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Ambient Water Quality Criteria for Endrin

AMBIENT WATER QUALITY CRITERIA FOR

ENDRIN

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FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

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CRITERIA DOCUMENT

ENDRIN

CRITERION

Aquatic Life

For endrin the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0023 µg/l as a 24-hour average, and the concentration should not exceed 0.18 µg/l at any time.

For endrin the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0023 µg/l as a 24-hour average, and the concentration should not exceed 0.037 µg/l at any time.

Human Health

The ambient water quality criterion for endrin is recommended to be identical to the existing water standard which is 1.0 µg/l. Analysis of the toxic effects data resulted in a calculated level which is protective of human health against the ingestion of contaminated water and contaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 g of aquatic organisms was not derived.

INTRODUCTION

Endrin is the common name of one member of the cyclodiene group of pesticides. It is a cyclic hydrocarbon having a chlorine-substituted methanobridge structure. Chemically pure endrin is a white crystalline solid, while the technical compound is a light tan powder. The specific gravity of this compound is 1.7 at 20°C; the vapor pressure is 2.7×10^{-7} at 25°C; and the substance begins to decompose at 200°C. Endrin was introduced into the United States in 1951. The endrin sold in the United States is a technical grade product, containing not less than 95 percent active ingredient, available in a variety of diluted formulations (Brooks, 1974). Jarvinen and Tyo (1978) found the solubility of endrin to be about 200 μg/l.

Known uses of endrin in the United States are as an avicide, rodenticide, and insecticide, the latter being the most prevalent. The largest single use of endrin domestically is for the control of lepidopteron larvae attacking cotton crops in the southeastern and Mississippi delta states. Its persistence in soil led to its discontinuation for control of tobacco worms. Thus, endrin enters the environment primarily as a result of direct applications to soil and crops. Waste material discharge from endrin manufacturing and formulating plants and disposal of empty containers also contribute significantly to observed residue levels. In the past several years, endrin utilization has been increasingly restricted and production has continued to decline. In 1978, endrin production was approximately 400,000 lbs (U.S. EPA, 1978).

REFERENCES

Brooks, G.T. 1974. Chlorinated Insecticides. Vol. I. Technology and Application. CRC Press, Cleveland, Ohio.

Jarvinen, A.W. and R.M. Tyo. 1978. Toxicity to fathead minnows of endrin in food and water. Arch. Environ. Contam. Toxicol. 7: 409.

U.S. EPA. 1978. Endrin-position document 2/3. Special Pest. Rev. Div., Off. Pest. Prog., Washington, D.C.

Aquatic Life Toxicology*

INTRODUCTION

Endrin is one of a group of chlorinated hydrocarbon pesticides developed after the broad scale use of DDT, and it was increasingly used during the 1950's. Perhaps because endrin has a high acute toxicity to aquatic organisms, it was more frequently tested in aquatic toxicity tests than related insecticides such as chlordane, heptachlor, and aldrin.

Because it is a broad spectrum pesticide, endrin was used to control many pests including termites, mice, and army worms. In the latter 1960's it was extensively used for cotton bollworm control. Its persistence in soil, while good for termite control, led to its discontinuation for control of tobacco worms. Early testing identified its high toxicity to mammals.

Endrin is very insoluble in water. Recently, Jarvinen and Tyo (1978) used a saturator in their toxicity tests and found the solubility in freshwater to be about 200 µg/l. Nearly all of the early work with endrin and aquatic animals used acetone or some other carrier solvent, and in those few tests where concentrations were measured, the actual concentrations were frequently considerably lower than the calculated ones. Some workers used a wetting agent such as Triton® X-100 in the acetone-endrin solution to improve dispersion in the test water. Because concentrations were not measured, the toxicity data reported may not reflect the true toxicity.

Ferguson and co-workers at Mississippi State University have published numerous articles on endrin resistance that developed in natural populations

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are calculations for deriving various measures of toxicity as described in the Guidelines.

of freshwater aquatic organisms exposed to high water concentrations of endrin as a result of its use on cotton. Nearly all of their work used static, unmeasured test procedures, and the data, at best, can be used only for relative toxicity purposes. Clearly, they did demonstrate a marked increased tolerance to endrin of a variety of species. None of the data on resistant populations has been included here since the criterion is expected to protect unacclimated populations as well. Ferguson and co-workers also showed that where resistant populations of organisms were found, top predators were absent; this demonstrates that acquisition of resistance is costly to species most important to humans.

The acute toxicity of endrin to saltwater organisms has been relatively well studied, particularly in the 1960's, although data on bioaccumulation of endrin and its chronic toxicity have been available only recently. Although the criterion for endrin is based on its bioconcentration, acute and chronic toxicity to invertebrate and fish species is only slightly above the Final Chronic Value. The similarity of these values is significant because only slight excursions above the Final Chronic Value may result in acute or chronic toxicity.

EFFECTS

Acute Toxicity

Twenty-two standard LC_{50} values have been reported for 15 freshwater invertebrate species (Table 1). None of the 22 data were based on measured concentrations, and only two were based on flow-through procedures. Most of the invertebrate species tested were substantially more tolerant than fishes, with few exceptions. Glass shrimp and stoneflies were comparable to fishes in sensitivity. *Daphnia magna* was among the more tolerant species. The generally higher tolerance of the insects and related groups was unexpected since endrin was an effective insecticide.

Table 1 also lists data on the acute toxicity of endrin to 13 freshwater fish species. Only six of these data from three different papers were based on measured concentrations and flow-through procedures. Of the seven data points for fathead minnows, two were derived from static tests with unmeasured concentrations, and these were not used in calculating the species mean acute value for that species. Few results of flow-through tests based on measured concentrations are available, due in part to the limited use of gas chromatography during the earlier work and the high toxicity which required very low detection limits which were not achievable until analytical procedures were improved.

All of the species mean acute values for freshwater fish species are between 0.15 and 2.1 µg/l, suggesting a relatively narrow range of species sensitivity for fishes. The Freshwater Final Acute Value for endrin, derived from the species mean acute values listed in Table 3 using the procedure described in the Guidelines, is 0.18 µg/l.

Acute toxicity tests with saltwater invertebrate species also demonstrate that endrin is very toxic (Tables 1 and 6). The variability in LC_{50} or EC_{50} values was greater than that for fishes, ranging from 0.037 µg/l for pink shrimp to 790 µg/l for the American oyster. The sensitivity of arthropods to endrin was not much different from the sensitivity of fishes. The penaeid shrimp was the most sensitive invertebrate family tested, with LC_{50} values from 0.037 to 0.3 µg/l (Schimmel, et al. 1975; Lowe, unpublished; Butler, 1963). LC_{50} values for five other arthropod species ranged from 0.3 µg/l for Korean shrimp (Schoettger, 1970) to 25 µg/l for blue crab (Butler, 1963). The sensitivity of different life stages of grass shrimp is similar, differing by only a factor of 3.4 (Tyler-Schroeder, 1979). American oysters were less sensitive than arthropods, with EC_{50}

values ranging from 14.2 to 790 µg/l, based on decreased shell deposition or abnormal development of larvae (Table 1).

The toxicity of endrin to oysters may vary depending on water temperature. Concentrations decreasing growth by 50 percent were: 400 µg/l at 12°C; 33 µg/l at 24°C; and 14 µg/l at 22°C (Table 1); these differences may however, be reflective of different laboratories' procedures. The range in LC_{50} values for saltwater invertebrate species was only slightly greater than the range for 17 species of freshwater molluscs and arthropods; the pink shrimp was the most sensitive invertebrate species tested.

Acute toxicity tests have been conducted with 17 species of saltwater fishes, and sensitivity varies (Tables 1 and 6) from 0.048 µg/l for chinook salmon (Schoettger, 1970) to 3.1 µg/l for northern puffer (Eisler, 1970b). Only two (usually tolerant) species, the sheepshead minnow (Hansen, et al. 1977) and the sailfin molly (Schimmel, et al. 1975) have been tested for 96 hours in flow-through tests with measured endrin concentrations. Sheepshead minnow fry, juveniles, and adults did not differ in their sensitivity to acute exposure to endrin (Hansen, et al. 1977).

Data on LC_{50} values for saltwater invertebrate species from acute toxicity tests on endrin support the hypothesis that the acute toxicity of endrin is underestimated by static tests and by not measuring concentrations of endrin in test water. Acute values based on nominal concentrations for grass shrimp, and American oysters were higher than acute values for measured concentrations (Table 1). Additionally, LC_{50} values based on static tests were greater than LC_{50} values for flow-through tests of the same duration for sheepshead minnow, sailfin mollies, shiner perch, dwarf perch, Korean shrimp, pink shrimp, and grass shrimp (Eisler, 1969; Schoettger, 1970; Earnest and Benville, 1972; Schimmel, et al. 1975; Tyler-Schroeder, 1979).

The Saltwater Final Acute Value for endrin, derived from the species mean acute values listed in Table 3 using the procedures described in the Guidelines, is 0.037 µg/l.

Chronic Toxicity

Life-cycle chronic tests have been completed with fathead minnow and flagfish, giving chronic values of 0.19 and 0.26 µg/l, respectively (Table 2). Mount (1962), working with the bluntnose minnow, a species closely related to the fathead minnow, found a no-observed-effect concentration between 0.1 and 0.4 µg/l for a 291-day exposure (Table 6). Spawning did not occur in this test, but the results are consistent with those for the fathead minnow.

Jarvinen and Tyo (1978) demonstrated that: (1) when food is contaminated with endrin, the toxicity of endrin in the water is greater than when uncontaminated food is fed; (2) the contribution of endrin to the body burden by food is only 10 to 15 percent of that contributed by water, and (3) residues contributed by food were additive to those contributed by water. Unfortunately, the existing data base is not sufficient to make a precise allowance for exposure through both routes for various species.

One saltwater invertebrate species, grass shrimp, has been exposed to endrin in a partial-life-cycle toxicity test (Table 2). Surivival of the parental generation was reduced by exposure to 0.11 µg/l (Tyler-Schroeder, 1979). Onset and duration of spawning were significantly delayed and lengthened for female grass shrimp at all exposure concentrations (0.03 to 0.79 µg/l). The number of females depositing embryos was less than that of controls, but embryo production and hatching success apparently were not affected. Larval mortality increased, time to metamorphosis increased, and growth of juvenile shrimp was decreased by endrin concentrations of 0.11 µg/l and higher. A chronic value of 0.039 µg/l endrin was obtained for

grass shrimp (Table 2), even though all tested concentrations significantly impaired some life-cycle function. A lower limit of 0.03 µg/l was selected because the only effect was a delay in onset of spawning of about one week; a delay of one week probably would not affect natural populations. The upper limit of 0.05 µg/l was set based on decrease in number of ovigerous females and delay in spawning of 3 to 4 weeks.

Sheepshead minnows (Schimmel, et al 1975; Hansen, et al. 1977), spot (Lowe, 1966), and mummichog (Eisler, 1970a) have been exposed to endrin for 10 days or longer (Tables 2 and 6). Of these tests with saltwater fish species, only the life-cycle exposure of sheepshead minnows (Hansen, et al. 1977) is suitable for obtaining a chronic value (Table 2). In this test, embryos exposed to 0.31 and 0.72 µg/l hatched early; all fry exposed to 0.72 µg/l, and about one-half of those exposed to 0.31 µg/l, died. Females died during spawning, fewer embryos were fertile, and survival of exposed progeny decreased in 0.31 µg/l. No significant effects were observed on survival, growth, or reproduction at an exposure concentration of 0.12 µg/l. The chronic limits, 0.12 to 0.31 µg/l, were not much less than the 96-hour LC_{50} of 0.34 µg/l, indicating that there is little difference between endrin concentrations that produce acute effects and the highest that produce no observed effect in chronic tests. Life-cycle tests with the freshwater fish species, fathead minnow and flagfish, also show little difference between acute and chronic toxicity of endrin (Table 2).

An early-life-stage test with sheepshead minnows (Schimmel, et al. 1975) was not used to obtain a chronic value because only LC_{50} values and nominal observed no-effect concentrations were reported (Table 6); however, results were similar to those reported in the life cycle test (Table 2). The LC_{50} value based on measured concentrations for fry on the 33rd day of the

experiment was 0.16 µg/l. Although mortality in fish exposed to a nominal concentration of 0.31 µg/l was not significant, they were visibly affected by endrin.

Fifty-seven percent of the juvenile spot exposed to 0.075 µg/l of endrin died within the first 19 days of an eight-month test; those exposed to 0.05 µg/l were apparently not affected (Lowe, 1966) (Table 6). Spot exposed to 0.05 µg/l for eight months exhibited no signs of poisoning, and their survival, length, and weight did not differ from those of control fish. The nominal, no-observed-effect concentration of 0.05 µg/l was 0.11 of the LC_{50} of 0.45 µg/l, and this also tends to support the conclusion of a minimal difference between the acute and chronic toxicity of endrin to fishes.

The only other datum on >96-hour effects of endrin on a saltwater fish species is a 10-day LC_{50} of 0.33 µg/l for the mummichog based on nominal concentrations (Eisler, 1970a); this is little different from the 96-hour LC_{50} values of 0.6 and 1.5 µg/l (Eisler, 1970b).

The acute-chronic ratios for the fathead minnow and the flagfish are 2.2 and 3.3, respectively (Table 2). For saltwater species, the acute-chronic ratios for the sheepshead minnow and grass shrimp are 1.9 and 18, respectively. The species mean acute values and acute-chronic ratios are summarized in Table 3.

Dividing the Freshwater Final Acute Value of 0.18 µg/l by the geometric mean (4.0) of the four acute-chronic ratios (Table 2) gives the Freshwater Final Chronic Value of 0.045 µg/l (Table 3). Dividing the Saltwater Final Acute Value of 0.037 ug/l by the geometric mean of acute-chronic ratios (4.0) gives the Saltwater Final Chronic Value of 0.0093 µg/l (Table 3).

Plant Effects

Data on the toxicity of endrin to five freshwater species of algae are listed in Table 4. Apparently, algae are not sensitive to endrin, and the lowest effect level for plants is 475 µg/l based on growth inhibition of *Anacystis nidularas*.

Three published studies on five species of saltwater algae and a natural phytoplankton community (Table 4) indicate that, like for freshwater species, effects of endrin on these plant species are unlikely at concentrations protective from acute effects on most invertebrate and fish species. Menzel, et al. (1970) in tests with four phytoplankton species found effects at concentrations greater than 1 µg/l. Productivity of natural phytoplankton communities was reduced by 46 percent in 1,000 µg/l (Butler, 1963). Growth rate of *Agmenellum quadruplicatum* was reduced in as little as 0.2 µg/l (Batterton, et al. 1971). Because none of the values is based on measured concentrations, a Final Plant Value has not been established.

Residues

Steady-state bioconcentration factors (BCF) have been measured for seven species of freshwater organisms (Table 5) including algae (140-122), mussels (3,000), and fishes (1,640-15,000).

Endrin seems to enter the body rapidly as indicated by the short time required for the tissues to reach equilibrium with the water concentration (Jarvinen and Tyo, 1978). The short biological half-life, as observed by Jackson (1976) (Table 6), demonstrates that endrin is different from related pesticides such as DDT. Jarvinen and Tyo (1978) observed metabolites of endrin in the tissues of their test fish suggesting an important rate of degradation as well as elimination.

The bioconcentration of endrin from water into the tissues of saltwater organisms has also been well studied (Tables 5 and 6). Steady-state biocon-

centration factors are available from studies with American oysters (Mason and Rowe, 1976), grass shrimp (Tyler-Schroeder, 1979), sheepshead minnows (Hansen, et al. 1977; Schimmel, et al. 1975), and spot (Lowe, 1966). Additional endrin BCF data (Table 6) are available from 96-hour exposures of oysters, grass shrimp, pink shrimp, sheepshead minnows, and sailfin mollies (Wilson, 1966; Schimmel, et al. 1975).

Bioconcentration factors (Table 5) for endrin in American oysters exposed for seven days ranged from 1,670 to 2,780 (Mason and Rowe, 1976). Endrin accumulated rapidly, reaching steady-state after about 48 hours of exposure. Oysters placed in endrin-free water depurated endrin at a rate of 0.005 μg/g/hour, resulting in a biological half-life of 67 hours. Based on this experiment, the oysters exposed to endrin for 10 days in a flow-through test by Wilson (1966) were probably at steady-state and had a BCF of 1,000, based on a nominal water concentration. Oysters exposed for only 96 hours contained 1,200 times the concentration in the exposure water (Schimmel, et al. 1975).

Bioconcentration factors for endrin from two experiments with grass shrimp averaged 1,490 and 1,600 (Tyler-Schroeder, 1979). In the first experiment, steady-state was reached after 2.5 days of a 21-day exposure. Ninety percent of the endrin was depurated within 4.2 days. In the second experiment, the average BCF of endrin was 1,600 in parental generation shrimp from a partial-life-cycle exposure lasting five months. Average bioconcentration factors after a 96-hour exposure were 830 for grass shrimp and 980 for pink shrimp (Schimmel, et al. 1975).

Bioconcentration data for two of three species of saltwater fishes differ little from those for invertebrate species. Bioconcentration factors calculated from nominal water concentrations were 1,340 for spot exposed for eight months and 1,560 for spot exposed five months (Lowe, 1966). The aver-

age BCF for juvenile sheepshead minnows exposed for 28 days was 2,500; for adults exposed for for 141 to 161 days the BCF was 6,400 (Hansen, et al. 1977), and for juvenile exposed for four days the BCF was 2,600 (Schimmel, et al. 1975). Sailfin mollies exposed to endrin for four days had an average BCF of 2,400 (Schimmel, et al. 1975).

The geometric mean of normalized BCF values for endrin for freshwater and saltwater aquatic life is 1,324 (Table 5). This value was obtained by first dividing each BCF for which a percent lipid value is available by that percent lipid value to obtain a normalized BCF, which is what the BCF would be if the percent lipids were 1 percent. Normalized BCF values obtained were: fathead minnow, 1,892; sheepshead minnow, 694 and 1,778; spot, 1,318. The geometric mean of all freshwater and saltwater normalized BCF values was then calculated.

Dividing the FDA action level of 0.3 mg/kg for edible fish and shellfish by the geometric mean of normalized BCF values (1,324) and by a percent lipid value of 15 for freshwater species (see Guidelines) gives a freshwater residue value of 0.015 μg/l. Dividing the FDA level by the geometric mean of normalized BCF values and by a percent lipid value of 16 for saltwater species (see Guidelines), a saltwater residue value of 0.014 μg/l is calculated similarly. Dividing the FDA action level of 0.3 mg/kg by the highest BCF for edible portion of an edible species, 2,780 for oyster (Mason and Rowe, 1976), provides an additional residue value for saltwater species of 0.11 μg/l.

Dividing the FDA action level of 0.3 mg/kg for fish oil by the geometric mean of normalized BCF values (1,324) and by a percent lipid value of 100 for fish oil gives a residue value for freshwater and saltwater of 0.0023 μg/l.

Other available residue data for effect levels are not appropriate for calculation of freshwater or saltwater residue values for wildlife protection. Therefore, the lowest residue value of 0.0023 µg/l is taken as the Freshwater Final Residue Value and the Saltwater Final Residue Value. The Final Residue Value may be too high because, on the average, the concentration in 50 percent of species similar to those used to derive the value will exceed the FDA action level.

Miscellaneous

Table 6, containing additional data for other effects not listed in the first five tables, does not indicate any significant effect levels that would alter the conclusions discussed previously.

Summary

Acute data are available for 28 freshwater species including a wide variety of organisms normally performing a spectrum of community functions. Only one of the 28 species has an acute value above 100 µg/l, the lowest species mean acute value is 0.15 µg/l, and most values are clustered near 1.0 µg/l. The data are predominantly from static tests in which toxicant concentrations were not measured and so probably underestimate true toxicity. The Freshwater Final Acute Value is 0.18 µg/l.

There are acute data for 21 species of saltwater organisms. None of the values is above 14.2 µg/l and four are below 0.1 µg/l. The Saltwater Final Acute Value is 0.037 µg/l, one-fifth that of the freshwater.

Life cycle tests with two freshwater fish species gave chronic endpoints near 0.2 µg/l and acute-chronic ratios of 3.3 and 2.2. Chronic data for the sheepshead minnow gave comparable estimates of 0.19 µg/l and 1.9 for the chronic value and acute-chronic ratio, respectively. The saltwater grass shrimp was more sensitive (0.039 µg/l) and gave a much larger acute-chronic ratio of 18. The geometric mean of these four estimates of the acute-

chronic ratio is 4.0. Using this value and the Freshwater and Saltwater Final Acute Values, the Freshwater Final Chronic Value is calculated to be 0.045 µg/l and the Saltwater Final Chronic Value is 0.0093 µg/l.

The residue data for freshwater and saltwater are similar and show relatively low bioconcentration factors as compared to related insecticides such as dieldrin. Further, the data agree that endrin uptake reaches steady-state quickly and is depurated quickly. Using the FDA action level of 0.3 mg/kg for fish oil, the geometric mean of normalized bioconcentration factors (1,324), and a percent lipid value of 100 for fish oil, a Final Residue Value of 0.0023 µg/l is calculated for both freshwater and saltwater. The Final Residue Value may be too high because, on the average, the concentration in 50 percent of species similar to those used to derive the value will exceed the FDA action level.

The plant data clearly indicate that plants are much more resistant than animals. Effect levels for plants are above 475 µg/l. Other data do not reveal any more sensitive effects. Saltwater algae appear more sensitive than freshwater, but all values are above 1 µg/l except one. Therefore, plant protection seems certain if animals are protected. Other data available do not suggest any lower effect levels.

CRITERIA

For endrin the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0023 µg/l as a 24-hour average, and the concentration should not exceed 0.18 µg/l at any time.

For endrin the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0023 µg/l as a 24-hour average, and the concentration should not exceed 0.037 µg/l at any time.

Table 1. Acute values for endrin

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
		FRESHWATER SPECIES		
Cladoceran, *Simocephalus serrulatus*	S, U	26	-	Sanders & Cope, 1966
Cladoceran, *Simocephalus serrulatus*	S, U	45	34	Sanders & Cope, 1966
Cladoceran, *Daphnia magna*	S, U	352	352	Gaufin, et al. 1965
Copepod (cyclopoid), (unidentified)	S, U	60	60	Naqvi & Ferguson, 1968
Sowbug, *Asellus brevicaudus*	S, U	1.5	1.5	Sanders, 1972
Scud, *Gammarus fasciatus*	S, U	4.3	-	Sanders, 1972
Scud, *Gammarus fasciatus*	S, U	1.3	-	Sanders, 1972
Scud, *Gammarus fasciatus*	FT, U	5.5	3.1	Sanders, 1972
Scud, *Gammarus lacustris*	S, U	3.0	-	Sanders, 1969
Scud, *Gammarus lacustris*	S, U	11.5	5.9	Nebeker & Gaufin, 1964
Glass shrimp, *Palaemonetes kadiakensis*	S, U	3.2	-	Sanders, 1972
Glass shrimp, *Palaemonetes kadiakensis*	FT, U	0.5	1.3	Sanders, 1972
Crayfish, *Orconectes nais*	S, U	320	-	Sanders, 1972
Crayfish, *Orconectes nais*	S, U	3.2	32	Sanders, 1972

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Mayfly, *Hexagenia bilineata*	S, U	64	64	Sanders, 1972
Mayfly, *Ephemerella grandis*	S, U	4.7	4.7	Gaufin, et al. 1965
Stonefly, *Acroneuria pacifica*	S, U	0.32	0.32	Jensen & Gaufin, 1966
Stonefly, *Pteronarcella badia*	S, U	0.54	0.54	Sanders & Cope, 1968
Stonefly, *Pteronarcys californica*	S, U	2.4	-	Jensen & Gaufin, 1966
Stonefly, *Pteronarcys californica*	S, U	0.25	0.78	Sanders & Cope, 1968
Stonefly, *Claassenia sabulosa*	S, U	0.76	0.76	Sanders & Cope, 1968
Damselfly, *Ischnura verticalus*	S, U	1.8	1.8	Sanders, 1972
Coho salmon, *Oncorhynchus kisutch*	S, U	0.51	-	Katz, 1961
Coho salmon, *Oncorhynchus kistuch*	S, U	0.27	-	Katz & Chadwick, 1961
Coho salmon, *Oncorhynchus kisutch*	S, U	0.76	0.47	Post & Schroeder, 1971
Chinook salmon, *Oncorhynchus tshawytscha*	S, U	1.2	-	Katz, 1961
Chinook salmon, *Oncorhynchus tshawytscha*	S, U	0.92	1.1	Katz & Chadwick, 1961
Cutthroat trout, *Salmo clarki*	S, U	0.113	-	Post & Schroeder, 1971

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Cutthroat trout, *Salmo clarki*	S, U	0.192	0.15	Post & Schroeder, 1971
Rainbow trout, *Salmo gairdneri*	S, U	0.405	-	Post & Schroeder, 1971
Rainbow trout, *Salmo gairdneri*	S, U	1.1	-	Macek, et al. 1969
Rainbow trout, *Salmo gairdneri*	S, U	0.58	-	Katz, 1961
Rainbow trout, *Salmo gairdneri*	S, U	0.9	0.69	Katz & Chadwick, 1961
Brook trout, *Salvelinus fontinalis*	S, U	0.355	-	Post & Schroeder, 1971
Brook trout, *Salvelinus fontinalis*	S, U	0.59	0.46	Post & Schroeder, 1971
Goldfish, *Carassius auratus*	S, U	2.1	2.1	Henderson, et al. 1959
Bluntnose minnow, *Pimephales notatus*	FT, U	0.27	-	Mount, 1962
Bluntnose minnow, *Pimephales notatus*	FT, U	0.29	-	Mount, 1962
Bluntnose minnow, *Pimephales notatus*	FT, U	0.47	0.33	Mount, 1962
Fathead minnow, *Pimephales promelas*	FT, M	0.50	-	Brungs & Bailey, 1966
Fathead minnow, *Pimephales promelas*	FT, M	0.49	-	Brungs & Bailey, 1966
Fathead minnow, *Pimephales promelas*	FT, M	0.40	-	Brungs & Bailey, 1966

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Fathead minnow, *Pimephales promelas*	FT, M	0.45	-	Brungs & Bailey, 1966
Fathead minnow, *Pimephales promelas*	S, U	1.1	-	Henderson, et al. 1959
Fathead minnow, *Pimephales promelas*	S, U	1.4	-	Henderson, et al. 1959
Fathead minnow, *Pimephales promelas*	FT, M	0.26	0.41	Solon, et al. 1969
Flagfish, *Jordanella floridae*	FT, M	0.85	0.85	Hermanutz, 1978
Mosquitofish, *Gambusia affinis*	S, U	0.75	0.75	Katz & Chadwick, 1961
Guppy, *Poecilia reticulata*	S, U	0.9	-	Katz & Chadwick, 1961
Guppy, *Poecilia reticulata*	S, U	1.6	1.2	Henderson, et al. 1959
Threespine stickleback, *Gasterosteus aculeatus*	S, U	0.44	0.44	Katz, 1961
Bluegill, *Lepomis macrochirus*	S, U	0.6	-	Katz & Chadwick, 1961
Bluegill, *Lepomis macrochirus*	S, U	8.25	-	Katz & Chadwick, 1961
Bluegill, *Lepomis macrochirus*	S, U	5.5	-	Katz & Chadwick, 1961
Bluegill, *Lepomis macrochirus*	S, U	2.4	-	Katz & Chadwick, 1961
Bluegill, *Lepomis macrochirus*	S, U	1.65	-	Katz & Chadwick, 1961

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Bluegill, *Lepomis macrochirus*	S, U	0.86	-	Katz & Chadwick, 1961
Bluegill, *Lepomis macrochirus*	S, U	0.33	-	Katz & Chadwick, 1961
Bluegill, *Lepomis macrochirus*	S, U	0.61	-	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S, U	0.41	-	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S, U	0.37	-	Macek, et al. 1969
Bluegill, *Lepomis macrochirus*	S, U	0.66	-	Henderson, et al. 1959
Bluegill, *Lepomis macrochirus*	S, U	0.61	1.0	Sanders, 1972
		SALTWATER SPECIES		
American oyster, *Crassostrea virginica*	S, U	790**	-	Davis & Hidu, 1969
American oyster, *Crassostrea virginica*	FT, M	14.2**	-	Schimmel, et al. 1975
American oyster, *Crassostrea virginica*	FT, U	33**	-	Butler, 1963
American oyster, *Crassostrea virginica*	FT, U	400**	14.2	Lowe, data sheets
Sand shrimp, *Cragon septemspinosa*	S, U	1.7	1.7	Eisler, 1969
Hermit crab, *Pagurus longicarpus*	S, U	12	12	Eisler, 1969

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Korean shrimp, *Palaemon macrodactylus*	S, U	4.7	-	Schoettger, 1970
Korean shrimp, *Palaemon macrodactylus*	FT, U	0.3	1.2	Schoettger, 1970
Grass shrimp (larva), *Palaemonetes pugio*	FT, M	1.2	-	Tyler-Schroeder, 1979
Grass shrimp (juvenile), *Palaemonetes pugio*	FT, M	0.35	-	Tyler-Schroeder, 1979
Grass shrimp (adult), *Palaemonetes pugio*	FT, M	0.69	-	Tyler-Schroeder, 1979
Grass shrimp, *Palaemonetes pugio*	FT, M	0.63	0.65	Schimmel, et al. 1975
Grass shrimp, *Palaemonetes vulgaris*	S, U	1.8	1.8	Eisler, 1969
Pink shrimp, *Penaeus duorarum*	FT, M	0.037	0.037	Schimmel, et al. 1975
American eel, *Anguilla rostrata*	S, U	0.6	0.6	Eisler, 1970b
Chinook salmon, *Oncorhynchus tshawytscha*	S, U	0.048	0.048	Schoettger, 1970
Sheepshead minnow (fry), *Cyprinodon variegatus*	FT, M	0.37	-	Hansen, et al. 1977
Sheepshead minnow (juvenile), *Cyprinodon variegatus*	FT, M	0.34	-	Hansen, et al. 1977
Sheepshead minnow (adult), *Cyprinodon variegatus*	FT, M	0.36	-	Hansen, et al. 1977
Sheepshead minnow (juvenile), *Cyprinodon variegatus*	FT, M	0.38	0.36	Schimmel, et al. 1975

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Mummichog, *Fundulus heteroclitus*	S, U	0.6	-	Eisler, 1970b
Mummichog, *Fundulus heteroclitus*	S, U	1.5	0.95	Eisler, 1970b
Striped killifish, *Fundulus majalis*	S, U	0.3	0.3	Eisler, 1970b
Sailfin molly, *Poecilia latipinna*	FT, M	0.63	0.63	Schimmel, et al. 1975
Atlantic silverside, *Menidia menidia*	S, U	0.05	0.05	Eisler, 1970b
Threespine stickleback, *Gasterosteus aculeatus*	S, U	1.65	-	Katz & Chadwick, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S, U	1.50	-	Katz & Chadwick, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S, U	1.20	-	Katz & Chadwick, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S, U	1.57	-	Katz & Chadwick, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S, U	1.57	-	Katz & Chadwick, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S, U	0.44	-	Katz, 1961
Threespine stickleback, *Gasterosteus aculeatus*	S, U	0.50	1.1	Katz, 1961
Striped bass, *Morone saxatilis*	FT, U	0.094	0.094	Korn & Earnest, 1974
Shiner perch, *Cymatogaster aggregata*	S, U	0.8	-	Earnest & Benville, 1972

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Shiner perch, *Cymatogaster aggregata*	FT, U	0.12	0.31	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	S, U	0.6	-	Earnest & Benville, 1972
Dwarf perch, *Micrometrus minimus*	FT, U	0.13	0.28	Earnest & Benville, 1972
Bluehead, *Thalassoma bifasciatum*	S, U	0.1	0.1	Elsler, 1970b
Striped mullet, *Mugil cephalus*	S, U	0.3	0.3	Elsler, 1970b
Northern puffer, *Sphaeroides maculatus*	S, U	3.1	3.1	Elsler, 1970b

* S = static, FT = flow-through, U = unmeasured, M = measured

**Abnormal development of oyster larvae; decreased growth of oyster; or loss of equilibrium of brown shrimp or blue crabs.

Table 2. Chronic values for endrin

Species	Test*	Limits (µg/l)	Chronic Value (µg/l)	Reference
		FRESHWATER SPECIES		
Fathead minnow, *Pimephales promelas*	LC	0.14-0.25	0.19	Jarvinen & Tyo, 1978
Flagfish, *Jordanella floridae*	LC	0.22-0.3	0.26	Hermanutz, 1978
		SALTWATER SPECIES		
Sheepshead minnow, *Cyprinodon variegatus*	LC	0.12-0.31	0.19	Hansen, et al. 1977
Grass shrimp, *Palaemonetes pugio*	LC	0.03-0.05**	0.039	Tyler-Schroeder, 1979

* LC = life cycle or partial life cycle

**Onset of spawning was delayed about one week in shrimp exposed to 0.03 µg/l. Because a delay of one week would probably not affect natural populations, limits were set on decreases in number of ovigerous females and delayed spawning of 3-4 weeks in 0.05 µg/l of endrin.

Acute-Chronic Ratios

Species	Acute Value (µg/l)	Chronic Value (µg/l)	Ratio
Fathead minnow, *Pimephales promelas*	0.42***	0.19	2.2
Flagfish, *Jordanella floridae*	0.85	0.26	3.3
Sheepshead minnow, *Cyprinodon variegatus*	0.36	0.19	1.9

Table 2. (Continued)

Acute-Chronic Ratios

Species	Acute Value (µg/l)	Chronic Value (µg/l)	Ratio
Grass shrimp, *Palaemonetes pugio*	0.72	0.039	18

***Since Jarvinen and Tyo (1978) did not provide a 96-hour LC50 value, the geometric mean of six 96-hour LC50 values for flow-through tests with measured concentrations was used as an estimate of the LC50 for calculating an acute-chronic ratio for fathead minnows.

Table 3. Species mean acute values and acute-chronic ratios for endrin

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
	FRESHWATER SPECIES		
28	Cladoceran, *Daphnia magna*	352	-
27	Mayfly, *Hexagenia bilineata*	64	-
26	Copepod (cyclopoid), (unidentified)	60	-
25	Cladoceran, *Simocephalus serrulatus*	34	-
24	Crayfish, *Orconectes nais*	32	-
23	Scud, *Gammarus lacustris*	5.9	-
22	Mayfly, *Ephemerella grandis*	4.7	-
21	Scud, *Gammarus fasciatus*	3.1	-
20	Goldfish, *Carassius auratus*	2.1	-
19	Damselfly, *Ischnura verticalus*	1.8	-
18	Sowbug, *Asellus brevicaudus*	1.5	-
17	Glass shrimp, *Palaemonetes kadiakensis*	1.3	-
16	Guppy, *Poecilia reticulata*	1.2	-
15	Chinook salmon, *Oncorhynchus tshawytscha*	1.1	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
14	Bluegill, *Lepomis macrochirus*	1.0	-
13	Flagfish, *Jordanella floridae*	0.85	3.3
12	Stonefly, *Pteronarcys californica*	0.78	-
11	Stonefly, *Claasenia sabulosa*	0.76	-
10	Mosquitofish, *Gambusia affinis*	0.75	-
9	Rainbow trout, *Salmo gairdneri*	0.69	-
8	Stonefly, *Pteronarcella badia*	0.54	-
7	Coho salmon, *Oncorhynchus kisutch*	0.47	-
6	Brook trout, *Salvelinus fontinalis*	0.46	-
5	Threespine stickleback, *Gasterosteus aculeatus*	0.44	-
4	Fathead minnow, *Pimephales promelas*	0.41	2.2
3	Bluntnose minnow, *Pimephales notatus*	0.33	-
2	Stonefly, *Acroneuria pacifica*	0.32	-
1	Cutthroat trout, *Salmo clarki*	0.15	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
	SALTWATER SPECIES		
21	American oyster, *Crassostrea virginica*	14.2	-
20	Hermit crab, *Pagurus longicarpus*	12	-
19	Northern puffer, *Sphaeroides maculatus*	3.1	-
18	Grass shrimp, *Palaemonetes vulgaris*	1.8	-
17	Sand shrimp, *Cragon septemspinosa*	1.7	-
16	Korean shrimp, *Palaemon macrodactylus*	1.2	-
15	Threespine stickleback, *Gasterosteus aculeatus*	1.1	-
14	Mummichog, *Fundulus heteroclitus*	0.95	-
13	Grass shrimp, *Palaemonetes pugio*	0.65	19
12	Sailfin molly, *Poecilia latipinna*	0.63	-
11	American eel, *Anguilla rostrata*	0.6	-
10	Sheepshead minnow, *Cyprinodon variegatus*	0.36	1.9
9	Shiner perch, *Cymatogaster aggregata*	0.31	-
8	Striped killifish, *Fundulus majalis*	0.3	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
7	Striped mullet, *Mugil cephalus*	0.3	-
6	Dwarf perch, *Micrometrus minimus*	0.28	-
5	Bluehead, *Thalassoma bifasciatum*	0.1	-
4	Striped bass, *Morone saxatilis*	0.094	-
3	Atlantic silverside, *Menidia menidia*	0.05	-
2	Chinook salmon, *Oncorhynchus tshawytscha*	0.048	-
1	Pink shrimp, *Penaeus duorarum*	0.037	-

* Ranked from least sensitive to most sensitive based on species mean acute value.

Final Acute-Chronic Ratio = 4.0

Freshwater Final Acute Value = 0.18 µg/l

Freshwater Final Chronic Value = 0.18 µg/l ÷ 4.0 = 0.045 µg/l

Saltwater Final Acute Value = 0.037 µg/l

Saltwater Final Chronic Value = 0.037 µg/l ÷ 4.0 = 0.0093 µg/l

Table 4. Plant values for endrin

Species	Effect	Result (µg/l)	Reference
	FRESHWATER SPECIES		
Alga, *Anacystis nidularas*	Growth	475	Batterton, et al. 1971
Alga, *Microcystis aeruginosa*	Growth	>1,000 <5,000	Vance & Drummond, 1969
Alga, *Anabaena cylindrica*	Growth	>15,000	Vance & Drummond, 1969
Alga, *Scenedesmus quadricauda*	Growth	>20,000	Vance & Drummond, 1969
Alga, *Oedogonium* sp.	Growth	>20,000	Vance & Drummond, 1969
	SALTWATER SPECIES		
Alga, *Agmenellum quadruplicatum*	Growth rate inhibited	0.2, 19, 95, 475, 950	Batterton, et al. 1971
Alga, *Dunaliella tertiotecta*	No effect on ^{14}C or cell division	1,000	Menzel, et al. 1970
Alga, *Skeletonema costatum*	^{14}C uptake reduced	>10	Menzel, et al. 1970
Alga, *Skeletonema costatum*	Growth reduced first 5 days of test	100	Menzel, et al. 1970
Alga, *Coccolithus huxlegi*	^{14}C uptake reduced	>10	Menzel, et al. 1970
Alga, *Coccolithus huxlegi*	Growth reduced	100	Menzel, et al. 1970
Alga, *Cyclotella nana*	^{14}C uptake reduced	>1.0	Menzel, et al. 1970

Table 4. (Continued)

Species	Effect	Result (µg/l)	Reference
Alga, *Cyclotella nana*	Growth reduced	100	Menzel, et al. 1970
Natural phytoplankton communities	46% decrease in productivity; ^{14}C	1,000	Butler, 1963

Table 5. Residues for endrin

Species	Tissue	Lipid (%)	Bioconcentration Factor	Duration (days)	Reference
		FRESHWATER SPECIES			
Alga, *Microcystis aeruginosa*	-	-	200	7	Vance & Drummond, 1969
Alga, *Anabaena cylindrica*	-	-	222	7	Vance & Drummond, 1969
Alga, *Scenedesmus quadricauda*	-	-	156	7	Vance & Drummond, 1969
Alga, *Oedogonium* sp.	-	-	140	7	Vance & Drummond, 1969
Mussels, (Mixed species)	Edible portion	-	3,000	21	Jarvinen & Tyo, 1978
Fathead minnow, *Pimephales promelas*	Whole body	-	10,000	47	Mount & Putnicki, 1966
Fathead minnow, *Pimephales promelas*	Whole body	3.7*	7,000	300	Jarvinen & Tyo, 1978
Channel catfish, *Ictalurus punctatus*	Whole body	-	2,000- 1,640	41 55	Argyle, et al. 1973
Flagfish, *Jordanella floridae*	Whole body	-	15,000	65	Hermanutz, 1978
		SALTWATER SPECIES			
American oyster, *Crassostrea virginica*	Edible portion	-	1,670- 2,780	7	Mason & Rowe, 1976
Grass shrimp, *Palaemonetes pugio*	Edible portion	-	1,490	10	Tyler-Schroeder, 1979
Grass shrimp, *Palaemonetes pugio*	Edible portion	-	1,600	145	Tyler-Schroeder, 1979
Sheepshead minnow (embryo-juvenile), *Cyprinodon variegatus*	Whole body	-	3,300- 4,800	33	Schimmel, et al. 1975

Table 5. (Continued)

Species	Tissue	Lipid (%)	Bioconcentration Factor	Duration (days)	Reference
Sheepshead minnow, *Cyprinodon variegatus*	Whole body	3.6**	2,500	28	Hansen, et al. 1977
Sheepshead minnow, *Cyprinodon variegatus*	Whole body	3.6**	6,400	141-161	Hansen, et al. 1977
Spot, *Leiostomus xanthurus*	Whole body	1.1	1,450	5-8 mos	Lowe, 1966

* Percent lipid data from Jarvinen (1980).

**Percent lipid data from Hansen (1980).

Maximum Permissible Tissue Concentration

Action Level or Effect	Concentration (mg/kg)	Reference
Fish and shellfish	0.3	U.S. FDA Guideline 7420.08, 1978
Fish oil	0.3	U.S. FDA Guideline 7426.04, 1977
Growth inhibition, Goldfish, *Carassius auratus*	0.43	Grant & Mehrle, 1970
Reduced survival, Fathead minnow, *Pimephales promelas*	0.63	Jarvinen & Tyo, 1978
Osmoregulation, Rainbow trout, *Salmo gairdneri*	0.725	Grant & Mehrle, 1973

Geometric mean of normalized BCF values (see text) = 1,324

Marketability for human consumption: FDA action level for fish and shellfish = 0.3 mg/kg

Percent lipid value for freshwater species (see Guidelines) = 15

Percent lipid value for saltwater species (see Guidelines) = 16

Table 5. (Continued)

Freshwater: $\frac{0.3}{1,324 \times 15}$ = 0.000015 mg/kg = 0.015 µg/l

Saltwater: $\frac{0.3}{1,324 \times 16}$ = 0.000014 mg/kg = 0.014 µg/l

Using highest BCF for edible portion of a consumed species

Saltwater: oyster = 2,780 (Mason and Rowe, 1976)

$\frac{0.3}{2,780}$ = 0.00011 mg/kg = 0.11 µg/l

FDA action level for fish oil = 0.3 mg/kg

Percent lipid value for fish oil = 100

Freshwater and Saltwater: $\frac{0.3}{1,324 \times 100}$ = 0.0000023 mg/kg = 0.0023 µg/l

Freshwater Final Residue Value = 0.0023 µg/l

Saltwater Final Residue Value = 0.0023 µg/l

Table 6. Other data for endrin

Species	Duration	Effect	Result (µg/l)	Reference
		FRESHWATER SPECIES		
Clam, *Eupera singleyi*	72 hrs	LC50	60	Naqvi & Ferguson, 1968
Snail, *Physa gyrina*	72 hrs	LC50	500	Naqvi & Ferguson, 1968
Glass shrimp, *Palaemonetes kadiakensis*	24 hrs	LC50	0.9	Naqvi & Ferguson, 1968
Stonefly, *Acroneuria pacifica*	30 days	LC50	0.035	Jensen & Gaufin, 1966
Stonefly, *Pteronarcys californica*	30 days	LC50	1.2	Jensen & Gaufin, 1966
Rainbow trout, *Salmo gairdneri*	15 min	ATPase inhibition	10^{-4} molar	Davis, et al. 1972
Goldfish, *Carassius auratus*	48 hrs	LC50	2	Iyatomi, et al. 1958
Carp, *Cyprinus carpio*	48 hrs	LC50	140	Iyatomi, et al. 1958
Carp, *Cyprinus carpio*	48 hrs	LC50	6	Iyatomi, et al. 1958
Carp, *Cyprinus carpio*	48 hrs	LC50	5	Iyatomi, et al. 1958
Carp (egg), *Cyprinus carpio*	24 hrs	LC50	19.9	Iyatomi, et al. 1958
Carp (fry), *Cyprinus carpio*	24 hrs	LC50	8.5	Iyatomi, et al. 1958
Carp (fry), *Cyprinus carpio*	24 hrs	LC50	10.7	Iyatomi, et al. 1958
Carp (fry), *Cyprinus carpio*	24 hrs	LC50	4.9	Iyatomi, et al. 1958

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Carp (fry), *Cyprinus carpio*	24 hrs	LC50	4.2	Iyatomi, et al. 1958
Carp (fry), *Cyprinus carpio*	24 hrs	LC50	0.061	Iyatomi, et al. 1958
Carp (fry), *Cyprinus carpio*	24 hrs	LC50	0.046	Iyatomi, et al. 1958
Golden shiner, *Notemigonus crysoleucas*	36 hrs	LC50	2.0	Ludke, et al. 1968
Bluntnose minnow, *Pimephales notatus*	291 days	Growth inhibition	0.4	Mount, 1962
Fathead minnow, *Pimephales promelas*	48 hrs	LC50	0.57	Lincer, et al. 1970
Fathead minnow, *Pimephales promelas*	48 hrs	LC50	0.77	Lincer, et al. 1970
Black bullhead, *Ictalurus melas*	36 hrs	LC50	0.37	Ferguson, et al. 1965
Yellow bullhead, *Ictalurus natalis*	36 hrs	LC50	1.25	Ferguson & Bingham, 1966
Channel catfish, *Ictalurus punctatus*	12 days	Half-life of residue	-	Jackson, 1976
Mosquitofish, *Gambusia affinis*	36 hrs	LC50	1.0	Ferguson, et al. 1966
Largemouth bass, *Micropterus salmoides*	48 hrs	LC50	0.27	Fabacher, 1976
Largemouth bass, *Micropterus salmoides*	20 days	LC20	0.1	Fabacher, 1976
Bluegill, *Lepomis macrochirus*	-	Weak inhibition of Mg^{2+} and Na^{+}-K^{+} ATPase	41.7 µM	Cutkomp, et al. 1971

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Bluegill, *Lepomis macrochirus*	24 hrs	LC50	2.0	Bennett & Day, 1970
		SALTWATER SPECIES		
American oyster, *Crassostrea virginica*	4 days	Bioconcentration factor = 1,200	-	Schimmel, et al. 1975
American oyster, *Crassostrea virginica*	10 days	Bioconcentration factor = 1,000	-	Wilson, 1966
Blue crab, *Callinectes sapidus*	2 days	LC50	25	Butler, 1963
Grass shrimp, *Palaemonetes pugio*	2 days	LC50	0.8	Lowe, data sheets
Grass shrimp, *Palaemonetes pugio*	4 days	Bioconcentration factor = 830	-	Schimmel, et al. 1975
Grass shrimp, *Palaemonetes pugio*	1.5 hrs	No avoidance	0.1, 1.0, 10	Hansen, et al. 1973
Pink shrimp, *Penaeus duorarum*	4 days	Bioconcentration factor = 980	-	Schimmel, et al. 1975
Pink shrimp, *Penaeus duorarum*	2 days	LC50	0.2	Lowe, data sheets
Brown shrimp, *Peneaus aztecus*	2 days	LC50	0.3	Butler, 1963
Gulf menhaden, *Brevoortia patronus*	24 hrs	LC50	0.80	Lowe, 1966
Sheepshead minnow, *Cyprinodon variegatus*	24 hrs	LC50	0.32	Lowe, 1966
Longnose killifish, *Fundulus similis*	24 hrs	LC50	0.23	Lowe, 1966

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Longnose killifish, *Fundulus similis*	2 days	LC50	0.3	Butler, 1963
Striped mullet, *Mugil cephalus*	24 hrs	LC50	2.6	Lowe, 1966
Striped mullet, *Mugil cephalus*	2 days	LC50	0.4	Lowe, data sheets
Sheepshead minnow, *Cyprinodon variegatus*	4 days	Bioconcentration factor = 2,600	-	Schimmel, et al. 1975
Sheepshead minnow, *Cyprinodon variegatus*	1.5 hrs	Avoidance	0.1, 1.0	Hansen, 1969
Sheepshead minnow (embryo-juvenile), *Cyprinodon variegatus*	33 days	LC50	0.16	Schimmel, et al. 1975
Mummichog, *Fundulus heteroclitus*	10 days	LC50	0.33	Eisler, 1970a
Sailfin molly, *Poecilia latipinna*	4 days	Bioconcentration factor = 2,400	-	Schimmel, et al. 1975
Spot, *Leiostomus xanthurus*	24 hrs	LC50	0.45	Lowe, 1966
Spot, *Leiostomus xanthurus*	8 mos	Death	0.075	Lowe, 1966
Spot, *Leiostomus xanthurus*	8 mos	No effect	0.05	Lowe, 1966
Northern puffer, *Sphaeroides maculatus*	4 days	Abnormal liver function	0.05	Eisler & Edmunds, 1966

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Mammalian Toxicology and Human Health Effects

INTRODUCTION

Wild and domestic mammals are exposed to endrin primarily through ingestion of treated foliage, although dermal contact and inhalation also occur. Endrin shows little tendency to accumulate in tissues other than adipose tissue; levels of up to 23.7 μg/g have been detected both in internal and external fat in a variety of species following ingestion of endrin-contaminated feed. Endrin was still detectable in the fat of these animals 42 days after the exposure (Long, et al. 1961).

Metabolism of endrin has been studied extensively in rats. Endrin is readily metabolized in the liver and excreted as hydrophilic metabolites. However, certain toxic metabolites such as 12-ketoendrin (also known as 9-ketoendrin) can be retained for longer periods of time. Rats excrete endrin and its metabolites primarily in the feces; in rabbits, excretion is primarily via the urine.

Endrin is highly toxic to all animals regardless of the route of exposure (Treon, et al. 1955). The primary toxic effect of acute exposure is on the central nervous system. When lethal concentrations are administered to experimental animals, convulsions may occur as soon as 30 minutes after exposure, and may culminate in death through respiratory failure in about 48 hours. The dose lethal to 50 percent of the experimental animals ranges from 3 mg/kg for the monkey to 50 mg/kg for the goat.

Many cases of mammalian fatalities have been reported outside the laboratory. For example, field application of endrin at rates of 0.55 to 2.75 kg/ha resulted in the death of 33 to 100 percent of

various species of wild mice inhabiting the target area (Dana and Shaw, 1958).

The chronic toxicity of endrin to mammals is greater than that of other organochlorine pesticides. Sublethal effects in wild animals manifest primarily as behavioral and reproductive disorders, i.e., improper maternal care, temporary loss of normal activity, increased vulnerability to predators, reduced reproductive potential, increased post-natal mortality, and fetal death. Chronic exposure to endrin may also be fatal. Doses of 0.49 to 0.81 mg/kg in the diet was fatal to dogs in 5 to 6 months. Twelve mg/kg in the diet for life decreased the survival time for mice. Deer mice succumbed to a diet which contained only 2 mg/kg endrin.

No malignancies attributable to endrin exposure have been reported in the literature; however, endrin has been found to cause chromosomal aberrations in rats following intratesticular injection. Teratogenesis, growth retardation, and increases in fetal mortality have been observed in mice and hamsters following endrin administration.

Human exposure to endrin occurs through the diet, from inhalation, and through dermal contact. The average dietary intake in the United States in 1973 was 0.033 μg/day (0.0005 μg/kg/day) for a 69.1 kg man. This is far below the maximum daily intake of 138.2 μg/day (2 μg/kg/day) established by the World Health Organization (WHO). Respiratory and/or dermal exposure to endrin occur during manufacture and distribution, but are more likely to result from agricultural uses.

Outbreaks of human poisoning have resulted from accidental contamination of foods and have been traced to doses as low as 0.2 mg/kg body weight. Endrin toxicity seems to result primarily from the effects of endrin and its metabolites on the central nervous system. Symptoms usually observed in victims of endrin poisoning were convulsions, vomiting, abdominal pain, nausea, dizziness, and headache. Respiratory failure was the most common cause of death. Significantly increased activity of the hepatic microsomal drug-metabolizing enzymes has occurred in individuals employed in the manufacture of endrin. No reports of irreversible adverse effects of occupational exposure to endrin have been found in the available literature.

Food contamination by endrin still occurs, but to a decreasing extent. At present, levels are approximately 4,000 times lower than those acceptable to the World Health Organization. Background concentrations in the atmosphere, hydrosphere, and lithosphere, far removed from agricultural areas where endrin is used and industrialized areas where endrin is manufactured, are generally below the levels of detection.

Humans ingest endrin-treated agricultural produce as well as meat from domesticated and wild animals and fish which feed on contaminated vegetation. Ingestion of 20 mg endrin per day by cows resulted in levels of up to 0.25 μg/g of endrin in milk. Aquatic invertebrates and fish bioconcentrate considerable quantities of endrin from water and pass it on to predatory birds. This contaminated fowl (or the fish themselves) may, in turn, be ingested by humans.

In animals, chronic exposure to endrin may result in damage to the liver, kidneys, heart, brain, lung, adrenal glands, and spleen. Effects, secondary to central nervous system disorders, have also been observed following chronic exposure of mammals to sublethal doses of endrin. These include behavioral abnormalities, changes in carbohydrate metabolism, and changes in the composition of the blood. Although no reports of malignancies attributable to endrin have been found, chromosomal abnormalities and teratogenesis have been induced by endrin in several mammalian species.

EXPOSURE

Ingestion from Water

Occasionally, groundwater may contain more than 0.1 µg/l of endrin, but levels as high as 3 µg/l have been correlated with precipitation and runoff following endrin applications (U.S. EPA, 1978). Drinking water from Franklin, Louisiana, an area of high endrin usage, was found to contain a maximum of 23 ng/l (Lauer, et al. 1966).

In a study conducted between March 1964 and June 1967, more than 500 grab samples of finished drinking water and corresponding raw water were collected from 10 selected municipal water treatment plants whose source was either the Mississippi or the Missouri Rivers. Of the 458 finished water samples assayed, 156 (34 percent), contained detectable concentrations of endrin. However, the number of finished water samples containing concentrations of endrin in excess of 0.1 µg/l decreased from 23 (10 percent) to 0 in a three year period from 1964 to 1967 (Schafer, et al. 1969).

A recent study of endrin contamination of drinking water was conducted by the U.S. EPA (1974). Endrin was detected in the finished water from the Carrollton Water Plant in New Orleans, Louisiana. The highest concentration measured from all samples was 4 ng/l.

Ingestion from Food

The general population has little exposure to endrin in the diet. In a series of analyses of total diets determined from "market basket" samples in five regions of the United States, the total average intake from food ranged from approximately 0.009 µg/kg body weight per day in 1965 to 0.0005 µg/kg body weight per day in 1970 (Table 1) (Duggan and Lipscomb, 1969; Duggan and Corneliussen, 1972). The six year average intake was 0.005 µg/kg body weight per day. A market basket consisted of 117 food items grouped into 12 composites required for the 14-day diet for a 16- to 19-year-old male. All foods were treated normally before analysis, i.e., meats were cooked, etc. The average daily intake remained at trace levels throughout the period 1965 to 1970; however, the frequency of occurrence decreased somewhat (Table 1). The breakdown of dietary endrin intake levels by food class is given in Table 2.

Processing of some foods before human consumption significantly changed endrin residues. Endrin increased in soybean oils (0.28 ppm) relative to whole crop levels (0.07 ppm) following the extraction process (Hill, 1970). Storage longer than 12 weeks decreased endrin residues in Irish and sweet potatoes by 20 percent (Solar, et al. 1971). Heat processing and freezing further lowered potato residues 65 and 52 percent, respectively. Studies on

TABLE 1

Average Incidence and Daily Intake of Endrin*

Year	Percent Positive Composites	Daily Intake (mg)	mg/kg body wt/day
1965	2.8	T[a]	0.000009
1966	2.0	T	0.000004
1967	1.7	T	0.000004
1968	1.1	0.001	0.00001
1969	3.3	T	0.000004
1970	1.4	T	0.0000005

*Source: Duggan and Corneliussen, 1972

[a]T = Trace, $<$ 0.001 mg

TABLE 2

Calculated Daily Intake of Endrin by Food Class (mg/day)[a]*

Year	Meat, Fish, and Poultry	Potatoes	Leafy Vegetables	Root Vegetables	Garden Fruit	Oils, Fats, Shortening
1965	---	T[b]	T	---	---	---
1966	---	T	---	T	T	T
1967	---	T	T	T	---	---
1968	---	T	---	---	---	0.001
1969	T	T	T	---	T	---
1970	---	T	---	T	T	---

*Source: Duggan and Corneliussen, 1972

[a]No detectable levels were found in dairy products, grains and cereals, legume vegetables, fruits, sugars and adjuncts, or beverages

[b]T=Trace, < 0.001 mg/day

turnips (Wheeler, et al. 1969) and carrots (Hermanson, et al. 1970) identified 50 to 80 percent of the endrin in the peels.

Endrin disappearance from growing and harvested crop is so variable that half-life data for endrin persistence on food plants should be viewed with skepticism (Hill, 1970). The loss of endrin from crops depends on the sum of many factors, including temperature, volatilization, metabolism, and dislodgement by wind and rain. Since generalizations cannot be made that endrin on a given crop will always "disappear" at the same rate, residue analyses on harvested crops are the most effective means of determining potential human exposure.

A bioconcentration factor (BCF) relates the concentration of a chemical in aquatic animals to the concentration in the water in which they live. The steady-state BCFs for a lipid-soluble compound in the tissues of various aquatic animals seem to be proportional to the percent lipid in the tissue. Thus, the per capita ingestion of a lipid-soluble chemical can be estimated from the per capita consumption of fish and shellfish, the weighted average percent lipids of consumed fish and shellfish, and a steady-state BCF for the chemical.

Data from a recent survey on fish and shellfish consumption in the United States were analyzed by SRI International (U.S. EPA, 1980). These data were used to estimate that the per capita consumption of freshwater and estuarine fish and shellfish in the United States is 6.5 g/day (Stephan, 1980). In addition, these data were used with data on the fat content of the edible portion of the same species to estimate that the weighted average percent

lipids for consumed freshwater and estuarine fish and shellfish is 3.0 percent.

Two laboratory studies, in which percent lipids and a steady-state BCF were measured, have been conducted on endrin. The mean of the BCF values, after normilization to 1 percent lipids, is 1,324 (see Table 5 in Section B). An adjustment factor of 3 can be used to adjust the mean normalized BCF to the 3.0 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average BCF for endrin and the edible portion of all freshwater and estuarine aquatic organisms consumed by Americans is calculated to be 3,970.

Because of the dynamic state of endrin in the biological tissues of lower animals (Mount, et al. 1966), the bioaccumulation is short-lived, and tissue burdens diminish rapidly once the environmental source is removed. (Toxic endrin metabolites, such as 12-ketoendrin, may persist for longer periods of time.) Commercial catfish from Arkansas and Mississippi were reported to contain average residues in the edible portions, ranging from 0.01 to 0.41 μg/g. Four percent of the samples exceeded the U.S. Food and Drug Administration (FDA) action level for maximum permissible endrin concentration of 0.3 μg/g in the edible portion of fish (Hawthorne, et al. 1974; Crockett, et al. 1975).

Humans may also be exposed to endrin in cow milk and steer, lamb, and hog meat. However, endrin is so rapidly metabolized and excreted that edible tissue levels are usually at or below the dietary concentrations of endrin. Residue levels in excess of 0.25 μg/g on a fat basis were detected in the milk of 40 Wisconsin dairy

herds between 1964 and 1967 (Moubry, et al. 1968). Endrin was presumably retained in the milk fat for up to four weeks. However, the quantities of endrin ingested during that period were not controlled. Williams and Mills (1964) studied the excretion of endrin in cows' milk under controlled feeding conditions. Endrin concentrations in the milk increased progressively during the first few days of feeding until they plateaued at 13 to 15 days. When ingestion of endrin ceased, residues in milk declined sharply and following 20 days on an endrin-free diet, detectable ($>$0.001 µg/g) levels were present only in milk samples from cows fed the highest levels of endrin (0.3 mg/kg). However, in this study animals were fed a mixture of pesticides, thus, interactions may have occurred. Endrin is apparently excreted in milk in higher concentrations when fed as a residue on hay than when fed dissolved in soybean oil (Ely, et al. 1957). However, in general, a total daily endrin intake of $>$20 mg as a residue sprayed in forage is necessary for excretion of measurable quantities of endrin in milk. In another study (Saha, 1969), the ratio of residue in milk to feed was 0.07.

Studies by Brooks (1969) demonstrated that steers, lambs, and hogs receiving 0.1 mg/kg endrin in the diet for 12 weeks showed little tendency to deposit endrin in body tissues. Continuous feeding of up to 2 mg/kg resulted in a maximum body fat content of 1 µg/g. Long, et al. (1961) reported high levels of storage (23.7 µg/g) in the adipose tissue of lambs. Higher levels were detected in the internal fat surrounding the stomach and thoracic cavity than in external fat deposits. After the lambs were transferred to untreated pasture, endrin levels in fat decreased somewhat, but

levels of approximately 6.4 to 13.8 μg/g were still present 42 days after termination of exposure. Pigs receiving 510 mg endrin over 30 days had endrin fat levels of no more than 2 μg/g, and no endrin was detected in any other tissue (Brooks, 1974).

Inhalation

Agricultural workers, home gardeners, and those involved in the manufacture or distribution of endrin might become exposed through the inhalation route. Respiratory exposure during periods of orchard spraying may generally be expected to reach 0.01 mg/hour (Wolfe, et al. 1963, 1967).

Wolfe, et al. (1963) reported that spraying of potatoes with a 1 percent solution of endrin dust produced levels of 0.41 mg/hour for respiratory exposure. During the high pressure spraying of row crops, the respiratory exposure rate was below the limits of detection of the analytical method employed (Jegier, 1964).

Another possible means of inhalation exposure to endrin is from the residues on tobacco plants used for smoking materials. Bowery, et al. (1959) found that tobacco retained an average of 0.2 μg of endrin per commercial cigarette. Forty percent of the residual endrin disappears during the curing process, but the remainder persists throughout the cigarette manufacturing process. Endrin residues in pipe tobacco increased approximately threefold from 1969 (0.05 μg/g) to 1971 (0.114 μg/g). Residues of endrin in cigars remained at approximately 0.06 μg/g from 1969 to 1972. Endrin residues in cigarettes decreased from 0.18 μg/g to 0.09 μg/g from 1969 to 1971 (Bowery, et al. 1959; Domanski and Guthrie, 1974).

In a survey of 45 sites in 1971, the highest level of endrin in ambient air was 25.6 ng/m^3 in Greely, Colorado (U.S. EPA, 1971). In a separate survey of three sites in 1975, the highest reported level of endrin in the ambient air was 0.5 ng/m^3 (U.S. EPA, 1979).

Dermal

The most significant occupational dermal exposure to endrin occurs during field applications. During dusting or spray-machine operations, dermal exposure is almost always greater than respiratory exposure. Dermal exposure during orchard spraying is likely to be as high as 3 mg/body/hour, for workers wearing standard protective clothing in which 3.15 ft^2 of the body is exposed. Potentially the greatest hazard associated with the use of endrin, however, occurs during measuring and pouring the emulsifiable concentrate solution (Wolfe, et al. 1963, 1967).

Wolfe, et al. (1963) studied exposure to endrin during several field situations. These situations included: spraying orchard cover crops for mouse control by various methods, dusting potatoes, spraying row crops, and piloting an airplane during application. The highest total exposure (dermal 18.7 mg/hr and respiratory 0.41 mg/hr) to endrin occurred during the dusting of potatoes with 1 percent endrin powder. In another study, a dermal exposure of 0.15 mg/hr was noted during the application of endrin to row crops (Jegier, 1964).

PHARMACOKINETICS

Absorption

Endrin is known to be absorbed by the skin, the lungs, and the gut (U.S. EPA, 1979), however, the rates of the absorption have not been adequately documented.

Distribution

Humans do not tend to store endrin in significant quantities. No residues were detected in plasma, adipose tissue, or urine of workers occupationally exposed to endrin (Hayes and Curley, 1968). Measurable levels of endrin have not been detected in human subcutaneous fat or blood, even in those areas where it is used extensively, such as India or the lower Mississippi delta area (Brooks, 1974). Despite its high acute toxicity, endrin is a relatively nonpersistent pesticide in humans. Endrin residues have only been detected in the body tissues of humans immediately after an acute exposure. However, little is known concerning the persistence and toxicity of endrin metabolites.

As a result of acute human poisoning, high levels of endrin have been observed in both blood and urine but not in cerebral spinal fluid (Coble, et al. 1967). Endrin-poisoned humans have been reported to have endrin levels as high as 400 μg/g in fat tissue and 10 μg/g in other tissues (Coble, et al. 1967). However, the 400 μg/g value was obtained using a bioassay technique presently regarded as unreliable (Curley, et al. 1970).

Much lower values of endrin were obtained from an autopsy of victims poisoned by eating endrin-contaminated bread (endrin levels ranged from 48 to 1,807 ppm) in Saudi-Arabia (Table 3). Blood and urine samples taken from patients 29 to 31 days after the outbreak were uniformly negative for endrin (Curley, et al. 1970). Low blood levels were detected in three humans who recovered after accidental ingestion of endrin. In one case, the concentration of endrin in the blood 30 minutes after convulsions occurred was

TABLE 3

Endrin Concentrations Found in Victims of Endrin Poisoning in Saudi Arabia*

Sample	Endrin Concentrations (µg/g)
Blood	0.007-0.032
Urine	0.004-0.007
Vomitus	5.24
Tissues (autopsy) from:	
Stomach	0.16
Liver	0.685
Kidney	0.116

*Curley, et al. 1970

0.053 μg/g and 20 hours after convulsions it was recorded at 0.038 μg/g. This same patient excreted 0.02 μg/g endrin via the urine during the following 24 hours (Coble, et al. 1967).

Richardson, et al. (1967) fed endrin to 9-month-old dogs for 128 consecutive days at a level of 0.1 mg/kg body weight per day. Blood concentrations during the experiment ranged from 0.001 to 0.008 μg/g. At the termination of the experiment, concentrations in the adipose tissue ranged from 0.3 to 0.8 μg/g; heart, pancreas, and muscle were at the lower end of this range, while the concentration in the hepatic tissue was 0.077 to 0.085 μg/g. The kidneys and lungs had similar concentrations.

The amounts of endrin detected in the tissues of dogs that were fed diets containing endrin in concentrations of 4 to 8 mg/kg for approximately six months were as follows: 1 μg/g in the fat; 1 μg/g in the liver; and 0.5 μg/g in the kidneys (Treon, et al. 1955).

Metabolism

Endrin is metabolized and excreted more rapidly than other chlorinated hydrocarbon insecticides (Jager, 1970). There is good evidence that endrin is quickly metabolized in mammals (probably in the liver) and excreted as a hydrophilic metabolite.

In vitro studies appear to support the hepatic metabolism of endrin. A metabolite behaving as a mono-hydroxy derivative was produced when endrin was incubated at 30°C for several hours with both rat liver and pig liver microsomes and NADPH (Brooks, 1969). Formation of the mono-hydroxy derivative was suppressed by sesamex, an inhibitor of microsomal oxidations.

Information regarding the metabolic fate of endrin *in vivo* is conflicting. Baldwin, et al. (1970) found that endrin is metabolized in the rat to at least three metabolites. One is 9-ketoendrin, which is found in tissues and in urine. The other two metabolites are excreted in the feces and have not been found in body tissues. The acute oral LD_{50} of 9-ketoendrin in rats (62 mg/kg) is higher than that of endrin (25 mg/kg), and the reaction appears to be a detoxication step (Brooks, 1969). Oxidation without skeletal rearrangement is the major metabolic route in mammals although details remain to be worked out (Brooks, 1974).

Bedford, et al. (1975) studied oral LD_{50} values based on 10-day mortalities for endrin and three of its mammalian metabolites (anti-12-hydroxyendrin, syn-12-hydroxyendrin, and 12-ketoendrin) in rats. All of the metabolites were more toxic than the parent compound. Rapidity of intoxication, sex differences, and analysis of the brain tissue indicated that 12-ketoendrin may be the acute toxicant in each case. Thus, the oxidative metabolism of endrin may be responsible for its acute toxicity.

Jager (1970) found, in feeding experiments with rats, that females metabolize endrin more slowly than males. When carbon-14 labeled endrin was fed to male and female rats, the males excreted 60 percent of it in the feces within the first 24 hours and the females only 39 percent. Less than 1 percent was excreted in the urine. Of the total radioactivity excreted in the feces, 70 to 75 percent occurred in the form of hydrophilic metabolites; the remainder was in unchanged endrin. Twenty-four hours after the last dose, only hydrophilic metabolites were excreted.

Sex differences in the rate of endrin metabolism in rats were also found by Hutson, et al. (1975). Although the major metabolite in both sexes was anti-12-hydroxyendrin, excreted via the bile as the glucuronide, male rats produced the metabolite at a higher rate than did females. A minor metabolite was trans-4,5-dihydroisodrin-4,5-diol. 12-Ketoendrin was the major urinary metabolite in male rats, whereas the major urinary metabolite in female rats was anti-12-hydroxyendrin-o-sulfate. These authors also found the formation of 12-ketoendrin to be directly related to the acute toxicity of endrin.

Excretion

At higher dosage levels in experimental animals, excretion of endrin appears to be slower. Tissue content of endrin declines fairly rapidly after a single dose or when a continuous feeding experiment is terminated (Brooks, 1969).

The major metabolite in both male and female rats was anti-12-hydroxyendrin, which was excreted via the bile as the glucuronide (Hutson, et al. 1975); trans-4,5-dihydroisodrin-4,5-diol is a minor biliary metabolite. 12-Ketoendrin was observed as the primary urinary metabolite in the male rat; the major urinary metabolite in female rats was anti-12-hydroxyendrin-o-sulfate. Syn-12-hydroxyendrin was not detected.

Cole, et al. (1968) also studied rates of excretion of carbon-14 labeled endrin in whole rats, bile-fistulated rats, and isolated perfused rat livers. Over 90 percent of the excreted radioactivity was found in the feces of the intact animals and in the bile of the fistulated animals. Fifty percent of the radioactive endrin was

excreted within the first 24 hours. In the fistulated animals, 50 percent of the endrin radioactivity was excreted in the bile in approximately one hour in the perfused experiments (Cole, et al. 1968).

With the exception of endosulfan, endrin is the least persistent of any of the chlorinated hydrocarbon pesticides in mammals. It is rapidly metabolized and eliminated from the tissues of vertebrates. Excretion occurs through the milk as well as through the urine and the feces (Brooks, 1974). Endrin metabolites, one of which is known to be several times more toxic than endrin itself, may persist for longer periods of time.

EFFECTS

Acute, Subacute, and Chronic Toxicity

Endrin is classified as "very highly hazardous"; meaning that, any contact with very small amounts of the substance may result in severe systemic toxicity or death (Thompson, 1971). Endrin is the most acutely toxic of the cyclodiene insecticides and yet, except for endosulfan, is least persistent in mammals (Brooks, 1974). Endrin toxicity can be elicited from any route of exposure. When ingested in one dose by rats, endrin is about three times as toxic as aldrin and about 15 times as toxic as DDT (Treon, et al. 1955). Upon intravenous administration to mice, endrin was five times as toxic as dieldrin (Walsh and Fink, 1972).

The onset of endrin toxicity symptoms is rapid. The return to normal among those who survive is also rapid. The recovery from endrin intoxication is faster than from other cyclodiene pesticides (Brooks, 1974).

Symptoms of acute endrin poisoning in mammals clearly indicate that endrin is a neurotoxicant. The first indication of acute endrin poisoning is usually central nervous system excitation as evidenced by hypersensitivity to external stimuli associated with generalized tremors and followed by severe tonic-clonic convulsions (Brooks, 1974). These convulsions may occur as early as 30 minutes after acute endrin exposure (Brooks, 1974). Convulsions can culminate in death from respiratory failure (Brooks, 1974). In the range of the acute oral LD_{50} (17 to 43 mg/kg), death of rats may result after 48 hours (Boyd and Stefec, 1969).

Other symptoms of acute endrin poisoning include bradycardia (slowed heartbeat); increase in blood pressure, salivation, and body temperature; leukocytosis (increase in number of white blood cells); increased hemoconcentration; decreased blood pH; increased cerebrospinal fluid pressure and cerebral venous pressure; increased renal vascular resistance with decreased renal blood flow and glomerular filtration rate; decrease in catecholamine concentration of the adrenals; and increased levels of circulating epinephrine and norepinephrine (Emerson, et al. 1964; Reins, et al. 1966). Histopathologic examinations of rat tissue at autopsy reveal signs of a stress reaction, degenerative changes in kidneys, liver and brain capillaries, and venous congestion, and loss of weight and dehydration of some organs (Boyd and Stefec, 1969).

The symptoms in man include headache, dizziness, abdominal disturbances, nausea, vomiting, mental confusion, muscle twitching, and epileptiform convulsions which may occur suddenly and without prior warning (Brooks, 1974; Coble, 1967).

Mammalian susceptibility to endrin toxicity varies greatly with age, sex, and species as shown in Table 4. The LD_{50} values range from 1.37 to 43 mg/kg. Apparently, mice and monkeys are most sensitive, and guinea pigs are more resistant. Rabbits seem to be somewhat more resistant than monkeys to a single dose of endrin. The acute toxicity of endrin is, however, high for all these species.

In rats and guinea pigs, females are more susceptible than males. The greater susceptibility of female rats six months of age than that of younger female rats is the reverse of the more normal relationship between age and susceptibility found in males.

When endrin was maintained in contact, as a dry 100-mesh powder, with either intact or abraded skin of female rabbits for 24 hours, the minimum lethal dosage was found to be greater than 60 and less than 94 mg/kg. Poisoned animals had convulsions, but there was not evidence of gross or microscopic damage to the skin. Degeneration of the cells in the central zones of the lobules of the livers in the rabbits was observed (Treon, et al. 1955).

Graves and Bradley (1965) determined an LD_{50} of 5.6 mg/kg for endrin injected into the peritoneal cavity of Swiss albino mice. An intravenous LD_{50} of 2.3 mg/kg was determined by Walsh and Fink (1972) for adult male mice. Endrin injected into dogs intravenously at a dosage of 3 mg/kg resulted in death in approximately 75 percent of the animals (Hinshaw, et al. 1966).

Target organs found in acute experiments are not always the same as those following repeated exposure over long periods of

TABLE 4

Acute Oral Toxicity of Endrin to Mammals

Animal (age, sex)	LD_{50} (mg/kg)
Mouse	1.37[a]
Rats (6 months, M)	43[b]
Rats (6 months, F)	7[b]
Rats (30 days, M)	30[b]
Rats (30 days, F)	17[b]
Rat	3[a]
Rabbits (F)	7-10[b]
Hamster	10[a]
Guinea pigs (F)	16[b]
Guinea pigs (M)	36[b]
Monkey	3[b]

[a]NIOSH, 1977
[b]Treon, et al. 1955

time. The central nervous system is the target of acute endrin poisoning. When an animal is repeatedly exposed to low doses (0.8 to 3.5 mg/kg/day) of endrin, it can often make compensatory adjustments to cope with the initial nervous system injury until damage to liver or other organs intervenes. However, Chernoff, et al. (1979) found that the threshold level for convulsions in hamsters was 10 mg endrin/kg body weight. This convulsive dose was approximately twice that required for the production of teratogenic effects.

Revzin (1968) found that chronic administration of endrin can lead to convulsions. He administered endrin to squirrel monkeys at a minimum rate of 0.2 mg/kg/day, which caused a characteristic change in the electroencephalogram (EEG) after seven days. With continued daily dosing electrographic seizures developed. Endrin administration was stopped after seizures, but after one month EEG's and behavior were still abnormal.

The chronic toxicity of endrin is greater than that of other organochlorine pesticides. In prolonged feeding experiments, rats can consume diets containing approximately three times as much aldrin and 12 times as much DDT as endrin without increase in relative weights of specific organs. On the basis of organ weights dogs are at least 10 times as susceptible to the toxic effects of endrin as to those of DDT (Treon, et al. 1955). Species and sex differences exist in susceptibility to chronic endrin toxicity. Females are generally more susceptible than males. Rabbits and dogs are more susceptible than rats (Treon, et al. 1955).

Mammalian species appear to be sensitive to the toxic effects of endrin at low levels in their diet. Significant mortality during a 7-month period appeared in deer mice when fed 2 mg/kg endrin in the diet (Morris, 1968). The deer mice exhibited symptoms of hypertension, uncoordination, muscle tremors, and convulsions which increased in intensity until death occurred. A 48-hour starvation period at the end of the feeding study increased mortality of young mice and suggests possible translocation of endrin from fatty tissues.

Endrin fed throughout the life to Osborne-Mendel rats at 12 mg/kg in the diet decreased viability. Mean survival time fell from 19.7 months to 17.6 months for males and from 19.5 months to 18.2 months for females. The endrin-fed rats experienced moderate increases in incidence of congestion and focal hemorrhages of the lung; slight enlargement, congestion and mottling of the liver; slight enlargement, discoloration or congestion of the kidneys (Deichmann, et al. 1970).

The paper published by Treon, et al. (1955) is perhaps the most extensive long-term toxicological study of endrin and will be reviewed in detail. This paper includes acute, subacute (3 to 6 months), and chronic (2 year) feeding studies in rats (male and female); a subacute oral study in rabbits (8 to 10 weeks); and a 19-month oral study in dogs (male and female). Body weights, organ weights, and histopathologic data are included.

The rabbit studies were limited to a single dose level. Four of five female rabbits given 1 mg/kg/day of endrin in peanut oil died in 8 to 10 weeks. The surviving animals sacrificed after

50 doses over 10 weeks showed "diffuse degenerative and fatty vacuolization of the hepatic and renal cells" and degeneration of the heart. Thus, to the rabbit a dose of 1 mg/kg/day of endrin is extremely toxic.

Initial subacute rat studies gave the following results. All rats survived 50 doses (in peanut oil) over 10 weeks at the 1 mg/kg/day level. At 2 mg/kg/day 1 of 2 young female rats and 1 of 3 adult female rats died during the 10 week study. All six of the male rats (young and old) survived the 10 week dosing at 2 mg/kg/day. Three of three male rats also survived a similar study at a dose level of 5 mg/kg/day. Thus, the female rat is apparently more sensitive to the effects of endrin than is the male. In addition, this study indicates that the rat is more resistant to multiple doses than is the rabbit.

In a 2-year rat feeding study (Treon, et al. 1955), animals were given 100, 50, 25, 5, 1, and 0 ppm of endrin in the diet. Groups of 20 male and 20 female rats (Carworth strain) were fed at each dosage level (total rats = 240). The mortality among these groups of rats is shown in Table 5. Since these dosage levels are given in ppm, it is necessary to calculate approximate daily intake on a mg/kg basis. If one estimates that a 200 g rat eats 20 g food/day then 100 ppm (100 μg/g) in the food translates to 10 mg/kg/day intake of endrin; 50 ppm to 5.0 mg/kg/day; and 25, 5, and 1 ppm to 2.5, 0.5, and 0.1 mg/kg/day, respectively. Endrin in the diet of female rats at 100, 50, or 25 ppm caused significant mortality at 80 weeks (Table 5). The male rats were somewhat less susceptible showing increased mortality only at the 100 and 50 ppm

TABLE 5

Mortality Among Groups of Control Rats and Rats Fed 2 Years on Diets Containing Endrin*

		No. That Died/No. Fed on Diet			
		Males		Females	
ppm	~ mg/kg/day	80 weeks	106 weeks	80 weeks	106 weeks
100	10	18/20[a]	18/20	18/20[a]	19/20[a]
50	5	13/20[b]	16/20	19/20[a]	20/20[a]
25	2.5	5/20	9/20	12/20[c]	15/20
5	0.5	5/20	13/20	7/20	12/20
1	0.1	5/20	9/19	4/20	9/20
0	0	7/20	12/20	5/20	13/20

*Source: Adapted from Treon, et al. 1955

[a] $p < 0.01$

[b] This value is only slightly above 0.05

[c] p 0.05 - 0.01

level. Dietary levels of 100 or 50 ppm resulted in the early deaths of all but a few resistant rats. Body weight gains were not particularly altered by these dosages of endrin, nor was the rate of live weight to body weight changed. In the male rats fed 25 ppm (2.5 mg/kg/day) or 5 ppm (0.5 mg/kg/day) the average liver weight to body weight ratios were significantly different (p. 0.05-0.01) from comparable controls. This was not true at the 1 ppm (0.1 mg/kg/day) dietary level, nor was there any effect in female rats at the 0.5 or 0.1 mg/kg/day level. Hypersensitivity to external stimuli and occasional convulsions were noted in rats at the 5 and 10 mg/kg/day level. Convulsions were not noted in the animals fed 2.5 mg/kg/day or less. Animals that died when fed at the three higher dosage levels (10, 5, and 2.5 mg/kg/day) exhibited "diffuse degeneration of brain, liver, kidneys, and adrenal glands." Survivors at the two highest dosage levels showed degenerative changes in the liver only. A single statement notes that the incidence of neoplasia was not greater among experimental rats than among the controls.

Treon, et al. (1955) also conducted an extensive dog study summarized in Table 6 which is taken directly from the published paper. This table provides the dosage in both ppm in the diet and daily intake as mg/kg body weight. All dogs died when fed 0.5 to 4.0 mg/kg/day (10 to 50 ppm) in the diet and more than half of those fed 0.20 to approximately 0.5 mg/kg/day (5 to 8 ppm) also died. All dogs survived when their diets contained 4 ppm (0.15 to 0.21 mg/kg/day) or less for periods up to 18.7 months. All dogs fed 10 ppm (0.49 to 0.81 mg/kg/day) suffered extensive weight loss;

TABLE 6

Fate of Dogs Given Endrin in Diet*
(insecticide introduced into diet 6 days of each week)

Daily Dosage in Relation to Food, ppm	Daily Dosage in Relation to Body Weight, mg/kg	Sex and (No. of Dogs)	Duration of Period of Feeding on Diet Containing Endrin, Months	Fate
50	2.50-4.00	M(1), F(1)	18-20 days	Both died
25	1.21-2.20	F(2)	18-30 days	Both died
5[a] 20	0.25-0.36 0.97-1.27	F(1)	4.7	Died
10	0.49-0.81	M(1), F(1)	24-44 days	Both died
8	0.29-0.62	M(1), F(1)	5.7	One survived
2[a] 8	0.09-0.17 0.31-0.65	M(1), F(1)	9.9	One survived
5	0.20-0.27	M(1)	47 days	Died
4	0.15-0.21	M(1), F(2)	5.7	All survived
3	0.12-0.25	M(2), F(2)	18.7	All survived
1	0.045-0.12	M(2), F(2)	16.4-18.7	All survived
0[b]	0	M(1), F(1)	18.7	All survived

*Source: Treon, et al. 1955

[a]Smaller dosage given during first portion (2.9 months) of feeding period, larger dosage during remainder of period

[b]Three additional control dogs survived 5.7 months

those fed at 8 ppm (0.29 to 0.62 mg/kg/day) gained weight intially, but eventually failed to continue growing. Those fed 4 ppm (0.15 to 0.21 mg/kg/day) did not grow normally, but those at 3 (0.12 to 0.25 mg/kg/day) or 1 ppm (0.045 to 0.12 mg/kg/day) grew as well as control dogs. Affected dogs became emaciated, developed respiratory distress, and signs of irritation of the central nervous system (hypersensitivity to stimulation, tremors, twitching, and severe convulsions). Dogs fed at the 4, 3, or 1 ppm level exhibited no such toxic manifestations. Dogs fatally poisoned were found to have "diffuse degenerative lesions in the brain, heart, liver, and kidneys, together with pulmonary hyperemia and edema." Renal damage was severe and characterized by diffuse degeneration and necrosis of the convoluted tubules. The liver exhibited diffuse degeneration, fatty vacuolization, and, in some instances, necrosis.

Dogs fed diets containing 8 ppm endrin (0.29 to 0.62 mg/kg/day) for six months had enlargement of the liver, kidney, and brain. At 3 ppm (0.12 to 0.25 mg/kg/day) the kidney and heart were significantly enlarged at sacrifice (18.7 months). Dogs fed at the 1 ppm level (0.045 to 0.120 mg/kg/day) for 18.7 months were comparable to controls by all parameters of comparison.

In summary, this paper (Treon, et al. 1955) demonstrates that dogs are apparently more susceptible to endrin than rats. Minimal effects (organ enlargement) were seen at the 3 ppm (0.12 to 0.25 mg/kg/day) level in dogs after 18.7 months. At higher dosage levels, effects were more severe with mortality beginning with the 5 ppm (0.20 to 0.27 mg/kg/day) group and no dogs surviving doses

greater than 10 ppm (0.49 to 0.81 mg/kg/day). The dog study included a total of 25 dogs, both male and female, with dosages ranging from 1 ppm (0.045 to 0.12 mg/kg/day) to 50 ppm (2.5 to 4.0 mg/kg/day) and demonstrated a no-effect level at the lowest dose of 1 ppm (0.045 to 0.12 mg/kg/day).

Although two monkeys were used in the Treon, et al. (1955) study, no data is included in their report other than the minimum lethal dosage of 1 to 3 mg/kg single oral dose for one male and one female monkey (unspecified). Thus, on an acute basis, the monkey appears more susceptible than the rodents.

Synergism and/or Antagonism

The acute oral toxicity (LD_{50}) of equitoxic doses of combinations of 15 pesticides was examined by Keplinger and Deichmann (1967). The results are presented in Table 7. Endrin plus diazinon, endrin plus toxaphene, and endrin plus malathion showed additive effects; while endrin plus parathion, endrin plus DDT and, particularly, endrin plus delnav showed lower than expected LD_{50}s, suggestive of antagonistic effects. Joint administration of endrin and its closely related compound aldrin showed a more than additive effect, and endrin plus chlordane was found to exert a potentiating effect.

No other information is available on synergistic and/or antagonistic effects of endrin.

Teratogenicity

Rats and mice were given 0.58 mg endrin/kg body weight four times weekly for a month, and then after a week or more without endrin treatment, the animals were allowed to become pregnant

TABLE 7

Expected and Observed Oral LD_{50}s of Endrin plus other Pesticides in Mice*

Other Pesticides	Expected LD_{50} (mg/kg)	Observed LD_{50} (mg/kg)	Ratio E/O
Chlordane	473	211	2.22
Aldrin	63	34	1.83
Dieldrin	63	50	1.25
Diazinon	93	93	1.00
Malathion	703	820	0.85
Toxaphene	63	77	0.81
Parathion	12	18	0.65
DDT	213	400	0.53
Delnav	87	195	0.44

*Source: Keplinger and Deichmann, 1967

(Nodu, et al. 1972). A reduced fetal survival rate was found in both species. Nine mouse fetuses with club foot were found in the treated group of 177, while only one fetus with club foot was in the control group of 303.

Endrin exerted embryocidal and teratogenic effects on pregnant hamsters. Both soft and skeletal tissue malformations were produced. Single oral doses of endrin (5 mg/kg) administered to pregnant Syrian golden hamsters on day 7, 8, or 9 of gestation caused a high incidence of fetal death, congenital abnormalities and growth retardation. Thirty-two percent of the implantations resulted in fetal mortalities. Teratogenic effects were observed in 28 percent of the fetuses from hamsters treated on day eight. Open eye occurred in 22 percent, webbed foot in 16 percent, cleft palate in 5 percent, cleft lip in 1 percent, and fused ribs in 8 percent (Ottolenghi, et al. 1974).

Ottolenghi, et al. (1974) also found endrin to be teratogenic in mice, but frequency and gravity of the defects produced were less pronounced than in the hamsters when a single dose (2.5 mg/kg in mice and 5 mg/kg in hamsters) of half the LD_{50} was administered. Abnormalities in the mice included open eye and cleft palate. No significant effects were found with respect to fetal survival or fetal weight.

Golden hamsters, intubated with endrin (0.75 and 1.5 mg/kg) on days 5 to 14 of gestation, had less reactive locomotor activity than controls during gestation but not at weaning (Gray, et al. 1979). The offspring of these dams were tested in open field at 15, 20, 27, 34, and 44 days of age. Fifteen-day-old pups at the

1.5 mg/kg dose were approximately 90 percent more active than controls but this difference disappeared by day 34. Prenatal endrin exposure appeared to have behavioral effects in hamsters and their offspring.

Chernoff, et al. (1979) found that a single dose of endrin administered to pregnant hamsters on day eight, produced meningoencephaloceles at doses above 1.5 mg/kg and fused ribs at doses above 5.0 mg/kg. Open eyes, cleft palates, and webbed feet were not noted. It was suggested that a teratogenic level of endrin in humans could be lower than the levels estimated to cause human convulsions since the convulsive dose in hamsters was approximately twice that required for the induction of terata.

Mutagenicity

Endrin, as well as aldrin and dieldrin, can cause chromosome damage (Grant, 1973). Evidence of cellular degeneration has been observed in germinal tissue of male albino rats treated with 0.25 mg endrin per testes administered intratesticularly (Dikshith and Datta, 1972). The most conspicuous effects were hypertrophy, chromosomal aberrations, including stickiness, bizarre configurations, formation of chromosome fragments, and abnormal restitution of chromosomes. Formation of single and double bridges with acentric fragments was very common, disturbing the normal disjunction of chromosomes and eventually affecting the chromosome complements of the division products (Dikshith and Datta, 1973). Unequal distribution of chromosomes at anaphase was also observed. Severe cell

damage resulted in liquefication and transformation of the chromatin mass into an amorphous lump (Dikshith and Datta, 1972). These were the only instances reported of mutagenicity related to endrin.

However, chlorinated cyclopentadienes, such as endrin, may undergo metabolic conversion forming acylating and, possibly, mutagenic tetrachlorocyclopentadienone although no data exists to support this hypothesis. Using mouse liver microsomes for metabolic activation and E. coli K12(343/113) to detect mutagenicity, tetrachlorocyclopentadiene and pentachlorocyclopentadiene were highly mutagenic after metabolic activation, whereas hexachlorocylcopentadiene was not (Goggelman, et al. 1978).

Carcinogenicity

No malignancies attributed to endrin exposure have been reported. In 2-year feeding studies in rats at dosage levels of 100, 50, 25, 5, 1, and 0 ppm Treon, et al. (1955) reported that the incidence of neoplasia was no greater among treated animals than among controls. The high dosage level (100 ppm) approximates 10 mg/kg/day. Endrin fed to weanling Osborne-Mendel rats for a lifetime at dietary levels of 2, 6, or 12 mg/kg was neither tumorigenic nor carcinogenic (Deichmann, et al. 1970; Deichmann and MacDonald, 1971; Deichmann, 1972).

A recently completed National Cancer Institute (NCI) bioassay for possible endrin carcinogenicity concluded that endrin was not carcinogenic for Osborne-Mendel rats or for B6C3F1 mice (NCI, 1979).

CRITERION FORMULATION

Existing Guidelines and Standards

In 1965, maximum permissable levels were assigned to each of the organochlorine compounds based on the "maximum acceptable concentrations" suggested on July 9, 1965, by the subcommittee on Toxicology to the Public Health Service Advisory Committee on Drinking Water Standards (Schafer, et al. 1969). This concentration for endrin was 0.001 ppm. In 1967, the "maximum reasonable stream allowance" for endrin of 0.1 ppb (0.1 μg/l) was suggested by Ettinger and Mount (1967) and was accepted as a guideline.

A maximum acceptable level of 0.002 mg/kg body weight/day was established by a Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Meeting on Pesticide Residues in Food held in Rome, November, 1972 (FAO, 1973).

A threshold limit value of 100 $\mu g/m^3$ was set for atmospheric levels of endrin by the American Conference of Governmental Industrial Hygienists (ACGIH) for 1971 (Yobs, et al. 1972). A threshold limit value of 100 $\mu g/m^3$ for an 8-hour time-weighted average occupational exposure has also been established by the Occupational Safety and Health Administration (OSHA) (29 CFR 1910.1000).

Toxic pollutant effluent standards (40 CFR 129.102) were promulgated by the U.S. EPA. These allowed an effluent concentration of 1.5 μg/l per average working day calculated over a period of one month, not to exceed 7.5 μg/l in any sample representing one working day's effluent. In addition, discharge is not to exceed 0.0006 kg per 1,000 kg of production.

Current Levels of Exposure

While no recent data are available on levels of exposure of humans to endrin it appears that the risk of exposure is decreasing because of the decreased usage of the pesticide.

In a survey of over 500 drinking water samples, the number of samples containing concentrations of endrin in excess of 0.1 μg/l, which has been established as a maximum reasonable stream allowance, decreased from 23 in the period 1964 to 1965 to 0 in the period 1966 to 1967 (Schafer, et al. 1969). The most recent study found only 4 ng/l in contaminated drinking water (U.S. EPA, 1974).

In a series of analyses of total diets, the average daily intake of endrin remained at trace levels ($<$0.001 mg) during the period 1965 to 1970, but the frequency of occurrence decreased considerably (Duggan and Lipscomb, 1969; Duggan and Corneliussen, 1972).

Exposure of the general public to endrin in the air decreased from a maximum level of 25.6 $\mu g/m^3$ in 1971 at Greeley, Colorado, to a maximum of 0.5 $\mu g/m^3$ in 1975 in Jackson, Mississippi (U.S. EPA, 1979).

Special Groups at Risk

Agricultural workers, home gardeners, and those involved in endrin manufacture and distribution are the most likely to be exposed to endrin. They may be exposed through inhalation or dermal exposure. The most significant occupational exposure comes during spraying of fields, and dermal exposure is almost always greater than respiratory exposure. Probably the greatest hazard associated with the use of endrin occurs when measuring and pouring the emulsifiable concentrate material. Because endrin has been

shown to cause teratogenic effects, pregnant women, particularly those whose diets may contain large amounts of fish, must also be considered a special group at risk. Evidence that endrin may cause chromosomal damage in germinal tissue suggests that men and women of child-bearing intent may also be a special risk group.

Endrin concentrations are highest in the atmosphere over agricultural areas and probably reach their peak levels during the pesticide use season. Of all urban communities, those surrounded by farm lands run the highest risk of atmospheric contamination. Endrin adsorbed to particulates could not be detected in the air over representative communities but, may be present at very low concentrations in the vapor phase. Urban communities far removed from agricultural areas are unlikely to experience significant contamination. The homes of occupationally exposed workers have higher levels of atmospheric contamination than do those of the general public.

Basis and Derivation of Criterion

Carcinogenicity studies with endrin have all been negative. The limited teratogenic and mutagenic studies on endrin suggest that effects are induced with high endrin doses. However, an unusual administration route was used in the positive mutagenic studies. More toxicological data must be gathered about these potential effects of endrin before a final conclusion can be reached.

On the basis of long-term dietary studies in mammals, a realistic drinking water criterion may be proposed. Maximum no-

observed-effect and gradual dosage dietary levels of endrin reported for experimental animals are shown in Table 8.

The data in Table 8 suggest that there is considerable species difference in the response to endrin. A 1.0 mg/kg single dose produced 4/5 deaths in rabbits, yet this amount is reported as a no-observed-effect level in the rat and mouse by other investigators. Obviously, the results of various studies are sensitive only to the extent to which the investigators pursue the study. In the Treon, et al. (1955) study large numbers of animals were used, both male and female, a range of dosages was fed and the animals followed by observation, body weight, organ weights, and histopathologic examination of tissues at sacrifice.

The rat study by Treon, et al. (1955) suggests a no-observed-effect level (NOEL) in a 2-year feeding study between 0.1 and 0.5 mg/kg/day. Dogs in an 18.7 month study were somewhat more sensitive with the NOEL at approximately 0.1 mg/kg/day. Monkeys may be more sensitive than the rat, but chronic studies in monkeys have not been reported. However, using two monkeys Treon, et al. (1955) found that single doses of 1 to 3 mg/kg were fatal.

Thus, long-term studies in both the rat and the dog suggest that the NOEL is approximately 0.1 mg/kg/day. Extrapolation from these two animal studies to man appears to be reasonable. Since data on chronic human ingestion are not available, but valid long-term feeding studies in more than one animal species have been reported, an uncertainty factor of 100 is appropriate in the absence of any indication of carcinogenicity for calculating a water criterion. Human exposure to endrin was calculated on the

TABLE 8

Maximum No-Effect and Graded Dosage Dietary Levels and Effects of Endrin in Various Experimental Animals

Species	Dose Level mg/kg/day	Duration	Effect	Reference
Mouse	1.0	Lifetime	NOEL	U.S. EPA, 1973
Rat	0.1 (1 ppm)	2 years	NOEL	Treon, et al. 1955
	0.5 (5 ppm)	2 years	>Liver wt.	Treon, et al. 1955
	2.5 (25 ppm)	2 years	Fatalities	Treon, et al. 1955
Rat	1.0	-	NOEL	Brooks, 1974
Rabbit	1.0	Single dose	4/5 deaths	Treon, et al. 1955
Hamster	1.5	Single dose	NOEL	Chernoff, et al. 1979
Dog	1.0	-	NOEL	Brooks, 1974
	0.29 -0.62 (8 ppm)	18.7 months	Approx. LD_{50}	Treon, et al. 1955
	0.12 -0.25 (3 ppm)	18.7 months	>Kidney, heart wt.	Treon, et al. 1955
	0.045-0.120 (1 ppm)	18.7 months	NOEL	Treon, et al. 1955
Dog	0.1	4 Months	NOEL	Richardson, et al. 1967
Monkey (2)	1-3	Single oral dose	Lethalities	Treon, et al. 1955

NOEL = No-observed-effect level

basis of daily ingestion of 2 l of water and 6.5 g fish with a BCF of 3,970 for endrin. Using a no-effect dosage level if 0.1 mg/kg/day the total acceptable daily intake (ADI) for a 70 kg person is:

$$0.1 \text{ mg endrin/kg} \times 70 \text{ kg} = \frac{7 \text{ mg/day}}{100 \text{ (uncertainty factor)}} = 70 \ \mu\text{g/day}$$

The criterion for endrin is thus:

$$x = \frac{70 \ \mu\text{g/day}}{2 \text{ l} + (0.0065 \text{ kg} \times 3{,}970)} = 2.51 \ \mu\text{g/l} \sim 2.5 \ \mu\text{g/l}$$

This approximates closely the 1 µg/l maximum allowable concentration for endrin proposed by the Public Health Service for drinking water. It is therefore, recommended that the endrin criterion be established at 1 µg endrin/l of ambient water (1 ppb).

This calculation assumes that 100 percent of man's exposure is assigned to the ambient water pathway. Although it is desirable to establish a criterion based upon total exposure potential, the data for other exposure conditions have not been factored into this analysis.

In summary, based upon the use of toxicologic data for dogs and rats, and an uncertainty factor of 100, the initial level for endrin corresponding to daily intake of 70 µg/day, is 2.5 µg/l. Since the existing 1 µg/l allowable concentration in the drinking water standards is reasonably close to 2.5 µg/l, it is recommended that 1.0 µg/l be used as the criterion with notation that there are

special groups at risk.* Drinking water contributes 5 percent of the assumed exposure while eating contaminated fish products accounts for 95 percent.

*If endrin was present in waters from which edible fish were located and if these fish concentrate endrin by a factor of 3,970, this criterion may not be sufficient to protect a special high risk group i.e., pregnant women who consume a single dose of endrin contaminated fish. Given the BCF, fish in water at the maximum recommended concentration of 1 µg/l, may contain 3.8 µg/g endrin. A 250 g portion of fish would contain approximately 1.0 mg endrin (or 0.02 mg/kg for a 50 kg female). This dose provides a margin of safety of only 75 over the NOEL of 1.5 mg/kg for teratogenicity in the hamster (Chernoff, et al. 1979). The adequacy of this margin of safety is highly questionable, especially given the likelihood of consumption of more than 250 g of fish at a given time. The recommended water quality criterion of 1 µg/l was based on a chronic exposure study, teratologic outcomes are more likely to occur with acute exposures at critical times in gestation.

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