4. Correlation of Exposure and Effect

4.1 Effects on Humans

Aldrin is converted to dieldrin both in the environment and by metabolism in mammals. Exposure of mammals to either is reflected by storage of dieldrin in the tissues, including the blood and fat. Where comparative data are available, toxic effects resulting from exposure to aldrin are similar, both qualitatively and quantitatively, to those resulting from exposure to dieldrin. Accordingly the two chemicals are treated together in this section correlating exposure with effect.

Table 4.1.1 summarizes the clinical and case reports of the effects of aldrin/dieldrin on humans and the studies with volunteers, which were cited in Sections 3.1 and 3.2, respectively. There are many reports of human poisonings, including a number of deaths, resulting from accidents or suicides. However, little quantitative information on the doses of aldrin/dieldrin responsible for the poisonings is available, and in some cases even the route of exposure is not clearly established. Many of the poisonings involved exposure to dust or spray formulations, and in these cases exposure may have been by dermal, respiratory, or oral routes. A few accidental poisonings resulted from ingestion, and there was one reported case of suicide by injection.

The AMA Committee on Toxicology (1960) suggested that the median lethal dose by ingestion in humans is probably about 65 mg/kg and "untoward symptoms" will result from a single dose of 10 mg/kg

or more. For long-term exposure, the concentration of HEOD in the blood or fat provides an indirect measure of cumulative exposure (Hunter et al 1969, Jager 1970). Jager (1970) summarized evidence suggesting that a concentration of HEOD in the blood of 0.15-0.20 ppm is the approximate threshold for clinical intoxication and a blood concentration of 0.30 ppm is the approximate threshold for convulsive seizures. According to the pharmacokinetic data summarized in Section 1.5.4, these blood concentrations correspond to about 30-40 ppm of HEOD in fat and to a continuous intake of about 15-20 µg/kg/day. Although a number of factors complicate these pharmacokinetic relationships, including intermittent exposures and interactions with other chemicals, these figures are a rough guide to the tissue levels and exposure that present toxic hazards.

The data in Table 4.1.1 are consistent with these figures but provide little additional quantitative information. One individual who survived a convulsive intoxication had 40 ppm HEOD in his fat 2 weeks after exposure (Bell 1960). A 4-year-old child who survived a severe intoxication had 0.27 ppm HEOD in blood serum and 47 ppm in fat 3 days after exposure (Garrettson and Curley 1969). One individual survived a single dose of 44 mg/kg (Hayes 1963), and another survived a single dose of 25.6 mg/kg (Spiotta 1951). The only report found of accidental long-term exposure was one by Gupta (1975) about two children who died after 6-12 months of exposure to contaminated food. Their average daily intake is

likely to have been less than 1 mg. However, in a study with volunteers, daily intake of 211 µg/day for 2 years by middle-aged men led to no measurable adverse effects (Hunter et al 1969).

Table 4.1.2 summarizes the results of studies of workers occupationally exposed to aldrin/dieldrin. These studies are described more fully in Section 3.3. Incidents of clinical intoxication, including convulsive seizures and at least one death, were frequently recorded in public health programs involving the spraying of liquid formulations containing 0.5-2.5% dieldrin (Hayes 1957, Blázquez and Bianchini 1956, Zavon et al 1961). In contrast, poisonings associated with the use of dust formulations have been much less frequent and have involved observation of inadequate safety precautions (Nelson 1953, Bell 1960). Little quantitative information from these incidents is available, except for an estimate by Fletcher et al (1959) that spraymen came into dermal contact with as much as 1.8 mg/kg/day of dieldrin without showing clinical symptoms. This figure is about 100 times the estimated threshold intake for clinical intoxication derived from the data of Jager (1970).

A few studies listed in Table 4.1.2 included data on tissue levels of HEOD. Blood concentrations as high as 0.14, 0.25, or 0.31 ppm were reported in individual workers with no overt symptoms (Hayes and Curley 1968, Avar and Czégledi-Jankó 1970, Mick et al 1971). However, one worker with a blood concentration of HEOD as low as 0.05 ppm showed clinical symptoms of intoxication and characteristic EEG changes (Avar and Czégledi-Jankó 1970).

In most of the studies summarized in Tables 4.1.1 and 4.1.2, the symptoms of aldrin/dieldrin intoxication involved the central nervous system, including headache, muscular jerking, convulsive seizures, and EEG changes. Other symptoms occasionally reported included dermatitis, enlarged liver, hematuria, transient bronchial complications, and elevated levels of serum enzymes (Avar and Czeglédi-Jankó 1970, Blázquez and Bianchini 1956, Nelson 1953, Jager 1970).

In two cases, biochemical changes occurred in association with low blood levels of HEOD. Hunter et al (1972) reported measurements of D-glutaric acid excretion that indicated significantly elevated microsomal enzyme activity in workers whose mean blood level of HEOD was only 0.026 ppm. Takahashi et al (1976) found elevated serum levels of C-reactive proteins and a correlation between alpha $_2$ globulin and HEOD levels in workers whose mean blood level of HEOD was only 0.012 ppm. These results suggest functional biochemical changes at exposure levels one order of magnitude lower than the threshold for overt intoxication.

Few data were found which can be used to assess the possibility that aldrin/dieldrin has carcinogenic, teratogenic, or mutagenic effects on the human population, or affects human reproduction. In two studies, cancer victims were shown to have higher tissue levels of HEOD than persons without cancer (see Section 3.4). However, these findings do not prove a cause-and-effect relationship. No evidence of chromosome abnormalities was

found in one study of 22 exposed workers (Dean et al 1975). Workers exposed for up to 19 years had no excess incidence of cancer (Jager 1970, Versteeg and Jager 1973), but the number of workers who were "highly exposed" was small and even their exposure appears to have been comparatively modest (see Section 3.3). No studies of female workers or of the reproductive performance of male workers were found.

4.2 Effects on Experimental Animals

Table 4.2.1 summarizes the reported effects of oral exposure to aldrin/dieldrin on experimental animals. Teratogenic, carcinogenic, and mutagenic effects are listed in Tables 4.3.1, 4.3.2, and 4.3.3, respectively. No studies of the effects of dermal exposure of animals to aldrin/dieldrin were found. The only study of the effects of respiratory exposure of animals to aldrin/dieldrin is that of Medved' et al (1964), who reported that exposure of cats to aldrin at a concentration of 0.1 mg/m^3 for an unspecified period caused marked lowering of conditioned and unconditioned reflexes.

At high dietary levels (10-150 ppm), the most striking effects of aldrin/dieldrin were on the central nervous system, the liver, and the kidney. Dose-response relationships for these effects appear to have comparatively small slopes. For example, although rats developed kidney and liver lesions and occasional convulsions at a dietary level of 10 ppm, some rats have survived for up to 2 years at dietary levels of 50, 100, and even 150 ppm (Fitzhugh et al 1964).

At dietary levels between 1 and 10 ppm, the most pronounced effects of aldrin/dieldrin were on the liver and the reproductive system. At a dietary level of 1 ppm dieldrin, reported effects included liver enlargement, liver lesions, and induction of hepatic microsomal enzymes in rats and mice, enzyme induction in rhesus monkeys, and liver enlargement in dogs (Street et al 1969; Wright 1974; Jager 1970; Walker et al 1969, 1972; Treon et al 1955). Adverse effects on reproduction were reported in rats and mice exposed at 2.5 ppm (Cleveland 1966, Virgo and Bellward 1975) and in dogs exposed at about 3 ppm (Deichmann et al 1971, Kitselman 1953). The importance of these observations is that dietary exposure to dieldrin at 1 ppm led to blood levels of HEOD in the range 0.017-0.086 ppm in these species (Table 1.5.4). These blood concentrations are in the lower part of the range observed in occupationally exposed workers (Table 4.1.2).

Several experiments showed effects of aldrin/dieldrin at dietary levels even below 1 ppm. Raccoons exposed at 0.73 ppm in the diet suffered severe adverse effects on reproduction (Frederickson 1973). Rats exposed at 0.5 ppm had increased liver weights and liver lesions (Fitzhugh et al 1964). In another study, rats exposed at 0.31, 0.16, and 0.08 ppm developed brain and vascular lesions, and those exposed at 0.31 and 0.16 suffered impaired reproduction (Harr et al 1970a,b). Mice exposed at 0.1 ppm had an increased incidence of liver tumors (Walker et al 1972).

4.3 Teratogenic, Carcinogenic, and Mutagenic Effects

Table 4.3.1 summarizes the experiments on teratogenesis, which are cited in Section 3.4. Aldrin and dieldrin were teratogenic in mice and Syrian golden hamsters when administered at about one-half the median lethal doses (Ottolenghi et al 1974). However, dieldrin had no effects on mice (other than minor effects on ossification) and no effects in rats exposed at lower doses (Chernoff et al 1975). A third experiment with dieldrin was inconclusive (Boucard et al 1970).

Table 4.3.2 summarizes the experiments on carcinogenesis, which are cited in Section 3.5. Aldrin and dieldrin were carcinogenic in mice, having produced increased incidence of tumors in 20 experiments, usually in males and females independently. The principal site of action is the liver, although treatment with dieldrin was associated with an increase in tumors of the lung and other sites in several experiments for which age-adjusted statistical analysis of tumor incidence was reported. In most of the experiments, dietary levels were 2.5-10 ppm, but in the most extensive experiment dietary exposure to dieldrin at 1 and 0.1 ppm led to significant increases in incidence of liver and lung tumors.

The results of carcinogenicity tests with rats are more equivocal. If several inadequately reported experiments are discounted, aldrin/dieldrin has been tested for carcinogenicity in rats in eight experiments. In six of these experiments, there

was a statistically ($P<0.01$) or marginally significant ($P<0.05$) increase in tumor incidence at one or more of the lower doses (0.1-30 ppm). However, the sites at which these increases were observed were inconsistent (thyroid, lung, adrenal, pancreas, lymphatic system, mammary gland, and liver), and in five cases tumor incidence was reduced at higher doses (10-150 ppm). The only statistically significant effects at these higher doses were liver lesions of disputed biologic significance. If only the data from the higher dose levels were available, the results would be accepted as consistently negative. On the other hand, if only the data from the lower dose levels were available, aldrin and dieldrin would be accepted as strongly carcinogenic, at least on the basis of the NCI experiments. The reasons for the apparent reversal in dose-response relationships are not clear, although the results of one experiment suggested that the pathways of metabolism of dieldrin may be different at low and high dose levels (Mueller et al 1975a,b).

Table 4.3.3 summarizes the experiments on mutagenesis, which are cited in Section 3.6. Several studies indicated that aldrin and dieldrin can damage chromosomes, primarily by causing breaks and gaps, in mammalian cells, both in vitro and in vivo (Ahmed 1975, Majumdar 1976, Georgian 1975). Aldrin and dieldrin yielded consistently negative results in bacterial reversion bioassays, with or without metabolic activation. In other mutagenicity tests, including dominant lethal and host-mediated assays, aldrin and

dieldrin generally gave negative results, although the sensitivity of some of the systems used is questionable. Dieldrin caused unscheduled DNA repair in human fibroblast cultures (Ahmed et al 1977).

Most of the positive results of damage to chromosomes were obtained at high concentrations, close to cytotoxic levels both in vitro and in vivo. However, Majumdar et al (1976) reported statistically significant increases in chromosome aberrations at the lowest doses tested (1 mg/kg in mice exposed in vivo and 1 ppm in human embryonic lung cell cultures).

4.4 Summary

Aldrin is converted to dieldrin in the environment and in mammalian tissues. The toxic effects of the two chemicals are similar, qualitatively and quantitatively.

When mammals are exposed to either aldrin or dieldrin, dieldrin is circulated in their blood and is stored in their tissues, primarily in the fat. After ingestion, humans store dieldrin in their tissues at much higher concentrations than those measured in experimental animals exposed at comparable levels. Consequently, target tissues in humans are exposed to dieldrin at concentrations proportionately higher than in experimental animals that ingest comparable quantities.

Aldrin/dieldrin is neurotoxic, and many cases of poisoning, including a few deaths, caused by accidental or imprudent overexposure have been reported. In a study conducted in a manufacturing plant,

concentrations of dieldrin in the blood were reported to be indicative of toxic hazard. A concentration of 0.15-0.20 ppm in the blood was considered the threshold for EEG changes and other CNS effects, whereas 0.30 ppm was considered the threshold for convulsive seizures. Corresponding average daily intakes were about 15-22 μg/kg and 30 μg/kg, respectively. Only minor biochemical changes (induction of hepatic microsomal enzymes and elevated levels of C-reactive protein in serum) were reported in workers with lower blood concentrations of dieldrin (0.012-0.026 ppm). Although a few workers who were exposed to aldrin/dieldrin for up to 19 years have been studied, the available reports are inadequate for determining whether aldrin/dieldrin may have carcinogenic, mutagenic, or teratogenic effects in humans, or may affect reproduction.

In experimental animals, the most conspicuous effects of aldrin/dieldrin are on the liver and on the CNS. A concentration of 1 ppm in the diet has been reported to be the approximate threshold for induction of hepatic microsomal enzymes in rats and mice. Rats exposed at a dietary concentration of 0.08-0.31 ppm have had brain and vascular lesions and impaired reproduction.

Aldrin/dieldrin is carcinogenic in mice, increasing the incidence of tumors primarily in the liver but also in the lung and perhaps other sites. In one experiment, carcinogenic effects occurred even at 0.1 ppm, the lowest dietary concentration tested. In rats, aldrin/dieldrin appeared to increase the incidence of

tumors at a variety of sites when administered at low dietary concentrations (0.1-30 ppm) but consistently failed to do so when administered at higher concentrations (10-150 ppm). The reasons for this apparent reversal in dose-response relationships are not clear.

Aldrin/dieldrin administered at about one-half the median lethal dose was teratogenic in mice and hamsters, but lower doses had no teratogenic effects in mice and rats. Aldrin/dieldrin has yielded consistently negative results in bacterial mutagenesis bioassays. However, aldrin/dieldrin has repeatedly caused chromosome damage in mammalian cells, even at low exposure levels (1 mg/kg in mice exposed in vivo and 1 ppm in human embryonic lung cultures). Dieldrin caused unscheduled DNA repair in human fibroblast cultures.

TABLE 4.1.1

SUMMARY OF EFFECTS OF ALDRIN/DIELDRIN EXPOSURE ON HUMANS (CLINICAL AND CASE REPORTS)

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin (aerosol)	84-214 hr respiratory	176 mg/m^3 "per day"	-	No detectable effect	Hodge et al 1967
Dieldrin	Unknown dermal and perhaps oral	4% powder	-	Convulsions, fever, cyanosis, death in 20 hr (9-mo-old girl)	Committee on Toxicology 1960
Aldrin (dust)	2 working days dermal, respiratory (packaging)	-	40 ppm in fat after 2 wk	Convulsions, EEG changes	Bell 1960
Dieldrin	18 hr dermal (dusting sheep)	3% solution	5-7 ppm in fat after 1 mo	Twitching of arms and legs	"
"	6 wk	0.4% solution	1 ppm in fat after 8 mo	"Symptoms of dieldrin poisoning"	"
Aldrin (field residues)	1-2 mo dermal	-	-	Myoclonic jerks, paresthesia, muscle weakness, tachycardia, motor polyneuropathy	Jenkins and Toole 1964

TABLE 4.1.1 (continued)

SUMMARY OF EFFECTS OF ALDRIN/DIELDRIN EXPOSURE ON HUMANS (CLINICAL AND CASE REPORTS)

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin (impregnated wool)	Unknown dermal	-	-	Nonspecific dermatitis	Ross 1964
"	"	0.1-0.5% in wool	-	No sensitization of skin	Hodge et al 1967
Dieldrin	Single dose oral	5% solution	0.27 ppm in serum, 47 ppm in fat (3 d after ingestion)	Convulsions, death in 2-yr-old girl; convulsions, cyanosis, EEG changes, elevated serum alkaline phosphatase after 6 mo in 4-yr-old boy	Garrettson and Curley 1969
Aldrin	Single dose oral (in food)	20% powder	-	Nausea, vomiting, hyperirritability, convulsions, death in 4/9 cases	Preda et at 1963
Aldrin or dieldrin	Single dose oral	65 mg/kg	-	Estimated median lethal dose	Committee on Toxicology 1960

TABLE 4.1.1 (continued)

SUMMARY OF EFFECTS OF ALDRIN/DIELDRIN EXPOSURE ON HUMANS (CLINICAL AND CASE REPORTS)

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin	Single dose oral	44 mg/kg	-	Convulsions	Hayes 1963
Aldrin	Single dose oral (attempted suicide)	-	0.279 ppm in plasma	Survived	Hayes and Curley 1968
Aldrin (liquid mixture)	Single dose oral	25.6 mg/kg	-	Convulsions within 20 min, EEG changes, generalized cerebral dysrhythmia, hematuria, albuminuria; treatment with barbiturates, EEG normal within 5 mo	Spiotta 1951
Dieldrin	"	-	-	Convulsions after 30 min, hematuria, amnesia; no EEG abnormalities, normal kidney and liver function	Jacobs 1967

TABLE 4.1.1 (continued)

SUMMARY OF EFFECTS OF ALDRIN/DIELDRIN EXPOSURE ON HUMANS (CLINICAL AND CASE REPORTS)

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin	6-12 mo oral	About 0.5% dust (mixture of aldrin and HCH) in flour	-	Myoclonic jerks, convulsions, EEG changes, death in 2/12	Gupta 1975
Dieldrin	Single dose oral	10 mg/kg	-	"Untoward symptoms"	Committee on Toxicology 1960
Dieldrin (99% HEOD in gelatin capsules)	2 year oral	50 or 211 ug daily	0.005-0.025 ppm in blood, 0.4-4.9 ppm in fat	None	Hunter et al 1967, 1969
Dieldrin in hydrocarbon solvent	Single dose iv injection (suicide)	5 ml of solution (unspecified concentration)	50 ppm in blood	Convulsions, frothing at the mouth, death within 3 min	Schwar 1965

*Aldrin is converted to dieldrin in the body, and the presence of dieldrin in tissues reflects exposure to either.

TABLE 4.1.2

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE TO ALDRIN/DIELDRIN

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin	1-5 yr unknown	-	0.024-0.4 ppm in blood	Muscular jerking, myoclonia, convulsions, psychic disturbances, EEG changes; clinical symptoms and EEG changes associated with blood levels of HEOD as low as 0.05 ppm; no symptoms in one worker with HEOD blood level of 0.25 ppm	Avar and Czegledi-Janko 1970
Dieldrin	Unknown dermal, respiratory	2.5% spray applied to surfaces at 0.5 g/m^2	-	Muscle jerking, convulsions, one death	Hayes 1957
"	1-18 mo dermal, respiratory	1.25-2.5% emulsion applied to surfaces at 1 g/m^2	-	Vertigo, nausea, myoclonia, convulsions, tremors, dermatitis, enlarged liver	Blazquez and Bianchini 1956

TABLE 4.1.2 (continued)

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE TO ALDRIN/DIELDRIN

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin	14-154 d respiratory, dermal	1.25 or 2.5% spary	-	Giddiness, headache, muscle twitching, convulsions, loss of consciousness	Patel and Rao 1958
Aldrin ("empty drums")	-	-	-	Nausea, vomiting, malaise, headache, fainting, convulsions, hematuria, EEG changes	Nelson 1953
Aldrin and dieldrin (technical product and various formulations; also exposure to Telodrin and Endrin in some cases)	1-13 yr respiratory, dermal	-	0.022-0.078 ppm in blood in most workers; occasionally up to 0.23 ppm in blood in highly exposed workers	No significant effects in most workers, adverse effects associated with blood levels of dieldrin 0.05-0.20 ppm: convulsions in 15; headache, dizziness, drowsiness, hyperirritability, malaise in 8 others; EEG abnormalities; elevated serum alkaline phosphatase and SGOT levels, increased urinary excretion of D-glutaric acid	Hoogendam et al 1962, 1965; Jager 1970; Hunter et al 1972

TABLE 4.1.2 (continued)

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE TO ALDRIN/DIELDRIN

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin or dieldrin	Long-term respiratory, dermal	30 µg/kg/d (estimated)	0.30 ppm in blood	Threshold for convulsive seizures	Jager 1970
"	"	15-20 µg/kg/d (estimated)	0.15-0.20 ppm in blood	Threshold for EEG changes and other CNS effects	Brown et al 1964, Jager 1970
Aldrin	1-2 yr respiratory, dermal	25% dust	-	Contact dermatitis, furunculi, "transient bronchial complications"	Nelson 1953
Aldrin and dieldrin (manufacture)	-	-	-	No significant increase in chromosome abnormalities	Dean et al 1974
Dieldrin	180 d dermal (estimated as 1.8 mg/kg/d)	0.55-1.1% emulsions, sprayed on surfaces at 0.5-1.0 g/m^2	-	No clinical symptoms	Fletcher et al 1959

TABLE 4.1.2 (continued)

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE TO ALDRIN/DIELDRIN

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin technical (formulating plant)	5 wk dermal, respiratory	-	0.100-0.312 ppm in plasma	No complaints or health problems reported to the company physician	Mick et al 1971
Aldrin and dieldrin (manufacture)	1-19 yr dermal, respiratory	-	0.0012-0.137 ppm (mean 0.025 ppm) in plasma; 0.60-32 ppm (mean 6.1 ppm) in fat; 0.0014-0.066 ppm (mean 0.028 ppm) in urine	No meaningful association of tissue levels with history of sick leave	Hayes and Curley 1968
Dieldrin (also exposure to pentachlorophenol)	Long-term unknown	-	Mean 0.012 ppm in blood	Elevated levels of C-reactive protein in serum; significant correlation between alpha-2-globulin and dieldrin levels in serum	Takahashi et al 1976

TABLE 4.1.2 (continued)

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE TO ALDRIN/DIELDRIN

Substance	Duration and Route of Exposure	Concentration or Dose	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin (spray)	1-8 yr dermal, respiratory	-	0.001-0.009 ppm in blood	No symptoms	Morgan and Hickin 1966

*Aldrin is converted to dieldrin in the body, and the presence of dieldrin in tissues reflects exposure to either.

TABLE 4.2.1

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin or dieldrin (99% pure)	Rat	50, 100, or 150 ppm 2 yr	-	Dose-related reduction in survival, increased liver weight, liver lesions, nephritis, renal necrosis, distended and hemorrhagic urinary bladders	Fitzhugh et al 1964, Reuber 1974
Dieldrin	"	75 ppm 396-440 d	-	Increased liver weight, liver cell changes, nephritis	Ferrigan et al 1965
Dieldrin (technical)	"	50 or 100 ppm 8 wk	-	Increase in smooth endoplasmic reticulum, atypical mitochondria	Kimbrough et al 1971
Dieldrin	"	40 ppm 2 yr	-	Reduced survival, convulsions, reproductive failure, brain and vascular lesions	Harr et al 1970a,b
"	"	25 or 50 ppm 60 d	-	Reduced muscular performance (as measured by speed of pulling a weight along a runway)	Khairy 1960

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin or dieldrin	Rat	25 ppm 2 yr	-	Increased liver weight, liver lesions	Treon et al 1955
"	"	12.5 or 25 ppm 3 generations	-	Inconsistent effects on pregnancy rates, severe reduction in survival of offspring	Treon and Cleveland 1955, Cleveland 1966
Aldrin	"	3-4.5 mg/kg/day 13 mo	-	Increased chronaxy	London and Pallade 1964
Dieldrin	"	20 ppm 2 yr	-	Reduced survival, convulsions, reproductive failure, brain and vascular lesions	Harr et al 1970a,b
Aldrin or dieldrin	"	12.5 ppm 2 yr	-	Increased liver weight, liver lesions	Treon et al 1955
Dieldrin (99% pure)	"	10 ppm 2 yr	0.03-0.11 ppm in blood, 8-50 ppm in fat	Increased liver weight in females, lesions, irritability, convulsions	Walker et al 1969

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin or dieldrin (99% pure)	Rat	10 ppm 2 yr	-	Increased liver weight, liver lesions, nephritis	Fitzhugh et al 1964
Dieldrin	"	"	-	Neural spasms, severely impaired reproduction, brain and vascular lesions	Harr et al 1970a,b
"	"	6.2 ppm 5 d	-	Increased level of serum luteinizing hormone, decreased prostate weight	Blend and Lehnert 1973
"	"	5 ppm 2 yr	-	Severely impaired reproduction, brain and vascular lesions	Harr et al 1970a,b
Aldrin or dieldrin	"	2.5 ppm 2 yr	-	Increased liver weight, liver lesions	Treon et al 1955
"	"	2.5 ppm 3 generations	-	Slightly decreased pregnancy rate, slightly to moderately decreased survival of offspring	Treon and Cleveland 1955, Cleveland 1966

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin or dieldrin (99% pure)	Rat	2 ppm 2 yr	-	Increased liver weight, liver lesions	Fitzhugh et al 1964, Reuber 1974
Dieldrin (99% pure)	"	1 ppm 2 yr	0.009-0.069 ppm in blood, 1.3-16 ppm in fat	Increased liver weight in females	Walker et al 1969
Dieldrin	"	1 ppm 2 wk	-	"Threshold" level for induction of hepatic microsomal enzymes	Street et al 1969
"	"	0.7 ppm 5 d	-	Decreased prostate weight	Blend and Lehnert 1973
"	"	0.31, 0.63, 1.25, or 2.5 ppm 2 yr	4-50 ppm in fat	Impaired reproduction; brain and vascular lesions	Harr et al 1970a,b

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN IN ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissues Levels of Dieldrin*	Reported Effects	Reference
Dieldrin (99% pure)	Rat	0.1 ppm 2 yr	0.003-0.013 ppm in blood, 0.17-3.1 ppm in fat	No significant effects	Walker et al 1969
Dieldrin	"	0.08 or 0.16 ppm 2 yr	1-2 ppm in fat	Impaired reproduction in second breeding, brain and vascular lesions	Harr et al 1970a,b
Aldrin or dieldrin (99% pure)	"	0.5 ppm 2 yr	-	Increased liver weight, liver lesions	Fitzhugh et al 1974, Reuber 1974
Dieldrin (99% pure)	"	1 ppm	-	Increased hepatic microsomal enzyme activity	Wright 1974
Aldrin	Mouse	2 or 4 mg/kg/d 7 d late in pregnancy	-	Significant reduction in body weight and significant increase in electroshock seizure threshold in offspring tested at 38 d	Al-Hachim 1971

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin	Mouse	1.25, 2.5, or 5 mg/kg/d 5 d	-	Increased hepatic microsomal protein and cytochrome P-450, alteration in uptake and metabolism of testosterone	Schein and Thomas 1975
Dieldrin (technical)	"	10 or 15 ppm 76 d	-	Reduced fertility and litter size, 100% mortality of offspring	Virgo and Bellward 1975
Aldrin or dieldrin	"	10 or 25 ppm 6 generations	-	Reductions in fertility, lactation indices, and viability of pups	Deichmann and MacDonald 1971, Keplinger et al 1966, 1968
Dieldrin (99% pure)	"	10 ppm 2 yr	0.42-0.52 in blood, 11-12 ppm in fat	Reduced survival, enlarged livers, liver lesions	Walker et al 1972, Thorpe and Walker 1973

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin (99% pure)	Mouse	5 ppm 2 yr	-	Reduced survival, enlarged livers, liver lesions	Walker et al 1972
Dieldrin (technical)	"	5 ppm 90 d	-	Reduced litter size	Good and Ware 1969
Aldrin or dieldrin	"	1 mg/kg single dose	-	Reduced toxic reaction to parathion and paraoxon 1-12 days later	Triolo and Coon 1966a,b
"	"	3 ppm 6 generations	-	No significant effect on reproduction	Deichmann and MacDonald 1971
Dieldrin (technical)	"	2.5 or 5 ppm 76 d	-	Increased mortality of offspring	Virgo and Bellward 1975
Dieldrin (99% pure)	"	2.5 ppm 2 yr	-	Reduced survival in females, enlarged livers, liver lesions	Walker et al 1972
"	"	1.25 ppm 2 yr	-	Enlarged livers, liver lesions	"

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin (99% pure)	Mouse	1.0 ppm 2 yr	0.044 ppm in blood, 1.27-1.55 ppm in fat	Enlarged livers, liver lesions	Walker et al 1972
Dieldrin	"	1 ppm	-	Increased hepatic microsomal enzyme activity	Wright 1974
Dieldrin (99% pure)	"	0.1 ppm 2 yr	0.0026-0.0039 ppm in blood, 1.27-1.55 ppm in fat	Enlarged livers, liver lesions	Walker et al 1972
Aldrin or dieldrin	Dog	2-10 mg/kg/d 2-5 wk	-	Fatty changes in liver and renal tubules; death in 9/10	Fitzhugh et al 1964
Dieldrin (99% pure)	"	2 mg/kg/d 1 wk	-	Proliferation of smooth endoplasmic reticulum, increased hepatic microsomal enzyme activity	Wright 1974

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin or dieldrin	Dog	1 mg/kg/d 12-49 wk	-	Fatty change in liver and renal tubules; reduced number of erythrocytes in bone marrow; death in 4/4	Fitzhugh et al 1964
Aldrin or dieldrin (recrystallized)	"	0.6 or 2.0 mg/kg/d 1 yr	-	36/37 pups stillborn or died within 3 d of birth	Kitselman 1953
Aldrin	"	0.5 mg/kg/d up to 2 yr	-	Convulsions; death	Fitzhugh et al 1964
Dieldrin	"	"	-	Convulsions; survival for 2 yr in 3 of 4	"
"	"	0.2 mg/kg/d 6 yr	-	Increased serum alkaline phosphatase activity, increased bromosulphthalein clearance	Jager 1970

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Aldrin or dieldrin	Dog	0.2 mg/kg/d 2 yr	-	No clinical effects	Fitzhugh et al 1964
Aldrin or dieldrin (recrystal-lized)	"	0.2 mg/kg/d 1 yr	-	10/16 pups stillborn or died within 3 d of birth	Kitselman 1953
Aldrin (technical)	"	0.15 or 0.3 mg/kg/d 14 mo	0.012-0.14 ppm in blood, 11-150 ppm in fat	Reduced fertility, mammary development, and lactation; stillbirths and increased pup mortality	Deichmann et al 1971
Aldrin	"	3 ppm 15 mo	-	Increased liver weight; liver cell changes	Treon et al 1955
Dieldrin	"	"	-	Increased liver weight	"
Aldrin	"	1 ppm 15 mo	-	No reported effects	"

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin	Dog	1 ppm 15 mo	-	Increased liver weight	Treon et al 1955
Dieldrin (recrystallized)	"	0.05 mg/kg/d 2 yr	0.03-0.087 ppm in blood	Increased serum alkaline phosphatase activity, increased liver weight in females	Walker et al 1969
"	"	0.005 mg/kg/d 2 yr	0.005-0.024 ppm in blood	No reported effects	"
Dieldrin	Rhesus monkey	5 ppm 6 yr	-	Increased hepatic microsomal enzyme activity; death in 2/5	Jager 1970, Wright 1974
"	"	1.75 ppm 6 yr	0.075 ppm in blood, 19 ppm in fat	Increased hepatic microsomal enzyme activity	"
"	"	1 ppm 6 yr	0.033 ppm in blood, 8.3 ppm in fat	Increased hepatic microsomal enzyme activity, marginal increase in microsomal protein	"

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF ORAL ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin	Rhesus monkey	0.01, 0.10, or 0.50 ppm 6 yr	0.004-0.022 ppm in blood, 0.39-5.0 ppm in fat	No reported effects	Jager 1970, Wright 1974
Dieldrin (technical)	Squirrel monkey	0.1 mg/kg/d 55-109 d	-	Impaired learning of a discrimination reversal task	Smith et al 1976
"	"	0.01 mg/kg/d 55-109 d	-	No measurable effect on learning	"
Dieldrin	Sheep	10 mg/kg/d 30 d	-	Impaired learning	Van Gelder et al 1970
"	"	25 ppm 40 mo	-	Death of all lambs shortly after birth	Harris and Greenwood 1963
"	"	1 or 5 ppm 40 mo	-	No measurable effects on reproduction	"

TABLE 4.2.1 (continued)

SUMMARY OF EFFECTS OF DIETARY ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Dietary Concentration or Oral Dose and Duration	Tissue Levels of Dieldrin*	Reported Effects	Reference
Dieldrin	White-tailed deer	25 ppm 3 yr	-	Reported growth, increased liver weight, reduced pituitary weight, increased thyroid size, reduced size of fawns at birth, increased postpartum mortality	Murphy and Korschgen 1970
"	"	5 ppm 3 yr	-	Increased postpartum mortality in offspring	"
"	Raccoon	2.2 ppm 2 yr	-	Death of most females under the stress of breeding	Frederickson 1973
"	"	0.73 ppm 2 yr	-	Reduced pregnancy rate and litter size, fetal deaths and resorption of embryos; adverse effects on sperm production and fertility in males	"
"	Cottontail rabbit	0.07-0.25 ppm 1 yr	0.11-0.66 ppm in brain	No measurable effect on reproduction	Malecki et al 1974

*Aldrin is converted to dieldrin in the body, and the presence of dieldrin in tissues reflects exposure to either.

TABLE 4.3.1

TERATOGENIC EFFECTS OF ALDRIN/DIELDRIN ADMINISTERED TO ANIMALS BY ORAL INTUBATION

Substance	Species	Dose and Time of Administration*	Reported Effects	Reference
Aldrin (recrystallized)	Rat	25 mg/kg d 9	Anomalies in 33%: open eye, webbed foot, cleft palate	Ottolenghi et al 1974
Dieldrin (recrystallized)	"	15 mg/kg d 9	Anomalies in 17%: webbed foot, cleft palate	"
Dieldrin (technical)	"	6 mg/kg/d d 7-16	Maternal deaths and weight loss; no anomalies in offspring	Chernoff et al 1975
"	"	1.5 or 3.0 mg/kg/d d 7-16	None	"
Dieldrin	"	3.4 mg/kg/d d 6, 6-14, or 1-14	Nonsignificant increase in anomalies	Boucard et al 1970
"	"	2.5 µg/kg/d d 6, 6-14, or 1-14	"	"
Photo-dieldrin	"	0.15, 0.3, or 0.6 mg/kg/d d 7-16	15% maternal mortality at 0.6 mg/kg/d, no increase in anomalies in offspring	Chernoff et al 1975

TABLE 4.3.1 (continued)

TERATOGENIC EFFECTS OF ALDRIN/DIELDRIN ADMINISTERED TO ANIMALS BY ORAL INTUBATION

Substance	Species	Dose and Time of Administration*	Reported Effects	Reference
Dieldrin (technical)	Mouse	3.0 or 6.0 mg/kg/d d 7-16	Increased maternal liver weight; increase in supernumerary ribs and decrease in caudal ossification centers in offspring	Chernoff et al 1975
"	"	1.5 mg/kg/d d 7-16	No significant effects	"
Dieldrin	"	3.4 mg/kg/d d 6, 6-14, or 1-14	Nonsignificant increase in anomalies	Boucard et al 1970
"	"	2.5 µg/kg/d d 6, 6-14, or 1-14	"	"
Photodieldrin	"	0.15, 0.30, or 0.60 mg/kg/d d 7-16	No significant effects	Chernoff et al 1975
Aldrin (recrystallized)	Hamster	50 mg/kg d 7, 8, or 9	Anomalies in 11-22%: open eye, webbed foot, cleft palate, cleft lip, others	Ottolenghi et al 1974

TABLE 4.3.1 (continued)

TERATOGENIC EFFECTS OF ALDRIN/DIELDRIN ADMINISTERED TO ANIMALS BY ORAL INTUBATION

Substance	Species	Dose and Time of Administration*	Reported Effects	Reference
Dieldrin (recrystal-lized)	Hamster	30 mg/kg d 7, 8, or 9	Anomalies in 4-33%: open eye, cleft lip, cleft palate, exencephaly, platycrania, micrognathia, ectrodactyly	Ottolenghi et al 1974

*Day of pregnancy

TABLE 4.3.2

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Concentration and Duration	Reported Effects	Reference
Aldrin (technical)	Rat	30 or 60 ppm 74 wk followed by 37-38 wk observation for females, 80 wk followed by 32-33 wk observation for males	At 60 ppm, no significant increases in tumor incidence; at 30 ppm, significant increases (compared to pooled controls) in three types of tumor: thyroid follicular cell tumors and adrenal cortical adenomas in both sexes, pancreatic islet tumors in males	NCI 1978a
Dieldrin (technical)	"	"	Significant dose-related increase in thyroid follicular cell tumors in females; at 30 ppm, significant increase (compared to pooled controls) in incidence of adrenal cortical adenomas and carcinomas in females	"
Aldrin	"	5 ppm 25 mo	No significant increase in tumor incidence	Deichmann et al 1967
Dieldrin (recrystallized)	"	2, 10, or 50 ppm 104-105 wk	"	NCI 1978b

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Concentration and Duration	Reported Effects	Reference
Dieldrin	Rat	1 ppm	Significant increase in lung and other tumors in males; nonsignificant incidence of liver lesions of disputed significance	Reuber 1974, Epstein 1975
Aldrin (recrystallized)	"	0.5, 2, 10, 50, 100, or 150 ppm 2 yr	Reduced survival at 50, 100, and 150 ppm; significant increase in lymphatic and mammary tumors at 0.5, 2, and 10 ppm (25/60 in pooled groups vs 2/17 in controls) but not at higher doses, significant increase in liver lesions of disputed significance (probably neoplastic or preneoplastic)	Fitzhugh et al 1964, Reuber 1974, Epstein 1975, Thorpe 1974
Dieldrin (recrystallized)	"	"	Reduced survival at 50, 100, and 150 ppm; marginally significant increase in lymphatic and mammary tumors at 0.5, 2, and 10 ppm (16/63 in pooled groups vs 2/17 in controls) but not at higher doses; significant increase in liver lesions of disputed significance (probably neoplastic or preneoplastic)	"

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Concentration and Duration	Reported Effects	Reference
Dieldrin (recrystallized)	Rat	0.1, 1.0, or 10 ppm 2 yr	Marginally significant increase in thyroid and mammary tumors in females exposed at 1.0 and 0.1 ppm (15/23 and 14/23 vs 19/43 in controls) but not at 10 ppm; liver lesions at 10 ppm	Walker et al 1969, Gross 1974, Stevenson et al 1975
Photodieldrin (recrystallized)	"	5 or 10 ppm (males); 3.4 or 7.5 ppm time-weighted average (females) 80 wk followed by 30 wk observation	No significant increases in tumor incidence	NCI 1977
Dieldrin (recrystallized)	Mouse	10 ppm 2 yr (series of nine experiments)	Increased incidence of liver tumors in males and females in nine independent experiments; lung metastases from 0-17% of tumors; some tumors successfully transplanted; significant increase in age-adjusted incidence of lung tumors in three experiments; increase in lymphoid and other tumors in two experiments	Walker et al 1972, Thorpe and Walker 1973, Hunt 1974, Epstein 1975, Gross 1974

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Concentration and Duration	Reported Effects	Reference
Dieldrin	Mouse	10 ppm 2 yr	Mean survival time 51 wk vs 59.8 wk in controls, 24% incidence of liver tumors vs 7% in controls	Davis and Fitzhugh 1962
Dieldrin (recrystallized)	"	10 ppm 2, 4, 8, 16, 32, or 64 wk sacrifice at 104 wk	Increased incidence of liver tumors, which was statistically significant in 64-wk group; malignant tumors in 64-, 8-, and 4-wk groups	Walker et al 1972
Aldrin	"	10 ppm 2 yr	Mean survival time 51.6 wk vs 59.8 wk in controls, 23% incidence of liver tumors vs 7% in controls	Davis and Fitzhugh 1962
Dieldrin	"	10 ppm 2 yr	Reduced survival, 39% vs 64% in controls at 2 yr; increased incidence of liver tumors, 87% in males and 87% in females vs 30% in male and 4% in female controls; lung metastases in 5% of exposed females; 8/9 tumors transplanted successfully	Davis 1965, Reuber 1974, Epstein 1975

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Concentration and Duration	Reported Effects	Reference
Aldrin	Mouse	10 ppm 2 yr	Reduced survival, 31% at 2 yr vs 64% in controls, increased incidence of liver tumors, 82% in males and 85% in females vs 30% in male and 4% in female controls; lung metastases in 4% of exposed males; 9/10 tumors transplanted successfully	Davis 1965, Reuber 1974, Epstein 1975
Dieldrin (recrystallized)	"	5 ppm (with 50 ppm DDT) 2 yr	Incidence of liver tumors 58% in males and 94% in females vs 0 in controls, 6% in males exposed to DDT only, and 16% in females exposed to DDT only	Walker et al 1972, Reuber 1974, Epstein 1975
Aldrin (technical)	"	4 or 8 ppm (males) 3 or 6 ppm (females) time-weighted average 80 wk followed by 10-13 week observation	Hepatocellular carcinomas in 56% of males at 8 ppm, 33% of males at 4 ppm, and 18% of pooled control males; non-significant increase in females	NCI 1978a

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Concentration and Duration	Reported Effects	Reference
Dieldrin	Mouse	3 or 10 ppm lifetime	Marked increase in liver lesions, including some diagnosed as hepatocellular carcinomas	MacDonald et al 1972, 1973; Reuber 1974; Epstein 1975
Dieldrin (technical)	"	2.5 or 5 ppm time-weighted average 80 wk followed by 10-13 wk observation	Hepatocellular carcinomas in 36% of males at 5 ppm, 24% of males at 2.5 ppm, and 18% of pooled control males; non-significant increase in females	NCI 1978a
Dieldrin (recrystallized)	"	1.25, 2.5, or 5 ppm 2 yr	Increased incidence of liver tumors in both sexes in all exposed groups; lung metastases from 3 tumors in exposed mice; significant dose-related increase in age-adjusted incidence of lung tumors	Walker et al 1972, Hunt 1974
"	"	0.1 or 1 ppm 2 yr	Increased incidence of liver tumors in both sexes at both dose levels independently; lung metastases from 3 tumors in exposed mice; increased incidence of pulmonary adenomas and carcinomas in males and females	Walker et al 1973, Gross 1974, Epstein 1975

TABLE 4.3.2 (continued)

CARCINOGENIC EFFECTS OF DIETARY ADMINISTRATION OF ALDRIN/DIELDRIN TO ANIMALS

Substance	Species	Concentration and Duration	Reported Effects	Reference
Photo-dieldrin	Mouse	0.32 or 0.64 ppm 80 wk followed by 10-13 wk observation	No statistically significant increases in tumor incidence	NCI 1977

TABLE 4.3.3

SUMMARY OF MUTAGENIC EFFECTS OF ALDRIN/DIELDRIN

Substance	Species or System	Strain	Dose	Reported Effects	Reference
Aldrin or dieldrin (technical)	Salmonella typhimurium	TA 1535 TA 1536 TA 1537 TA 1538	20 µg in DMSO	No increase in number of revertants without microsomal activation	Shirasu et al 1976
Dieldrin	"	"	1,000 µg	No increase in number of revertants with and without rat liver microsomal activation	Marshall et al 1976
Aldrin or dieldrin	"	-	-	No increase in number of revertants with mouse liver microsomal activation	Van Dijck and Van de Voorde 1976
Dieldrin	"	TA 1535 TA 1536 TA 98 TA 100	10 mg	No increase in number of revertants with and without rat liver microsomal activation	McCann et al 1975
"	"	5 unspecified strains	-	No increase in number of revertants with and without microsomal activation (no details given in abstract)	Bidwell et al 1975

TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF ALDRIN/DIELDRIN

Substance	Species or System	Strain	Dose	Reported Effects	Reference
Aldrin or dieldrin (technical)	Bacillus subtilis	H17 Rec^+ M45 Rec^-	20 µg in DMSO	Negative results in recombination assays	Shirasu et al 1976
Aldrin or dieldrin	Escherichia coli	B/r try WP2 WP2 try hcr	20 µg in DMSO	No increase in number of mutants without microsomal activation	"
Aldrin	Saccharomyces cerevisiae	-	5 and 50 µg/ml	Significant mutagenic activity	Guerzoni et al 1976
Dieldrin	Chinese hamster cells	V79	0.1, 0.3, 1.0, or 3.0 mM	Negative results in vitro in alkaline elution assay for DNA damage, with rat liver microsomal activation	Swenberg et al 1976
"	"	"	-	Significant increase in ouabain resistant mutants	Ahmed 1975
Dieldrin (recrystallized)	Chinese hamster	-	30 or 60 mg/kg single dose in DMSO	Nonsignificant decrease in polyploidy in bone marrow cells, no increase in chromatid gaps	Dean et al 1975

TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF ALDRIN/DIELDRIN

Substance	Species or System	Strain	Dose	Reported Effects	Reference
Aldrin	Human lymphocytes	-	19 or 38 µg/ml	Increase in chromosome aberrations: gaps, breaks, deletions, fragments, and interchanges	Georgian 1975
Aldrin or dieldrin	Human fibroblasts	VA-4	1, 10, 100, or 1,000 µM	Induction of unscheduled DNA repair in VA-4 cells transformed by SV-40 virus, with and without rat liver microsomal activation	Ahmed et al 1977
Dieldrin (purified)	Human lung cells	WI-38	1, 10, or 30 µg/ml	Significant dose-related increases in chromosome abnormalities: breaks, fragments, interchanges, and rings	Majumdar et al 1976
Dieldrin (technical)	Duck lymphocytes	-	0.1, 1, 10, or 100 µg/ml	Significant increase in chromosomal aberrations, including gaps and breaks, at 100 µg/ml; mitotic indices reduced at all concentrations	Bunch and Low 1973
Dieldrin (recrystallized)	Saccharomyces cerevisiae (host-mediated assay in CF1 mice)	D4	25 or 50 mg/kg single dose or repeated doses of 0.2, 3, or 10 mg/kg/d	No changes in rate of mitotic gene conversion	Dean et al 1975

TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF ALDRIN/DIELDRIN

Substance	Species or System	Strain	Dose	Reported Effects	Reference
Dieldrin (purified)	Mouse	STS	1, 30, or 50 mg/kg single ip injection	Pronounced mitotic inhibition and significant 2- to 6-fold increases in chromosome abnormalilities in bone marrow cells	Majumdar et 1976
Aldrin or dieldrin	"	-	1.2 or 2 mg/kg single dose	Mitotic inhibition, chromosome aberrations including breaks, fragments, chromosome and chromatid bridges, and stickiness	Markaryan 1966
Dieldrin (recrystallized)	Mouse (dominant lethal assay)	CF1	12.5, 24, or 50 mg/kg single dose in DMSO	Negative results in one assay, reduced number of fetal implantations in another	Dean et al 1975
Aldrin	Mouse	-	9.6, 19, or 38 mg/kg single ip injection	Dose-related increase in chromosome and chromatid aberrations; no effect at 9.6 mg/kg	Georgian 1975
"	Rat	-	"	Significant increase in chromosome and chromatid aberrations at 19 mg/kg; inconclusive results at 38 mg/kg	"

TABLE 4.3.3 (continued)

SUMMARY OF MUTAGENIC EFFECTS OF ALDRIN/DIELDRIN

Substance	Species or System	Strain	Dose	Reported Effects	Reference
Dieldrin	Mammal (unspecified)	-	0.08, 0.8, or 8 mg/kg by	Negative for mutagenicity in 4 tests (unspecified)	Bidwell et al 1975
Dieldrin (technical)	Mallard duck	-	4, 10, or 30 ppm in diet for 60 days	No significant increase in chromosome aberrations	Bunch and Low 1973