diet for 12 weeks. Two steers received rations with 2 mg/kg diet for the same period. The control groups consisted of two animals each. No evidence of illness and no postmortem pathology were found.

Goats administered 50 mg aldrin/kg body weight showed mild degenerative changes, congestion and petechial haemorrhages, in various organs. In the kidneys degenerative changes of the proximal convoluted tubules were found. Clinical changes were also found, e.g., salivation and convulsions (Singh et al., 1985).

8.2.2 Dermal

In studies by Treon et al. (1953), aldrin and dieldrin, as dry powders or in solutions, were applied daily to the skin of groups of three female rabbits for 2 h on each of 5 days per week over a period of 10 weeks. A series of graded doses was used to determine the doses resulting in no mortality. It was clear that aldrin or dieldrin dissolved in kerosene was very toxic (LD_{50} of approximately 5 mg/kg body weight). Dissolved in vegetable oil they were about 6 times less toxic and as dry powder about 20 times less toxic than when dissolved in kerosene.

8.2.3 Inhalation

Mice, hamsters, and guinea-pigs did not show any adverse effects when exposed to vapourized aldrin at a concentration of 18 mg/m^3 for 178 days (Baker et al., 1959).

8.3 Skin and Eye Irritation; Sensitization

8.3.1 Skin and eye irritation

Treon et al. (1953) reported that technical aldrin or dieldrin applied on the intact rabbit skin for 24 h occasionally caused slight erythema. Repeated application of aldrin or dieldrin for 10 weeks (2 h per day, 5 days per week) as a dry powder did not alter the gross condition of the rabbit skin. Slight irritation and scaliness were observed when the compounds were applied in vegetable oil, but their application in kerosene resulted in damage, attributable to the solvent.

An undiluted aldrin emulsifiable concentrate formulation (48% aldrin in high aromatic hydrocarbon solvent), applied at a dose of 0.5 ml at each test site for 24 h on the intact skin and abraded skin of rabbits under an occlusive patch, caused severe irritation and necrosis of the skin. One male died on day 13. When applied to the rabbit eye, this undiluted 48% emulsifiable concentrate caused severe initial pain and mild irritation (Rose, 1982).

8.3.2 Sensitization

In the Magnusson and Kligman guinea-pig maximization test, 48% aldrin emulsifiable concentrate caused positive responses (at 24 h and 48 h after removal of the challenge patches) in 3 out of the 20 test animals. Rechallenge of these animals, one week later, confirmed that they had been sensitized to the test material (Rose, 1982).

Aldrin emulsifiable concentrate (48%) is not a skin sensitizer under the EEC Dangerous Substances Directives (EEC, 1983).

No cases of skin sensitization occurred over a period of 20 years among a group of over 1000 workers involved in the manufacture and formulation of aldrin and dieldrin (Jager, 1970).

8.4 Long-Term Toxicity and Carcinogenicity

8.4.1 Mouse

Davis & Fitzhugh (1962) fed groups of 100 male and 100 female C3HeB/Fe mice a diet containing aldrin or dieldrin at 0 or 10 mg/kg diet for 2 years. The average lifespan of the treated mice was shortened by 2 months. A significant increase in the incidence of benign liver tumours was observed.

In a further study, 100 male and 100 female C3HeB/Fe/J mice received aldrin or dieldrin at 0 or 10 mg/kg diet for 2 years. An increase in the number of animals with hepatic hyperplasia and benign liver tumours was seen in the treated groups, but no increase in malignant liver tumours was found. The survival in the treated groups was lower than that of controls (Davis et al., 1965).

Groups of 300, 125, 125, and 200 CF1 mice of each sex were fed diets containing dieldrin (> 99%) at 0, 0.1, 1, or 10 mg/kg, respectively, for 2 years. A positive control group fed 600 mg 4-amino-2,3-dimethylazobenzene for 6 months, followed by a control diet, was used. After 9 months, the morbidity of the mice fed 10 mg/kg started to increase, but the lifespan of the mice fed 0.1 or 1 mg/kg was unaffected. The animals with 4-amino-2,3-dimethylazobenzene died within 14 months. The frequency of liver tumours was increased in all groups fed dieldrin. Two types of tumours were observed, one of which was considered benign (hyperplastic nodules) and the other malignant. The malignant tumours were clearly hepatocarcinomas, though no fibrosis or bile duct proliferation, as seen in the positive control group, occurred in the dieldrin-treated groups. A reversibility study in a separate group fed 10 mg dieldrin/kg in the diet for up to 15 months, followed by a control diet for the rest of the 2-year study, showed that the tumours did not regress or disappear upon discontinuation of the treatment. However, the dieldrin induced hepatomegaly, and cytoplasmic changes were found to be reversible (Walker et al., 1972; Hunt et al., 1975).

In a study by Thorpe & Walker (1973), a group of 30 CF1 mice of each sex were fed a diet containing 10 mg dieldrin/kg for 2 years. The

control group consisted of 45 mice of each sex. Liver enlargement was detected after 50 weeks in both sexes, and liver lesions were observed, classified as hyperplastic nodules (Type a) and hepatocellular carcinoma (Type b) (sometimes associated with lung metastases). In a separate study, it was shown that dieldrin Type b liver cell tumours were capable of growing as subcutaneous transplants in mice of the same strain and sex (Thorpe, 1973).

To compare the pathological responses to dieldrin in different mouse strains, groups of 30 mice of each sex of the CF1, LACG, and hybrid CF1-LACG strains were fed diets containing 10 mg dieldrin/kg for 2 years. There was also a control group of 45 animals of each sex for each strain. The incidence of liver tumours, particularly Type b tumours, in male CF1 and hybrid mice and in females of all three strains was higher than in controls. In male LACG mice, the incidence of liver tumours was low. Qualitatively, there was no difference in tumours between strains, and there was no increased incidence of neoplasms in other tissues, nor were unusual tumours found. Metastases of liver carcinoma were found in the lungs in some of the mice (Thorpe & Hunt, 1975).

In studies by Benitz et al. (1977), nine groups of 100 Charles River CD1 mice of each sex were given dieldrin in the diet at concentrations ranging from 0.15 to 15 mg/kg. Six hundred mice of each sex were used as controls. Groups of animals were sacrificed at time intervals ranging from 2 to 25 months. Initial changes in the liver consisted of various degrees of centrilobular and pericentral hypertrophy. These changes were later associated with the appearance of hepatic nodules, the occurrence of which was time and dose related. These nodules consisted of hypertrophic hepatocytes, which, in a few instances, were mixed with hyperplastic cells. Various degrees of loss and distortion of lobular architecture were seen within these nodules. Metastases in the lung were observed in three nodule-bearing animals given 15 mg dieldrin/kg for 25 months. These metastases contained similar hypertrophic hepatocytes as did the primary liver tumours.

Groups of 50 B6C3F1 mice of each sex were fed diets containing aldrin (4 or 8 mg/kg diet for males and 3 or 6 mg/kg diet for females) or dieldrin (2.5 or 5 mg/kg for both sexes) for 80 weeks, followed by an observation period of 10-13 weeks. Concurrent controls consisted of groups of 20 male and 10 female mice. The pooled controls, used for statistical evaluation, consisted of the concurrent control groups combined with 92 male and 79 female mice from similar bioassays of other chemicals. All surviving mice were killed at 90-93 weeks. Body weight was not affected in the treated animals, but there was a dose-related increase in mortality, especially in the high-dose groups in the second half of the study. In the dieldrin-treated mice, clinical symptoms, such as irritability, tremors, and alopecia occurred. Hepatocellular carcinomas were found, as indicated in Table 39. The incidence of hepatocellular carcinomas was clearly higher in male than female mice. There was no difference in tumour frequencies in other tissues (NCI, 1978a).

Table 39. Incidence of hepatocellular tumours in mice (NCI, 1978[a])

Groups	Males	Females
Concurrent controls	3/20 (15%)[a] 3/18 (17%)[b]	0/10 (0%)[a] 0/20 (0%)[b]
Pooled controls	17/92 (18%)	3/78 (4%)
Aldrin (4 mg)	16/49 (33%)	
(8 mg)	25/45 (56%)	
Aldrin (3 mg)		5/48 (10%)
(6 mg)		2/43 (5%)
Dieldrin (2.5 mg)	12/50 (24%)	6/50 (12%)
(5 mg)	16/45 (36%)	2/49 (4%)

[a] Concurrent controls of aldrin study.
[b] Concurrent controls of dieldrin study.

Groups of weanling male C3H/HE mice were fed a diet containing 10 mg dieldrin/kg diet until an age of 57 weeks and then were either administered a control diet (12 mice) or continued on the dieldrin diet (11 mice) for another 10 weeks. A third group served as an untreated control group (21 mice). Laparatomies were performed and biopsy specimens taken when about 30% of the mice in each dieldrin-treated group had tumours. Further biopsy samples were taken approximately 10 weeks later. Tumours were observed at the first laparotomy in 6/21 controls and 14/23 dieldrin-treated animals. At the second laparotomy, adenomas were seen in some animals in which there had been no tumour at the first laparotomy. In one animal in the continuous dieldrin-treatment group, there was histological progression from adenoma to hepatocellular carcinoma. Additional hepatocellular carcinomas were observed in some animals autopsied at 2 years of age. A strong tendency to tumour progression was found in both treated and control mice (Ruebner et al., 1984a,b).

In a study by Meierhenry et al. (1983), groups of 50-70 male mice of three strains (C57Bl6J, C3H/He, and C57Bl6J x C3H/He B6C3F1 hybrid) were administered a diet containing 10 mg dieldrin/kg diet for 85 weeks. The control groups consisted of approximately 60 mice of the same strains. After 4 months, the livers in a small number of animals showed swellings of hepatocytes in the central zone with nuclear atypia, small nodules containing basophilic or eosinophilic foci, and multiple tumours. The percentage of benign hepatic tumours was 28, 20, and 29, respectively, and in the control groups, 19, 18, and 4. The percentage of hepatocellular carcinomas was 30, 38, and 42, respectively, and, in the controls, 0, 12, and 4%. Mallory bodies were seen in all the dieldrin-treated mice that had either benign or malignant tumours, but only rarely in mice without tumours.

It seems from the available studies that dieldrin facilitates and exacerbates the expression of an endogenous oncogenic factor in CF_1 mice (Tennekes et al., 1981). The dose-response characteristics of dieldrin-mediated enhancement of liver tumour formation in CF_1 mice were analysed using existing tumour data from long-term feeding studies at six levels of continuous exposure, involving a total of more than 1500 animals. Using the Druckrey equation, the actual contribution of dieldrin to tumour formation was considered to be negligible (Tennekes et al., 1985).

8.4.1.1 Appraisal

A number of long-term carcinogenicity studies have been carried out in which mice of different strains were fed aldrin and/or dieldrin at one or more dose levels. In all these studies, there was an increased incidence of liver changes, some of which were of the nature of hepatocellular carcinomas while others were regarded as non-malignant. Females seem to be less sensitive than males. No other tumours were induced.

8.4.2 Rat

Borgmann et al. (1952a) fed six groups of 10 male and 10 female weanling Sprague Dawley rats a diet containing 0, 5, 10, 50, 100, or 150 mg aldrin/kg diet over a period of 2 years. At the two highest dose levels, an increased mortality was found at 16 months, which was not seen in the other groups. Liver enlargement was observed in the groups with high dose levels, but not in the groups with 10 mg/kg diet or less.

When groups of 40 Carworth rats of each sex were given diets containing aldrin or dieldrin at 0, 2.5, 12.5, or 25 mg/kg diet for 2 years, there was no increase in mortality and the growth rate was comparable with that of controls. At all dose levels, the liver/body weight ratio was increased in males and there were histological liver cell changes characteristic of CHIRL. No tumours were reported (Treon & Cleveland, 1955). In a review of all the aldrin and dieldrin studies, it was reported that there was no excess of tumours in these rats (Cleveland, 1966).

When groups of 12 Osborne-Mendel rats of each sex were given diets containing aldrin or dieldrin (0, 0.5, 2, 10, 50, 100, or 150 mg/kg diet) for 2 years, growth was not affected. However, survival was markedly decreased at dose levels of 50 mg or more in a dose-related manner. The liver/body weight ratio was increased in males fed 10 mg/kg or more, while, in females, an increase at all dose levels was found (no dose-response relationship at the lower doses). CHIRL was observed in all treated groups, although at 0.5 mg/kg only a few animals showed a trace of CHIRL. Rats at dose levels of 50 mg/kg or more showed haemorrhagic urinary bladders and nephritis. An overall increase in tumour incidence was noted, but this was not dose related. On the

contrary, the lowest dose levels showed the highest tumour incidence. Only one liver tumour was found (Fitzhugh et al., 1964).

In a study at the National Institute of Public Health of the Netherlands, no increased incidence of tumours was found in rats fed diets containing 75 mg dieldrin/kg for 2 years (Van Genderen, 1965, 1979).

When groups of 30 Osborne-Mendel rats of each sex were fed 5 mg/kg aldrin (95%) or a control diet for 2 years, there was no increase in mortality, liver/body weight ratios, or tumour incidence in the aldrin-fed group (Deichmann et al., 1967).

In studies by Walker et al. (1969b), groups of 25 Carworth Farm E rats of each sex were given dieldrin at 0.1, 1, or 10 mg/kg diet for 2 years. A control group consisted of 45 males and 45 females. There was no effect on body weight. After 2-3 months, the animals fed 10 mg/kg exhibited irritability and, as the study progressed, tremors and occasional convulsions, usually during handling. Mortality, haematology, serum enzyme levels, and urinalysis were not affected. The females fed 1 mg/kg and 10 mg/kg had increased liver/body weight ratios. At 10 mg/kg, one male and six females exhibited CHIRL. In two females of the group fed 10 mg/kg and in one female control rat, microscopic nodules in the liver parenchyma were seen. There was no increase in tumour incidence. Subsequent re-evaluation of these data (Stevenson et al., 1976) confirmed that there was no treatment-related increase in tumour incidence.

Nine groups of 50 Osborne-Mendel rats of each sex were fed diets containing aldrin or dieldrin at 0, 20, 30, or 50 mg/kg for up to 31 months. A control group consisted of 100 male and 100 female rats. Dose-related tremors and convulsions, always associated with weight loss, occurred at all dose levels, particularly in females. Female rats fed 50 mg aldrin/kg or 30 or 50 mg dieldrin/kg had a shortened lifespan. The liver/body weight ratio was increased in all dieldrin-treated groups and in males fed 30 or 50 mg aldrin/kg, but was decreased in females fed 20 mg/kg. A moderate increase (not dose related) in the incidence of hepatic centrilobular cloudy swelling, necrosis, or, rarely, foci of acute or chronic inflammatory cellular infiltration was observed in all treated groups. Hyperplasia in the liver was found in two male rats fed 30 mg aldrin/kg. There was no increase in tumour incidence (Deichmann et al., 1970; Deichmann, 1974).

Groups of 50 Osborne-Mendel rats of each sex were given diets containing aldrin at levels of 30 or 60 mg/kg. Treatment of male rats lasted 74 weeks followed by 37-38 weeks of observation, while that of female rats lasted 80 weeks followed by 32-33 weeks of observation. In a similar study, dieldrin was fed at a level of 29 mg/kg diet (time-weighted average dose) for 80 weeks followed by observation for 30-31 weeks or 65 mg/kg diet (time-weighted average dose) for 59 weeks followed by observation for 51-52 weeks. Concurrent control groups consisted of 10 rats of each sex. Pooled controls, used for statistical evaluation, consisted of concurrent control groups combined with 58 males and 60 females from similar bioassays with other chemicals.

All surviving rats were killed at 110-111 weeks. Typical signs of organochlorine intoxication (such as hyperexcitability) were observed with increasing frequency and severity, especially in the second year, but mortality was not affected. No significant increase in tumour incidence was found (NCI, 1978a) (table 40).

Groups of 24 Fischer 344 rats of each sex were given dieldrin at 0, 2, 10, or 50 mg/kg diet for 2 years. Typical signs of organochlorine intoxication were observed during the second year in the 50 mg/kg group. Body weight and survival were not adversely affected in any of the dieldrin groups. Liver tumours were not observed. No significant increase in tumours was found (NCI, 1978b) (Table 40).

Table 40. Incidence of hepatocellular tumours in rats (NCI, 1978[a,b])

Groups	Males	Females
Osborne-Mendel rats		
Concurrent controls	1/10 (10%)[a] 1/10 (10%)[b]	1/10 (10%)[a] 0/9 (0%)[b]
Pooled controls	?	5/59 (8.5%)[a]
Aldrin (30 mg/kg diet) (60 mg/kg diet)	1/47 (2%) 1/47 (2%)	0/48 (0%) 3/49 (6%)
Dieldrin (40-20 mg/kg diet)[d] (80-40 mg/kg diet)[e]	0/44 (0%) 1/47 (2%)	1/47 (2%) 1/44 (2.3)
Fischer F 344 rats		
Concurrent controls	2/24 (8.3%)	0/24 (0%)
Pooled controls	?	?
Dieldrin (2 mg/kg diet) (10 mg/kg diet) (50 mg/kg diet)	0/23 (0%) 0/23 (0%) 4/23 (17%)[c]	0/24 (0%) 0/24 (0%) 0/23 (0%)

[a] Concurrent controls of aldrin study.
[b] Concurrent controls of dieldrin study.
[c] Nodular hyperplasia.
[d] Time-weighted average dose = 29 mg/kg.
[e] Time-weighted average dose = 65 mg/kg.

When groups of 50 female rats of two different strains (Osborne-Mendel and Sprague Dawley) were fed 0, 20, or 50 mg aldrin/kg diet, the survival rate was reduced at 50 mg/kg but not at 20 mg/kg. There was no increase in the incidence of mammary or liver tumours (Deichmann, 1974; Deichmann et al., 1979).

Photodieldrin, which has metabolites identical to those of dieldrin, was fed to groups of rats for 80 weeks at concentrations of up to 7.5 mg/kg diet NCI (1977). No increase in tumour incidence was found (see section 8.8.1.3).

Ito et al. (1983) studied the promoting activity of dieldrin on the induction of hyperplastic (neoplastic) liver nodules using a short-term test system. F344 rats received a single dose (200 mg/kg body weight) of *N*-nitrosodiethylamine, and 2 weeks later, were treated for 6 weeks with dieldrin in the diet at a concentration of 100 mg/kg. Dieldrin had a weak promoting potential in this test system.

8.4.2.1 Appraisal

A number of long-term/carcinogenicity studies have been carried out in which rats of different strains were fed one or more dose levels of aldrin and/or dieldrin. The overall no-effect level in these long-term studies, both for aldrin or dieldrin, was 0.5 mg/kg diet. At feeding levels of 1 mg/kg or more, an increasing, dose-related hepatomegaly and histological changes in the liver characterized as CHIRL occurred. At levels of 10 mg/kg diet or more, typical signs of organochlorine toxicity occurred such as irritability, tremors, and convulsions. In all these studies, no increase in tumour incidence in liver or other organ/tissue systems was found.

8.4.3 Hamster

When groups of 34-40 Syrian golden hamsters of each sex were fed diets containing dieldrin (99%) at 0, 20, 60, or 180 mg/kg for 120 weeks, there was no significant increase in tumour incidence (Cabral et al., 1979b).

8.4.4 Monkey

In studies on rhesus monkeys, groups of five males were given diets containing dieldrin (88.4%) at 0, 0.01, 0.1, 0.5, 1, or 5 mg/kg (0.0002-0.07 mg/kg body weight) for approximately 6 years. After two monkeys in the group fed 5 mg/kg died, the level of exposure to the remaining three animals was reduced to 2.5 mg/kg and, later, to 1.75 mg/kg. Subsequently, one of these animals had his dieldrin intake progressively increased until at the end of the second year, he was receiving dieldrin at the initial dietary concentration of 5 mg/kg. Clinical and haematological examinations, liver and kidney function studies, urinalysis, and pathology did not reveal any abnormalities. The liver/body weight ratios and liver DNA and RNA of the test animals were not different from those of control animals. No subcellular changes were seen in the hepatocytes. Dose-related increases in microsomal cytochrome P-450 and in the activity of the liver monooxygenase enzyme system were observed at the two highest dose levels. These alterations in cytochrome P-450 in the liver microsomes were

significant in the monkeys fed 0.1 mg/kg or more. No effect was observed at 0.01 mg/kg. The concentrations of dieldrin in the subcutaneous fat of the monkeys fed 0.1 mg/kg were similar to those measured in human beings receiving a daily oral intake of similar concentration. The dieldrin concentrations in the monkey livers were approximately 200 times higher than those in male rats receiving a daily intake of dieldrin 3 times higher than the monkeys, and they were similar to the concentration in the livers of male mice daily ingesting dieldrin at a level approximately 50 times higher (Zavon & Stemmer, 1975; Wright et al., 1977, 1978).

8.4.5 Mode of Action

From long-term feeding experiments, it seems that aldrin and dieldrin may be carcinogenic to mice, but not to rats or hamsters. Mutagenicity findings have been consistently negative (see section 8.6). There is insufficient knowledge of the mechanism by which these chemicals might behave epigenetically.

The latest evaluation of IARC (1987) is that there is inadequate evidence of carcinogenicity in humans and limited evidence for carcinogenicity in experimental animals.

8.5 Reproduction, Embryotoxicity, and Teratogenicity

8.5.1 Reproduction

8.5.1.1 Mouse

Groups of 100 pairs of male and female virgin CFW Swiss mice were fed diets containing 5 mg dieldrin/kg for 30 days before mating, after which time they were randomly paired and fed the same diet for a further 90 days. Mortality in the dieldrin-treated group was similar to that of a control group (size not specified). No major biological effects on fertility, fecundity, gestation period, size of the first litters, or numbers of young produced per day were noted as a result of feeding dieldrin. A statistically significant (6%) decrease in mean size of all litters combined was the only difference observed between the dieldrin-treated and control groups (Good & Ware, 1969).

In a reproductive study, groups of 4 male and 14 female Swiss white mice (120 days old) were fed diets containing 3, 5, 10, or 25 mg aldrin/kg or 3, 10, or 25 mg dieldrin/kg. Six groups served as controls. The study covered six generations, and two litters per generation. For both aldrin and dieldrin, the 25 mg/kg dose was too toxic and resulted in high litter mortality in the few dams reaching gestation. This dose level was therefore discontinued. Pup survival was low in mice fed 10 mg dieldrin/kg, and so treatment was terminated after the first generation. The most pronounced effect observed in the group fed 10 mg aldrin/kg and, to a lesser extent, 5 mg aldrin/kg was a low pre-weaning pup survival. No effects on fertility, viability,

or gestation were observed in six generations of mice fed 3 mg dieldrin/kg. A decrease in pre-weaning survival was observed in the F_{2b} litters, but a similar decrease was also found in one of the six control groups (Keplinger et al., 1970).

In studies by Virgo & Bellward (1975), groups of 18-19 uniparous female Swiss-Vancouver mice were given diets containing 0, 2.5, 5, 10, 15, 20, or 25 mg dieldrin/kg, 4 weeks prior to their second mating, continuing until day 28 postpartum. Significant mortality of the females occurred at 20 and 25 mg/kg, all deaths occurring before parturition (89 and 56%, respectively). Fertility in the groups fed 10 and 15 mg/kg was decreased, though survivors at higher doses were fertile. Oestrus and gestation period were not affected. Litter size was decreased only in the group receiving 25 mg/kg. The major effect was an increase in pre-weaning pup mortality; 47% at 2.5 mg/kg, 80% at 5 mg/kg, and 100% at 10 mg/kg or more (31% mortality in control animals). Dams receiving 10 mg/kg or more exhibited hyperactivity, which was a contributory factor to the high pup mortality. No gross abnormalities were detected in the pups, none of whom showed tremors or convulsions. Within the litters raised at 2.5 and 5 mg/kg, pup survival was not different from controls. The only effect on reproductive capacity or pup survival observed in female mice fed 2.5 mg/kg was an increase in pre-weaning pup mortality.

A study was carried out on primiparous female Swiss-Vancouver mice to investigate whether diets containing up to 15 mg dieldrin/kg affect maternal behaviour and pup viability. Viability was investigated in dams fed diets containing 0, 5, 10, or 15 mg dieldrin/kg for 4 weeks prior to mating. Pups fed 10 mg/kg were nursed by foster dams not fed dieldrin, and all died by day 4; the foster dams' own pups showed a very low mortality and survived until weaning. Similar results were obtained at 5 mg/kg. Dieldrin did not have any influence on serum progesterone levels, milk production, or the dam's tendency to retrieve pups or build nests. However, at 5 mg/kg or more, nursing was reduced. It was concluded that dieldrin causes irreversible congenital inviability (not through any effect on progesterone levels) and it was suggested that the inviability and the reduced tendency to nurse increased the pup mortality (Virgo & Bellward, 1977).

8.5.1.2 Rat

In studies by Treon & Cleveland (1955), rats (Carworth strain) were fed aldrin or dieldrin at dietary concentrations of 2.5, 12.5, or 25 mg/kg for three consecutive generations, two litters being produced for each generation. (There was no mention of a control group, and tabulation and description of results was limited in this report). A reduction in the number of pregnancies, which gradually disappeared over successive generations, was initially observed at 12.5 and 25 mg aldrin/kg and at all three doses of dieldrin. No effects on litter size or pup weights were observed at any dietary concentration. A marked increase in mortality in pre-weaning pups was found at dietary

concentrations of 12.5 and 25 mg/kg for both compounds. This was thought by the authors to be due to the high concentration of dieldrin in the milk of the mothers. Neither aldrin nor dieldrin had any effect on reproductive capacity. No effects, except a "slight to moderate" increased pre-weaning pup mortality, were observed in the rats fed for three generations with aldrin or dieldrin at 2.5 mg/kg.

When groups of 10 male and 20 female Long Evans rats were fed dietary concentrations of 0, 0.1, 1, or 2 mg dieldrin/kg over three generations (each generation producing two litters), no effects were observed on the general health (including weight gain), behaviour, fertility, gestation, viability, lactation, or organ weight ratios. No pathological changes were found in parents or pups. Increased pre-weaning mortality (compared to that in controls) in the F_{1a} litter was observed in the animals fed 2 mg/kg. This effect was not found in the five subsequent litters from this group and was not considered to be a major toxic effect. No changes in reproductive capacity were observed over three generations at dietary concentrations up to and including 2 mg/kg dieldrin (Eisenlord et al., 1967).

In studies by Harr et al. (1970), groups of 20 male and 20 female 28-day-old OSU-Wistar rats were fed 0, 0.08, 0.16, 0.31, 0.63, 1.25, 2.5, 5, 10, 20, or 40 mg dieldrin/kg diet throughout their lifespan. Ten females from each group were mated at 146 days of age. Mortality occurred in dams at 20 and 40 mg/kg. Fertility and litter size were decreased in several dose groups without a clear dose relationship. The number of pups at weaning was markedly reduced at 2.5 mg/kg or more; none survived at 20 and 40 mg/kg. The nursing pups died in convulsions or starved. No effects were noted at 1.25 mg/kg or less. Neural lesions, such as cerebral oedema and hydrocephalus, occurred in pups of nursing dams at dieldrin concentration of 0.08 mg/kg. Hepatic lesions were found in rats fed concentrations of 0.31 mg/kg or more.

When groups of 18-20 Long Evans pregnant rats were given 4 mg dieldrin/kg body weight daily by gavage from day 15 of gestation to 21 days post partum, fecundity, number of stillbirths, perinatal mortality, and total litter weights did not differ from the control group. No malformations in pups were observed (Coulston et al., 1980).

8.5.1.3 Dog

In study by Kitselman (1953), seven groups of three dogs, each group having at least one member of each sex, were fed either aldrin or dieldrin for one year at dietary concentrations equivalent to 0, 0.2, 0.6, or 2 mg/kg body weight (in corn oil). Out of a total of 11 bitches fed either aldrin or dieldrin, 9 conceived. All pregnant bitches produced litters of at least four pups/litter. The survival of pups was generally lower in the groups fed aldrin or dieldrin. Histopathological examinations of dead pups revealed degenerative changes in the liver and mild degenerative changes in renal tubules. Liver changes were also observed in treated bitches. The design and size of this study was too limited to deduce a dose-response relationship for pup

survival, but no effects were observed in dogs receiving 0.2 mg dieldrin/kg body weight.

8.5.1.4 Appraisal

In the reproductive studies (over one to six generations) carried out with aldrin or dieldrin on mice and rats, the major effect observed in most of the studies was an increased mortality rate in pre-weaning pups. Reproductive performance, *per se*, was only affected at doses causing maternal intoxication. The studies on dogs are of a too limited nature to draw firm conclusions, apart from the consistent increase in pre-weaning pup mortality.

The results of these reproductive studies indicate that dieldrin at levels of 2 mg/kg in the rat diet and 3 mg/kg in the mouse diet (equivalent to 0.1 and 0.4 mg/kg body weight per day, respectively) are no-effect levels for reproduction. It is not possible to establish a no-effect level for aldrin for reproduction, because no adequate data are available.

8.5.2 Embryotoxicity and teratogenicity

8.5.2.1 Mouse

Ottolenghi et al. (1974) gave groups of 10 pregnant CD-1 mice single oral doses of 25 mg aldrin/kg body weight or 15 mg dieldrin/kg body weight (in corn oil; equivalent to half the LD_{50} values) on day 9 of gestation. Control groups consisted of untreated and corn-oil-dosed mice. No effects on fetal survival or weight were observed. Abnormalities, such as webbed feet, cleft palate, and open eyes, were increased in both treated groups, but they may have been related to maternal toxicity. The percentage of the total live fetuses that were malformed was 33% for aldrin-treated mice and 17% for dieldrin-treated ones.

In two comparable studies, pregnant CD-1 mice (6-16 per group) were given daily oral doses of dieldrin in peanut oil at 0, 1.5, 3, or 6 mg/kg body weight from day 7 to day 16 of gestation. At 6 mg/kg, reduced body weight gain and increased liver/body weight ratio were observed. There was an increase in supernumerary ribs and a decreased number of caudal ossification centres in the fetuses of mice given 6 mg/kg. In one study, the number of supernumerary ribs was increased at all three dose levels, (significant at the two highest dose levels) (Chernoff et al., 1975). In the other study, the increase in supernumerary ribs at 6 mg/kg was not significant. The increase in the number of supernumerary ribs may be an expression of developmental toxicity.

Doses of dieldrin (99%) were given either in corn oil (0, 1.5, or 4 mg/kg body weight) or in dimethylsulfoxide (DMSO) (0, 0.25, 0.5, or 1 mg/kg) daily by gavage to pregnant CF-1 mice (7-14 mice/group) on days 6-14 of gestation. No maternal or fetal toxicity was seen in

groups treated with dieldrin in corn oil or in the corn oil control groups, but some was seen in the dieldrin/DMSO and DMSO-control groups. No compound-related teratogenic effects were observed (Dix et al., 1978).

8.5.2.2 Rat

In a study by Chernoff et al. (1975), pregnant CD rats (9-25 per group) were given daily oral doses of dieldrin in peanut oil (0, 1.5, 3, or 6 mg/kg body weight) from days 7 to 16 of gestation. At 6 mg/kg, increased mortality and reduced body weight gain were observed in the dams, but no changes in the liver/body weight ratios were found. Fetuses did not show any differences from the controls in mortality, body weight, or occurrence of anomalies. There were no differences in the average number of sternal or caudal ossification centres (as were seen in mice). No evidence of teratogenicity was observed at a dose level of 6 mg aldrin/kg body weight per day.

No malformations were observed in fetuses or pups from 18-20 Long Evans rats given 0 or 4 mg dieldrin/kg, by gavage, daily from day 15 of gestation to day 21 of lactation (Coulston et al., 1980).

8.5.2.3 Hamster

Pregnant Syrian golden hamsters (41-43 per group) were given single oral doses in corn oil of either 50 mg aldrin/kg body weight or 30 mg dieldrin/kg body weight on either day 7, 8, or 9 of gestation. Untreated and vehicle-control groups (respectively, 57 and 41 animals) were used. The high dose levels of both aldrin and dieldrin caused reductions in the number of live fetuses and fetal weight and an increased incidence of abnormalities (cleft palate, open eyes, and webbed feet). The effects were more pronounced after treatment on days 7 and 8 of gestation than on day 9. It was suggested that, since webbed foot and open eye were frequently associated with low fetal weight, these effects might be simply the expression of growth retardation (Ottolenghi et al., 1974).

8.5.2.4 Rabbit

No teratogenic effects were observed in the offspring of groups of pregnant Banded Dutch rabbits dosed with dieldrin in carboxymethylcellulose (2 or 6 mg/kg body weight per day) from days 6 to 18 of gestation. The animals were killed on day 28 of gestation and the fetuses were examined for visceral and skeletal abnormalities (Dix & Wilson, 1971).

8.5.2.5 Appraisal

No evidence of a teratogenic potential has been found from studies on rats, mice, or rabbits using oral doses up to 6 mg/kg body weight.

Single high oral doses, equivalent to half the LD_{50}, have been found to cause fetotoxicity and abnormal development of the fetuses in hamsters and, to a lesser extent, in mice. The significance of these abnormalities in the presence of severe maternal toxicity is doubtful but a specific teratogenic potential cannot be ruled out completely. No gross malformations have been reported in reproductive studies.

8.6 Mutagenicity and Related End-Points

8.6.1 Microorganisms

Most research workers have reported that aldrin and dieldrin, with or without microsomal activation, are not mutagenic in bacterial or yeast test systems. In one study, it was reported that dieldrin, without activation, was mutagenic in two out of three strains of *Salmonella typhimurium*, but there was no dose-response relationship (Majumdar et al., 1977). The results of the other mutagenicity studies with aldrin and dieldrin in bacterial test systems have been negative (Table 41). A critical survey of the published reports indicates clearly that neither aldrin nor dieldrin is mutagenic in microbial systems (Ashwood-Smith, 1981).

8.6.2 Mammalian cell point mutations

Only one study on the *in vitro* mutagenicity of dieldrin to mammalian cells has been reported. Dieldrin was weakly mutagenic when tested at a single concentration (0.01 mmol/litre) in ouabain-resistant Chinese hamster V-79 cells. The significance of this result is difficult to assess because of the lack of a dose-response relationship, and a positive control group was not used (Ahmed et al., 1977a).

8.6.3 Dominant lethal assays and heritable translocation assays in mice

Aldrin did not show any detectable dominant lethality when given as a single intraperitoneal dose (8 or 40 mg/kg) or in daily oral doses (0.5 or 1 mg/kg body weight) for 5 days to male ICR/Ha Swiss mice (Epstein et al., 1972).

Dieldrin, also, revealed no detectable dominant lethality in four assays in male mice following a single intraperitoneal injection (5.2 or 26 mg/kg) or daily oral doses of 2 or 3 mg/kg body weight for 5 days (Epstein et al., 1972). Likewise, a single oral dose of 12.5, 25, or 50 mg/kg body weight did not produce dominant lethality in CF-1 mice (Dean et al., 1975). Bidwell et al. (1975) carried out a dominant lethal test on B6D2F1/J mice orally administered 0.08, 0.8, and 8 mg/kg body weight dieldrin for 5 days, but no effects were seen.

In further studies by Bidwell et al. (1975), a heritable translocation test was performed on male mice after oral intake of 0.008, 0.08, or 0.2 mg dieldrin/kg body weight per day for a period of 6

Table 41. Aldrin and dieldrin: mutagenicity tests in microorganisms

Organism	Strain	Activation system	Compound/dose	Result	Reference
E. coli	WP2 Try⁻	none	aldrin and dieldrin; 1000 µg/plate	negative	Ashwood-Smith et al. (1972)
E. coli	WP2 hcr	rat S9	up to 5000 µg/plate	negative	Moriya et al. (1983)
E. coli *Serratia marcescens* *Saccharomyces cerevisiae*	Gal R^s alpha 21 and 742	none	aldrin and dieldrin; dose not stated	negative	Fahrig (1974)
Aspergillus nidulans	diploid P1 and haploid strain 35	none	dieldrin; 13 or 26 mmol	negative	Crebelli et al. (1986)
Saccharomyces cerevisiae	632/4	none	aldrin; 5 µg/ml on disc	positive	Guerzoni et al. (1976)
Bacillus subtilis *Salmonella typhimurium* *E. coli*	(Rec-assay) TA 1535, 1536, 1537, 1538 WP2 hcr$^+$, hcr$^-$	none	aldrin and dieldrin;	negative	Shirasu (1975)
Salmonella typhimurium	TA 98, 100, 1535, 1536, 1537, 1538, G46	rat S9	dieldrin; 10, 50, 100, or 500 µg/plate	negative	Bidwell et al. (1975)
Salmonella typhimurium	TA 98, 100, 1535, 1537	rat S9	dieldrin; dose not stated	negative	McCann et al. (1975)
Salmonella typhimurium	TA 1535, 1536, 1537, 1538	rat S9	dieldrin; 1000 µg/plate	negative	Marshall et al. (1976)
Salmonella typhimurium	TA 98, 100	none	dieldrin; 10, 30, 100, 300, 1000, 3000 µg/plate	negative	Glatt et al. (1983)

Table 41 (contd).

Organism	Strain	Activation system	Compound/dose	Result	Reference
Salmonella typhimurium	TA 90, 100, 1535, 1537, 1538	rat S9	up to 5000 µg/plate	negative	Moriya et al. (1983)
Salmonella typhimurium	TA 98, 100, 1535, 1537, 1538, 1950, 1978	mouse S9	dieldrin; 1000 µg/plate	negative	Van Dijck & Van de Voorde (1976)
Salmonella typhimurium	not specified	S9	dieldrin; dose not stated	"weak" response	Ercegovich & Rashid (1977)
Salmonella typhimurium	TA 98, 100, 1535	mouse S9	dieldrin; 1, 25, or 50 µg/ml	positive	Majumdar et al. (1977)
Salmonella typhimurium	TA 98, 100, 1535, 1538	rat S9	dieldrin; up to 2500 µg/plate	negative	Purchase et al. (1978)
Salmonella typhimurium	TA 98, 100	rat S9	dieldrin; 50 or 1000 µg/plate	negative	Wade et al. (1979)
Salmonella typhimurium	TA 98, 100, 1535, 1537, 1538	rat, mouse, and human S9	aldrin; dose not stated	negative	Simmon et al. (1977)
Salmonella typhimurium	TA 98, 100	rat S9	aldrin and dieldrin; 364 and 380 µg/plate	negative	Nishimura et al. (1982)
Salmonella typhimurium	TA 98, 100 1535, 1537, 1538	rat S9	dieldrin 2.6×10^4 nmoles/plate	negative	DeFlora (1981)

weeks. The cytogenetic determination of somatic cells using the micronucleus test and the usual analysis of spermatocytes did not reveal an increase in the rate of translocations.

8.6.4 Micronucleus test

Aldrin did not induce a significant increase in the frequency of micronuclei in the bone marrow of mice treated orally with 13 mg/kg body weight (Usha Rani et al., 1980).

No cytogenetic abnormalities were seen in a standard metaphase analysis and micronucleus test after oral gavage of mice with 0.8 or 8 mg dieldrin/kg body weight per day for 5 days (Bidwell et al., 1975).

8.6.5 Chromosome and cytogenicity studies

Chinese hamsters (three groups of four males and four females) were orally dosed with 30 and 60 mg dieldrin/kg body weight. No chromosome abnormalities were found in femoral bone marrow cells (Dean et al., 1975).

The effect on the bone marrow cells of STS mice was examined after applying a single dose of dieldrin intraperitoneally at 0, 1, 30, or 50 mg/kg body weight. A decrease in the mitotic index was noted, as dieldrin concentration increased, and differences in chromosome aberrations (a slight increase in breaks, fragments, and interchanges) were found (Majumdar et al., 1976).

Seventy-one juvenile mallard ducks, the parents of which had been exposed to various dietary levels of dieldrin for 6 months or longer, were grouped and fed dieldrin at a level that corresponded to the diet fed to the parents (0, 4, 10, or 30 mg dieldrin/kg diet) for approximately 60 days. At the end of this period, no chromosomal aberrations were found in femoral bone marrow cultures. However, the mitotic index of ducks exposed to 30 mg/kg was significantly reduced (Bunch & Low, 1973).

When lymphocytic cultures from adult mallard ducks (which had not been exposed to dieldrin) were treated with 0, 0.1, 1, 10, 30, or 100 mg dieldrin/kg, there was a significant increase in the incidence of chromosome structural alterations, but only at the highest dose level. The mitotic index was significantly reduced at all dose levels, the greatest decreases occurring at the two highest dose levels (Bunch & Low, 1973).

Chromosome studies in cultured lymphocytes from current dieldrin plant workers (12) former plant workers (9), and control (17) did not show any differences in the frequency of chromosome aberrations (Dean et al., 1975). In one study, it was reported that aldrin produced chromosomal aberrations in cultured human lymphocytes at concentrations of 19 and 38 μg/ml. In mice and rats, an intraperitoneal injection of a dose of 19 mg/kg body weight was reported to induce chromosomal gaps, breaks, deletions, and fragments in bone marrow cells (Georgian, 1975).

Cultured human peripheral lymphocytes from agricultural and public health (anti-Chagas' disease) workers with at least 10 years exposure to dieldrin were examined for structural chromosome aberrations and sister chromatid exchange. No differences were seen when they were compared with lymphocytes derived from a control group (Bordon, 1980).

8.6.6 Host-mediated assays

Bidwell et al. (1975) carried out a host-mediated assay, incorporating blood- and urine-recovery studies, for mutagenic substances on B6D2F1/J mice. Five daily oral doses of 20 mg dieldrin/kg body weight were given, and the mice were then injected intraperitoneally with *Salmonella* tester strains. The results were negative. In a further host-mediated assay using *Saccharomyces cerevisiae* (strain D_4, heteroallelic at the ade-2 and trp-5 loci) as tester microorganism, CF-1 mice were treated with a single oral dose of 25 or 50 mg dieldrin/kg body weight or with five daily doses of 5 or 10 mg/kg body weight. No mutagenic activity was found (Dean et al., 1975).

8.6.7 Cell transformation in mammalian cell systems

Dieldrin (0.08-250 mg/litre) proved negative in mammalian cell transformation tests using cell lines derived from baby Syrian hamster kidney (BHK-21 C13) and from human lung (WI-38), either with or without metabolic activation by rat liver S9 microsomal fraction (Purchase et al., 1978).

In a 6-thioguanine resistance mutation assay using FM 3A mouse cell cultures, aldrin was weakly mutagenic (Morita & Umeda, 1984).

8.6.8 Drosophila melanogaster and other insect systems

There is no evidence of a mutagenic activity of aldrin or dieldrin in *Drosophila melanogaster* (Benes & Sram, 1969; Bidwell et al., 1975). No increase in recessive or dominant lethal mutations was found following exposure of the wasp *Bracon hebetor* to sublethal doses of dieldrin (95%) (Grosch & Valcovic, 1967).

8.6.9 Effects on DNA

DNA strand breakage was not detected in Chinese hamster V-79 cells exposed to dieldrin (0.1-1 mmol/litre) in the presence of rat liver S9 microsomal fraction using the alkaline elution assay (Swenberg et al., 1976).

Aldrin (1-1000 µmol/litre) and dieldrin (1-100 µmol/litre) induced unscheduled DNA synthesis in SV-40 transformed human fibroblast cells (VA-4) both in the presence and absence of rat liver microsomes (Ahmed et al., 1977b). This study was repeated by Zelle & Lohman (1977). After exposure to dieldrin, the rate of DNA synthesis in normal primary human fibroblasts (AH) decreased, but returned to the

control level in a few hours. This suggests that dieldrin interferes with semiconservative DNA replication without damaging DNA. The effect of dieldrin on the induction of repair replication was studied with both AH cells and SV-40 transformed human cells (MM-SV-40). No evidence that dieldrin could induce DNA repair was found (Zelle & Lohman, 1977).

The DNA breakage rates in an *Escherichia coli* plasmid after treatment with aldrin or dieldrin did not differ from those in untreated plasmid DNA, suggesting that, at least in these studies, the compounds did not interact directly with DNA (Griffin & Hill, 1978).

The effects of aldrin and dieldrin (both at 100 μg/ml) on the uptake of tritiated thymidine by cultured rat thymocytes and human lymphocytes were tested under different experimental conditions. Both compounds appeared to have marginal effects on thymidine uptake, suggesting inhibition of DNA synthesis (Rocchi et al., 1980).

Aldrin (100 mmol/litre) and dieldrin (500 mmol/litre) did not induce unscheduled DNA synthesis in primary cultures of Fischer 344 rat hepatocytes (Probst et al., 1981). Williams (1982) reported the results of the hepatocyte primary culture/DNA repair test, using freshly isolated hepatocytes of high metabolic capability to monitor the production of DNA damage by measuring DNA repair synthesis. Aldrin and dieldrin gave equivocal results concerning DNA repair, but there was no damage to DNA. Aldrin (0.3-3 mmol/litre) induced DNA strand breaks in an alkaline elution/rat hepatocyte assay (Sina et al., 1983).

Cultured hepatocytes from male Balb/c mice treated with dieldrin at a concentration of 4×10^{-4} mol/litre showed no unscheduled DNA synthesis. The results were no different with cells from mice treated *in vivo* with phenobarbital (Klaunig et al., 1984).

A DNA synthesis inhibition/damage test on HeLa cells with S9 showed inhibition to 60% of the control value within 90 min of treatment with 4×10^{-4} mol dieldrin/litre (Painter, 1981).

8.6.10 Cell to cell communication

Both aldrin and dieldrin inhibited gap junctional intercellular communication between 6-thioguanine-sensitive and 6-thioguanine-resistant human teratocarcinoma cells in culture (Zhong-Xiang et al., 1986).

The inhibition of cell to cell communication was observed in human teratocarcinoma cells in culture in the presence of dieldrin, using dye transport methods (Wade et al., 1986).

Metabolic cooperation between 6TG-resistant and HGPRT-deficient Chinese hamster V79 cells was inhibited when aldrin (2.5-10 μg/ml) or dieldrin (2.5-5 μg/ml) was added to the medium (Kurata et al., 1982).

Trosko et al. (in press) studied the inhibition of gap junctional-mediated intercellular communication using co-cultures of Chinese hamster cells. To do this, an *in vitro* assay (in which the metabolic cooperation between V79-6-thioguanine-sensitive (6 TGs) and resistant

(6 TGr) cells is studied) has been developed to detect the ability of non-cytotoxic and non-mutagenic chemicals to inhibit gap junctional communication. Aldrin and dieldrin inhibited metabolic cooperation at concentration of about 4 μg/ml or more.

8.6.11 Appraisal

Aldrin and dieldrin are not mutagenic to mammals in a variety of mutagenicity test systems with unrelated different end-points.

8.7 Special Studies

8.7.1 Liver enzyme induction

Aldrin and dieldrin have been shown to increase the activity of liver microsomal enzymes, generally associated with enlargement of the liver. They have also been found to induce microsomal dimethylamino-antipyrine-N-demethylase and aldrin-epoxidase, and increase the cytochrome P-450 level (Campbell et al., 1983). This enzyme induction is the earliest and most sensitive indicator of an effect of exposure in mouse, rat, beagle dog, and rhesus monkey (Wright et al., 1972).

Studies on rats indicated a no-effect level for enzyme induction, by either aldrin or dieldrin, at 1 mg/kg diet (Gillett & Chan, 1968; Kinoshita & Kempf, 1970; Den Tonkelaar & Van Esch, 1974).

In the rhesus monkey, the activity of the liver microsomal monooxygenase system was increased by dieldrin (at daily feeding levels of 1.75 and 5 mg/kg diet for approximately 6 years), but no associated liver enlargement was observed. The dietary intake of dieldrin required for the induction of this enzyme system in monkeys was approximately 1 mg/kg diet, corresponding to an intake of 25-30 μg/kg body weight per day (section 8.4.4) (Wright et al., 1978).

In human beings, oral dosing with 211 μg dieldrin/day (approximately 3 μg/kg body weight per day) for two years, in addition to the daily intake of 19 μg dieldrin from the diet, did not increase the activity of microsomal liver enzymes as measured by the concentration of *p,p'*-DDE in adipose tissue and blood. No evidence of enzyme stimulation was observed in a group of 10 workers (at the time, they were the most highly exposed workers) in a manufacturing plant with a mean exposure equivalent to a daily oral intake of 17 μg/kg body weight (maximum 24 μg/kg body weight) (Hunter & Robinson, 1967; Hunter et al., 1969; Jager, 1970).

8.7.2 Nervous system

8.7.2.1 Rat

When three groups of eight male albino rats were fed diets containing 0, 25, or 50 mg dieldrin/kg for 60 days, there was no effect on body weight or learning, but muscular efficiency, measured by pulling

weights of increasing magnitude in a 250-cm runway, was decreased (Khaïry, 1960). This finding is in agreement with the results of a study on nerve muscle (gastrocnemius) preparations of pre-treated rats (Ibrahim, 1964).

8.7.2.2 Dog

Groups of five dogs of each sex, given daily oral doses of dieldrin (0.05 mg/kg body weight) by capsule for 2 years, did not show any changes in behaviour or EEG recordings compared with controls (Walker et al., 1969b).

8.7.2.3 Monkey

When groups of three or four adult male squirrel monkeys were given daily oral doses of 0, 0.01, or 0.1 mg dieldrin/kg body weight for 54 days, learning ability was impaired and changes (high amplitude slow waves) in the EEG occurred in both test groups (Van Gelder & Cunningham, 1975).

8.7.3 Weight loss and stress

It is known that in birds, and perhaps in some small mammals, dieldrin intoxication may be induced by starvation, weight loss, and stress in animals having a previously harmless body burden of dieldrin. Concern is sometimes expressed that, by analogy to these observations, a similar course of events might occur in human beings. Therefore, this phenomenon was studied in rats as well as in human beings (for human beings see section 9.1.3.2).

8.7.3.1 Rat

In studies by Treon & Cleveland (1955), rats previously fed diets containing aldrin or dieldrin at levels of 5, 10, or 15 mg/kg diet for 7–18 months were starved. The complete withdrawal of food did not result in the release of aldrin or dieldrin from the adipose tissue stores to an extent sufficient to induce symptoms of intoxication of any type.

When Osborne-Mendel rats fed 7.5 mg aldrin/kg diet for 4 weeks were subsequently starved for 6 days with free access to water, there was a marked loss of body weight and fat and a decrease in the liver/body weight ratio. The total body burden of dieldrin decreased during starvation regardless of age, sex, or the previous level of exposure. The total quantity of dieldrin in the liver decreased in all rats. In females, particularly older females, the concentration of dieldrin in abdominal fat increased, whereas in all males, the level in fat decreased. The concentration of dieldrin in the blood was not increased. Young weanling rats reacted similarly (Deichmann et al., 1972).

8.7.4 Immunosuppressive action

Loose et al. (1981) found that macrophages from mice fed 50 mg dieldrin/kg diet had a marked impairment in antigen processing. The effect was statistically significant in Kupffer cells at 50 mg/kg diet, in alveolar and splenic macrophages at 0.5, 5 and 50 mg/kg diet, and in peritoneal macrophages at 5 and 50 mg/kg diet. There was an impairment of *in vivo* phagocytic clearance in mice receiving 5 or 50 mg/kg diet for 8 weeks but not at 0.5 mg/kg diet. This was related to a decrease in serum fibronectin. Tumour cell killing after challenge with EL-4, P388, or mKSA tumour cells was significantly impaired in mice fed either 1 or 5 mg dieldrin/kg diet. The mean survival time after challenge with EL-4 was reduced by 3 weeks, and with the P388 or mKSA tumour cells impairment was observed after 3 or 18 weeks, respectively. There was no alteration in the oxygen uptake by isolated macrophages either at rest or during phagocytosis, and no effect on phagocytic activity or capacity or on chemotaxis *in vitro* was observed.

Loose (1982) found that dieldrin caused immunosuppression in mice. Levels of 1 or 5 mg dieldrin/kg diet were fed to BALB/c mice for 3.5 or 10 weeks, and the mice were challenged intradermally with *Leischmania tropica*. Dieldrin acted synergistically on lethality in a dose- and time-related manner, indicating an effect on host mechanisms. It also resulted in decreased antibody formation to PVP, a T-independent antigen (direct splenic plague assay). The mitogenic response of cultured T-cells to phytohaemagglutinin (PHA) in dosed mice was depressed. Mitomycin C and anti-Thy-1 abolished the mitogenic response. When splenic T-cells from treated mice were mixed with T-cells from control mice, there was inhibition of PHA mitogenesis. The data indicated an active cell-mediated suppressor. A soluble macrophage factor from the hepatic Kupffer cells (but not from alveolar or peritoneal macrophages) suppressed the T-cell response to PHA. It was concluded that administration of 5 mg dieldrin/kg diet to mice for 10 weeks caused a profound impairment of macrophage antigen processing.

8.8 Toxicity of Photodieldrin and Major Metabolites

The relevance of photodieldrin lies in the fact that it has metabolites identical to those of dieldrin and is quantitatively and qualitatively similar in toxicity.

8.8.1 Photodieldrin

The photodecomposition of deposits of dieldrin on leaves and grass has been reported (Roburn, 1963), and the physical and chemical properties and structure of this decomposition product have been determined (Robinson et al., 1966b; Rosen et al., 1966). It appears to be the pentacyclo isomer of dieldrin (hexacyclo isomer by the alternative nomenclature used by Rosen et al. (1966)). Photodieldrin residues were less than the limits of detection in most of the food samples analysed (Robinson et al., 1966a).

8.8.1.1 Acute toxicity

Photodieldrin is more acutely toxic than dieldrin for mice, rats, and guinea-pigs (Table 42). The toxicity for dogs is about equal to that of dieldrin. Dieldrin-like convulsions have been observed in all species given photodieldrin.

Table 42. Oral LD_{50} values for photodieldrin

Species	Vehicle	LD_{50} (mg/kg body weight)		Reference
		Photodieldrin	Dieldrin	
Mouse	dimethyl-sulfoxide	6.8	77.3	Brown et al. (1967)
Rat	dimethyl-sulfoxide	9.6	46.8	Brown et al. (1967)
Guinea-pig	dimethyl-sulfoxide	2.3-3.9	18-30	Brown et al. (1967)
Dog (male)	gelatin capsule	120-160	120	Brown et al. (1967)
Dog (female)	gelatin capsule	80-120	80-100	Brown et al. (1967)

8.8.1.2 Short-term toxicity

(a) *Mouse*

When groups of five male and five female Carworth Farm No. 1 mice were fed 1, 3, or 10 mg photodieldrin/kg diet for 1 month, all animals fed 10 mg/kg and two animals fed 3 mg/kg died. No changes were observed at necropsy (Brown et al., 1967).

(b) *Rat*

Groups of five male and five female Carworth Farm E rats were fed 3 or 10 mg photodieldrin/kg diet for one month without apparent ill effects (Brown et al., 1967).

In studies by Walton et al. (1971), groups of 28 male and 28 female Charles River rats were fed 0, 1, 5, or 25 mg photodieldrin/kg diet for 3 months. A similar study was carried out concurrently with dieldrin. The concentrations of photodieldrin given in the diet were lowered from 25 to 12.5 mg/kg diet within the first week of the study because of high mortality. At the end of 3 months, no significant differences were found in growth or food intake, and no gross evidence of toxicity

was observed. Liver/body weight ratios were increased at 12.5 mg/kg diet. Increases in the activity or concentration of liver mixed-function oxidase and microsomal cytochrome P-450 at 5 and 12.5 mg/kg diet indicated the occurrence of a dose-dependent enzyme induction. The total protein content of the liver was not affected. The short-term toxicities of photodieldrin and dieldrin appeared to be similar.

Walker et al. (1971) fed groups of 12 Carworth Farm E rats of each sex diets containing 0.1, 1, 10, or 30 mg photodieldrin/kg diet for 3 months. The control group consisted of 24 male and 24 female rats. Six females given 30 mg/kg and two females given 10 mg/kg died. The animals in these groups that survived were irritable and showed tremors when handled. Growth was reduced, increases in serum urea and glutamic pyruvic transaminase (SGPT) activity were seen in females fed 30 mg/kg, and the liver/body weight ratio was increased in this group. In the groups fed 10 or 30 mg/kg, kidney/body weight ratio was increased in males. At autopsy, no gross lesions were seen. Some of the animals fed 10 or 30 mg/kg showed CHIRL and centrilobular fatty changes in the liver. Eosinophilic droplets were seen in the cytoplasm of the proximal convoluted tubules and in the lumen of affected tubules in the kidneys of males fed 10 or 30 mg/kg. No evidence of nephron damage was found. No effects were observed in the animals dosed with 1 mg/kg.

(c) *Dog*

In a study by Walker et al. (1971), groups of four male and four female beagle dogs received photodieldrin in olive oil by capsule (daily oral doses of 0.005, 0.05, or 0.2 mg/kg body weight) for 3 months. A control group of six males and six females received olive oil in gelatine capsules. The health, behaviour, body weight, and haematology were unaffected. In the 0.2 mg/kg males, increases occurred in the plasma alkaline phosphatase and SGPT activities, and, after 13 weeks, their serum protein levels were slightly reduced. Increases in the liver/body weight ratios occurred in the 0.2 mg/kg animals and the 0.05 mg/kg females. At autopsy, no pathological changes associated with photodieldrin were observed. No effects were observed at 0.005 mg/kg body weight.

8.8.1.3 Long-term toxicity

(a) *Mouse*

In a study on the long-term toxicity of photodieldrin, groups of 50 B6C3F1 mice of each sex were fed diets containing 0.32 or 0.64 mg/kg for 80 weeks. After 80 weeks, the animals were fed a control diet for 12 or 13 weeks. Concurrent control groups consisted of 10 untreated mice of each sex. Pooled controls, used for statistical evaluation, consisted of the concurrent controls plus 60 male and female mice from similarly performed bioassays with six other test chemicals. All surviving mice were killed at 93 weeks. Mean body weights and mortality

were not affected by treatment, but convulsions and hyperactivity were noted in treated male mice. No statistically significant increase in tumour incidence was found (NCI, 1977).

(b) *Rat*

In similar studies to those on mice, groups of 50 Osborne-Mendel rats of each sex were given 5 or 10 mg photodieldrin/kg diet for 80 weeks. After 80 weeks, the animals were fed a control diet until sacrifice at 111-112 weeks. Because of neurotoxicity, the doses in the females were reduced after 30 weeks, so that the time-weighted average doses were 3.4 or 7.5 mg/kg diet for the females. Concurrent control groups consisted of 10 rats of each sex. Pooled controls, used for statistical evaluation, consisted of the concurrent controls combined with 65 rats of each sex from similarly performed bioassays with six other chemicals. All surviving animals were killed at 111-112 weeks. Mean body weights and mortality were not affected by treatment, but convulsions and hyperactivity occurred in treated male and female rats. Photodieldrin was not carcinogenic in this study (NCI, 1977).

8.8.1.4 Reproduction, embryotoxicity, and teratogenicity

(a) *Mouse*

Chernoff et al. (1975) fed groups of pregnant CD-1 mice (16-20 per group) photodieldrin in peanut oil (daily oral doses of 0, 0.15, 0.3, or 0.6 mg/kg body weight) from day 7 to day 16 of gestation. At a dose of 0.6 mg/kg, one animal died. Liver/body weight ratios were increased in a dose-related manner, but no significant differences in fetal mortality, litter weight, percentage of supernumerary ribs, or sternal or caudal ossification centres were observed at any of the doses used. Photodieldrin was not teratogenic or fetotoxic in CD-1 mice at doses up to and including 0.6 mg/kg body weight.

(b) *Rat*

In a study by Chernoff et al. (1975), groups of 24-27 pregnant CD rats were given daily oral doses of photodieldrin in peanut oil (0, 0.15, 0.3, or 0.6 mg/kg) on days 7-16 of gestation. Some maternal mortality (5 out of 24 animals) occurred in the 0.6-mg/kg group. No significant differences in liver/body weight ratios, fetal mortality, weight of the pups, or occurrence of anomalies in litters of treated animals, compared with the controls, were noted. No evidence of teratogenicity in CD rats was observed at doses of photodieldrin up to and including 0.6 mg/kg per day.

8.8.1.5 Appraisal

The acute oral toxicity of photodieldrin to rodents is greater than that of dieldrin. In short-term toxicity and teratogenicity studies,

no major differences between the two compounds were found. Photodieldrin did not induce tumours in mice and rats. The accumulation of photodieldrin in the adipose tissue of experimental animals was less than that of dieldrin (section 6.2.3).

8.8.2 Major metabolites of dieldrin

8.8.2.1 Acute toxicity

The acute oral toxicity of the major metabolites of dieldrin is far less than that of dieldrin itself (Table 43).

Table 43. Oral LD_{50} values for metabolites of aldrin and dieldrin in mice

Compound	LD_{50} (mg/kg body weight)	Reference
trans-6,7-dihydroxy-dihydroaldrin	1250	Korte & Arent (1965)
9-hydroxy-dieldrin	> 400	Baldwin et al. (1970)
hexachlorohexahydromethanoindenedicarboxylic acid (aldrin dicarboxylic acid)	> 850	Baldwin et al. (1972)

8.8.2.2 Short-term toxicity

In a study by Granville et al. (1973), groups of 12 male and 12 female rats (control group of 24 males and 24 females) were fed diets containing aldrin dicarboxylic acid (0, 0.1, 1, 10, 100, or 1000 mg/kg diet) for 13 weeks. No adverse effects attributable to the dosing were observed in general health, behaviour, body weight, clinical chemical and haematological values, organ weights, or on pathological examination of the viscera.

8.9 Mechanisms of Toxicity; Mode of Action

Like most chemicals, aldrin and dieldrin do not have a single mechanism of toxicity. The main target organs of these chemicals are the central nervous system and the liver.

8.9.1 Central nervous system

Intoxication following acute or long-term overexposure is characterized by involuntary muscle movements and epileptiform convulsions.

Survivors, after a short period of residual signs and symptoms, recover completely (Hoogendam et al., 1962; Avar & Czegledi-Janko, 1970; Jager, 1970). In rare cases, a residual brain injury has been reported, but this has been found to be due to the convulsive state or prolonged cerebral anaemia rather than to the dieldrin *per se*. Apparently, a still unidentified receptor site in the central nervous system is reversibly occupied, and when this occupation exceeds a certain degree, myoclonics and convulsions occur (Van Genderen, 1979). *In vitro*, the dieldrin metabolite aldrin transdiol appears to be more potent in this respect that is dieldrin itself (Van den Bercken, 1972; Van den Bercken & Narahashi, 1974). However, in cats, the aldrin transdiol appeared to be inactive (Joy, 1977). The mechanism of action seems to be a pre-synaptic inhibition as well as an increased release of an unidentified transmitter (Akkermans, 1974; Akkermans et al., 1975; Joy, 1976).

Joy (1982) suggested that dieldrin acts by intensifying synaptic activity through a presynaptic locus of action and possibly a post-synaptic action as well. Neurons having a large number of synapses will be affected most. There does not appear to be any selective action on a particular neurotransmitter or neurotransmitter system. The modification of behaviour is dose dependent and performance in complex behavioural tasks is readily disrupted.

Aldrin and dieldrin and other cyclodiens inhibit the gamma amino butyric acid (GABA)-induced chloride ion uptake into skeletal muscles and the binding of tritiated dihydropicrotoxinin (anion channel probe) to the membrane. This results in central nervous system excitation and convulsions due to the blocking of GABA transmitters (Lawrence & Casida, 1984; Abalis et al., 1985).

8.9.2 Liver

The mode of action of aldrin and dieldrin on the liver involves an increase in the activity of microsomal biotransformation enzymes, particularly of the monooxygenase system with cytochrome P-450. This induction of liver microsomal enzymes is reversible and, if exceeding a certain degree, appears to be associated with the occurrence of CHIRL and hepatomegaly in the liver of rodents (sections 6.3 and 8.2) (Jager, 1970; Wright et al., 1972, 1977, 1978).

9. EFFECTS ON HUMAN BEINGS

9.1 General Population Exposure

9.1.1 Acute toxicity - poisoning incidents

When a toxic dose of aldrin or dieldrin has been ingested or has contaminated the skin, effects appear from 20 min to 24 h afterwards. Signs and symptoms may include headache, dizziness, nausea, general malaise, and vomiting, followed by muscle twitchings, myoclonic jerks, and convulsions. Death may result from cerebral anoxaemia (Nelson, 1953; Princi, 1954; Hayes, 1957, 1963; Hoogendam et al., 1962, 1965; Kazantzis et al., 1964; Schafer, 1968; Jager, 1970).

The duration of the interval between oral intake or skin contact and onset of symptoms (as well as the clinical picture) depends on the dose absorbed. With massive over-exposure, convulsions may occur even in the absence of any premonitory symptoms.

Initially, there is no fever or change in blood count or in blood chemistry. However, later the temperature may be elevated and leukocytosis may occur. Terminal hyperthermia has been reported. Abnormal EEG patterns showing spike and dome complexes and multiple spike and wave discharges, or in less serious intoxications, bilateral synchronous theta discharges may be seen. The diagnosis needs to be confirmed by determining the insecticide concentration in the blood.

The onset of clinical intoxication is practically always acute also in those cases where the accumulation of dieldrin in the target tissues has taken place during a much longer period. The latter cases are, therefore, usually indistinguishable from acute intoxication. Survivors almost always recover completely (Jager, 1970; Hayes, 1982).

Estimates of dosages in anecdotal cases suggest that fatalities have occurred with ingestion of approximately 10 mg dieldrin/kg body weight, (Hayes, 1982) but Hodge et al. (1967) estimate the lethal dose of aldrin and/or dieldrin for the adult man to be about 5 g.

Cases of poisoning have occurred by ingestion of formulated material, mostly in children by mistake (for instance when aldrin is used in granules as bait to control ants) or by adults with suicidal intent. Several cases of poisoning have been the result of ingesting food contaminated with aldrin or dieldrin during storage or transport.

Van Raalte (1965) surveyed the world literature for all cases of fatal poisoning by aldrin and dieldrin, and found 13 cases: four suicides, three due to accidental ingestion, five due to accidental contamination, and only one (a spray operative) due to occupational exposure. No cases of fatal poisoning have been reported during the course of aldrin and dieldrin manufacture and formulation.

A non-exhaustive overview of published poisoning cases is given in Table 44. A more complete review is provided by Hayes (1982).

Table 44. Case reports on accidental and suicidal acute aldrin and dieldrin poisoning

Number of cases	Fatal cases	Causative agent	Circumstances	Reference
1	-	aldrin emulsifiable concentrate	attempted suicide	Spiotta (1951)
53	-	aldrin and other pesticides	consumption of seed grain	WHO (1958)
	13	aldrin and dieldrin	review of all fatal cases from literature: - 4 suicides, 3 accidental ingestion, 5 accidental contaminations, 1 sprayer	Van Raalte (1965)
2	1	5% dieldrin	accidental ingestion	Garrettson & Curley (1969)
79			consumption of dieldrin-contaminated rice in Mali	WHO (1977)
1	-	dieldrin (120 mg/kg)	attempted suicide	Black (1974)
2	-	dieldrin		Fry (1964)
12	-	aldrin + BHC	consumption of seed grain	Gupta (1975)

9.1.2 *Effects of short- and long-term exposure - controlled human studies*

9.1.2.1 Accidental poisoning

Twelve cases of neurotoxicity, resulting from the repeated consumption of wheat into which aldrin dust and gammexane (BHC) powder had been mixed accidentally, have occurred in India (Gupta, 1975). The patients consumed this wheat for 6-12 months before showing typical clinical symptoms, including convulsions. Electroencephalographic tracings were consistent with a diagnosis of organochlorine insecticide poisoning. The patients were treated with phenobarbital and diazepam. The latter was more effective in controlling seizures. All patients recovered.

The threshold dieldrin concentration in the blood below which no adverse effects have been observed (and none are to be expected) is 105 µg/litre (see also section 9.2.1.1). The dieldrin concentration in the blood of the general population, in the countries where this has been investigated, is well below this threshold level. However, there are rare cases in which it seems that low concentrations of dieldrin have induced effects.

A rare, well investigated and well reported case of dieldrin-induced immunohaemolytic anaemia was observed in Iowa, USA. The patient had a haemolytic anaemia with a positive direct antiglobulin (Coombs) test and a positive Ham test in the serum. The serum contained antibodies selectively active against erythrocytes coated with dieldrin. The patient improved following splenectomy. Dieldrin concentrations in blood and fat were similar to those of the general Iowa population (Hamilton et al., 1978). A similar case was reported by Muirhead et al. (1959).

9.1.2.2 Controlled human studies

In section 6.2.2.4, reference was made to a pharmacodynamic study in human volunteers. This study had three objectives:

(a) to establish the relationship between the daily intake of dieldrin and its concentration in human blood and adipose tissue;
(b) to establish the blood/fat ratio in human beings; and
(c) to establish the relationship between the concentrations of dieldrin in blood and fat and the length of exposure (Hunter & Robinson, 1967, 1968; Hunter et al., 1969).

In addition, the opportunity was taken to monitor the health of the human subjects during and after the exposure by full clinical, physiological, and laboratory examinations as well as full electroencephalographic (EEG) studies, polygraphic recording of cardio-respiratory function, measurement of basal metabolic rate, and electroneuromyo-

graphic studies at frequent intervals to detect the possible occurrence of changes in physiological function. The study involved 13 adult male college graduates without a history of recent occupational exposure to pesticides. The subjects received 0, 10, 50, or 211 μg dieldrin per day for 2 years. All the men continued in excellent health. Clinical, physiological, and laboratory findings remained essentially unchanged throughout the whole experimental period of 24 months and the 8 months after exposure. No departures from what is regarded as normal for the general population were observed. The concentration of *p,p'*-DDE in adipose tissue and blood did not show any significant change during or after the study, indicating that the liver microsomal enzyme activity had not been induced. Thus, the total daily intake of 230 μg (211 μg plus intake from food) of dieldrin per person for 2 years had no effect on health. The concentrations of dieldrin in both adipose tissue and blood were shown to be proportional to the daily intake (section 6.2.2.4).

9.1.3 Tissue concentrations of dieldrin in hospitalized people

9.1.3.1 Pathological findings

Specimens of human abdominal subcutaneous fat, obtained from four hospitals in Chicago were analysed for residues of dieldrin. Dieldrin was not present in 103 out of 221 samples analysed for this pesticide. Positive samples contained 0.01-1.39 mg dieldrin/kg fat (mean value 0.14 mg/kg). There was no correlation between the dieldrin concentration in adipose tissue and pathological findings (Hoffman et al., 1967).

When organochlorine pesticide concentrations were determined in the adipose tissue and liver of 271 hospital patients in Miami, USA, patients with typical alcoholic (Laennec's) cirrhosis of the liver had about twice the dieldrin concentration in the liver of that found in the normal population. In patients with post-necrotic cirrhosis, fatty metamorphosis of the liver, metastatic malignancy of the liver, or primary hepatocellular carcinoma, dieldrin concentrations were "normal". Terminal cases with carcinomas of different organs had elevated concentrations of organochlorine pesticides in the fat, but no association with any particular neoplastic disease was found (Radomski et al., 1968).

In Hawaii, emaciated patients who had carcinoma and/or focal or generalized liver pathology were found to have "normal" (for the USA) concentrations of dieldrin in the liver and body fat (Casarett et al., 1968).

When concentrations of organochlorine pesticides were determined in specimens of liver, brain, and adipose tissue from autopsies of patients with cirrhotic liver disease in Vancouver (Canada) hospitals, the concentrations of dieldrin appeared to be no higher than in tissues from controls (Oloffs et al., 1974).

In a case-control study on 122 matched cancer patients in south Florida, USA, a comparison was made of dieldrin residues in the adipose

tissue of cancer patients and controls. The mean dieldrin concentration in the adipose tissue was 0.3 mg/kg fat in both cancer patients and controls (Davies et al., 1975).

9.1.3.2 Influence of weight loss and stress on dieldrin concentrations in tissues

It is well known that, in birds, and perhaps in some small mammals, dieldrin intoxication may be induced by starvation, weight loss, or stress in animals having a previously harmless body burden of dieldrin. Concern is sometimes expressed that, by analogy to these observations, a similar course of events might occur in human beings.

Twenty-nine patients (14 males, 15 females) undergoing surgery were investigated. The concentrations of dieldrin in the blood were unaffected by the catabolic responses to surgery. In another study, these authors determined the concentrations of dieldrin in the blood of 4 women undergoing voluntary near-starvation for slimming purposes, which resulted in weight losses of up to 7.5 kg/week. There was no increase in the concentration of dieldrin in the blood (Hunter & Robinson, 1968).

No significant difference was found between the dieldrin blood concentrations of slimming or non-slimming mothers before and after delivery (Eckenhausen et al., 1981).

On the basis of these results and calculations, it is suggested that significant weight loss does not result in increased concentrations of dieldrin in human tissues (Van Raalte, 1965; Hunter & Robinson, 1968).

9.1.4 Exposure in treated homes

From the data on aldrin concentrations in the air of houses treated for termite control (section 5.1.2), an estimate of the dieldrin concentration in the blood of occupants of these houses can be made using the mathematical formulas given by Hunter et al. (1969) for deriving blood concentrations from the average daily intake. The average daily intake is based on an estimated average in-house volume of air inhaled per day (15 m^3). The dieldrin blood levels of home dwellers, calculated in this way, remain far below the blood concentration no-effect level for the general population (secton 9.2.1.1).

The blood dieldrin concentrations of 59 female residents of Dade County (Florida, USA), where many houses had been treated for termite control, were of the order of 1 µg/litre (Barquet et al., 1981).

Also relevant to the health of home dwellers is the experience obtained in the 1950s and 1960s when tens of thousands of houses in more than 30 countries were sprayed with dieldrin for malaria and yellow fever eradication. Although exposures were presumed to have been high, as a result of surface spraying inside and outside houses, no adverse health effects were reported in home dwellers. Neither were adverse effects observed in well-trained and medically-supervised spray

operators (Soper, 1955 (Personal communication at the 2nd Meeting of the Industrial Council on Tropical Health, Boston); Fletcher et al., 1959).

9.2 Occupational Exposure

9.2.1 Acute toxicity - poisoning incidents

With the exception of poisoning cases resulting from massive acute overexposure, most reported cases of poisoning with aldrin and dieldrin in occupationally-exposed men have been the result of a slow build-up of the insecticide in the body, the daily intake exceeding the daily excretion (Jager 1970; Hayes 1982).

Based on the experience of Jager (1970), it was suggested that the classification of types of intoxication by Hayes (1963) be modified as follows:

Type 1: an acute convulsive intoxication with no (or only minor) prodomi, resulting from one or several gross overexposures.

Type 2: a greater number of smaller doses may cause an accumulative intoxication. Clinically, this results in a syndrome of headache, dizziness, drowsiness, hyperirritability, general malaise, nausea, anorexia, occasional vomiting. At times muscle twitchings, myoclonic jerks and convulsions may occur. In these circumstances minor increases in the insecticide level in the blood, perhaps caused by minor fluctuations in exposure, may bring about a convulsive intoxication.

Type 3: this is actually a combination of Types 1 and 2. In this type an over-exposure, in itself not significant, causes an acute convulsive intoxication superimposed upon a subclinical accumulative intoxication of Type 2.

These three types of intoxication are schematically illustrated in Fig. 3.

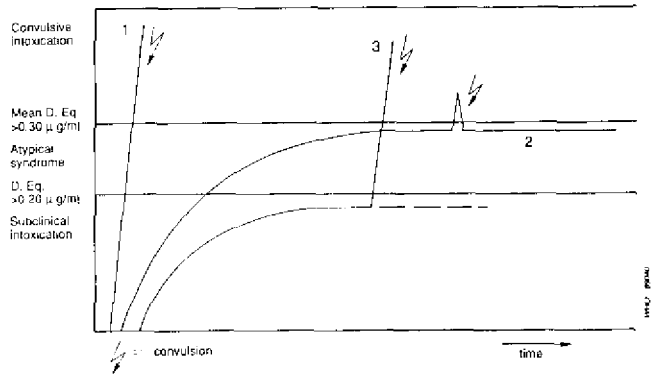

Fig. 3. Three types of organochlorine insecticide intoxication. From: Jager (1970).

Table 45 gives a non-exhaustive overview of occupational aldrin and dieldrin poisonings. Hayes (1982) contains further information on this subject.

No cases of fatal poisoning have been reported during the manufacture and formulation of aldrin and dieldrin (Jager, 1970). However, there has been one case of a spray operator being fatally poisoned (Van Raalte, 1965).

In developing countries it is, however, difficult to establish the actual number of poisoning cases. Experience shows that even when pesticides are banned, cases may occur in areas where control is poor and where large quantities of pesticide are stocked. In May 1987, four cases of occupational poisoning with aldrin were reported from an area of cocoa plantations in Bahia (Brazil). One of them was fatal, while three recovered. The fatal case had a dieldrin level in whole blood exceeding 600 μg/litre two days after poisoning (Rahde, personal communication).

9.2.1.1 Blood levels diagnostic of aldrin/dieldrin poisoning

Because the symptoms of aldrin/dieldrin intoxication are non-specific, a differential diagnostic test is required to confirm that the symptoms, signs, and clinical course of a particular case are the result of aldrin or dieldrin intoxication.

The results of animal studies, together with those obtained subsequently during medical surveillance of workmen employed in the manufacture (or formulation) of aldrin/dieldrin, have shown that adverse effects induced by aldrin/dieldrin are related to the dieldrin blood concentration (Brown et al., 1964; Jager, 1970). Therefore, the determination of this concentration provides a specific differential diagnostic test.

Concentrations of dieldrin ranging from 40 to 530 μg/litre have been reported in the blood of people who had been poisoned relatively recently and who had recovered (Kazantzis et al., 1964; Jager, 1970; Avar & Czegledi-Janko, 1970; Siyali & Simson, 1973).

From the limited information available, Brown et al. (1964) concluded that the threshold concentration of dieldrin in the blood of human beings, critical for intoxication, is approximately 150-200 μg/litre.

Dieldrin is present in the blood at very low concentrations in the general population of many countries throughout the world. It is also found at considerably higher concentrations in the blood of healthy workers. These "healthy workmen" were men between 18 and 60 years of age who had no complaints or clinical or laboratory signs attributable to occupational exposure, but they were, of course, subject to the same ailments and diseases as are members of the general population (Hayes & Curley, 1968; Jager, 1970). No complaints of ill health and no positive results in objective clinical or laboratory tests of ill health have ever been noted in workers whose blood contained less than 200 μg/litre. This concentration may, therefore, be considered to be

Table 45. Published case reports on occupational aldrin and dieldrin poisoning

Number of cases	Fatal cases	Acute cases	Causative agent	Circumstances	Reference
3	-	?	25% aldrin dust	formulation with inadequate safety precautions	Nelson (1953)
~100	-	?	various	spraying in malaria-eradication programmes	Hayes (1957, 1959)
1	-	1	aldrin	gross overexposure in aldrin packer	Bell (1960)
1	1	?	dieldrin	sprayer	Van Raalte (1965)
4	-	?	aldrin	formulation of aldrin	Kazantzis et al. (1964)
17	-	some	aldrin and dieldrin	manufacturing and formulation	Hoogendam et al. (1962, 1965)
32 (15 in addition to previous reference)	-	some	aldrin, dieldrin, endrin, isobenzan	manufacturing and formulation	Jager (1970)

a no-observed-adverse-effect level in human beings. Higher concentrations may have effects. The maximum concentration reported to be without complaints or clinical signs or symptoms was 430 μg/litre (Jager, 1970).

Studies on animals have shown that the earliest physiological sign of exposure to dieldrin is an increase in the activity of certain liver microsomal enzymes. No enzyme induction has ever been found in workers with dieldrin blood concentrations at or below 105 μg/litre (Jager, 1970). (When liver enzyme induction test methods became available, workers with dieldrin levels in the blood exceeding 105 μg/litre were no longer encountered.)

Sometimes, dieldrin concentrations in plasma or serum, rather than in whole blood, have been reported. The ratio of the dieldrin concentration in plasma to that in erythrocytes is approximately 4 : 1 (Dale et al., 1965; Mick et al., 1972) (the conversion factor to calculate the concentration of dieldrin in whole blood from the concentration in plasma or serum is 0.66).

Great differences exist between the average concentrations of dieldrin in the blood of the general population and of occupationally exposed workers with or without complaints (Table 46).

Among 13 adolescent patients with colon-rectal adenocarcinomas, who had lived in rural areas of Mississippi, USA, where pesticides are widely sprayed, dieldrin blood levels were no higher than those in controls (Caldwell et al., 1981).

9.2.1.2 Electroencephalography

Changes in the electroencephalogram (EEG) are sometimes of practical importance for confirming a diagnosis of aldrin/dieldrin intoxication (Spiotta, 1951; Winthrop & Felice, 1957; Hoogendam et al., 1962, 1965; Kazantzis, 1964; Avar & Czegledi-Janko, 1970; Jager, 1970). These EEG changes were first used as a practical tool for monitoring workers and determining when they should discontinue exposure and when they could be allowed to resume work with aldrin/dieldrin. Characteristic changes - which, however, are not pathognomonic for aldrin/dieldrin poisoning - include bilateral synchronous spikes, spike and wave complexes, and slow theta waves, thought to be possibly associated with brain stem stimulation (Hoogendam et al., 1962, 1965). The interesting parallelism between the rate of diminution of the EEG changes and the rate of decrease in the dieldrin blood concentration was also reported in the case of an accidentally poisoned child (Garrettson & Curley, 1969).

Nowadays, analysis for dieldrin in the blood has replaced EEG examination as the method of choice for monitoring exposed workers (Jager, 1970).

9.2.2 Effects of short- and long-term exposure

Occupational exposure occurred in the 1950s and early 1960s among sprayers in malaria and yellow fever control programmes. These men

Table 46. Concentrations of dieldrin in whole blood of human beings (μg/litre)

Subjects	No. of persons involved	Geometric mean	Range	Reference
General population	4592	<1	<1-16.1[a]	US EPA (1983)
Unexposed persons	25	0.5	0-3.3	Sandifer et al. (1981)
	20	2.5	0.5-10	Brown et al. (1964)
Healthy workers	35	29	<10-90	Jager (1970)
	21	120[e]		Mick et al. (1972)
	37	55	-[f]	Morgan & Roan (1974)
	27	20	4.5-54	Sandifer et al. (1981)
	89	38[g]	2-220	Brown et al. (1964)
Patients with clinical symptoms	18	160[g]	8-280	Avar & Czegledi-Janko (1970)
	4		40-530[b]	Kazantzis et al. (1964)
	5		130-370[c]	Brown et al. (1964)
	5		160-430[d]	Brown et al. (1964)
Deceased (suicide)	1		850	Hayes (1982)

[a] In serum.
[b] The low level of 40 μg/litre was found in a man with chronic nephritis, complaining of headache and nausea; the occupational cause of the symptoms is, therefore, doubtful. In one other worker, a blood level of 530 μg/litre was found 1 month after a mild acute episode when he was exposed to aldrin again.
[c] Determined some time after the acute episode.
[d] Estimated to be the concentration at the time of the acute episode.
[e] Converted from plasma figures using a factor of 0.66 (see 9.2.1.1).
[f] Highest value 231 kg/litre.
[g] Average.

sprayed dieldrin inside houses day after day in prolonged cycles without appreciable intervals of non-exposure. Quite often, precautions and supervision were less than would be required today. At the time, methods for the determination of blood concentrations had not been developed. A significant percentage of these sprayers became sick after having worked for as little as 2 days or as much as 2 years (Hayes, 1957, 1959; Patel & Rao, 1958; Zavon & Hamman, 1961). According to communications by the Pan-American Sanitary Bureau (Soper, 1955[a]), it appeared that no clinical symptoms were observed in well-executed, well-supervised malaria and yellow fever control programmes.

In a study carried out in East Africa, where workers were spraying dieldrin 6 h/day for 180 days per year (with an interim of 2 months between spraying cycles) no clinical symptoms were seen. The potential average dermal exposure of spray operators who observed the protective measures laid down was 1.8 mg/kg body weight per day (Fletcher et al., 1959).

Long et al. (1969) studied 159 farmers in Iowa, USA. Extensive clinical and laboratory examinations of 33 pesticide users among these farmers did not reveal evidence of any disease that could be attributed to the use of pesticides, neither was the dieldrin blood concentration correlatable with any parameter examined.

The dieldrin blood concentrations in 8 locust-control workers in Ethiopia were measured on two occasions and were found to range between 0 and 9 μg/litre (MacCuaig, 1976).

Wolfe et al. (1963) studied the hazards from spraying orchards with dieldrin in the US Pacific Northwest. Potential contamination of the skin and respiratory exposure were measured. From the results, potential skin and respiratory exposures were calculated to amount to 14.2 and 0.25 mg/h, respectively.

Princi & Spurbeck (1951) studied a group of workers exposed to chlordane, aldrin, and dieldrin for several years in a manufacturing and formulating plant. The atmospheric concentrations of aldrin were reported to be as high as 2.6 mg/m^3. Physical examinations and chest-röntgenograms did not reveal respiratory anomalies.

A study was carried out on 71 men employed in the manufacture and formulation of aldrin, dieldrin, endrin, and some other non-related pesticides. Twenty-eight of these workers each contributed a sample of blood and a sample of fat on the same day. The average concentration of dieldrin in fat (6.12 ± 1.24 mg/kg) was 247 times greater than the mean plasma concentration (0.025 ± 0.006 mg/litre). There was no relation between the amount of dieldrin in the samples and the use of sick leave (Hayes & Curley, 1968).

In another study, 68 pesticide workers (including pest control operators) and 29 unexposed controls were examined quarterly over a

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[a] Personal communication at the 2nd Meeting of the Industrial Council on Tropical Health, Boston.

period of four years. Determinations of serum pesticide concentrations and enzyme activity, blood chemistry, haematology, and urinalysis were carried out. The mean serum dieldrin concentration was 3.6 ± 6.3 μg/litre (1.1 ± 1.6 μg/litre in the controls). There was no difference between the exposed workers and the controls in the incidence of disease or disability (Warnick & Carter, 1972).

In a pesticide formulation plant, the blood of 21 employees was examined at the conclusion of a 5-week period during which 900 kg of technical aldrin was formulated. The mean dieldrin concentration in plasma was 11 and 182.5 μg/litre for herbicide formulators and aldrin formulators, with a maximum of 317 μg/litre in the latter case. No mention was made of any intoxications (Mick et al., 1972).

In a group of 42 occupationally exposed pesticide workers with a dieldrin serum concentration 5 times as high as that in a group of 23 controls, no indication of disturbed renal- or adrenocortical function was found (Morgan & Roan, 1969, 1973).

A study was carried out in California, USA, where aldrin (EC as a 0.5% solution) at 480 g/litre was applied as a termiticide to typical slab and crawl space type houses. Personal air samples, samples of blood, and samples of pads on clothes and gloves were taken to monitor the exposure of the pest-control operators. The personal air samples during application contained less than 0.3 μg/m^3 aldrin for the slab houses and 30-75 μg/m^3 for the crawl space houses. The total work day (9-18 h) time-weighted average concentration of aldrin in air was 6-17 μg/m^3. This is far below the threshold limit value (TLV) for aldrin established by the American Conference of Governmental Industrial Hygienists (ACGIH, 1986) of 250 μg/m^3. Data from dermal exposure samples showed large variation. However, the maximum calculated percentage of the toxic dose per h, based on the acute percutaneous toxicity (rat LD_{50}) of the formulation, was less than 0.01%. The concentration of aldrin and dieldrin in the blood of the operators was below the limit of detection (less than 1 μg/litre) (Marlow et al., 1982).

A case-control study, carried out on 27 pesticide workers (4 formulators and 23 pest-control operators) with elevated blood concentrations of dieldrin, revealed a mean blood concentration of 19.59 μg/litre (range: 4.45-54 μg/litre). In an extensive clinical examination, including physical examination, comprehensive neurological examinations, laboratory tests, and physiological and psychomotor testing, no important differences were found compared with results in a control group of 25 people with a mean dieldrin blood concentration of 0.48 μg/litre (range of 0-3.34 μg/litre) (Sandifer et al., 1981).

9.2.3 Epidemiological studies

An extensive study on workers in an aldrin/dieldrin manufacturing plant has been in progress since the plant began operations in the 1950s. The results from the first 15 years of this epidemiological study were reported in 1970 (Jager, 1970). From a total of more than

800 exposed workers, all those exposed for more than 4 years (233 men) or those who had experienced an intoxication (20 men) underwent extensive physical, neurological, haematological, and other laboratory examinations. Clinical chemical determinations, including SGOT, SGPT, LDH, alkaline phosphatase, total serum protein, and serum protein spectrum, were made every 3 months and remained within normal limits. A no-effect level in this group of workers, including those who had previously suffered intoxications, was established at a dieldrin blood concentration of 200 μg/litre. This level corresponds to a total equivalent daily oral intake of 33 μg/kg body weight or a total daily intake of 2300 μg/person per day (Hunter & Robinson, 1967).

In experimental animals, the earliest, reversible effect of dieldrin is the induction of liver microsomal enzyme systems (Wright et al., 1977, 1978). This finding led to an investigation of a group of 10 workers. At the time, due to further improvements in the industrial hygiene of the above-mentioned plant, the geometric mean concentration of dieldrin found in the blood of workers was 105 μg/litre. As criteria of enzyme induction measurements were made of the blood levels of *p,p'*-DDE, the urinary ratio of 6-beta-hydroxycortisole and 17-hydroxycorticosteroids, and the urinary excretion of D-glucaric acid. No difference in these values was found between the 10 exposed workers and a control group. On the basis of these data, the no-effect level was 105 μg dieldrin/litre blood, equivalent to an oral daily intake of 17.4 μg/kg body weight per day (or 1220 μg/person per day) (Jager, 1970; Hunter et al., 1969; Hunter & Robinson, 1967; Versteeg & Jager, 1973).

Further results from this long-term survey of an industrial population were subsequently published, based on a study of 1000 workers. Because not all of the workers had severe and/or prolonged exposure, smaller groups with an exposure meaningful enough for carcinogenicity evaluation were included. One group consisted of 166 men (including workers who were still exposed and workers who had left the company), with a mean exposure time of 16.9 years (range 4-19 years), who had been under observation for more than 15 years (mean observation period 17 years; range, 15-20 years). A sub-group comprised 69 men with a mean exposure time of 14.9 years (range 10-19 years) and a mean observation period of 17.2 years. Among the group of 166 workers, 51 were more than 50 years old. One man with only 5 years of comparatively mild exposure died because of a gastric carcinoma. A lymphosarcoma occurred in a man with 7 years of very mild exposure. Both incidences occurred before 1964. No new cases were noted in the final 11 years of study, and no undue mortality from other causes that could have masked a higher cancer incidence was observed (Versteeg & Jager, 1973; Van Raalte, 1977).

In a follow-up study on the original group of 233 men with more than 4 years of exposure and an observation period ranging from 4 to 29 years (mean, 24 years), there were no indications of a specific carcinogenic activity. Total observed mortality was 25 deaths versus 38 expected. Of nine cancer deaths, three were caused by lung cancer,

while the remaining six were each of a different nature. No primary liver tumours were observed (Ribbens, 1985).

In a study by Morgan & Roan (1974), 28 pesticide formulators and applicators, plus a separate group of 43 termite-control workers, with occupational exposures of 5-22 years were examined, together with 56 controls. The highest levels of dieldrin among these 71 workers were found in a group of 37 men who had a mean serum dieldrin concentration of 84 μg/litre (equivalent to about 55 μg/litre whole blood). There were no signs of liver cell injury and the serum enzyme activities SGOT, SGPT, LDH, alkaline phosphatase and creatine phosphokinase (CPK) were within normal limits. There was no indication of drug-metabolizing enzyme induction and urinary excretion of D-glucaric acid was not different from that in a control group.

A study comparing liver cancer deaths in the USA and the "domestic disappearance" of organochlorine pesticides, revealed that, in 1962, 18 and 10 years after the introduction of DDT and aldrin/dieldrin, respectively (when an increase in primary liver cancer due to the organochlorines would be manifest), the cases of primary liver cancer as a percentage of the total number of liver cancer deaths began a gradual and steady decline (from 61.3% in 1962 to 56.9% in 1972). The death rate (per 100 000 per year) of primary liver cancer for this period declined from 3.46 to 3.18 (Deichmann & MacDonald, 1977).

An epidemiological mortality study in a plant manufacturing aldrin, dieldrin, and endrin was carried out on a cohort of 1155 workers who had been employed for at least 6 months between 1946 and 1976 (almost 25 000 man-years of observation). The mortality due to all malignant neoplasms was 31, lower than expected (standardized mortality ratio (SMR) 82). The total mortality from all causes was 173 (SMR 84). The only disease with an SMR above 100 (SMR 212) was "non-malignant respiratory system disease", specifically pneumonia. There was a slight excess of oesophagus and rectum cancer (two and three cases observed with an SMR of 235 and 242, respectively), liver cancer (two cases observed versus 0.57 expected), and cancer of the lymphatic and haematopoietic system (six cases observed versus 4.07 expected). However, there was a deficit of cancer of other sites. The authors concluded that "the study has not identified a specific cancer risk associated with employment at this manufacturing plant, but several causes should be examined further" (Ditraglia et al., 1981).

In a 1981 health survey, a total of 567 serum samples from 1811 Florida citrus workers were collected during the spraying and the harvest season and were compared with the national ("Hanes") sample. There were no differences in serum dieldrin levels; the mean in both groups being 1.8-1.9 μg/litre serum (Griffith & Duncan, 1985).

10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT

10.1 Evaluation of Human Health Risks

Aldrin and dieldrin, organochlorine pesticides, were used throughout the world from 1950 until the early 1970s as insecticides in agriculture and as a seed treatment, for the control of soil pests and other types of insects (e.g., termites, grasshoppers, and textile pests), and for the control of tse-tse flies and other disease vectors. The compounds act as contact and stomach poisons in the insects. Since the early 1970s, both compounds have been restricted or banned from use in several countries, especially in agriculture. Nevertheless, use continues in other countries for termite control.

Both compounds are practically insoluble in water and moderately to highly soluble in many organic solvents. The vapour pressure is low.

Dairy and meat products, fish, oils and fats, and certain vegetables such as root vegetables often contain dieldrin. Maximum residue limits recommended by the FAO/WHO Joint Meeting on Pesticide Residues range from 0.02 to 0.2 mg/kg product. Recent measurements have shown that actual levels are lower, and this has been confirmed by total diet studies. Since the use of these two compounds has been restricted, a steady but slow decrease in residue levels in the different food commodities has taken place.

The intake by human beings of low concentrations in the daily diet has resulted in dieldrin being present in adipose tissue and in some other tissues and organs. Global surveys have shown that mean values range from 0.1 to 0.4 mg/kg adipose tissue. Since the early 1970s, this concentration has slowly decreased.

Transplacental exposure of the fetus occurs, with the result that the fatty tissues of the fetus also contain dieldrin, but at concentrations 10-50% of those of the mother. There seems to be an equilibrium between levels in the fetus and those in the mother. Dieldrin is also excreted with the milk. Inhabitants of houses that have been treated for termite control may be exposed by inhalation. Concentrations in the air found after indoor treatment may range from 0.01 to 7 $\mu g/m^3$, depending on the type of applications, concentration used, type of ventilation, and time of sampling. Under these conditions food may also be contaminated by direct contact or by sorption from the atmosphere.

Metabolism takes place mainly in the liver where aldrin is readily transformed to dieldrin. Dieldrin is degraded at a slower rate to hydrophilic metabolites, which are then excreted via the bile and urine. The structures of these metabolites have been established. In all species examined, including human beings, it has been shown that there is a steady state of aldrin/dieldrin storage corresponding to the level of intake and a linear relationship between the log of intake and storage has been demonstrated. The concentration of dieldrin in body

tissues decreases exponentially on termination of exposure to the compounds.

The acute oral toxicity of aldrin and dieldrin for mammals is high, while the dermal toxicity is moderate. Dermal sensitization has not been found. Effects observed in acute, short-term and long-term studies involve the central nervous system. The liver is also a target organ. In the liver of mice and rats, changes known as "chlorinated hydrocarbon insecticide rodent liver" are found.

Aldrin and dieldrin do not appear to cause teratogenic effects at doses below those causing maternal toxicity and fetotoxicity. Male or female reproductive toxicity has not been reported.

Numerous *in vitro* and *in vivo* mutagenicity studies have demonstrated that neither aldrin nor dieldrin have mutagenic potential.

In long-term studies, aldrin and dieldrin induced benign and malignant liver tumours in the mouse. However, no increased incidence of liver tumours or other tumours were found in rats and hamsters.

IARC (1987) has stated that there is inadequate evidence of carcinogenicity in human beings and limited evidence of carcinogenicity in experimental animals. Both aldrin and dieldrin have been classified in Group 3: the chemicals cannot be classified as to their carcinogenicity in human beings.

On the basis of available short-term and long-term toxicity data, the overall no-observed-adverse-effect level in the rat is 0.5 mg dieldrin/kg diet, equivalent to 0.025 mg/kg body weight. In the dog, the lowest no-observed-adverse-effect level found was 0.04 mg/kg body weight. The Joint Meeting on Pesticide Residues (JMPR) established an Acceptable Daily Intake (ADI) of 0.1 µg/kg body weight in 1966 and 1977 based on the conclusion that aldrin and dieldrin were not human carcinogens.

Aldrin and dieldrin are highly toxic to human beings. Both accidental and occupational cases of poisoning have occurred but reported fatalities have been rare. Survivors of acute or subacute intoxications recovered completely. Adverse effects are related to the dieldrin blood concentration, the determination of which provides a specific diagnostic test for aldrin/dieldrin exposure. At a dieldrin blood concentration below 105 µg/litre, no adverse effects can be expected. This level is considered a threshold no-observed-adverse-effect level and corresponds to a daily intake of 0.02 mg dieldrin/kg body weight per day.

Environmental, mainly dietary, exposure leads to the presence of dieldrin in low concentrations in the human body. The results of extensive clinical and epidemiological studies indicate that these body burdens do not present a health hazard to human beings.

No signs of any premonitory change in liver function were found in a 20-years study, involving more than 1000 industrial workers exposed to aldrin and dieldrin. In this study and another study in the USA, no specific cancer risk could be identified associated with occupational exposure to (sometimes high levels of) aldrin and dieldrin.

All the available information on aldrin and dieldrin taken together, including studies on human beings, supports the view that for practical purposes, these chemicals make very little contribution, if any, to the incidence of cancer in human beings.

Photodieldrin, the photo-decomposition product of dieldrin, is similar to dieldrin in its short-term toxicity. It is not teratogenic or carcinogenic in mice and rats. The accumulation of photodieldrin in the adipose tissue of experimental animals was less than that of dieldrin.

10.2 Evaluation of Effects on the Environment

Aldrin, used as a soil insecticide, is the major source of dieldrin (up to 97%) in the environment. Aldrin and its reaction product dieldrin are rapidly adsorbed on soils, especially soils containing a high level of organic matter. Consequently there is little penetration into the soil, and contamination of groundwater does not generally occur. Transport of both compounds takes place mainly through soil erosion (as wind drift) and sediment transport (surface run off), but not through leaching.

The use of aldrin and dieldrin in agriculture leads to residues (mainly of dieldrin) in the soil that can persist for years; the estimated half-life of dieldrin is between 4 and 7 years. Under tropical conditions, the compounds are less persistent than under temperate conditions.

Aldrin and dieldrin enter the atmosphere through volatilization from treated crops and soil or, directly, during the application of the pesticide. Dieldrin returns to soil and water surfaces by washout and dry deposition. Thus, the compounds are found either in the vapour phase (very low levels, in general 1-2 ng/m^3), adsorbed by dust particles, or in rainwater (of the order of 10-20 ng/litre).

The occurrence of dieldrin in the aquatic environment has been reported by several authors. The concentrations in surface water are mainly very low, less than 5 ng/litre. However, concentrations in areas of soil erosion or agricultural use may be higher. Sediment in rivers in these areas may contain up to 1 mg dieldrin/kg. The high capacity for aquatic organisms to concentrate dieldrin from very low levels in water could lead to toxic levels in aquatic organisms. Concentration through aquatic foodchains is of less importance than direct uptake from water.

Because of the widespread occurrence of dieldrin in the environment and its persistence, there is a wide range of concentrations in non-target organisms. Whereas the concentrations previously ranged from 0.001 mg to 100 mg/kg tissue, they are now mostly below 1 mg/kg tissue.

In terrestrial ecosystems, aldrin and dieldrin are accumulated by a wide variety of organisms, principally as dieldrin. Dieldrin is probably responsible for the deaths of mammals in the field and for the decline in population size in some species, such as the otter. Small

mammals would be killed by eating dieldrin-dressed grain, but populations of these animals are likely to have been replenished by immigration from surrounding areas. Birds of prey eating small mammals and small birds contaminated by dieldrin take up and accumulate dieldrin in their own tissues and eggs. Granivorous birds have been killed by eating dressed grain. It is probable that the population decline in birds of prey was caused by dieldrin residues (among other organochlorine residues) in their tissues. The effects of dieldrin are seen some time after the exposure, because residues are stored in fat over winter, to be released in the spring. When dieldrin was used only at certain times of the year, this did not prevent bird mortalities.

The widespread use of aldrin and dieldrin, in conjunction with other organochlorine pesticides, has led to severe detrimental effects on the environment, though with drastic curtailment of use, particularly in seed dressings, there has been some recovery in bird populations.

10.3 Conclusions

(a) Both aldrin and dieldrin have been subjected to intensive and wide-ranging study, toxicologically, clinically, and epidemiologically. The body burden is mainly the result of the oral ingestion of residues in the diet (which seem generally to fall within the promulgated ADIs) and, to a lesser extent, of inhalation. Evaluation of the data suggests strongly that the body burden resulting from the present level of exposure constitutes no health risk to the general population.

(b) Dieldrin occurs almost ubiquitously in human breast milk. However, its concentration in the blood and adipose tissue of suckling infants does not increase with age during the first six months, nor is their blood dieldrin level higher than that of bottle-fed babies. Under these circumstances, the benefits of natural breast feeding still make it the preferred method of infant feeding, in spite of the dieldrin residues.

(c) In the treatment of premises, notably for termite control, the exposure of occupants does not appear to be increased to a level that endangers their health, as long as the directions for safe practice are conscientiously respected.

(d) Despite the highly toxic nature of aldrin and dieldrin, both of these chemicals can be handled safely as long as the recommended precautions to minimize worker exposure are always observed. Neglect of these rules may lead to the poisoning of operators.

(e) During the period of high aldrin and dieldrin use between 1950 and 1970, detrimental effects were undoubtedly inflicted upon species in the environment. These effects were due partly to dieldrin and partly to other organochlorines. Since the drastic curtailment of the use of these materials, the affected species have recovered in numbers.

11. RECOMMENDATIONS

1. A further, properly designed, teratogenic investigation is required in the hamster, with dieldrin at realistic dose levels.

2. Research into the mechanism of carcinogenesis should be directed to explaining why the hepatic reaction in the mouse is different from that of other species.

3. Dieldrin should be selected as an agent for further study of neurotoxic mechanisms, both experimentally and clinically.

4. To protect the environment, large-scale use of aldrin and dieldrin must not be resumed, and applications should be confined to those situations in which no safer, equally effective alternatives can be recommended.

5. For the health and welfare of workers and the general population, the handling and application of aldrin and dieldrin should only be entrusted to well trained competent operators, who will follow adequate safety measures.

6. To avoid accidental poisoning from aldrin, especially among children, the use of aldrin granules as an ant bait should be forbidden.

12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

Aldrin and dieldrin were evaluated by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) in 1963, 1965, 1966, 1967, 1968, 1969, 1970, 1974, 1975, and 1977 (FAO/WHO, 1964, 1965a,b, 1967a,b, 1968a,b, 1969a,b, 1970a,b, 1971a,b, 1975a,b, 1978a,b). From 1966 onwards, the JMPR established an acceptable daily intake (ADI) of 0-0.0001 mg/kg body weight (combined total for aldrin plus dieldrin). This was based on a level causing no toxicological effect of:

0.5 mg/kg diet, equivalent to 0.025 mg/kg body weight, in the rat; and

1 mg/kg diet, equivalent to 0.025 mg/kg body weight, in the dog.

The maximum residue limits (MRLs) listed in Table 47 were recommended by the FAO/WHO Joint Meeting on Pesticide Residues in 1970 and 1975 and are quoted as the sum of aldrin plus dieldrin.

Table 47. Maximum residue limits (MRL's) recommended by the Codex Alimentarius Commission (FAO/WHO, 1986)

Commodity	Aldrin and dieldrin (mg/kg)
Potatoes	0.1
Fat of meat	0.2[a]
Carrots, lettuce, fat of meat	0.1[a]
Asparagus, aubergines, broccoli, Brussels sprouts, cabbage, cauliflower, cucumbers, horse radish, onions, parsnips, peppers, pimentos, radishes, radish tops	0.1
Eggs (shell-free)	0.1[a]
Milk and milk products (fat basis)	-
Milk	0.006[a]
Fruit	0.05
Rice (in husks)	0.02
Raw cereals (other than rice)	0.02[a]

[a] Extraneous residue limit.

WHO (1984) recommended that the level of aldrin and dieldrin in drinking-water should not exceed 0.03 µg/litre.

IARC evaluated aldrin and dieldrin on several occasions. Aldrin and dieldrin were found to be carcinogenic in the liver in mice, but there was no evidence for carcinogenicity in other organs. The data available did not provide evidence of carcinogenicity in rats. Data on dogs, monkeys, and human beings were too limited to allow any conclusions (IARC, 1974). IARC considered that there was inadequate evidence of carcinogenicity in humans and limited evidence of carcinogenicity in experimental animals. Accordingly, both chemicals were classified in Group 3 (IARC, 1987).

The Pesticide Development and Safe Use Unit, Division of Vector Biology and Control, WHO, classified the acute hazard to health for technical dieldrin as "highly hazardous" (WHO, 1988). The same division published a data sheet on aldrin (79.41) and dieldrin (75.17) (WHO/FAO, 1975-85).

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APPENDIX I. NOMENCLATURE

Two major systems are currently used for the nomenclature of these compounds: "polyhydroaromatic" names used by Chemical Abstracts (American Chemical Society) and IUPAC and the von Baeyer/IUPAC system for polycylic aliphatic compounds. That the latter system should be used for the cyclodiene insecticides was proposed by Benson (1969) and Bedford (1974). The "polyaromatic" system has, unfortunately, been subject to historical variation, and there are differences between the IUPAC, British and American conventions for defining the 3-dimensional stereochemistry in this system. As a consequence of the differences in the numbering of the carbon atoms in the two major systems, and the modification of the Chemical Abstracts "polyaromatic" name for dieldrin since 1971, considerable confusion can occur regarding the nomenclature of metabolites.

The various alternative names for aldrin, dieldrin, and photodieldrin are summarized in Table 48. A useful discussion of nomenclature is given by Brooks (1974).

For convenience, in view of the much more extensive usage in the literature of the former Chemical Abstracts names for aldrin and dieldrin, the names of their metabolites in this review are based (if appropriate) on the former Chemical Abstracts names of the parent compounds given in Table 48. The names of the metabolites are given in Table 49, together with some alternative names based on either the current Chemical Abstracts name for dieldrin or the von Baeyer/IUPAC system.

The possible misunderstandings that may occur, particularly for those not familiar with the various conventions of chemical nomenclature, are illustrated by the different names that may be given to the major faecal metabolite of dieldrin. This one compound may be designated:

(a) 9-hydroxy dieldrin (former CA system);
(b) 8-hydroxy dieldrin (current CA system); or
(c) 12-hydroxy dieldrin (von Baeyer/IUPAC system).

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Table 48. Alternative chemical names for aldrin, dieldrin, and photodieldrin

Compound[a]	Polyhydroaromatic name		Polycyclic aliphatic name (von Baeyer/IUPAC)
	Chemical Abstracts	IUPAC	
Aldrin (HHDN) (I)	*Formerly:* 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-endo-1,4-exo-5,8-dimethanonaphthalene	*Formerly:* 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-exo-1,4-endo-5,8-dimethanonaphthalene	1,8,9,10,11,11-hexachloro-2,3-7,6-endo-2,1-7,8-exo-tetracyclo[6.2.1^{3,6}.0^{2,7}] dodeca-4,9-diene
	Currently: 1,2,3,4,10,10-hexachloro-1 alpha,4 alpha,4a-beta, 5 alpha,8a,8a beta-hexahydro-1,4:5,8-dimethanonaphthalene	*Currently:* (1R,4S,5S,8R)-1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-dimethanonaphthalene	
Dieldrin (HEOD) (II)	*Formerly:* 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-endo-1,4-exo-5,8-dimethanonaphthalene	*Formerly:* 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-exo-1,4-endo-5,8-dimethanonaphthalene	1,8,9,10,11,11-hexachloro-4,5-exo-epoxy-2,3-7,6-endo-2,1-7,8-exo-tetracyclo[6.2.1.1^{3,6}.0^{2,7}] dodec-9-ene
	Currently: 3,4,5,6,9,9-hexachloro-1a alpha,2 beta,2a alpha, 3 beta,6 beta,6a alpha,7 beta, 7a alpha-octahydro-2,7:3,6-dimethanonaphth[2,3-b]oxirene	*Currently:* (1R,4S,5S,8R)-1,2,3,4,10,10-hexachloro-1,4,4a,5,6,7,8,8a-octahydro-6,7 epoxy-1,4:5,8-dimethanonaphthalene	
Photodieldrin (III)	1,1,2,3,3a,7a-hexachloro-6,7-epoxy-2,4,7-metheno-decahydro-3H-cyclopenta[a]-pentalene		3,exo-4,5,6,6,7-hexachloro-11,12-exo-epoxy-pentacyclo[6.4.0.0^{2,10}.0^{3,7}.0^{5,9}]-dodecane

[a] Roman numerals in parentheses refer to the structures in Fig. 2 of the main document.

Table 49. Chemical nomenclature of metabolites of aldrin and dieldrin

Trivial name(s)[a]	Chemical name used in this review	Alternative chemical names
9-Hydroxy dieldrin (VI) (9-Hydroxy HEOD)	9-hydroxy-1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-endo-5,8-exo-dimethanonaphthalene	9-(syn-epoxy)hydroxy-1,2,3,4,10,10-hexachloro-6,7,-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-endo,exo-5,8-dimethanonaphthalene 8-hydroxy-3,4,5,6,9,9-hexachloro-1a alpha, 2 beta, 2a alpha, 3 beta, 6 beta, 6a alpha, 7 beta, 7a alpha-octahydro-2,7:3,6-dimethanonapth[2,3-b]oxirene 1,8,9,10,11,11-hexachloro-4,5-exo-epoxy-12-(synepoxy)hydroxy-2,3-7,6-endo-2,1-7,8-exo-tetracyclo[6.2.1.1^{3,6}0^{2,7}]dodec-9-ene
Aldrin trans-diol (IV)	trans-6,7-dihydroxy-1,2,3,4,10,10-hexachloro-1,4,4a,6,7,5,8,8a-hexahydro-1,4-endo-5,8-exo-dimethanonaphthalene	1,8,9,10,11,11-hexachloro-4,5-trans-dihydroxy-2,3-7,6-endo-2,1-7,8-exo-tetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodec-9-ene
Aldrin dicarboxylic acid (V)	4,5,6,7,8,8-hexachloro-4,7-methano-3a,4,7,7a-tetrahydro-indane-1,3-dicarboxylic acid	1,7,8,9,10,10-hexachloro-2,3-6,5-endo-tricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-exo-dicarboxylic acid
Bridged pentachloroketone (VII) (PCK, Klein's metabolite)	3,5,6,6,7-pentachloro-11,12-exo-epoxy-pentacyclo[6.4.0.0^{2,10}.0^{3,7}.0^{5,9}]dodecan-4-one	
Dechloro-aldrin dicarboxylic acid (VIII)	4,5,6,7,8-pentachloro-4,7-methano-3a,4,7,7a-tetrahydro-indane-1,3-dicarboxylic acid	

Table 49 (contd).

Trivial name(s)[a]	Chemical name used in this review	Alternative chemical names
Dieldrin ketone (IX)	1,2,3,4,10,10-hexachloro-1,4,4a,5,6,7,8,8a-octahydro-6-keto-endo-1,4-exo-5,8-dimethanonaphthalene	1,8,9,10,11,11-hexachloro-2,3-7,6-endo-2,1-7,8-exo-tetracyclo[6.2.1.$1^{3,6}$.$0^{2,7}$]-dodec-9-en-4-one
Photodieldrin ketone (X)	3-exo-4,5,6,6,7-hexachloro-pentacyclo[6.4.0.$0^{2,10}$.$0^{3,7}$.$0^{5,9}$] dodecan-11-one	
Photodieldrin trans-diol (XI) (caged aldrin trans-diol)	3,exo-4,5,6.6,7-hexachloro-11,12 dihydroxy-pentacyclo[6.4.0.$0^{2,10}$. $0^{3,7}$.$0^{5,9}$]dodecane	
Photoaldrin dicarboxylic acid (XII) (caged aldrin acid)	1,7,8,exo-9,10,10-hexachlorotetra-cyclo[5.2.1.$0^{2,6}$.$0^{4,8}$]decane-3,5-exo,exo-dicarboxylic acid	
Photoaldrin (XIII)	3,exo-4,5,6,6,7-hexachloropenta-cyclo[6.4.0.$0^{2,10}$.$0^{3,7}$.$0^{5,9}$]dodec-11-ene	

[a] Roman numerals in parentheses refer to the structures in Fig. 2 of the main document.

RESUME

1. Généralités

L'aldrine et la dieldrine qui sont l'une et l'autre des pesticides organochlorés fabriqués industriellement depuis 1950, ont été utilisés dans le monde entier jusqu'au début des années 70 comme insecticides en agriculture, contre de nombreux ravageurs présents dans le sol, et pour le traitement des semences. Ces insecticides étaient actifs contre les termites, les sauterelles, les xylophages, les coléoptères et les ravageurs des textiles. La dieldrine a également été employée en santé publique, pour la lutte contre la mouche tsé-tsé et d'autres vecteurs de maladies tropicales invalidantes. L'aldrine comme la dieldrine agissent par contact et par ingestion.

Depuis le début des années 70, ces deux composés sont interdits ou font l'objet de limitations rigoureuses dans un certain nombre de pays, spécialement en agriculture. Néanmoins, ils continuent d'être employés pour la destruction des termites dans d'autres pays. La production annuelle mondiale, estimée à 13 000 tonnes en 1972, est tombée à moins de 2500 tonnes en 1984.

L'aldrine et la dieldrine de qualité technique ont une pureté respective de 90% et plus de 95%. Les principales impuretés sont, pour l'aldrine, l'octachlorocyclopentène, l'hexachlorobutadiène et des produits de polymérisation et, pour la dieldrine, des polychloroépoxy-octahydrodiméthanonaphtalènes.

Les deux composés sont pratiquement insolubles dans l'eau et modérément à très solubles dans la plupart des alcanes, des hydrocarbures aromatiques et des hydrocarbures halogénés, ainsi que dans les esters, les cétones et les alcools.

La tension de vapeur de l'aldrine est de $6,5 \times 10^{-5}$ mmHg à 25°C et celle de la dieldrine de $3,2 \times 10^{-6}$ mmHg à 25°C.

Les méthodes utilisables pour le dosage de l'aldrine et de la dieldrine dans les aliments, les aliments pour animaux et le milieu sont décrites à la section 2.

2. Transport, distribution et transformation dans l'environnement

L'aldrine est principalement utilisée comme insecticide épandu au niveau du sol. Les sols ainsi traités constituent donc dans l'environnement une source importante d'aldrine et de son produit de réaction, la dieldrine.

L'aldrine n'a qu'une faible capacité de migration à partir des zones traitées, par volatilisation ou lessivage. Elle s'adsorbe préférentiellement, et rapidement, sur les sols riches en matières organiques, mais faiblement sur les sols argileux. Il est rare que l'aldrine et la dielrine pénètrent au-delà des 20 premiers centimètres de la couche de sol traité. L'aldrine adhère si solidement aux

particules du sol que seules des traces peuvent être retirées par l'eau. C'est pourquoi il n'y a généralement pas contamination des eaux souterraines.

L'aldrine s'élimine du sol selon une cinétique qui évoque une réaction du premier ordre. Immédiatement après épandage, on observe une courte période d'élimination rapide par volatilisation, suivie d'une seconde période, plus longue, de décroissance exponentielle, principalement du fait de la transformation en dieldrine, plus lente à se dissiper. Néanmoins, il peut y avoir une certaine migration du fait de l'érosion du sol, sous l'action du vent, des eaux de ruissellement de du déplacement des sédiments. Les observations faites sur les résidus d'aldrine dans la nature montrent que, apparemment, ce composé est essentiellement retenu dans le sol et que pour 97%, le résidu essentiel n'est pas le composé d'origine mais l'époxyde correspondant, la dieldrine.

La photodieldrine est un produit de photodégradation de la dieldrine, peu répandu dans l'environnement.

Apres épandage sur le sol, l'aldrine disparaît lentement dans les régions tempérées puisque, dans le cas type, il faut un an pour qu'elle s'élimine aux trois quarts. La vitesse d'élimination diminue ensuite à mesure que l'aldrine se transforme en dieldrine. Il semblerait que la vitesse d'élimination soit plus élevée en anaérobiose, comme c'est le cas dans les rizières, qu'en aérobiose. Dans les régions tropicales, la dieldrine s'élimine du sol très rapidement, jusqu'à hauteur de 90% au cours du premier mois, alors que, dans le sol des régions tempérées, la dieldrine a une demi-vie d'environ 5 ans. La volatilisation semble être le principal mécanisme d'élimination à partir du sol, bien que la teneur atmosphérique de la dieldrine et de l'aldrine soit généralement faible. Une partie de la dieldrine est éliminée de l'atmosphère par les précipitations, mais la concentration de ce produit est très faible dans les eaux souterraines par suite de son adsorption énergique sur les particules telluriques. On trouve de la dieldrine en petites quantités dans les eaux de surface qui sont contaminées par les eaux de ruissellement provenant de terres agricoles.

3. Concentrations environnementales et exposition humaine

On trouve de l'aldrine et de la dieldrine dans l'atmosphère en phase vapeur, adsorbées sur des poussières ou dans les eaux de pluie, à des teneurs variables selon la situation. Ces produits s'observent principalement dans les régions agricoles où leur concentration atmosphérique moyenne est de l'ordre de 1-2 ng/m^3 avec des maximums d'environ 40 ng/m^3. Dans l'eau de pluie, on relève des concentrations de l'ordre de 10-20 ng/litre ou parfois plus.

Dans les habitations traitées avec ces produits contre les termites, on observe une concentration dans l'air allant de 0,04 à 7 μg/m^3, selon le moment de l'échantillonnage (c'est-à-dire le nombre de jours après l'épandage) et le type d'habitation. Au bout de

8 semaines, la concentration a très nettement diminué. Lorsqu'on traite le bois en profondeur dans ces maisons, la concentration de la dieldrine dans l'air va de 0,01 à 0,5$\mu g/m^3$. On a constaté que l'aldrine et la dieldrine migraient dans les produits alimentaires à partir de panneaux lamellés et de contreplaqués traités, ainsi que par contact direct ou sorption à partir de l'atmosphère.

On a signalé la présence de dieldrine en milieu aquatique. Mais les concentrations étaient très faibles, le plus souvent inférieures à 5 ng/litre. Les concentrations plus élevées ont généralement été attribuées au rejet d'effluents industriels ou à l'érosion du sol à la suite de l'utilisation de ces produits en agriculture. Dans les cours d'eau, les sédiments peuvent présenter des teneurs beaucoup plus élevées (allant jusqu'à 1 mg/kg).

On trouve rarement de l'aldrine dans les aliments, alors que la dieldrine est plus courante, spécialement dans les produits laitiers, les produits carnés, le poisson, les huiles et les graisses, les pommes de terre et certains autres légumes (principalement des légumes-racines). Des limites maximales de résidus (LMR) de l'ordre de 0,02-0,2 mg/kg de produit ont été recommandées lors des réunions conjointes successives FAO/OMS sur les résidus de pesticides. Les études récentes réalisées dans différents pays montrent que la concentration effective de la dieldrine dans les denrées alimentaires est généralement plus faible. Le recul est net au Royaume-Uni. En 1966-67, la concentration moyenne des résidus de dieldrine observée lors d'une étude sur la ration totale était de 0,004 mg/kg d'aliments tandis que, pendant la période 1975-77, elle n'était plus que de 0,0015 mg/kg pour tomber à 0,0005 mg/kg en 1981. Cette évolution en baisse est confirmée dans d'autres pays, par exemple aux Etats-Unis d'Amérique. Cela tient peut-être à l'interdiction ou à la limitation d'emploi de ces composés.

Dans un grand nombre de travaux publiés, on a recherché la présence de dieldrine dans le tissu adipeux, les organes, le sang et d'autres tissus, chez des sujets de la population générale. Au cours des 25 dernières années, des enquêtes ont été réalisées dans de nombreux pays, partout dans le monde. La plupart des concentrations moyennes observées dans le tissu adipeux se situent entre 0,1 et 0,4 mg/kg. Aux Etats-Unis d'Amérique, aux Pays-Bas et au Royaume-Uni, on note une diminution de la concentration dans les tissus adipeux depuis le milieu de la décennie 70. La concentration sanguine varie de 1 à 2 μg/litre. Dans le foie, elle est inférieure à 0,4 mg/kg tandis que, dans les autres tissus, à savoir les reins, l'encéphale et les gonades, elle est inférieure à 0,1 mg/kg.

A la suite d'une exposition par voie transplacentaire, on trouve de la dieldrine dans le sang, les tissus adipeux et d'autres tissus du foetus et du nouveau-né. Les concentrations sont 2 à 10 fois plus faibles que chez la mère. Il n'existe aucune différence entre le nourrisson et l'adulte pour ce qui est des concentrations relatives de la dieldrine dans le cerveau, le foie et les tissus adipeux. La dieldrine est également excrétée dans le lait maternel. Depuis une quinzaine d'années, on recherche dans divers pays la présence de

pesticides organochlorés dans le lait de femme. Dans la plupart des pays, la concentration plafonne à 6 µg/litre, sauf cas exceptionnels.

4. Cinétique et métabolisme

Chez les animaux comme chez l'homme, l'aldrine et la dieldrine passent rapidement des voies digestives dans le courant sanguin. L'absorption a également lieu au niveau de la peau ou des poumons après inhalation de la vapeur. Une étude sur des volontaires a montré que la quantité résorbée par la peau intacte représente 7-8% de la dose appliquée. Selon des études d'inhalation conduites sur des volontaires, le taux d'absorption et de rétention de l'aldrine dans l'organisme peut atteindre 50% de la vapeur inhalée. Après absorption, le composé se répartit rapidement dans tous les organes et tissus, et il existe un échange permanent entre le sang et les autres tissus. Entre-temps, l'aldrine se transforme en dieldrine, principalement au niveau du foie mais aussi, dans une moindre proportion, dans d'autres tissus comme les poumons. Cette conversion est très rapide.

Après administration par voie orale d'une dose de 10 mg d'aldrine par kg de poids corporel à des rats de 1 jour, on a retrouvé ce composé dans le foie des animaux d'expérience 2 heures après l'administration. Au cours des quelques heures suivantes, la dieldrine s'est concentrée dans une beaucoup plus large mesure dans les tissus lipidiques.

Comme l'ont montré de nombreuses études effectuées avec de l'aldrine ou de la dieldrine marquées au ^{14}C, une partie du produit ingéré passe telle quelle dans l'intestin d'où elle est éliminée de l'organisme, une partie est excrétée telle quelle à partir du foie dans la bile, une autre fraction est stockée dans les divers organes et tissus, en particulier le tissu adipeux, et une dernière fraction est métabolisée dans le foie en produits à caractère hydrophile et polaire plus prononcé. Chez l'homme et la plupart des animaux, les métabolites sont principalement éliminés dans les excreta, par l'intermédiaire de la bile. On a établi par ailleurs que la biodégradation de l'aldrine et de la dieldrine aboutit aux mêmes métabolites.

La plupart des connaissances actuelles sur le catabolisme de la dieldrine chez les mammifères proviennent d'études chez la souris, le rat, le lapin, le mouton, le chien, les petits singes, le chimpanzé et l'homme. Dans l'ensemble, on n'observe que des différences quantitatives entre les diverses espèces et les mécanismes sont apparemment semblable chez le rat et les primates.

Le principal métabolite, sauf chez le rat, est le dérivé hydroxylé en 9. On le trouve dans les déjections ainsi que dans l'urine, sous forme libre ou conjuguée. On a découvert et identifié chez les animaux d'expérience trois autres métabolites, présents en petites quantités. Il s'agit d'un dérivé 6,7-dihydroxylé en position *trans*, d'un acide dicarboxylique dérivé du composé dihydroxylé et d'une pentachlorocétone pontée.

Seul le composé hydroxylé en 9 a été mis en évidence chez l'homme, dans les matières fécales, tandis que ni ce composé ni les autres métabolites n'apparaissaient dans le sang ou les autres tissus. On a observé la présence de dieldrine dans les selles d'ouvriers professionnellement exposés, tandis que, dans la population générale, les quantités étaient inférieures au seuil de détection. L'examen des urines de cinq ouvriers a montré que l'excrétion de la dieldrine et de ses quatre métabolites par voie urinaire était minime par rapport à l'élimination du métabolite hydroxylé en 9 par voie fécale.

La transformation de l'aldrine en dieldrine dans le foie, sous l'action de mono-oxygénases à fonction mixte (aldrine-époxydase) et la distribution, puis le dépôt ultérieur, de la dieldrine (principalement dans les tissus à contenu lipidique, tels que le tissu adipeux, le foie, les reins, le coeur et le cerveau) sont beaucoup plus rapides que le catabolisme et l'élimination finale de la dieldrine intacte et de ses métabolites. Dans ces conditions, pour un apport quotidien moyen déterminé d'aldrine ou de dieldrine, il y a accumulation lente de dieldrine dans l'organisme. Mais cette accumulation n'est pas indéfinie. Quand l'administration se poursuit, on finit par aboutir à un état d'équilibre dynamique, la quantité excrétée compensant exactement l'apport. La quantité stockée maximale dépend de l'apport quotidien, tout comme on l'a montré chez le rat, le chien et l'homme.

Quand l'apport d'aldrine/dieldrine est réduit ou interrompu, la charge de l'organisme diminue. Chez l'homme, la demi-vie biologique est de l'ordre de 9 à 12 mois. Chez le rat, le chien et l'homme, on a démontré l'existence de relations significatives entre la concentration de la dieldrine dans le sang et sa concentration dans d'autres tissus.

De nombreuses études sur la concentration de la dieldrine dans divers tissus, dont le sang et les tissus adipeux, aussi bien dans la population générale que dans des catégories particulières, ont été réalisées dans plusieurs pays et ont montré que, à l'équilibre, les concentrations respectives dans les tissus adipeux, le foie, le cerveau et le sang sont sensiblement proportionnelles à 150, 15, 3 et 1.

La dieldrine est transportée par le placenta jusqu'au foetus. Il y a accumulation dans les mêmes organes et tissus que chez l'adulte, mais en quantités moindres. Il existe apparemment un équilibre entre les concentrations chez la mère et chez le foetus.

Chez le rat et le chien, la photodieldrine est également métabolisée sous forme de pentachlorocétone pontée. On a retrouvé les deux composés dans les tissus adipeux, le foie et les reins des animaux à qui l'on avait administré de la photodieldrine à forte dose. Chez l'homme, aucun résidu de ces composés n'a été mis en évidence dans le tissu adipeux, les reins ni le lait maternel. L'accumulation de photodieldrine dans les tissus adipeux des animaux d'expérience était beaucoup moins importante que celle de la dieldrine.

5. Effets sur les êtres vivants dans leur milieu natural

5.1 Accumulation

La plupart des résidus présents chez les êtres vivants sont des résidus de dieldrine, car l'aldrine se transforme facilement chez eux en dieldrine.

Les champignons, les streptomycètes et les bactéries concentrent la dieldrine du milieu ambiant dans une proportion qui peut aller en 4 h de 0,3 à plus de 100. Les protozoaires absorbent la dieldrine davantage que les algues. Celles-ci absorbent très rapidement la dieldrine présente dans le milieu de culture, les concentrations maximales étant souvent atteintes en quelques heures.

De nombreuses espèces d'invertébrés aquatiques concentrent fortement la dieldrine à partir d'une eau à très faible teneur. L'équilibre est atteint en quelques jours. Lorsqu'on les remet en eau pure, la dieldrine s'élimine rapidement, avec une demi-vie de 60-120 h.

Pour les poissons entiers, le facteur de bioconcentration dépasse 10 000. Chez une espèce de poissons, la demi-vie d'élimination de la dieldrine accumulée s'est établie à 16 jours.

La bioconcentration de dieldrine chez les organismes aquatiques se fait principalement à partir de l'eau et non par ingestion d'aliments.

Les lombrics absorbent la dieldrine présente dans le sol et la concentrent jusqu'à un facteur maximal d'environ 170. Pour la plupart des types de sol, il n'existe guère de corrélation entre la concentration atteinte chez le lombric et la concentration dans le sol.

De nombreux travaux ont été consacrés à la présence de la dieldrine dans les tissus ou dans les oeufs d'espèces non visées. Les concentrations observées sont extrêmement variables, allant de 0,001 mg/kg à 100 mg/kg de tissu, mais elles restent le plus souvent inférieures à 1 mg/kg de tissu.

Chez les oiseaux, il y a accumulation rapide de dieldrine aussi bien dans les tissus que dans les oeufs. De même, on a montré que diverses espèces de mammifères accumulent la dieldrine, en particulier dans les graisses.

5.2 Toxicité pour les micro-organismes

La dieldrine a des effets très variables sur les algues unicellulaires, avec une action sensible sur certaines espèces dès la concentration de 10 µg/litre tandis que d'autres espèces ne sont pas touchées même à la concentration de 1000 µg/litre. L'aldrine et la dieldrine n'ont que peu d'effets sur les bactéries terricoles, même à des concentrations très supérieures aux valeurs habituelles. Dans la plupart des études, aucun effet n'a été constaté après exposition à une concentration de 2000 mg/kg de terre. Des effets ont été signalés sur la photosynthèse chez différentes espèces d'algues, avec une action plus marquée de l'aldrine que de la dieldrine à concentrations égales.

Mais ces effets minimes sur la biochimie des algues n'étaient que transitoires.

5.3 Toxicité pour les organismes aquatiques

L'aldrine et la dieldrine sont extrêmement toxiques pour les crustacés aquatiques, avec des valeurs de la DL_{50} à 96 h inférieures à 50 µg/litre. Cependant, les quelques résultats plus élevés signalés (jusqu'à 4300 µg/litre) illustrent les différences de sensibilité selon les espèces. Les daphnies sont moins sensibles à la dieldrine qu'à l'aldrine, avec des DL_{50} à 48 h de 23-32 µg/litre dans le premier cas et de 190-330 µg/litre dans le second. Les mollusques sont nettement plus résistants, les CL_{50} à 48 h pouvant atteindre plus de 10 000 µg/litre. Des études de plusieurs semaines ont confirmé la résistance relative des daphnies et des mollusques. Les invertébrés aquatiques les plus sensibles sont les stades larvaires des insectes, avec des CL_{50} à 96 h de 0,5-39 µg/litre pour la dieldrine et de 1,3-180 µg/litre pour l'aldrine.

Lors d'épreuves de toxicité aiguë, l'aldrine comme la dieldrine se sont montrées très toxiques vis-à-vis des poissons. Chez diverses espèces de poisson, on a relevé des valeurs de la CL_{50} à 96 h allant de 2,2 à 53 µg/litre pour l'aldrine et de 1,1 à 41 µg/litre pour la dieldrine. De nombreuses études ont montré que la toxicité augmente avec la température. Dans une étude prolongée sur *Poecilia latipinna*, on a obtenu un taux de mortalité de 100% en présence d'une concentration de dieldrine égale ou supérieure à 3 µg/litre. L'addition de dieldrine à la nourriture de truites arc-en-ciel jusqu'à des concentrations de 430 µg/kg de poids corporel par jour, n'a exercé aucune influence sur la mortalité mais a entraîné des modifications enzymatiques. Des altérations morphologiques ont été observées au microscope électronique dans les mitochondries hépatiques. Le mécanisme de détoxification de l'ammoniaque chez les poissons est sensible à la dieldrine, la dose sans effet nocif apparent étant inférieure à 14 µg/kg de poids corporel par jour. La sensibilité à la dieldrine s'est révélée variable selon le stade de développement des poissons. Les oeufs étaient résistants et les formes juvéniles moins sensibles que les adultes.

La toxicité aiguë de l'aldrine comme de la dieldrine est élevée pour les larves d'amphibiens, avec des CL_{50} à 85 h de l'ordre de 100 µg/litre.

5.4 Toxicité pour les organismes terrestres

La dieldrine est peu toxique pour les végétaux supérieurs puisque les cultures ne sont affectées que par des doses supérieures à 22 kg/ha. La phytotoxicité de l'aldrine est plus importante, notamment pour les tomates et les concombres, mais uniquement à des doses plusieurs fois supérieures aux valeurs recommandées. Le chou est la plante cultivée la plus sensible à l'aldrine.

Vis-à-vis des abeilles, la DL_{50} par voie orale varie, selon les observations publiées, de 0,24 à 0,45 µg/abeille pour l'aldrine et de 0,15 à 0,32 µg/abeille pour la dieldrine. Les quantités toxiques par contact vont de 0,15 à 0,80 µg/abeille pour l'aldrine et de 0,15 à 0,41 µg/abeille pour la dieldrine. D'après deux études, la dieldrine est relativement plus toxique vis-à-vis des insectes prédateurs qui se nourrissent de ravageurs.

Selon des études effectuées en laboratoire, le lombric supporte des doses d'aldrine de 13 mg/kg en sol artificiel, le taux de mortalité étant inférieur à 1%. La CL_{50} à six semaines était de 60 mg d'aldrine par kg de sol.

Pour 13 espèces d'oiseaux, la toxicité aiguë de l'aldrine et de la dieldrine variait de plus du simple au décuple, avec des valeurs de 6,6-520 mg/kg de poids corporel pour l'aldrine et de 6,9-381 mg/kg de poids corporel pour la dieldrine. Chez quatre espèces d'oiseaux, la toxicité subaiguë par voie orale correspondait à des doses comprises entre 34 et 155 mg/kg pour l'aldrine et 37 et 169 mg/kg pour la dieldrine. Des épreuves répétées au cours d'une certaine période n'ont révélé aucun signe de résistance acquise chez ces espèces. D'après des études sur la reproduction de plusieurs espèces de volaille, une concentration de la dieldrine dépassant 10 mg/kg dans les aliments provoque une certaine mortalité chez les adultes. Aucun effet ne s'est fait sentir sur la production des oeufs, la fécondité, le taux d'éclosion ni la survie des poussins en présence de dieldrine dans les aliments à des concentrations qui ne sont pas toxiques pour la mère. La dieldrine n'a aucune influence directe sur l'épaisseur de la coquille des oeufs. Cependant, la diminution de la consommation de nourriture, qui constitue un symptôme de l'intoxication par la dieldrine, peut entraîner une diminution de l'épaisseur de la coquille.

Chez le mammifères non élevés au laboratoire, la réponse à la dieldrine varie selon les espèces. Chez quatre espèces de campagnols, on a observé des valeurs de la DL_{50} aiguë, allant de 100 à 210 mg/kg de poids corporel, ce qui montre que ces animaux sont moins sensibles à la dieldrine que les animaux de laboratoire. Des musaraignes ont survécu à la consommation d'une nourriture contenant 50 mg de dieldrine par kg mais sont mortes quand la concentration est passée à 200 mg/kg. Des damalisques (une espèce d'antilope) ont survécu 90 jours à une nourriture contenant de la dieldrine à raison de 5 ou 15 mg/kg mais sont toutes mortes dans les 24 jours pour une concentration égale ou supérieure à 25 mg/kg. Tous les damalisques d'une région où l'on avait pulvérisé de la dieldrine à raison de 0,16 kg/ha sont mortes et le calcul a montré que l'apport alimentaire était de 1,82 mg/kg par jour. Trente pour cent des springboks ont survécu aux épandages, sans manifester d'effets tardifs. Les signes toxicologiques de l'intoxication par la dieldrine étaient sensiblement les mêmes que chez les mammifères de laboratoire.

5.5 Effets sur les populations et les écosystèmes

Certaines études donnent à penser que des populations de mammifères ont été intoxiquées par de la dieldrine. Il est probable que de petits mammifères sont morts après avoir mangé des semences enrobées de dieldrine mais les populations se sont reconstituées par immigration. Des chauves-souris ont été tuées par la dieldrine contenue dans les agents de protection du bois.

Des résidus de dieldrine ont été signalés chez de nombreuses espèces d'oiseaux. Partout dans le monde, c'est chez les oiseaux de proie que les résidus sont les plus abondants car les animaux se situent en fin de chaîne alimentaire. La teneur en dieldrine des tissus et des oeufs d'oiseau suit l'évolution de l'emploi de l'aldrine et de la dieldrine, et elle a diminué à la suite des restrictions imposées à leur usage. Il n'est pas facile de repérer les effets de la dieldrine car les résidus de cet insecticide s'accompagnent de résidus d'autres organochlorés. La dieldrine est plus toxique que le DDT pour les oiseaux et il est probable qu'elle a provoqué chez les adultes une plus forte mortalité que le DDT. Il est encore plus difficile de démontrer l'existence d'effets de la dieldrine sur la reproduction à l'état naturel. En outre, il se peut que les effets interviennent longtemps après l'exposition.

6. Effets sur les animaux d'expérience et les systèmes d'épreuve *in vitro*

L'aldrine et la dieldrine sont extrêmement toxiques : pour ces deux composés, la DL_{50} varie, chez la souris et chez le rat, de 40 à 70 mg/kg de poids corporel. Par voie percutanée, la dose toxique se situe entre 40 et 150 mg/kg de poids corporel selon l'espèce en cause et le solvant utilisé. On a constaté que l'aldrine et la dieldrine de qualité technique déterminent chez le lapin une irritation cutanée légère à intense, mais la cause en est le solvant. Dans l'épreuve de maximalisation de Magnusson & Kligman chez le cobaye, l'aldrine a provoqué un effet de sensibilisation. Pourtant, au cours de 20 années de fabrication et de préparation des formules, aucun cas de sensibilisation cutanée n'a été observé dans un groupe comptant plus de 1000 travailleurs.

L'aldrine, comme la dieldrine, a une faible tension de vapeur de sorte que, en principe, il n'y a aucun effet aigu par inhalation. Les effets observés lors des études de toxicité aiguë après exposition par toutes les voies possibles concernent le système nerveux central et consistent en hyperexcitabilité, tremblements et convulsions.

Des études d'exposition par voie orale, de courte ou longue durée, ont été réalisées avec l'aldrine et la dieldrine, chez la souris, le rat, le chien, le hamster et les petits singes. Chez le rat et la souris, le foie est le principal organe-cible : on observe une augmentation de son poids par rapport au poids du corps et une hypertrophie des hépatocytes centrilobulaires, la réversibilité étant possible à un

stade précoce. Au microscope, ces altérations se traduisent par une augmentation de l'oxyphilie cytoplasmique et une migration périphérique des granules basophiles. Ces altérations ne se rencontrent pas au niveau du foie chez le hamster et le singe. Chez le chien, l'atteinte hépatique est peu prononcée (dégénérescence graisseuse et légère atrophie des hépatocytes); elle s'accompagne d'une atteinte rénale consistant dans une vacuolisation de l'épithélium des tubules distaux et une dégénérescence tubulaire. Chez le rat, la dose sans effet nocif observable se situe dans l'ensemble, d'après les résultats dont on dispose sur le court et le long terme, aux alentours de 0,5 mg/kg de nourriture, soit l'équivalent de 0,025 mg/kg de poids corporel. En augmentant les quantités incorporées à la nourriture, jusqu'à obtenir l'équivalent de 0,05 mg/kg de poids corporel ou davantage, on observe une hépatomégalie et des altérations histologiques d'importance proportionnée à la dose. Chez le chien une dose de 0,04-0,2 mg/kg de poids corporel s'est révélée sans effet.

Plusieurs études de cancérogénicité à long terme ont été effectuées sur différentes souches de souris, avec de l'aldrine ou de la dieldrine. Chaque fois, on a observé des tumeurs hépatocellulaires bénignes ou malignes. Apparemment, les femelles étaient plus sensibles que les mâles. Aucun autre type de tumeur ne s'est manifesté dans ces études.

Des études à long terme sur d'autres espèces (rat, hamster) n'ont révélé aucune augmentation de l'incidence tumorale. L'administration de photodieldrine incorporée à la nourriture, jusqu'à une concentration de 7,5 mg/kg d'aliments, ne s'est pas révélé tumorigène.

En outre, on a publié un certain nombre d'études spéciales qui n'ont, jusqu'ici, pas permis d'élucider le mécanisme de la production des tumeurs hépatiques chez la souris.

Dans la plupart des études de reproduction (sur 1 à 6 générations), réalisées avec l'aldrine ou la dieldrine sur des souris et des rats, le principal effet constaté a été l'augmentation du taux de mortalité dans la descendance, avant sevrage. La capacité génésique n'a été atteinte qu'à des doses toxiques pour la mère. Les études sur le chien étaient trop limitées pour permettre les conclusions catégoriques, si ce n'est qu'on a noté une augmentation systématique de la mortalité des chiots à la mamelle.

D'après les résultats de ces études sur la reproduction, on peut conclure que, de ce point de vue, les doses sans effet nocif décelable sont de 2 mg de dieldrine par kg de nourriture chez le rat et de 3 mg de dieldrine par kg de nourriture chez la souris, soit l'équivalent quotidien de 0,1 et 0,4 mg/kg de poids corporel respectivement.

Aucun signe de tératogénicité n'a été observé chez la souris, le rat ou le lapin, après administration par voie orale de doses d'aldrine et de dieldrine atteignant 6 mg/kg de poids corporel. L'administration d'une dose unique d'aldrine et de dieldrine, représentant environ la moitié de la DL_{50}, a provoqué des effets toxiques intenses chez le foetus de souris et de hamster, ainsi qu'une incidence accrue d'anomalies tératogènes. La signification de ces observations est

douteuse en présence d'effets toxiques probables chez les femelles gravides.

Les études de mutagénicité *in vivo* ou *in vitro* ont été nombreuses, mais elles ont presque toujours donné des résultats négatifs.

La toxicité aiguë de la photodieldrine par voie orale est plus élevée que celle de la dieldrine chez la souris, le rat et le cobaye. Lors d'études de toxicité aiguë ou à long terme, on a observé des symptômes d'intoxication et des effets sur les organes cibles analogues à ceux de la dieldrine, tant sur le plan quantitatif que sur le plan qualitatif. La photodieldrine ne s'est pas montrée tumorigène chez la souris ni chez le rat.

Comme la plupart des autres substances chimiques, l'aldrine et la dieldrine exercent leurs effets toxiques selon plusieurs mécanismes. Les organes cibles sont le système nerveux central et le foie. Chez l'homme et les autres vertébrés, l'intoxication secondaire à une exposition aiguë ou chronique, se caractérise par des mouvements musculaires involontaires et des convulsions épileptiformes. En cas de survie, la récupération est totale après une courte durée marquée par des symptômes résiduels. Au niveau du foie, on observe une activité accrue des enzymes microsomales de biotransformation, en particulier du système enzymatique cytochrome P-450/monooxygénase. Cette induction des enzymes mircosomales est réversible et, au-delà d'un certain niveau, elle semble liée aux altérations cytoplasmiques au niveau du foie et à l'hépatomégalie chez les rongeurs.

Dans l'ensemble, d'après les observations faites sur l'aldrine et la dieldrine, notamment dans le cadre des études sur l'homme, on peut penser que, en pratique, ces produits ne contribuent guère à l'incidence des cancers humains.

7. Effets chez l'homme

L'aldrine et la dieldrine sont très toxiques pour l'homme. Il y a eu de graves cas d'intoxication accidentelle ou professionnelle mais il est rare qu'ils aient fait des victimes. La plus faible dose ayant provoqué une issue fatale a été estimée à 10 mg/kg de poids corporel. Les personnes ayant survécu à une intoxication aiguë ou subaiguë se sont complètement rétablies. Aucun effet irréversible ni atteinte anatomopathologique résiduelle n'a été signalée.

Les effets nocifs de l'aldrine et de la dieldrine sont fonction de la concentration de la dieldrine dans le sang. Le dosage de la dieldrine dans le sang permet de diagnostiquer avec précision une exposition à l'aldrine/dieldrine. Chez les travailleurs, le taux sanguin au-dessous duquel on n'observe aucun effet nocif (dose limite sans effet nocif décelable) est de 105 µg/litre de sang. Cela correspond à un apport quotidien de dieldrine de 0,02 mg/kg de poids corporel.

L'exposition environnementale (principalement par l'intermédiaire des aliments mais aussi, dans une faible mesure, par voie respiratoire) entraîne l'apparition de dieldrine à une très faible concentration dans

les organes, le sang et le lait maternel. Autant qu'on puisse en juger d'après des études épidémiologiques et cliniques poussées, il n'existe aucun raison de penser que les taux couramment observés dans l'organisme constituent une menace pour la santé de la population en général. Lors d'une étude poursuivie pendant plus de 20 ans auprès de 1000 travailleurs de l'industrie, employés dans une fabrique d'insecticides à base d'aldrine/dieldrine, aucune augmentation de l'incidence des cancers n'a été observée chez les sujets fortement exposés à ces deux produits. Phénomène encore plus significatif, aucun signe avant-coureur, sous forme d'une altération de la fonction hépatique, n'a été observé.

Une étude épidémiologique sur la mortalité a été réalisée dans une unité de production aux Etats-Unis, sur une cohorte de 870 travailleurs exposés à l'aldrine, à la dieldrine et à l'endrine. Malgré près de 25 000 années-homme d'observation, il n'a pas été possible de repérer un risque particulier de cancer attributable au travail dans cette usine.

EVALUATION DES DANGERS POUR LA SANTE DE L'HOMME ET DES EFFETS SUR L'ENVIRONNEMENT

1. Evaluation des dangers pour la santé de l'homme

L'aldrine et la dieldrine sont des pesticides organochlorés qui ont été utilisés partout dans le monde entre 1950 et le début des années 70 comme insecticides en agriculture et pour le traitement des semences, pour la destruction des ravageurs terricoles et d'autres types d'insectes (par exemple les termites, les sauterelles et les ravageurs des textiles) ainsi que pour la lutte contre les glossines et autres vecteurs de maladies. Chez les insectes, ces composés exercent leur effet toxique par contact et par voie digestive. A partir des années 70, on en a limité ou interdit l'emploi dans plusieurs pays, spécialement en agriculture. Pourtant, ils continuent d'être utilisés dans d'autres pays pour la destruction des termites.

Les deux composés sont pratiquement insolubles dans l'eau et modérément à très solubles dans de nombreux solvants organiques. Leur tension de vapeur est faible.

On trouve souvent de la dieldrine dans des produits laitiers ou carnés, le poisson, les huiles et les graisses et certains légumes, notamment des légumes-racines. La limite maximale de résidus recommandée par les instances compétentes de la FAO/OMS lors des réunions conjointes sur les résidus de pesticides varie de 0,02 à 0,2 mg/kg de produit. Des mesures récentes ont montré que les teneurs effectives sont plus faibles, comme l'ont d'ailleurs confirmé les études sur la ration globale. Comme l'utilisation de ces deux composés fait maintenant l'objet de restrictions, on observe une diminution lente mais régulière de la teneur en résidus des différentes denrées alimentaires.

Les quantités ingérées par l'homme avec sa ration quotidienne se traduisent, malgré la faible concentration de ces produits dans les aliments, par la présence de dieldrine dans le tissu adipeux et dans certains autres tissus et organes. Des enquêtes à l'échelle mondiale montrent que les teneurs moyennes varient de 0,1 à 0,4 mg/kg de tissu adipeux. Depuis le début des années 70, cette concentration diminue lentement.

Comme le foetus est exposé par voie transplacentaire, ses tissus adipeux contiennent également de la dieldrine, mais à une concentration qui n'est que de 10 à 50% de la concentration chez la mère. Il semble exister un équilibre entre les concentrations foetales et les concentrations maternelles. La dieldrine est également excrétée dans le lait. Une exposition est possible par inhalation dans les habitations où l'on utilise ce produit pour la destruction des termites. Après traitement, on observe des concentrations atmosphériques allant de 0,01 à 7 $\mu g/m^3$, selon le mode d'épandage, la concentration utilisée, les modalités de l'aération et le moment où les échantillons sont prélevés. En pareilles circonstances, les aliments peuvent aussi être contaminés, par contact direct, ou par sorption à partir de l'air ambiant.

Le métabolisme s'effectue principalement dans le foie où l'aldrine se transforme rapidement en dieldrine. Le catabolisme de la dieldrine est plus lent que celui de ses métabolites hydrophiles qui sont excrétés dans la bile et dans les urines. La structure de ces métabolites a été établie. Chez toutes les espèces étudiées, notamment l'homme, on a montré que les quantités d'aldrine/dieldrine accumulées se stabilisent à un niveau qui est fonction de l'apport puisqu'il existe une relation linéaire entre les quantités accumulées et le logarithme de l'apport. Quand l'exposition prend fin, la concentration de la dieldrine dans les tissus de l'organisme diminue selon une loi exponentielle. La toxicité aiguë de l'aldrine et de la dieldrine est importante chez les mammifères par voie orale, tandis que la toxicité par voie cutanée est modérée. Aucune sensibilisation cutanée n'a été observée. Les effets constatés à la suite d'une exposition expérimentale aiguë ou de courte ou longue durée intéressent le système nerveux central. Le foie est également un organe cible. Chez les souris et les rats, on observe à ce niveau des altérations désignées sous le nom de "foie de rongeur sous insecticide organochloré".

Apparemment, l'aldrine et la dieldrine ne sont pas tératogènes à des doses inférieures à celles qui sont toxiques chez la femelle gravide et chez le foetus. On n'a pas fait état de toxicité pour la fonction de reproduction chez le mâle ou la femelle.

De nombreuses études de mutagénicité *in vitro* et *in vivo* ont montré que ni l'aldrine ni la dieldrine ne sont mutagènes.

Lors d'études à long terme, ces deux produits ont déterminé chez la souris des tumeurs hépatiques, bénignes ou malignes. En revanche, aucune augmentation de l'incidence des tumeurs hépatiques ou autres n'a été observée chez le rat ni le hamster.

Selon le CIRC (1987), il n'existe pas de preuves suffisantes d'un pouvoir cancérogène chez l'homme et les preuves de cancérogénicité chez l'animal d'expérience sont limitées. L'aldrine comme la dieldrine ont été classées dans le groupe 3, à savoir celui des produits chimiques dont il est impossible de préciser le pouvoir cancérogène chez l'homme.

Compte tenu des résultats obtenus lors des études de toxicité de courte ou de longue durée, la dose globale sans effet nocif décelable se situe chez le rat à 0,5 mg de dieldrine par kg de nourriture, soit l'équivalent de 0,025 mg/kg de poids corporel. Chez le chien, la dose sans effet nocif décelable est de 0,04 mg/kg de poids corporel. Lors des réunions conjointes FAO/OMS de 1966 et 1977 sur les résidus de pesticides, on a fixé la dose journalière admissible (DJA) à 0,1 µg/kg de poids corporel, en tenant compte de la non-cancérogénicité de ces deux substances pour l'homme.

L'aldrine et la dieldrine sont très toxiques pour l'homme. On connaît des cas d'intoxication accidentelle ou professionnelle, mais qui ont rarement fait des victimes. Les survivants à une intoxication aiguë ou subaiguë se sont entièrement rétablis. Les effets nocifs sont fonction de la concentration sanguine de la dieldrine, dont le dosage permet de diagnostiquer avec précision une exposition à l'aldrine/dieldrine. Pour taux sanguins inférieur à

105 µg/litre, aucun effet indésirable n'est à craindre. Cette concentration constitue la dose limite sans effet nocif décelable et correspond à un apport quotidien de 0,02 mg de dieldrine par kg de poids corporel.

L'exposition liée à l'environnement, principalement par la voie alimentaire, entraîne la présence de faibles concentrations de dieldrine dans l'organisme. D'après des études épidémiologiques et cliniques poussées, ces teneurs ne constituent pas une menace pour la santé humaine.

Aucun signe avant-coureur d'une altération de la fonction hépatique n'a été observé lors d'une enquête de 20 ans portant sur plus de 1000 ouvriers de l'industrie exposés à l'aldrine et à la dieldrine. Dans cette étude ainsi que dans une autre effectuée aux Etats-Unis d'Amérique, aucun risque particulier de cancer n'a été repéré chez les personnes profesionnellement exposées à l'aldrine et à la dieldrine (parfois à de fortes concentrations).

Dans l'ensemble, d'après les observations faites sur l'aldrine et la dieldrine, notamment dans le cadre des études sur l'homme, on peut estimer que, en pratique, ces produits chimiques ne contribuent que très peu, sinon pas du tout, à l'incidence des cancers humains.

La photodieldrine, produit qui résulte de la dégradation de la dieldrine sous l'action de la lumière, est analogue à la dieldrine pour ce qui est de sa toxicité sur une courte durée. Elle n'est ni tératogène ni cancérogène chez la souris et le rat. L'accumulation de photodieldrine dans les tissus adipeux d'animaux d'expérience s'est révélée inférieure à celle de la dieldrine.

2. Evaluation des effets sur l'environnement

La principale source de dieldrine (jusqu'à 97%) dans l'environnement est l'aldrine, un insecticide épandu au niveau du sol. L'aldrine et son produit de réaction, la dieldrine sont rapidement absorbé par les sols, spécialement ceux qui sont riches en matières organiques. De ce fait, la pénétration est limitée et il n'y a généralement aucune contamination des eaux souterraines. Les deux composés sont entraînés principalement du fait de l'érosion (sous l'action du vent) et du transport des sédiments (eaux superficielles de ruissellement), mais non par lessivage.

L'emploi d'aldrine et de dieldrine en agriculture donne lieu à la présence de résidus (principalement de dieldrine) dans le sol où ils peuvent persister plusieurs années; la demi-vie de la dieldrine est estimée à 4-7 ans. La persistance de ces composés est moindre dans les régions tropicales que dans les régions tempérées.

L'aldrine et la dieldrine passent, par volatilisation, des récoltes et du sol traités à l'atmosphère; elles peuvent aussi y pénétrer directement lors de l'épandage. La dieldrine retourne au sol ou dans les étendues d'eau par les précipitations ou par dépôt de particules sèches. Les composés se rencontrent donc soit en phase vapeur (à des concentrations très faibles, en général de l'ordre de

1-2 ng/m^3), soit adsorbés sur des particules de poussière, soit encore dans les eaux de pluie (à des concentrations de l'ordre de 10-20 ng/litre).

Plusieurs auteurs ont signalé la présence de dieldrine en milieu aquatique. Dans les eaux de surface, les concentrations sont le plus souvent très faibles, inférieures à 5 ng/litre. Mais des valeurs plus élevées s'observent dans les régions soumises à l'érosion ou dans celles où l'on utilise ce produit en agriculture. Dans ces régions, les sédiments des cours d'eau peuvent renfermer jusqu'à 1 mg de dieldrine par kilogramme. La forte capacité qu'ont les organismes aquatiques à concentrer la dieldrine à partir de teneurs très faibles peut aboutir à l'accumulation de doses toxiques. La concentration de ce produit tout au long de la chaîne alimentaire aquatique est moins importante qu'une absorption directe à partir de l'eau.

Comme la dieldrine est très répandue dans l'environnement et qu'elle y persiste, on observe des concentrations très variées chez les organismes non visés. Alors qu'auparavant les valeurs observées allaient de 0,001 mg à 100 mg/kg de tissu, elles sont aujourd'hui le plus souvent inférieures à 1 mg/kg de tissu.

Dans les écosystèmes terrestres, l'aldrine et la dieldrine s'accumulent chez divers organismes, principalement sous forme de dieldrine. Cette dernière est probablement responsable de la mort de mammifères dans la nature et de la raréfaction de certaines espèces, comme la loutre. Certains petits mammifères périssent sans doute après avoir mangé des céréales traitées mais il est probable que leurs populations se reconstituent par immigration à partir des zones voisines. Les oiseaux de proie qui mangent de petits mammifères et de petits oiseaux contaminés par la dieldrine absorbent et concentrent cet insecticide dans leurs tissus et leurs oeufs. Des oiseaux granivores ont été tués par la consommation de céréales traitées. Il est probable que la raréfaction des oiseaux de proie s'explique par la présence dans leurs tissus de résidus de dieldrine (entre autres organochlorés). Les effets de la dieldrine se manifestent avec un certain retard car les résidus s'accumulent dans les graisses pendant l'hiver d'où ils ne se libèrent qu'au printemps. Le fait de n'utiliser la dieldrine qu'à certaines époques de l'année n'a pas réduit la mortalité des oiseaux.

La large utilisation d'aldrine et de dieldrine, parallèlement à celle d'autres organochlorés, a exercé des effets très nocifs sur l'environnement mais grâce à des restrictions draconiennes, particulièrement en ce qui concerne les semences traitées, les populations d'oiseaux commencent à se reconstituer.

3. Conclusions

a) L'aldrine et la dieldrine ont donné lieu à des études poussées et variées sur le plan toxicologique, clinique et épidémiologique. La charge de l'organisme résulte principalement de l'ingestion de résidus présents dans la nourriture (les quantités ingérées semblant diminuer de façon générale et tomber en-dessous des DJA fixées) et, dans une

moindre mesure, de l'inhalation de ces produits. D'après l'étude des données, on a tout lieu de penser que la charge de l'organisme résultant du niveau actuel d'exposition ne menace en aucun cas la santé de la population dans son ensemble.

b) La dieldrine se rencontre presque partout dans le lait maternel. Mais, sa concentration dans le sang et dans le tissu adipeux des nourrissons n'augmente pas avec l'âge au cours des six premiers mois de leur vie et le taux sanguin n'est pas plus élevé que chez un enfant nourri au biberon. Dans ces conditions, l'allaitement au sein reste la méthode de choix pour nourir les nourissons malgré la présence de résidus de dieldrine.

c) Lors du traitement de locaux, notamment pour la destruction des termites, l'exposition des occupants ne semble pas présenter des risques pour leur santé, pour autant que le traitement s'effectue correctement.

d) Malgré leur toxicité élevée, l'aldrine et la dieldrine peuvent être manipulées sans danger dans la mesure où l'on observe toujours les précautions recommandées en vue de réduire au minimum l'exposition des opérateurs. Dans le cas contraire, il y a risque d'intoxication.

e) Pendant la période où l'on a massivement utilisé l'aldrine et la dieldrine, c'est-à-dire de 1950 au début des années 70, il est certain que cette pratique a eu des effets dommageables sur diverses espèces. Ces effets sont imputables en partie à la dieldrine à côté d'autres organochlorés. Depuis qu'on a limité de façon draconienne l'utilisation de ces produits, les espèces touchées se sont reconstituées.

RECOMMENDATIONS

1. Il faut effectuer des études de tératogénicité complémentaires sur le hamster, bien conçues, avec des doses réalistes de dieldrine.

2. Dans l'étude du mécanisme de la cancérogenèse, on s'efforcera d'expliquer pourquoi les réactions hépatiques sont si différentes chez la souris et chez les autres espèces.

3. On continuera d'utiliser la dieldrine pour l'étude des mécanismes neurotoxiques, à la fois sur le plan expérimental et sur le plan clinique.

4. Pour des raisons écologiques, toute reprise d'une utilisation massive d'aldrine et de dieldrine est exclue, et on n'utilisera ces produits que s'il n'existe pas de produit moins nocif d'efficacité équivalente.

5. Afin de préserver la santé et le bien-être des travailleurs et de la population en général, il convient de ne confier la manipulation et l'épandage de l'aldrine et de la dieldrine qu'à des opérateurs compétents et dûment formés, qui devront appliquer les mesures de sécurité qui s'imposent.

6. En raison du risque d'intoxication accidentelle par l'aldrine, spécialement chez les enfants, il faut en interdire l'utilisation sous forme de granulés contre les fourmis.

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