Biological Report 85 (1.8)
May 1986

Contaminant Hazard Reviews
Report No. 8

DIOXIN HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

By

Ronald Eisler

Patuxent Wildlife Research Center
U.S. Fish and Wildlife Service
Laurel, MD 20708

SUMMARY

Polychlorinated dibenzo- *para*- dioxins (PCDDS) are present as trace impurities in some manufactured chemicals and industrial wastes. The chemical and environmental stability of PCDDs and their tendency to accumulate in fat have resulted in their detection within many ecosystems. In general, wherever high levels of PCDDs have been detected, the source has been a hazardous waste dump, an industrial discharge, or an application of PCDD-contaminated herbicide.

There are 75 PCDD isomers; some are extremely toxic, while others are believed to be relatively innocuous. The most toxic and most extensively studied PCDD isomer is 2,3,7,8-tetrachlorodibenzo- *para*- dioxin (2,3,7,8-TCDD). In the United States and elsewhere, accidental contamination of the environment by 2,3,7,8-TCDD has resulted in deaths in many species of wildlife and domestic animals. High residues of 2,3,7,8-TCDD in fish, i.e., more than 50 parts-per-trillion (ppt) wet weight, have resulted in closing rivers to fishing. In the most seriously affected areas, hospitalization and permanent evacuation of humans has been necessary. Laboratory studies with birds, mammals, aquatic organisms, and other species have demonstrated that exposure to 2,3,7,8-TCDD can result in acute and delayed mortality as well as carcinogenic, teratogenic, mutagenic, histopathologic, immunotoxic, and reproductive effects. These effects varied greatly among species.

No regulations governing PCDD contamination exist at present to protect sensitive species of wildlife and aquatic organisms. However, the limited data available suggest that 2,3,7,8-TCDD concentrations in water should not exceed 0.01 ppt to protect aquatic life, or 10 to 12 ppt in food items of birds and other wildlife. Additional data are needed in several areas: background levels of PCDDs in natural systems; identification of fish and wildlife populations at risk; relative importance of PCDD sources; toxicological effects of various PCDDs to aquatic biota and wildlife, especially reproductive and immunosuppressive effects; and toxic and other interaction effects of PCDDs with other groups of polychlorinated chemicals having similar structure and properties, such as biphenyls, dibenzofurans, and biphenylenes.

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This report should be cited as:

Eisler, R. 1986. Dioxin hazards to fish, wildlife, and invertebrates: a synoptic review. U.S. Fish and Wildlife Service Biological Report. 85(1.8).

TABLES

ACKNOWLEDGMENTS

I thank L.J. Garrett and J.E. Haber for library services; I.E. Moore for secretarial help; D.L. Stalling, C.E. Grue, and D.M. Swineford for reviewing the manuscript; and C.H. Halvorson and J.R. Zuboy for editorial assistance.

INTRODUCTION

Accidental contamination of the environment by polychlorinated dibenzopara- dioxins (PCDDs), especially 2,3,7,8-tetrachlorodibenzo -*para*- dioxin (2,3,7,8-TCDD), has been associated with poor reproduction of herring gulls (*Larus argentatus*) in Lake Ontario (Stolzenburg and Sullivan 1983), with the closure of selected rivers in Missouri to anglers due to high residues in fish (Powell 1984), with the destruction of fish and wildlife in Vietnam during. military defoliation operations using phenoxy herbicides (Rappe 1984), and with the death of livestock and wildlife in Missouri (Powell 1984) and Italy (Fanelli et al. 1980b). For example, in 1976, massive kills of small animals (predominantly rabbits and poultry) occurred within the first few weeks after a chemical plant explosion in Seveso, Italy, in which 2,3,7,8-TCDD was released; many humans were hospitalized (Fanelli et al. 1980b). Levels of 2,3,7,8-TCDD in milk from dairy cows and tissues of pigs, chickens, cattle, goats, and sheep from Seveso were sufficiently elevated to pose a risk to human health. Accordingly, all domestic livestock in the most seriously afflicted areas were destroyed. In eastern Missouri during 1971, waste oil contaminated with 2,3,7,8-TCDD was applied to control road dust (Powell 1984). Later, hundreds of horses kept in riding arenas became sick, and 75 died; deaths were also observed among dogs, rodents, chickens, cats, and birds near the treated areas. Soils in Times Beach, Missouri were so heavily contaminated with 2,3,7,8-TCDD that it was permanently evacuated in December 1982. The U.S. Environmental Protection Agency had earlier announced that they would buy the dioxin-contaminated city of Times Beach; once purchase is completed the city will no longer exist officially (Powell 1984). Approximately 22 kg (48.4 pounds) of 2,3,7,8-TCDD were involved in the Times Beach incident (Westing 1978).

PCDDs are present as trace impurities in some commercial herbicides and chlorophenols. They can be formed as a result of photochemical and thermal reactions in fly ash and other incineration products. Their presence in manufactured chemicals and industrial wastes is neither intentional nor desired. The chemical and environmental stability of PCDDs coupled with their potential to accumulate in fat has resulted in their detection throughout the global ecosystem. The number of chlorine atoms in PCDDs can vary between one and eight to produce up to 75 positional isomers. Some of these isomers are extremely toxic, while others are believed to be relatively innocuous. The most toxic and extensively studied PCDD isomer is 2,3,7,8-TCDD. In fact, it is the most toxic synthetic compound ever tested under laboratory conditions. This isomer is produced during the synthesis of 2,4,5-trichlorophenol, which is used in the manufacture of the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), and other trichlorophenoxy acids, and the germicide hexachlorophene. There is general agreement that 2,3,7,8-TCDD is exceedingly stable, readily incorporated into aquatic and terrestrial ecosystems, extraordinarily persistent, and virtually impossible to destroy. PCDD-contaminated phenoxy herbicides are not the only sources of 2,3,7,8-TCDD, others include polychlorinated biphenyls and pentachlorophenols. The other 74 isomers enter the biosphere from a variety of sources (NRCC 1981). The fate and effects of PCDDs--with special reference to 2,3,7,8-TCDD and its role in poisonings of humans, aquatic organisms, wildlife, livestock, poultry, and its contamination of vegetation, soils, and sediments--have been extensively reviewed (Blair 1973; Cattebeni et al. 1978; Ramel 1978; Nicholson and Moore 1979; NRCC 1981; Hay 1982; Kociba and Schwetz 1982a,b; Choudhary et al. 1983; Josephson 1983; Long et al. 1983; Stolzenburg and Sullivan 1983; NIOSH 1984; Nriagu and Simmons 1984; Rappe 1984; Webb 1984; Kamrin and Rodgers 1985; Stalling et al. 1985a,b; Young and Cockerham 1985).

This account summarizes available data on ecological and toxicological aspects of PCDDs in the environment, with special reference to fish, wildlife, and their diets. In addition, it reviews and provides recommendations for the protection of sensitive species of wildlife and aquatic biota. This report is part of a continuing series of synoptic reviews prepared in response to requests for information from Resource Contaminant Specialists of the U.S. Fish and Wildlife Service.

ENVIRONMENTAL CHEMISTRY

The PCDDs consist of 75 isomers that differ in the number and position of attached chlorine atoms; each isomer has its own unique identity and toxicological properties. The most toxic of the chlorinated dioxin isomers is 2,3,7,8-TCDD (Figure 1). It is one of 22 possible congeners of tetrachlorodibenzo- *p*- dioxin. There is general agreement that PCDDS, including 2,3,7,8-TCDD, are (or were, until recently) found in chlorophenols, especially trichlorophenol and pentachlorophenol (Table 1), in certain phenoxy pesticides (2,4,5-T; 2,4-D; Fenoprop; Silvex; Ronnel; Erbon; Agent Orange), in hexachlorophene, and in polychlorinated biphenyls (used in electrical transformers and capacitors, and contaminated with trichlorobenzenes). PCDDs enter the environment through accidental release during chlorophenol production, through aerial application of some phenoxy herbicides, and through improper disposal of wastes into terrestrial and aquatic ecosystems (Ramel 1978; NRCC 1981; Ogilvie 1981: Choudhary et al. 1983; Josephson 1983; Stolzenburg and Sullivan 1983; NIOSH 1984; Rappe 1984;

Kamrin and Rodgers 1985). The PCDD content of technical products varies between manufacturers, between lots and grades, and between various formulations of pesticidal chemicals (NRCC 1981). More recently, PCDDs have been identified in effluents from combustion products of municipal and industrial incinerators, including fly ash and flue gas (Czuczwa and Hites 1984). These PCDDs may be associated with small particles which have long residence times in the atmosphere and can become distributed over large areas. For example, in the Great Lakes atmospheric transport of combustion products is the major source of PCDDs (mostly octa-, hepta-, and hexa-CDDs) in sediments (Czuczwa et al. 1984). High-temperature combustion of bituminous coal in an oxidized and chlorinated atmosphere (produced experimentally) yielded chlorodioxins, mostly octa-, hepta-, and hexa-CDDs and measurable quantities of tetra-CDDs (Mahle and Whiting 1980). Other potential sources of PCDDs include fossil fuel power plants, internal combustion engines, home fireplaces, and cigarette smoke (Kociba and Schwetz 1982a,b), but they require verification.

In general, PCDDs exhibit a relative inertness to acids, bases, oxidation, reduction, and heat. With increasing halogen content, they become more environmentally and chemically stabile (NRCC 1981). PCDDs are usually destroyed at temperatures greater than 1,000 C. They are resistant to biological breakdown, concentrated in fat, not readily excreted, extremely toxic to some animals, and the cumulative effects of small doses to both animals and humans are a source of increasing concern (Stolzenburg and Sullivan 1983). Most PCDDs are relatively insoluble in water, sparingly soluble in organic solvents, and will decompose on exposure to UV light, including sunlight (NIOSH 1984), or to hydroxyl compounds (Josephson 1983). The isomer 2,3,7,8-TCDD is a colorless crystalline solid at room temperature and decomposes when heated at greater than 700 C (Table 2).

Data on the bioavailability of PCDDs are scarce. It is known that PCDDs incorporated into wood as a result of chlorophenol (preservative) treatement are bioavailable. Swine and poultry using chlorophenol-treated wooden pens or litter have been found to be contaminated with PCDDs (NRCC 1981). Toxicities of individual PCDD isomers can vary by a factor of 1,000 to 10,000 for isomers as closely related as 2,3,7,8-TCDD and 1,2,3,8-TCDD or 1,2,3,7,8-penta CDD and 1,2,4,7,8-penta CDD (Rappe 1984). Isomers with the hightest biological activity and acute toxicity have 4 to 6 chlorine atoms, and all lateral (i.e., 2,3,7, and 8) positions substituted with chlorine. On this basis, the most toxic PCDD isomers are 2,3,7,8-TCDD, 1,2,3,7,8-penta CDD, 1,2,3,6,7,8-hexa CDD, 1,2,3,7,8,9-hexa CDD, and 1,2,3,4,7,8-hexa CDD (Rappe 1984).

Although PCDDs are highly persistent, volatilization and photolysis are major removal processes (NRCC 1981). In soils, 2,3,7,8-TCDD undergoes photolysis rapidly on the surface in a few hours, but more deeply buried 2,3,7,8-TCDD could have a chemical half-time greater than 10 years (NRCC 1981). Microbial degradation of 2,3,7,8-TCDD in soils is slow, with biological half-times estimated at 1.0 to 1.5 years (Ramel 1978). However 2,3,7,8-TCDD was detected in northwestern Florida from samples of soils, rodents, birds, lizards, fishes, and insects 12 years after application. This half-time in soil was estimated at 2.9 years (Westing 1978). Uptake of 2,3,7,8-TCDD from soils by vegetation is considered negligible (Blair 1973;Ramel 1978).

Other than 2,3,7,8-TCDD, identification difficulties with specific isomers make quantification difficult. To date, there has been little effort towards resolution of deficiencies in analytical methodology (NRCC 1981). A detection level of 1 pg (10^{-12}g), or lower, might be requried to find 2,3,7,8-TCDD in a one gram sample. Analyses at such low levels are complicated by interference from a multitude of other compounds, as well as by the large number of PCDD isomers and their variation in chemical properties (Rappe 1984). Although 2,3,7,8-TCDD is the most extensively studied PCDD isomer, data on its fate and persistence are generally poor, interpretations are frequently absent, and extrapolations from case to case usually impossible. The general result is a qualitative concept of this compound's behavior in environmental situations (NRCC 1981). This issue is further confounded by the presence in biological and abiotic samples of chemicals of similar structure and toxicological properties to that of 2,3,7,8-TCDD. These isosteric compounds include: 2,3,6,7-tetrachlorobiphenylene; 2,3,7,8-chlorine substituted dibenzofurans; and 3,3',4,4'-tetra-, 3,3',4,4',5-penta-, and 3,3',4,4',5,5'-hexachlorobiphenyl (Stalling et al. 1985a,b). For example, analytical results of fish, birds, and sediments indicated that every sample that was positive for 2,3,7,8-TCDD also contained 2,3,7,8-chlorine substituted dibenzofurans (Stalling et al 1985a,b).

Table 1. Levels of PCDDs in commercial chlorinated phenols, and levels of 2,3,7,8-TCDD in 2,4,5-T acid and ester formulations (Hardell 1983).

Formulation	Geographic locale (year)	Concentration, in mg/kg (ppm) PCDDs	2,3,7,8-TCDD
2,4,5-T Acid	Sweden (1952)	-	1.10
2,4,5-T Ester	Sweden (1960)	-	0.40
2,4,5-T Ester	Finland (1962)	-	0.95
2,4,5-T Ester.	Finland (1967)	-	0.22
2,4,5-T Acid	USA (1964)	-	4.8
2,4,5-T Acid	USA (1969)	-	6.0
Agent Orange	USA (-)	-	0.12
Agent Orange	USA (-)	-	5.1
2,4,6-trichlorophenol	Sweden (-)	3.0	-
2,4,6-trichlorophenol	USA (-)	0.3	-
2,3,4,6-tetrachlorophenol	England (-)	12.0	-
Pentachlorophenol	USA (-)	1,900-2,625	-
Pentachlorophenol	Germany (-)	6.8	-

Table 2. Chemical and physical properties of 2,3,7,8-TCDD, also known as CAS Registry No. 1746-01-6 (NIOSH 1984).

Criterion	Property
Empirical formula	$C_{12}H_4Cl_40_2$
Percent by weight	
Carbon	44.70
Oxygen	9.95
Hydrogen	1.25
Chlorine	44.1
Molecular weight	322
Vapor pressure, mm Hg at 25 C	$1.7x10^{-6}$
Melting point, C	305
Decomposition temperature, C	>700
Solubilities, g/liter	
o - dichlorobenzene	1.4
Chlorobenzene	0.72
Benzene	0.57
Chloroform	0.37
n - octanol	0.05
Methanol	0.01
Acetone	0.11
Water	$2.0x10^{-7}$

BACKGROUND CONCENTRATIONS

Data are accumulating that indicate many PCDDS, in addition to 2,3,7,8-TCDD, are present in biological and abiotic samples (NRCC 1981; O'Keefe et al. 1983; Petty et al. 1983; Stalling et al. 1983; Czuczwa et al. 1984; Lamparski et al. 1984; Kamrin-and Rodgers 1985; Stalling et al. 1985a). In general, wherever high levels of dioxins have been detected in the environment, a local application of TCDD-contaminated herbicide, hazardous waste site, or industrial discharge has usually been implicated as the source (Stolzenburg and Sullivan 1983). At Eglin Air Force Base (EAFB), located in northwestern Florida, contamination of a 208 hectare section with 2.778 kg of 2,3,7,8-TCDD (equivalent to 13 mg/ha) occurred between 1962 and 1970 as a result of repeated, massive herbicide applications (Young and Cockerham 1985). The 2,3,7,8-TCDD isomer was present as an impurity in 76,740 kg of 2,4-D and 73,010 kg of 2,4,5-T applied to this section of EAFB during the 9-year span. Ecological surveys conducted between 1970 and 1975 showed an apparently healthy and diverse wildlife fauna, although soil levels of 520 ppt of 2,3,7,8-TCDD were frequently encountered, and 2,3,7,8-TCDD residues were elevated in some species examined. The highest residues recorded in various trophic levels were 283 ppt in whole beetle grubs, up to 1,360 ppt in whole southern toads (*Bufo terrestris*), 360 ppt in viscera and 430 ppt in-carcass of a lizard, the six-lined racerunner (*Cnemidophorus sexlineatus*), 18 ppt in gonad and 85 ppt in gut contents of the spotted sunfish (*Lepomis punctatus*), 100 to 1,200 ppt in stomach contents of the southern meadowlark (*Sturnella magna argutula*), and 300 to 2,900 ppt in liver and 130 to 200 ppt in pelt of a beachmouse (*Peromyscus polionotus*) (Young and Cockerham 1985). The significance of these elevated residues will be discussed later.

In some cases, 2,3,7,8-TCDD has constituted up to 95% of the total body PCDD burden, as was true in lake trout, *Salvelinus namaycush* (O'Keefe et al. 1983), and rainbow trout, *Salmo gairdneri* (Petty et al. 1983) from Lake Ontario. Concentrations of 2,3,7,8-TCDD in whole carp (*Cyprinus carpio*), varied from 24% of total body PCDDs in Saginaw Bay, Michigan (Stalling et al. 1983), to 45 to 56% in the Niagara River (NRCC 1981). In herring gulls from Saginaw Bay, 2,3,7,8-TCDD comprised 40 to 60% of the whole body PCDD content (NRCC 1981; Petty et al. 1983), and 72 to 78% in gulls from Lakes Huron and Ontario (Stalling et al. 1983, 1985a). In 1983, Forster's tern (*Sterna forsteri*) from Green Bay, Wisconsin, contained 114 ppt of PCDDs in egg, of which 41% was 2,3,7,8-TCDD; double-crested cormorants (*Phalacrocorax auritus*) from the same area contained 25 to 214 ppt of PCDDs in whole body, of which only 10 to 31% was 2,3,7,8-TCDD (Stalling et al. 1985a). The causes of the observed variations are not known, but may be associated with localized inputs from municipal sewage treatment plants (Lamparski et al. 1984) and with atmospheric transport of incinerated domestic and industrial chemical wastes (Czuczwa et al. 1984). For example, the PCDD composition of sewage sludge from Milwaukee, Wisconsin, was relatively constant, as judged by analysis of samples from 1933, 1981, and 1982 (Lamparski et al. 1984). Total PCDD content in these samples ranged between 60,950 and 70,191 ppt, of which the great majority was in the form of octa-CDDs (82-86%), hepta-CDDs (11.0-15.4%), and hexa-CDDs (1.3-2.1%). However, the tetra-CDDs increased from 34 ppt in 1933, to 138 in 1981, and to 222 in 1981; corresponding values for the 2,3,7,8-TCDD isomer in 1933, 1981 and 1982 were 2.2, 11.0, and 16.0 ppt, respectively. Other TCDD isomers also showed increases from 6 ppt in 1933 to 22 ppt in 1982 (1,3,7,8-TCDD), and during that same period from 2.2 ppt to 140 ppt (1,2,3,7-, and 1,2,3,8-TCDD). It seems that chlorinated dibenzodioxins have been present in dried sludge from this plant for at least 50 years. Their presence in this material suggests that they may have been formed by the condensation of chlorophenols resulting from the chlorination of naturally occurring phenolic compounds (Lamparski et al. 1984). PCDDs were also found in sediments from Siskiwit Lake on Isle Royale in Lake Superior, a location which can receive only atmospheric inputs. The source of these compounds is the atmospheric transport of dioxins formed by combustion of domestic and chemical wastes. For example, particulates from a chemical waste incinerator in Midland, Michigan had 260,000,000 ppt of octa-CDDs and 170,000,000 ppt of hepta-CDDs; lower, but still elevated levels of 440,000 ppt of octa-CDDs and 310,000 ppt of hepta-CDDs were measured in municipal trash incinerator particulates (Czuczwa et al. 1984).

Data are limited on 2,3,7,8-TCDD concentrations in field collections of biological and other materials (Table 3). In the Great Lakes area, fish from the Tittabawasee and Saginaw Rivers, two tributaries of Lake Huron's Saginaw Bay, contained up to 695 ppt of 2,3,7,8-TCDD (Stolzenburg and Sullivan 1983). High 2,3,7,8-TCDD levels (87 to 162 ppt) were also recorded in fish. from the Niagara River, New York, and from parts of Lake Ontario; lower concentrations (2 to 28 ppt) were noted in fish from Lakes Erie, Huron, Michigan, and Superior (Stolzenburg and Sullivan 1983). Muscle from larger specimens of commercial fish collected from Lake Ontario in 1980 had higher levels of 2,3,7,8-TCDD than smaller fish (Ryan et al. 1984), suggesting that accumulation increases with age. The larger fish also contained high concentrations (1.2 to 4.9 parts per million, fresh weight)

of polychlorinated biphenyls (Ryan et al. 1984), demonstrating a need to elucidate TCDD interaction kinetics with other contaminants. Bottom-feeding fish, such as carp and catfish, from rivers in Michigan during 1978, contained higher 2,3,7,8-TCDD residues than surface feeders (Marless et al. 1982), indicating an association with contaminated sediments. Sediments from the Spring River, Missouri, contained 12 ppt of 2,3,7,8-TCDD immediately downstream of a now defunct hexachlorophene facility (Kleopfer and Zirschky 1983); concentrations in fish were measurable 111 km downstream from this disposal site (Table 3). Fish from the Spring River (and also the Meremac River, Missouri) contained inordinately high levels of 18 to 78 ppt of 2,3,7,8-TCDD, prompting the U.S. Food and Drug Administration to issue a health advisory in 1982 against fish consumption from these areas (Powell 1984). In Massachusetts, 6 ponds were surveyed for 2,3,7,8-TCDD in 1983 after prior treatment with phenoxy herbicides between 1958 and 1978 (Anon. 1984). Only one fish, a brown bullhead (*Ictalurus nebulosus*), age 3+ years, contained measurable (25 ppt) dioxin levels. Residues were not detectable in other species of fish sampled, including several species of ictalurid catfish, yellow perch (*Perca flavescens*), and chain pickerel (*Esox niger*). Negative results (less than 10 ppt 2,3,7,8-TCDD) were also documented in freshwater fish from Arkansas and Texas following spraying of the herbicide 2,4,5-T (Shadoff et al. 1977).

In birds, the levels of 2,3,7,8-TCDD have been decreasing, according to analysis of herring gull eggs from Lake Ontario. During the decade 1970-1980, there was a reduction of about 50% in 2,3,7,8-TCDD levels every two years (Ogilvie 1981; NRCC 1981; Nriagu and Simmons 1984). The reasons for the decline are unknown, and the relevance to higher-chlorinated PCDDs has not yet been determined. Until these questions are resolved and more substantative data are acquired on dioxin residues in birds, the current predictive trends on decline rates should be interpreted with caution.

Table 3. Concentrations of 2,3,7,8-TCDD measured in selected organisms and nonbiological materials collected from various locales. All values are in parts-per-trillion (ng/kg) fresh weight.

Ecosystem, taxonomic group, collection locale, year of collection, species, tissue, and other variables	Concentration[a] (ppt)	Reference[b]
Aquatic organisms		
Amphibians		
Seveso, Italy, 1978		
Toad, *Bufo* sp., whole	200	Fanelli et al. 1980c
Molluscs		
South Vietnam, during military defoliation operations with 2,4,5-T		
Various species, whole	Max. 810	Ramel 1978
Fish		
Massachusetts, 1983		
Lake Winthrop		
Muscle with skin		
Brown bullhead, *Ictalurus nebulosus*	25	Anon. 1984
Other fish species	ND	
Other bodies of water (5)		
Muscle with skin, 8 spp.	ND	
Missouri, 1982		
Spring River		

Whole fish	26	Powell 1984
Fillets	18	
Meremac River		
Whole	78	
Missouri, 1981		
Spring River, whole		
Distance, in km downstream from hexachlorophene manufacturing facility		
1	19	Kleopfer and Zirschky
5	37	1983
9	36	
74	1.1	
111	0.8	
Niagara River, New York, 1981		
Spottail shiner, *Notropis hudsonius*		
Whole	(4–60)	Suns et al. 1983
Cayuga Creek, New York, 1980		
Fillets, 4 spp.	(12–27)	O'Keefe et al. 1983
Coho salmon, *Oncorhynchus kisutch*		
Fillet	21	
Lake Ontario, 1980		
Muscle fillet, skinless		
White sucker, *Catostomus commersoni*	3 (2–4)	Ryan et al. 1984
Yellow perch, *Perca flavescens*	3.8 (3.2–4.3)	
Brown bullhead, *Ictalurus nebulosus*	6.0 (3.4–8.6)	
Channel catfish, *Ictalurus punctatus*	15.5 (12.8–17.7)	
American eel, *Anguilla rostrata*	19.8 (6.4–38.5)	
Rainbow smelt, *Osmerus mordax*	20.0 (11.3–32.9)	
Rainbow trout, *Salmo gairdneri*	32	O'Keefe et al. 1983
Lake trout, *Salvelinus namaycush*	41	NRCC 1981
Whole		
Lake trout	51	O'Keefe et al. 1983
Lake Ontario, 1979		
Rainbow trout		
Muscle	17	O'Keefe et al. 1983
Lake Ontario, 1978		
Lake trout		
Muscle	107	NRCC 1981

Brown trout, *Salmo trutta fario*		
Muscle	162	
Michigan Rivers, 1978		
Muscle, edible		
Lake trout	ND	Harless et al. 1982
Smallmouth bass,		
Micropterus dolomieui	8 (7–8)	
Catostomids	11 (4–21)	
Yellow perch	14 (10–20)	
Carp,		
Cyprinus carpio	55 (20–153)	
Channel catfish	157 (28–695)	
Cayuga Creek, New York 1978		
Coho salmon		
Fillet	20	O'Keefe et al. 1983
Amsterdam, Netherlands		
Eel, *Anguilla anguilla*		
From sediments containing		
5,000 ppt (dry weight)		
Whole	1.1	Heida 1983
Fat	3.9	
Terrestrial organisms		
Higher plants		
Seveso, Italy, 1976		
Various species, leaves	Max. 50,000,000	Ramel 1978
Annelids		
Seveso, Italy, 1978		
Earthworms, whole	12,000	Fanelli et al. 1980c
Reptiles		
Seveso, Italy, 1978		
Snakes, various spp.		
Liver	2,700	
Adipose tissue	16,000	
Mammals		
Seveso, Italy, 1978		
Field mouse, *Microtus arvalis*		
Whole	1,200 (70–49,000)	
Rabbit, *Lepus* sp.		
Liver	7,700 (2,700–13,000)	
Seveso, Italy, 1976		
Domestic goat, *Capra* sp.		
Liver	1,253	Fanelli et al. 1980b
Rabbit		
Liver		

Precontamination	13 (0.3–55)	
Postcontamination	85 (3.7–633)	
Cow, *Bos* sp.		
Milk		
July 9	ND	Fanelli et al. 1980a
July 28	7,900	
August 2	5,100	
August 10	2,500	
Birds		
Herring gull, *Larus argentatus*		
Egg		
Lake Ontario		
1983	90	Stalling et al. 1985a
1980	(44–68)	Ogilvie 1981
1971–72	(800–1,000)	
1970	1,200	Nriagu and Simmons 1984
Other Great Lakes		
1980	(2–14)	Ogilvie 1981
Saginaw Bay		
1980	(43–86)	
Great Lakes area,		
Green Bay and Lake Michigan		
Black-crowned night-heron,		
Nycticorax nycticorax		
Whole		
1982	21	Stalling et al. 1985a
1978	(12–59)	
Double-crested cormorant,		
Phalacrocorax auritus		
Whole, 1983	4	
Forster's tern, *Sterna forsteri*		
Wisconsin, 1983		
Egg		
Green Bay	47	
Lake Poygan	9	
Nonbiological materials		
Soils		
Seveso, Italy		
1978	3,500 (10–12,000)	Fanelli et al. 1980c
1976		
Precontamination	ND	Fanelli et al. 1980b
Postcontamination	2,300 (<0.75–51,000)	
Southwest Missouri		
1974	(220,000–440,000)	Kimbrough 1984

1971	(31,800,000–33,000,000)	
Pond sediments		
Massachusetts, 1983		
Lake Winthrop	5.9	Anon. 1984
Other ponds (5)	ND	
Municipal sewage sludge		
Milwaukee, Wisconsin		
1933	2	Lamparski et al. 1984
1981	11	
1982	16	
Industrial chemical and sludge samples		
Trichlorophenol process		
Still, bottom	111,000,000	Van Ness et al. 1980
Sump fluid		
Upper layer	63	
Lower layer	676,000	
Sludge		
Liquid	445,000	
Solid	374,000	
Process	79	
Discharge	22,000	

[a]Concentrations are listed as mean, (minimum-maximum), maximum=max., or nondetectable=ND, values recorded.

[b]Each reference applies to the values in the same row, and in the rows that follow for which no other reference is indicated.

Much of the information on 2,3,7,8-TCDD levels in wildlife and domestic livestock are from the vicinity of Seveso, Italy (Table 3). There, on July 10, 1976, a chemical cloud containing 2,3,7,8-TCDD was released as a result of an industrial accident. It contaminated the food (hay, grass, cut-up corn) of dairy cows (Fanelli et al. 1980a). Grossly elevated levels (7,900 ppt) were measured in milk from these herds at concentrations considered hazardous to human health, i.e., more than 7,000 ppt (Fanelli et al. 1980a). Wildlife from the most heavily-contaminated area appeared to accumulate 2,3,7,8-TCDD. Field mice (*Microtus arvalis*), for example, contained very high whole body concentrations of 2,3,7,8-TCDD (up to 49,000 ppt) almost 2 years after the critical contamination. The mechanisms for this phenomenon included ingestion of contaminated soil and licking of their dioxin-contaminated pelt (Fanelli et al. 1980c). In another study, no 2,3,7,8-TCDD was detected in livers of mountain beavers (*Aplodontia rufa*) that fed for 45 to 60 days in Oregon forests that had been sprayed with 2.2 kg of 2,4,5-T/ha (Newton and Snyder 1978). Although it was presumed that the herbicide was heavily contaminated with dioxins, no chemical analysis of the 2,4,5-T was performed.

TOXIC AND SUBLETHAL EFFECTS

GENERAL

Information is lacking or scarce on the biological properties of PCDD isomers, except 2,3,7,8-TCDD. The latter has been associated with lethal, carcinogenic, teratogenic, reproductive, mutagenic, histopathologic, and immunotoxic effects. There are substantial inter- and intraspecies differences in sensitivity and toxic responses to 2,3,7,8-TCDD. Typically, animals poisoned by 2,3,7,8-TCDD exhibit weight loss, atrophy of the thymus gland, and eventually death. The toxicological mechanisms are imperfectly understood.

TERRESTRIAL INVERTEBRATES

Reinecke and Nash (1984) reported that two species of earthworms (*Allolobophophora caliginosa, Lumbricus rubellus*) showed no adverse effects when held for 85 days in soils containing grossly elevated levels

of 5 ppm of 2,3,7,8-TCDD, but both species died at 10 ppm. In soils containing lower concentrations of 50 ppb of 2,3,7,8-TCDD, earthworms accumulated 5X soil levels in 7 days. There was no avoidance of soils contaminated with 2,3,7,8-TCDD, suggesting indifference. No surface penetration of dioxins into the body of earthworms was noted, and there was no biological breakdown of 2,3,7,8-TCDD during digestion as judged by the absence of mono-, di-, and tri-CDD's in excrement. Worm-worked soils had 2,3,7,8-TCDD retention times of 80 to 400 days, suggesting that earthworms may significantly alter half-time patterns of 2,3,7,8-TCDD in soils (Reinecke and Nash 1984).

Mutagenic responses were produced in *Escherichia coli* and certain strains of *Salmonella typhimurium* bacteria by 2,3,7,8-TCM,- but not by octa-CDD (Vos 1978). Further, chromosomal aberrations were induced in at least one species of higher plant and mammal (Ramel 1978). It must be concluded at this time that 2,3,7,8-TCDD is mutagenic or has mutagenic potential.

AQUATIC ORGANISMS

No data were available on lethal and sublethal effects of any PCDD isomer to aquatic organisms, except for 2,3,7,8-TCDD and freshwater biota (Table 4); 2,3,7,8-TCDD and liver microsomal enzyme activities in two marine species: winter flounder, *Pseudopleuronectes americanus*, and the little skate, *Raja erinacea* (Pohl et al. 1976); and 1,3,6,8-TCDD uptake and elimination by fathead minnows and rainbow trout (Corbet et al. 1983).

Sensitive species of teleosts exhibited reduced growth and fin necrosis at concentrations as low as 0.1 ppt of 2,3,7,8-TCDD after exposure for 24 to 96 hours. Concentrations of 1.0 ppt and higher were eventually fatal, and exposure to lower concentrations of 0.01 ppt for 24 hours had no measurable effect (Table 4). A typical 2.,3,7,8-TCDD poisoning sequence in guppies (*Poecilia reticulatus*) and coho salmon (*Oncorhynchus kisutch*) during a postexposure observation period included: declining interest in feeding (5-8 days postexposure); skin discoloration and fin necrosis (30 days), with caudal fin most severely affected; reduced resistance to fungal infestations; reduced swimming; and, finally, death several weeks to months after exposure (Miller et al. 1973). In general, older and larger fish die last, and smaller or younger specimens succumb first (Norris and Miller 1974).

Histopathologic and teratogenic effects were noted in fry of rainbow trout (*Salmo gairdneri*) exposed to 10 ppt of 2,3,7,8-TCDD for 96 hours as eggs, or is yolk-sac fry Helder 1981). Some fry showed extensive degeneration and necrosis of the liver, and subsequently developed edema prior to death. The remaining fry showed a high incidence of teratogenic changes, including opercular defects, and foreshortened maxillas.

Invertebrates, plants, and amphibians were comparatively resistant to 2,3,7,8-TCDD. For example, there were no adverse effects on growth, reproduction, or food consumption of algae, daphnids, and snails during immersion for 32 days in solutions containing 2.4 to 4.2 ppt of 2,3,7,8-TCDD (Yockim et al. 1978).

Accumulation of 2,3,7,8-TCDD from the aquatic environment was evident for all species examined (Table 4). The isomer 1,3,6,8-TCDD was also accumulated from the environment by freshwater teleosts, but accumulations were much lower than predicted when compared to 2,3,7,8-TCDD, and elimination was 10 to 15 times more rapid than. 2,3,7,8-TCDD (Corbet et al. 1983). In outdoor pond studies, a major portion of the added 2,3,7,8-TCDD concentrated in aquatic plants and at the sediment-water interface (Tsushimoto et al. 1982); however, most (85-99%) of the 2,3,7,8-TCDD originally added to the ecosystem remained in the sediments at the end of the study (Isensee and Jones 1975). Among teleosts, body burdens of 2,3,7,8-TCDD increased with increasing concentration in the water column and with increasing duration of exposure; on removal to uncontaminated water, less than 50% was lost in 109 days (Miller et al. 1979). The significance of 2,3,7,8-TCDD residues in aquatic organisms is not clear, and loss-rate kinetics are not fully documented; both areas merit additional research.

BIRDS

LD-50 values computed 37 days after a single oral dose of 2,3,7,8-TCDD varied from 15 ug/kg body weight in Northern bobwhite (*Colinus virginianus*), with 95% confidence limits of 9.2 and 24.5 ug/kg, to more than 810 ug/kg bodyweight for the ringed turtle-dove (*Streptopelia risoria*). Mallards (*Anas platyrhynchos*) were intermediate in sensitivity with an acute oral LD-50 value of more than 108 ug/kg body weight (Hudson et al. 1984). For all 3 species, death occurred 13 to 37 days after treatment; remission in survivors had apparently occurred by day 30 posttreatment. Gross necropsy of ringed turtle-doves that survived treatment showed enlarged livers, about twice normal size. Bobwhites showed severe emaciation, high accumulations of uric acid salts in connective tissues, and fluid accumulations in the pericardial and abdominal cavities (Hudson et al.

1984). Some birds regurgitated within a few minutes after treatment. Signs of intoxication that began 7 days after treatment included excessive drinking, loss of appetite, hypoactivity, emaciation, weakness, debility, muscular incoordination, increased reaction to stimuli, fluffed feathers, huddled position, unkempt appearance, falling, tremors, spasms, convulsions, and immobility (Hudson et al. 1984).

Table 4. Effects of 2,3,7,8-TCDD on selected species of freshwater organisms.

Taxonomic group, organism, and other variables	Dose[a]	Duration of exposure	Effects	Reference[b]
Algae and macrophytes	2.4–4.2 ppt (M)	32 days	Bioconcentration factor (BCF)	
Alga, *Odegonium cardiacum*			of 6X water at day 1; 654 to 2,083 at days 3 to 32; 500 at day 7 post-exposure (pe); 230 at day 14 pe	1
Pondweeds, *Elodea* sp. and *Ceratophyllum* sp.	53.7 ppt (M)	30 days	Residues of 7,000 ppt in 5 days; 2,500 ppt in 30 days	2
Molluscs				
Snail, *Helisoma* sp.	2.4–4.2 ppt (M)	32 days	Maximum BCF of 3,731	1
Snail, *Physa* sp.	200 ppt (M)	36 days	Reduced reproduction at day 12 pe	3
Annelids				
Worm, *Paranais* sp.	200 ppt (M)	55 days	Reduced reproduction	3
Arthropods				
Mosquito, *Aedes aegypti*				
Larvae	200 ppt (M)	17 days	No effect at day 30 pe	3
Cladoceran, *Daphnia magna*	2.4–4.2 ppt (M)	32 days	Maximum BCF of 7,125	3
Amphibians				
Bullfrog, *Rana catesbeiana*				
Tadpole	500 µg/kg (BW)	Single dose, injected intra-peritoneally (ip)	No effect through metamorphosis	4
Adult	500 µg/kg (BW)	Single dose, injected ip	No effect at day 35 pe	4

Fish				
Northern pike, *Esox lucius*				
Eggs and fry	0.1 ppt (M)	96 h	Growth retardation	5
Rainbow trout, *Salmo gairdneri*				
Eggs	0.1 ppt (M)	96 h	Growth retardation of fry at day 72 pe	6
Juveniles	10 ppt (M)	96 h	Growth retardation, edma; 26% dead at day 72 pe	6
Immature	107 ppt (M)	2 h	Whole body residues of 1,010 ppt	7
Immature	107 ppt (M)	6 h	Some deaths beginning at day 78 pe. At day 136 pe, survivors showed reduced growth and enlarged livers; tissue residues, in ppt fresh weight, were 650 in whole trout, 260 in muscle, 3,710 in liver, and 3,880 in fat	7
Juveniles	6.3 µg/kg (BW), oral route	33 days	Fin necrosis in 14 days; some deaths at day 33	3
Juveniles	0.0063 µg/kg (BW), oral route	33 days	No effect	3
Immature	1.2 µg/kg (BW)	Single dose, injected ip	Elevated liver cytochrome P-450 content	8
Guppy, *Poecilia reticulatus*	1.1 ppt (M)	24 h	Fin disease after 42 days	9
"	1.0 ppt (M)	24 h	LC-50 at day 42 pe	9
"	0.01 ppt (M)	24 h	No effect at day 32 pe	9
"	100 ppt (M)	24 h	Fin necrosis in 10 days; all dead at day 32 pe	10
Coho salmon, *Oncorhynchus kisutch*				
Juveniles	0.56 ppt (M)	48 h	12% dead in 60 days	3
Juveniles	5.6 ppt (M)	96 h	55% dead in 60 days	3
Juveniles	56 ppt (M)	24 h	All dead in 40 days	3
Juveniles	2.05 ppt (M)	96 h	Whole body residues of 125 ppt at day 114 pe	9
Juveniles	10.53 ppt (M)	96 h	Whole body residues of 2,177 ppt at day 114 pe; reduced growth and survival	9
Mosquitofish, *Gambusia affinis*	2.4–4.2 ppt (M)	15 days	BCF of 676 at day 1; 1,482 at day 7. All dead at day 15, preceded by	

			nasal bleeding and listless swimming	1
Channel catfish, *Ictalurus punctatus*	2.4–4.2 ppt (M)	20 days	Fin necrosis, erratic swimming, hemorrhaging from anus and lower jaw, BCF of 2,181; all dead between days 15 and 20	1
Fathead minnow, *Pimephales promelas*	53.7 ppt (M)	40 days	Whole body residues of 8,500 ppt in 10 days, 2,500 ppt in 40 days	2

[a]M=concentration in ambient medium at start; BW=body weight.

[b]References: 1, Yockim et al. 1978; 2, Tsushimoto et al. 1982; 3, Miller et al. 1973; 4, Neal et al. 1979; 5, Helder 1980; 6, Helder 1981; 7, Branson et al. 1985; 8, Vodicnik et al. 1981; 9, Miller et al. 1979; 10, Norris and Miller 1974.

Domestic chickens were relatively sensitive to PCDDS, especially 2,3,7,8-TCDD, with an estimated 2,3,7,8-TCDD oral LD-50 range of 25 to 50 ug/kg body weight (Kociba and Schwetz 1982a,b). Chickens fed 1 or 10 ug of 2,3,7,8-TCDD, 1,2,3,7,8,9-hexa CDD, or hepta-CDDs per kg body weight daily for 21 days showed signs of chick edema disease, i.e., pericardial, subcutaneous, and peritoneal edema; liver enlargement and necrosis with fatty degeneration; and frequently resulted in death (NRCC 1981; Gilbertson 1983). Autopsies of poultry killed by 2,3,7,8-TCDD in Seveso, Italy, in 1976 showed signs characteristic of chick edema disease (Fanelli et al. 1980b). Pathological signs of chick edema disease were also seen in herring gull chicks on the lower Great Lakes in the early 1970's (Gilbertson 1983). Concentrations of 2,3,7,8-TCDD in eggs of the herring gull declined from about 1,000 ppt in 1971 to less than 80 ppt in 1981. This was accompanied by a decrease in the frequency of chick edema disease (Gilbertson 1983). Decreases in levels of other contaminants notably mirex were probably more important to the survival of gulls in these colonies than 2,3,7,8-TCDD (Eisler 1985); however, little data exist on the interaction of PCDDS, including 2,3,7,8-TCDD, with other contaminants appearing concomitantly in bird tissues or their diets.

Although there presently is no evidence of biomagnification of PCDDs in birds (Gilbertson 1983), it is speculated that piscivorous birds have a greater potential to accumulate PCDDs than the fish that they eat (NRCC 1981).

MAMMALS

The greater toxic potential of certain PCDD isomers involves two properties: halogen atoms occupying at least 3 of the 4 lateral ring positions (2,3,7, 8 positions) and at least one of the adjacent ring positions being nonhalogenated (Kociba and Schwetz 1982a,b). Comparative toxicity data for selected PCDD isomers to the guinea pig (*Cavia* sp.) and the mouse (*Mus* sp.) confirmed this generalization and demonstrated significant interspecies differences in sensitivity (Table 5). Other PCDD isomers tested (2,8-di CDD, octa-CDD) were relatively nontoxic to mice and guinea pigs (NRCC 1981).

Acute toxicity studies with 2.,3,7,8-TCDD have shown marked differences--up to 8,400X--between the single oral LD-50 dose for the guinea pig and the hamster (*Cricetus* sp.) (Table 6). The acute oral LD-50 value of 0.6 ug/kg body weight for guinea pigs, suggests that 2,3,7,8-TCDD may be the most toxic compound ever tested on small laboratory animals. The unusual resistance of hamsters may be associated with its enhanced rate of metabolism and excretion of 2,3,7,8-TCDD relative to other PCDD isomers examined (Olson et al. 1980b; NRCC 1981). Poisoning in mammals by 2,3,7,8-TCDD is typically characterized by loss of body weight and delayed lethality; large interspecies differences exist in lethal dosages and toxic effects (Vos 1978; Neal et al. 1979; Kociba and Schwetz 1982a,b; Josephson 1983; Matsumura 1983; Kimbrough 1984; Seefeld et al. 1984). For example, 2,3,7,8-TCDD produces prominent chloracne-type skin lesions in man and monkeys, edema formation in birds, and severe liver damage in rats, mice, and rabbits.

Table 5. Acute toxicities of selected PCDD isomers to the guinea pig and the mouse (Kociba and Schwetz 1982b).

PCDD isomer	Oral LD-50, in µg/kg body weight Guinea pig	Mouse
2,8-di CDD	>300,000	-
2,3,7-tri CDD	29,444	>3,000
2,3,7,8-TCDD	2	284
1,2,3,7,8-penta CDD	3	338
1,2,4,7,8-penta CDD	1,125	>5,000
1,2,3,4,7,8-hexa CDD	73	825
1,2,3,6,7,8-hexa CDD	70–100	1,250
1,2,3,7,8,9-hexa CDD	60–100	>1,440
1,2,3,4,6,7,8-hepta CDD	>600	-

Table 6. Acute oral toxicities of 2,3,7,8-TCDD to mammals.

Organism	LD-50, in µg/kg body weight (ppb)	Reference[a]
Guinea pig	0.6- 2	1, 2
In corn oil	2.5	3
In aqueous methyl cellulose	19	3
Rat	22 - 45	2
Rhesus monkey	<70	4
Dog	100 - 200	2
Mouse	114 - 284	2
Rabbit	115	4
Hamster	1,157 -5,051	2

[a]References: 1, Harless et al. 1982; 2, Kociba and Schwetz 1982a, b; 3, Silkworth et al. 1982; 4, Olson et al. 1980a, b.

Intraspecies differences in sensitivity to 2,3,7,8-TCDD--up to 14 fold--were recently reported among 3 strains of mice; no reasons were given to account for these differences. Oral LD-50 (30 day) values varied from 182 ug 2,3,7,8-TCDD per kg body weight in strain C57, the most sensitive strain tested, and 296 for strain BD6, to 2,570 for strain DBA (Chapman and Schiller 1985). All 3 strains of mice evidenced a 25 to 34% weight loss prior to death; however, there was no measurable decline in food consumption.

Atrophy of the thymus is a consistent finding in mammals poisoned by 2,3,7,8-TCDD, and suppression of thymus-dependent cellular immunity, particularly in young animals, may contribute to their death. Although the mechanisms of 2,3,7,8-TCDD toxicity are unclear, current research areas include the role of thyroid hormones (Rozman et al. 1984), interference with plasma membrane functions (Matsumura 1983), alterations in, ligand receptors (Vickers et al. 1985), the causes of hypophagia (reduced desire for food) and subsequent attempts to alter or reverse the pattern of weight loss (Courtney et al. 1978; Seefeld et al. 1984; Seefeld and Peterson 1984), and excretion kinetics of biotransformed metabolites (Koshakji et al. 1984).

Developing mammalian fetuses are especially sensitive to 2,3,7,8-TCDD, and maternal exposure results in increased frequencies of stillbirths. Among live births, exposure to it produces teratogenic effects such as cystic kidney, cleft palate, and spinal column deformities (Ramel 1978). Effects of 2,3,7,8-TCDD on reproduction are reported for rats (McNulty 1977; Murray et al. 1979; Kociba and Schwetz 1982a,b) and monkeys (Ramel 1978; Barsotti et al. 1979; NRCC 1981; Kociba and Schwetz 1982a,b). In a 3-generation study with rats, daily dose levels of 0.01 ug of 2,3,7,8-TCDD/kg body weight (equivalent to 120 to 290 ppt or ng/kg in the diet), produce decreased litter size at birth, increased number of stillborns, and reduced survival and growth of young in both the Fl and F2 generations. Reproduction was not affected in rats at daily dosages of 0.001 ug/kg body weight, which are equivalent to 12 to 30 ppt or ng/kg of 2,3,7,8-TCDD in the diet. Abortion and weight loss were reported in rhesus monkeys (*Macaca mulatta*) at dietary levels as low as 50 ppt 2,3,7,8-TCDD (about 0.0017 ug/kg body weight daily) after 7 to 29 months. However, comparatively high dosages (200 ppt in diets equivalent to 0.0095 ug/kg body weight daily) could be tolerated by monkeys for short periods (3X weekly for 3 weeks) with no adverse effects on reproduction. Higher dose levels for extended periods (i.e., 500 ppt in diets equivalent to about 0.011 ug/kg body weight daily for 9 months) caused death (63%) or, among survivors, abortion, chloracne, nail loss, scaly and dry skin, and progressive weakness. Most treated monkeys remained fairly alert to external stimuli until just prior to death. On removal from the 500 ppt 2,3,7,8-TCDD diet and transfer to an uncontaminated diet, a severely affected monkey became pregnant and gave birth to a well-developed infant after an uneventful gestation. This suggests that some 2,3,7,8-TCDD damage effects are not permanent.

Androgenic deficiency in male rats given a single oral dose of 15 ug 2,3,7,8-TCDD/kg BW was evident as early as 2 days posttreatment, with persistence up to 12 days. These deficiencies may account for male reproductive pathology and dysfunction in rats treated with overtly toxic doses of TCDD. Findings included depression in plasma testosterone concentrations, as well as decreased weight of seminal vesicles (by 68%), ventral prostate gland (by 48%), testes, and epididymis (Moore et al. 1985).

Accumulation of 2,3,7,8-TCDD is reported in the liver of rats during lifetime exposure to diets containing 0.022 ug 2,3,7,8-TCDD/kg (Newton and Snyder 1978), or when administered orally at 0.01 ug/kg body weight once a week for 45 weeks (Cantoni et al. 1981). Liver residues of rats fed 2,3,7,8-TCDD were 0.54 ug/kg, or about 25X dietary levels; livers of rats dosed orally contained 1.05 ug/kg, or about 2.3X the total dose received on a unit weight basis.

Unlike toxicity, elimination rates of accumulated 2,3,7,8-TCDD were within a relatively narrow range. The estimated retention times of 2,3,7,8-TCDD in small laboratory mammals (rats, mice, guinea pigs, and hamsters) extended from 10.8 to 30.2 days for 50% elimination and seemed to be little influenced by species, concentration administered, duration of dose, or route of administration (Blair 1973; Olson et al. 1980b; NRCC 1981; Koshakji et al. 1984).

Histopathological effects have been reported in rabbits and horses poisoned by 2,3,7,8-TCDD. Rabbits surviving exposure to an industrial accident in Seveso, Italy, in which 2,3,7,8-TCDD was released, had edema, hemorrhagic tracheitis, pleural hemorrhage, and dystrophic lesions of hepatic tissue (Fanelli et al. 1980b). Horses from Missouri that died after waste oil contaminated with 2,3,7,8-TCDD was applied as a dust control agent in riding arenas had liver lesions, skin hyperkeratosis, gastric ulcers, and lung and kidney lesions (Kimbrough 1984). Since 2,3,7,8-TCDD is an extremely potent porphyrogenic agent, it is probable that these animals also exhibited porphyria, a condition characterized by fragility of the skin, photosensitivity, and accumulation of porphyrins in the liver (Cantoni et al. 1981).

Teratogenic and fetotoxic effects of 2,3,7,8-TCDD are well-documented in several species of animals (Marless et al. 1982; Kociba and Schwetz 1982a,b; Kimbrough 1984; Weber et al. 1985). Cleft palate in young mice was associated with daily dosages of 1.0 ug 2,3,7,8-TCDD per kg body weight in pregnant females (no-effect level at 0.1 ug/kg), and intestinal hemorrhage was found in sensitive strains of rats given daily dosages of 0.125 ug/kg body weight (no-effect level at 0.03 ug/kg) (Kociba and Schwetz 1982a,b). The 2,3,7,8-TCDD isomer has been studied for carcinogenic potential in rats and mice. There is a good correlation between carcinogenicity in both species and long-term ingestion of higher dose levels that induce toxicity. In rats, carcinomas in liver, pharynx, skin, lung, and thyroid were documented at daily dosages of 0.01 to 0.1 ug of 2,3,7,8-TCDD/kg body weight; comparable values for mice were 0.03 to 0.07 ug/kg body weight (Kociba and Schwetz 1982a,b). No response occurred at continuous daily dose levels of 0.001 to 0.0014 ug/kg body weight in rats and 0.001 to 0.03 in mice. Carcinogenic or cocarcinogenic effects were also induced by 1,2,3,6,7,8-hexa CDD and 1,2,3,7,8,9-hexa CDD, but only at higher dose levels (Rappe 1984). It appears that 2,3,7,8-TCDD has

a greater effect on growth, survival, and reproduction of animals than on tumor formation.

Interaction effects of PCDDs with other polychlorinated compounds or mixtures are not extensively documented. For example, certain polychlorinated hexachlorobiphenyls (PCBs) have a low toxic potency to induce cleft palate deformities in mice (Birnbaum et al. 1985). However, mixtures of 2,3,7,8-TCDD and 2,3,4,5,3',4' hexachlorobiphenyl resulted in a 10-fold increase in incidence of cleft palate in mice. Thus, the toxicity of compounds such as 2,3,7,8-TCDD may be enhanced by compounds of relatively low acute toxicity such as selected PCBs. Birnbaum et al. (1985) concluded that the widespread environmental occurrence of such combinations suggests a need for further evaluation of the mechanism of this interaction.

CURRENT RECOMMENDATIONS

At present, there are no criteria or standards promulgated for any of the 75 PCDD isomers, by any regulatory agency, for the protection of sensitive species of wildlife and aquatic organisms. Data are scarce or missing on the distribution and upper limits of background levels of PCDDs in natural resources, on the identification of fish and wildlife resources potentially at risk, on the relative importance of PCDD sources, and on the comparative toxicities of various PCDDs to fish and wildlife, especially reproductive and immunosuppressive toxicities (NRCC 1981). A similar situation exists for human health protection, except for the 2,3,7,8-TCDD isomer.

For protection of human health, concentrations of 2,3,7,8-TCDD (in ppt fresh weight) in fish muscle (and presumably other food items) considered acceptable are 10 in New York State (Kleopfer and Zirschky 1983), 20 in Canada (Kleopfer and Zirschky 1983), and 25 in other States within the U.S., according to the U.S. Food and Drug Administration (Stolzenburg and Sullivan 1983). Food items containing more than 50 ppt are considered unsafe for human consumption, but fish fillets containing between 25 and 50 ppt of 2,3,7,8-TCDD may be eaten once weekly by occasional consumers of fish, and twice monthly for those who eat contaminated fish year round (Stolzenburg and Sullivan 1983). It is not known at this time whether residues of 10 to 50 ppt (or higher) of 2,3,7,8-TCDD in fish flesh represents an unacceptable risk to the growth, survival, reproduction, metabolism, or behavior of the teleost, or to its predators; clearly, this is a high priority research topic.

For protection of aquatic life, it is conservatively estimated that water levels of 2,3,7,8-TCDD should not exceed 0.01 ppt as judged by laboratory studies with freshwater teleosts. The highest 2,3,7,8-TCDD concentration tested to date which has no measurable adverse effect on freshwater fish is 0.01 ppt (Miller et al. 1979). The next highest concentration tested, 0.1 ppt, was associated with fin disease in guppies (Miller et al. 1979) and reduced growth of northern pike (Helder 1981).

Diets containing up to 10 or 12 ppt of 2,3,7,8-TCDD may prove to be nonhazardous to birds and other wildlife, as judged by the results of laboratory studies with rats, monkeys, and chickens, and by the recommendations of New York State for human health protection. Higher dietary levels of 12 to 30 ppt of 2,3,7,8-TCDD (equivalent to about 1.0 ng/kg body weight daily) are not harmful to rats, based on the results of a 3-generation study (McNulty 1977; Murray et al. 1979). However, domestic chickens are relatively sensitive, with adverse effects recorded at daily dietary levels equivalent to almost 1.0 ng/kg body weight (NRCC 1981; Gilbertson 1983). Unacceptable dietary levels of 50 ppt (equivalent to 1.7 ng/kg body weight daily) are recorded for monkeys (Ramel 1978; Barsotti et al. 1979; NRCC 1981).

In the past, the major source of 2,3,7,8-TCDD in the environment was as a contaminant in phenoxy herbicides (such as 2,4,5-T; Silvex; 2,4-D; and Agent Orange), in hexachlorophene, and in other chlorophenol-type compounds. Concentrations of 2,3,7,8-TCDD in some of these products exceeded 60,000 ppb. However, this situation has been largely corrected by new manufacturing processes and by increasingly stringent Federal regulations (NRCC 1981; Choudhary et al. 1983; Stolzenburg and Sullivan 1983; NIOSH 1984; Rappe 1984). For example, 2,3,7,8-TCDD level in 2,4,5-T has decreased from 60,000 ppb in 1957 to 2,000 ppb in 1965 as a result of new manufacturing processes, and it was limited to 500 ppb in 1970 by the Canadian Federal Government. In 1970, the U.S. Department of Defense halted the spraying of Agent Orange. In 1972, the U.S. Food and Drug Administration banned the use of hexachlorophene in nonprescription soaps and deodorants. In 1978, 7 of 14 major producers of 2,4,5-T no longer manufactured this product, and the remainder claimed that their products contained less than 100 ppb of 2,3,7,8-TCDD. In 1979, production of 2,4,5-T and Silvex ceased in the United States, although stockpiles of both are still being distributed and permitted for use on rice fields, sugarcane fields, orchards, fence rows, vacant lots, and lumber yards. In 1982, the EPA required some industries to certify that chlorophenol-type compounds were no longer used as slime control agents. On

October 18, 1983, EPA published its intent to cancel the registration of pesticide products containing 2,4,5-T and Silvex, and to prohibit the transfer, distribution, sale, or importation of any unregistered product containing 2,4,5-T, Silvex, or their derivatives (NIOSH 1984).

At present, burning or heating of commercial and purified chlorophenates, and pyrolysis of polychlorinated biphenyls contaminated with trichlorobenzenes can result in the production of 2,3,7,8-TCDD and other PCDDs (NIOSH 1984). These sources together with discharges from various municipal and industrial incinerators of chlorinated compounds probably constitute the largest source of PCDDs in the environment today. In 1983, the U.S. Environmental Protection Agency proposed to monitor 2,3,7,8-TCDD in the environment (Stolzenburg and Sullivan 1983). Specific goals of the monitoring program include: determination of 2,3,7,8-TCDD concentrations in soils and biota, with emphasis on geographic areas where PCDDs may have been manufactured, used, or stored--and where concentrations may be in excess of 1,000 ppt; monitoring of industrial and municipal incinerators for TCDD emissions; and establishment of background levels for PCDDs in areas where these compounds are not expected to occur in high levels. It seems that information is also needed on the toxicological interactions of groups of polychlorinated chemicals (such as certain biphenyls, biphenylenes, and dibenzofurans) known to be isosteric with 2,3,7,8-TCDD and which frequently coexist with 2,3,7,8-TCDD in environmental samples. Acquisition of these data should provide the basis of a risk assessment analysis for dioxin and fishery and wildlife resources.

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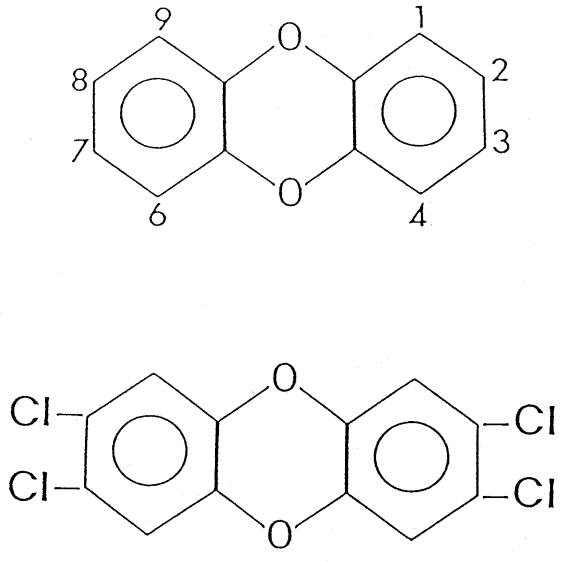

Figure 1. Upper. Numbering system used for identification of individual PCDD isomers. Lower. The isomer 2, 3, 7, 8-tetrachlorodibenzo-*para*-dioxin (2, 3, 7, 8-TCDD).