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EPA **Fact Sheet**

Polychlorinated Dibenzo-p-dioxins and Related Compounds Update: Impact on Fish Advisories

Dioxins are a group of synthetic organic chemicals that contain 210 structurally related individual chlorinated dibenzo-p-dioxins (CDDs) and chlorinated dibenzofurans (CDFs). For the purposes of this fact sheet, the term "dioxins" will refer to the aggregate of all CDDs and CDFs. These chemically related compounds vary in their physical and chemical properties and toxicity. Dioxins have never been intentionally produced, except in small quantities for research. They are unintentionally produced as byproducts of incineration and combustion processes, chlorine bleaching in pulp and paper mills, and as contaminants in certain chlorinated organic chemicals. They are distributed widely in the environment because of their persistence. Dioxin exposure is associated with a wide array of adverse health effects in experimental animals, including death. Experimental animal studies have shown toxic effects to the liver, gastrointestinal system, blood, skin, endocrine system, immune system, nervous system, and reproductive system. In addition, developmental effects and liver cancer have been reported. Skin rashes and a severe form of acne have been documented in humans following exposure to relatively high doses; however, other effects of dioxin exposure in humans are not well understood. There are some studies that suggest liver damage and cancer can occur in people exposed to dioxins. The available data do not provide sufficient evidence that dioxins are genotoxic; however dioxins are classified by EPA as probable human carcinogens (Group B2). As of 1998, 19 states have issued 59 fish advisories for dioxins. These advisories inform the public that dioxins have been found in local fish at levels of public health concern. State advisories recommend either limiting or avoiding consumption of certain fish from specific waterbodies or, in some cases, from specific waterbody types (e.g., all freshwater lakes or rivers).

The purpose of this fact sheet is to summarize current information on sources, fate and transport, occurrence in human tissues, range of concentrations in fish tissue, fish advisories, fish consumption limits, toxicity, and regulations for dioxins. The fact sheets also illustrate how this information may be used for developing fish consumption advisories. An electronic version of this fact sheet and fact sheets for mercury, PCBs, and toxaphene are available at **http://www.epa.gov/OST/fish**. Future revisions will be posted on the web as they become available.

Sources of Dioxins in the Environment

Dioxins are formed primarily as unintentional by-products of incomplete combustion and various chemical processes. Although forest fires and possibly other natural sources may produce dioxins, these sources are small compared with anthropogenic sources. Dioxins are produced in small quantities during the combustion of fossil fuels, wood, municipal and industrial waste. Bleaching processes which were used in pulp and paper production produced dioxins, and they occur as contaminants during the production of some chlorinated organic chemicals, such as chlorinated phenols.

Currently, the major environmental source of dioxins is incineration. Dioxins have been detected in soil, surface water, sediment, plants, and animal tissue in all regions of the earth.

Dioxins are highly persistent in the environment with reported half-lives in soil and sediment ranging from months to years. Because dioxins have very low solubility in water and low volatility, most are contained in soil and sediments that serve as environmental reservoirs from which dioxins may be released over a long period of time. Volatilization and particle resuspension from environmental reservoirs are probably important contributors to global distribution.

Fate and Transport of Dioxins

The global cycling of dioxins consists of particle resuspension and evaporation from soils and surface waters to the atmosphere and redeposition back to land and surface water. However, volatilization is slow. Adsorption to sediments and bioaccumulation are the primary loss mechanisms from surface water. Photolysis is an important transformation process for dioxins that are exposed to sunlight.

Dioxins in surface waters and sediments are accumulated by aquatic organisms and bio-accumulated through the aquatic food chain. Concentrations of dioxins in aquatic organisms may be hundreds to thousands of times higher than the concentrations found in the surrounding waters or sediments. Bioaccumulation factors vary among the congeners and generally increase with chlorine content up through the tetra congeners and then generally decrease with higher chlorine content. For example, experimental bioconcentration factors (BCFs) for fish exposed to 2,3,7,8-TCDD in water ranged from 37,900 to 128,000; whereas, BCFs for OCDD ranged from 34 to 2,226. In the presence of both water and sediment, BCFs were reduced by 15% to 82% (compared to water only experiments) for various congeners, with the greatest reduction associated with OCDD.

Six dioxin congeners and nine dibenzofuran congeners were measured in fish tissue and shellfish samples in the EPA's National Study of Chemical Residues in Fish (NSCRF). The various dioxin congeners were detected at 32% to 89% of the 388 sites surveyed, while the furan congeners were detected at 1% to 89% of the 388 sites surveyed. As shown in Table 1, the dioxin/furan congeners detected at more than 50% of the sites included four CDD compounds and three CDF compounds; 1,2,3,4,6,7,8 HpCDD (89%), 2,3,7,8 TCDF (89%), 2,3,7,8 TCDD (70%), 1,2,3,6,7,8 HxCDD (69%), 2,3,4,7,8 PeCDF (64%), 1,2,3,4,6,7,8 HpCDF (54%), and 1,2,3,7,8 PeCDD (54%). The most frequently detected CDD/CDF compounds (1,2,3,4,6,7,8-HpCDD and 2,3,7,8-TCDF) were also detected at the highest concentrations: 249 ppt and 404 ppt, respectively. The mean concentrations of these two compounds were considerably lower, at 10.5 and 13.6 ppt, respectively. The dioxin congener 2,3,7,8-TCDD, believed to be the most toxic to mammals, was detected at 70% of the sites at a maximum concentration of 204 ppt and a mean concentration of 6.8 ppt.

Table 1. Maximum and Average Concentrations of Dioxins Reported in Fish[a]

Chemical	Percent of Sites Where Detected	Maximum Concentration[b] (pg/g)	Mean Concentration[b] (pg/g)
Dioxins			
1,2,3,4,6,7,8-HpCDD	89	249	10.5
2,3,7,8-TCDD	70	204	6.89
1,2,3,6,7,8-HxCDD	69	101	4.3
1,2,3,7,8-PeCDD	54	54	2.38
1,2,3,7,8,9-HxCDD	38	24.8	1.16
1,2,3,4,7,8-HxCDD	32	37.6	1.67
Furans			
2,3,7,8-TCDF	89	404	13.6
2,3,4,7,8-PeCDF	64	56.4	3.06
1,2,3,4,6,7,8-HpCDF	54	58.3	1.91
1,2,3,4,6,7,8-PeCDF	47	120	1.71
1,2,3,4,7,8-HxCDF	42	45.3	2.35
2,3,4,6,7,8-HxCDF	32	19.3	1.24
1,2,3,6,7,8-HxCDF	21	30.9	1.74
1,2,3,4,7,8,9-HpCDF	4	25.7	1.24
1,2,3,7,8,9-HxCDF	1	0.96	1.22

[a]Species included freshwater, estuarine, and marine finfish; and a small number of marine shellfish.
[b]Concentrations reported on a wet weight basis (parts per trillion).
Source: U.S. EPA, 1992.

Potential Sources of Exposure and Occurrence in Human Tissues

Dietary intake is the most important source of exposure to dioxins for the general population. Meat, dairy products, fish and other seafood products, contribute more than 90% of the daily intake for the general population.

Individuals who may be exposed to higher than average levels of dioxins include those who ingest food containing higher concentrations of dioxins than are found in the commercial food supply. These groups include recreational and subsistence fishers who routinely consume large amounts of locally caught fish; subsistence hunters who routinely consume the meat and organ tissues of marine mammals, and subsistence farmers living in a contaminated area who consume farm-raised beef and dairy products. In addition, persons who live near industrial or municipal incinerators, and persons who live near hazardous waste sites contaminated with dioxins could be exposed to higher levels of dioxins than the general population.

Analytical methods can be used to measure dioxins in blood, lipid tissues, and breast milk.

Fish Advisories

The states have primary responsibility for protecting their residents from the health risks of consuming contaminated noncommercially caught fish. They do

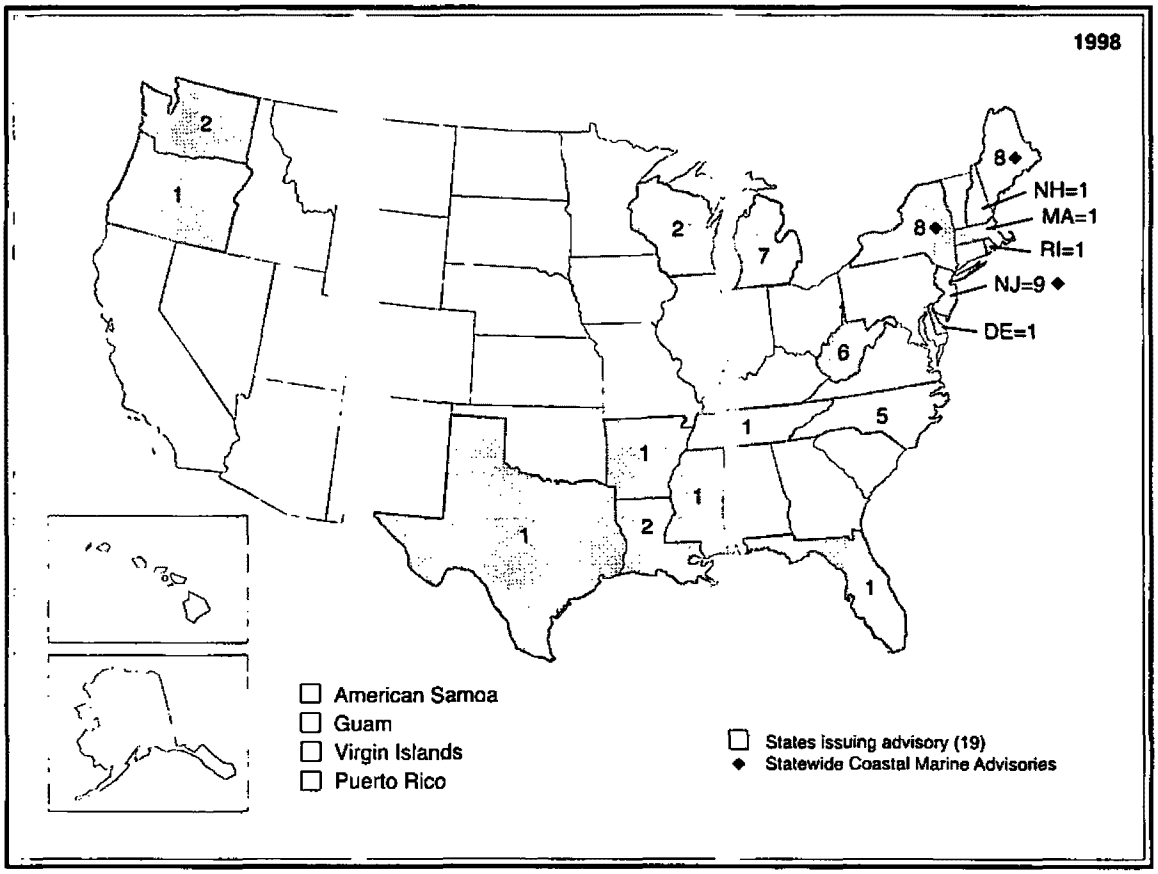
this by issuing consumption advisories for the general population, including recreational and subsistence fishers, as well as sensitive subpopulations (such as, pregnant women/fetus, nursing mothers, and children). These advisories inform the pubic that high concentrations of chemical contaminants have been found in local fish. The advisories recommend either limiting or avoiding consumption of certain fish from specific waterbodies or, in some cases, from specific waterbody types (such as lakes or rivers).

General recommendations regarding food preparation, such as trimming the fat and skinning the fish prior to cooking, also may be included in general advisory information. Lipophilic chemicals, such as dioxins, accumulate mainly in fatty tissues (belly flap, lateral line, subcutaneous and dorsal fat, dark muscle, gills, eye, brain, and internal organs). Therefore, removal of internal organs and skin and trimming the fat before cooking will decrease exposure. In addition, various cooking procedures can also reduce the amount of dioxins consumed (see Appendix section "Dose Modification Due to Food Preparation and Cooking" of EPA's *Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories*, Volume 2).

As of December 1998, dioxins/furans were the chemical contaminants responsible, at least in part, for the issuance of 59 fish consumption advisories by 19 states (see Figure 1). Only 2% of all advisories issued in the United States are a result of dioxin/furan contamination in fish and shellfish. The number of advisories for dioxins/furans fluctuated between 54 and 65 from 1993 through 1998. The maximum number of advisories for dioxin were in effect in 1997. Dioxins/furans are one of several chemical contaminants for which fish advisories have been rescinded by several states, in part because many pulp and paper mills have changed their bleach kraft processes, thereby reducing effluent levels of dioxins and furans.

The decline in the number of dioxin advisories in 1998 can be attributed primarily to the rescinding of advisories in three states (Arkansas, Michigan, and Virginia).

Figure 1. Fish Advisories for Dioxins.



It should also be noted that no states currently have statewide advisories in effect for dioxins/furans in their freshwater lakes and/or rivers. Three states (Maine, New York, and New Jersey) have statewide dioxin/furan advisories in effect for their coastal marine waters. To date, 65% of the 59 dioxin advisories in effect have been issued by the following five states; New Jersey (9), New York (8), Maine (8), West Virginia (6), and North Carolina (5).

Fish Consumption Limits—Table 2 shows the recommended monthly fish consumption limits for dioxins/furans for fish consumers based on EPA's default values for risk assessment parameters. . Consumption limits have been calculated as the number of allowable fish meals per month, based on the ranges of dioxins/furans in the consumed fish tissue. The following assumptions were used to calculate the consumption limits:

- Consumer adult body weight of 72 kg
- Average fish meal size of 8 oz (0.227 kg)
- Time-averaging period of 1 month (30.44d)
- EPA's cancer slope factor for dioxin (1.56×10^5 per mg/kg-d) from EPA's Health Effects Assessment Summary Tables (U.S. EPA, 1997)
- Maximum acceptable cancer risk level (10^{-5} over a 70-year lifetime)

For example, when dioxin levels in fish tissue are 0.1 ppq, then four 8-oz. meals per month can safely be consumed.

For sensitive populations, such as pregnant women, nursing mothers, and young children, some states have issued either "no consumption" advisories or "restricted consumption" advisories for dioxins/furans. Additional information on calculating specific limits for these sensitive populations is available in *EPA's Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories,* Volume 2, Section 3.

Toxicity of Dioxins

Pharmacokinetics—Dioxins are absorbed through the gastrointestinal tract, respiratory tract, and skin and distributed throughout the body. Absorption is congener-specific, with decreased absorption of hepta- and octa-congeners compared with dioxins with fewer chlorines. Because of their lipophilic nature, dioxins tend to accumulate in fat and the liver. Dioxins are slowly metabolized by oxidation or reductive dechlorination and conjugation, and the major routes of excretion are the bile and feces. Reported half lives in the body range from 5 to 15 years. Small amounts may be eliminated in the urine.

Table 2. Monthly Fish Consumption Limits for Dioxins/Furans

Risk Based Consumption Limit	Cancer Health Endpoints
Fish meals/month	Fish Tissue Concentrations, (ppq[b],-TEQ)
16	>0.019 - 0.039
12	>0.039 - 0.052
8	>0.052 - 0.077
4	>0.077 - 0.15
3	>0.15 - 0.21
2	>0.21 - 0.31
1	>0.31 - 0.62
0.5	>0.62 - 1.2
None (<0.5)[a]	>1.2

[a]None = No consumption recommended.
[b]ppq = parts per quadrillion on a wet weight basis.
Note: In cases where >16 meals per month are consumed, refer to EPA's *Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories*, Volume 2, Section 3 to determine safe consumption limits.

The current evidence indicates that metabolites are less toxic than the parent compounds.

The predominant forms retained in the tissues are the 2,3,7,8-substituted congeners. Tissue deposition depends on the route of exposure, congeners present, dose, and age. Based on a study of a human volunteer, about 87% of a single dose of dioxins dissolved in corn oil was absorbed, and about 90% of the absorbed dose was distributed to fatty tissue.

The half-lives for various dioxin congeners in humans are reported to range from 2.9 to 26.9 years. Some studies suggest longer half-lives in individuals with higher levels of body fat.

Dioxins induce mixed function oxidases and hepatic aryl hydrocarbon hydroxylase (AHH). Dioxins bind to a cytosolic protein, the Ah receptor, which regulates the synthesis of a variety of proteins. The Ah receptor has been found in many human tissues, including the lung, liver, placenta, and lymphocytes. Although evidence indicates that the Ah receptor is involved in many biological responses to dioxins, the diversity of biological effects observed cannot be accounted for by characteristics of this receptor alone.

Acute Toxicity—The LD_{50} values for dioxins vary over several orders of magnitude depending on the congener, species, and strain of animal tested. The most toxic congener is 2,3,7,8-TCDD, with LD_{50} values ranging from 22 to 340 mg/kg in various strains of laboratory rats. Guinea pigs are the most sensitive species tested (LD_{50} values from 0.6 to 2.1

mg/kg), and hamsters are the most resistent (LD_{50} values from 1,157 to 5051 mg/kg). In all studies, the animals died from a pronounced wasting syndrome characterized by weight loss and depletion of body fat that lasted 1 to 6 weeks. By contrast, laboratory animals have survived acute doses of 1 to 4 g/kg of 2,7-DCDD and OCDD. Single exposures to dioxins have also affected the heart, liver, kidneys, blood, stomach, and endocrine systems of laboratory animals. No human deaths have been directly associated with exposure to dioxins.

Chronic Toxicity—In animal studies, numerous effects have been documented, including hepatic, gastrointestinal, hematological, dermal, body weight changes, endocrine, immunological, neurological, reproductive, and developmental effects. Most of the studies have involved oral exposure. Despite the variety of adverse effects observed in animals exposed to dioxins, adverse health effects in humans have generally been limited to highly exposed populations in industrial factories or following chemical accidents and contamination episodes. The adverse human health effect most commonly associated with high-level exposure to dioxin-like agents is the skin disease chloracne, a particularly severe and prolonged acne-like skin disorder. Adverse human health effects were also noted following consumption of heated rice oil contaminated with PCBs and CDFs. Conclusive evidence of other adverse human health effects at lower dioxin exposure levels is generally lacking because of incomplete exposure data, concomitant exposure to other compounds, and/or small numbers of study participants. Some epidemiological studies have suggested that dioxins may cause immuno-suppression, respiratory effects, cardiovascular effects, and liver effects in humans.

Developmental Toxicity—Dioxins have been shown to cause adverse developmental effects in fish, birds, and mammals at low exposure levels. Several studies in humans have suggested that dioxin exposure may cause adverse effects in children and in developing fetuses. These include effects on the skin, nails, and meibomian glands; psychomotor delay; and growth retardation. However, study limitations, including lack of control for confounding variables, and deficiencies in the general areas of exposure make it difficult to interpret these results. Overall, the human data are inconclusive; however, the animal data suggest that developmental toxicity is a concern.

In mammals, learning behavior and development of the reproductive system appear to be among the most sensitive effects following prenatal exposure. In general, the embryo or fetus is more sensitive than the adult to dioxin-induced mortality across all species.

Mutagenicity—The majority of mutagenicity assays of dioxins have been negative. An increased incidence of chromosomal aberrations was found in fetal tissue but not in maternal tissue in a group of women exposed to dioxins following an industrial accident in Italy; however, cases treated for chloracne did not have an increased incidence of chromosomal aberrations. Animal studies also are inconclusive. The available data do not provide strong evidence that dioxins are genotoxic.

Carcinogenicity—Dioxins are classified by EPA as Group B2 (sufficient evidence in animals, insufficient evidence in humans) when considered alone and Group B1 (sufficient evidence in animals, limited evidence in humans) when considered in association with chlorophenols and phenoxyherbicides. This is based on studies that have found multiple-site sarcomas and carcinomas in rats and mice exposed to various dioxin mixtures and congeners. Epidemiological studies suggest an increased incidence of cancer mortality (all types of cancers combined) and of some specific cancers (soft-tissue sarcoma, non-Hodgkin's lymphoma, respiratory tract cancer, and gastrointestinal cancers). In addition, there is evidence that 2,3,7,8-TCDD acts as a tumor promoter. As with all epidemiological studies, it is very difficult to obtain clear unequivocal results because of the long latency period required for cancer induction and the multiple confounders arising from concurrent exposures, lifestyle differences, and other factors. The currently available evidence suggests that dioxins may cause cancer in humans.

Summary of EPA Health Benchmarks

- Carcinogenicity: 1.56×10^5 per mg/kg-d (U.S. EPA, 1997)

Special Susceptibilities—There is evidence that children are more susceptible than adults to the dermal toxicity of dioxins. Animal data suggest that the developing reproductive, immune, and nervous systems of the fetus are sensitive to dioxin toxicity.

Interactive Effect—Environmental exposure to dioxins includes various mixtures of CDDs and CDFs. These mixtures of dioxin-like chemicals cause multiple effects that vary according to species susceptibility, congeners present, and interactions. Risk assessment of these complex mixtures is based on the assumption that effects are additive, and there is some experimental evidence to support this. However, there also is evidence that some interactions may result in inhibition and others in potentiation. Co-treatment of mice with various commercial PCB mixtures (Aroclors) and 2,3,7,8-TCDD has resulted in inhibiting some of the Ah receptor mediated responses. An increased incidence of cleft palate was reported when mice were treated with both 2,3,7,8-TCDD and a hexachlorobiphenyl compared with treatment with

2,3,7,8-TCDD alone. Both synergistic and antagonistic responses have been observed following co-exposure of 2,3,7,8-TCDD with other chemicals as well.

Critical Data Gaps—The following data gaps have been identified for dioxins: inhalation and dermal toxicity studies; toxicity studies of dioxin compounds other than 2,3,7,8-TCDD; continued medical surveillance of individuals with known past high exposures to dioxins; mechanistic studies; immune function tests in human cohorts; neurological tests in ongoing prospective studies of humans; congner-specific human toxicokinetic studies to better assess human dosimetry; further studies to identify potential biomarkers for exposure and effects; and additional studies to support exposure modeling.

EPA Regulations and Advisories

- Maximum Contaminant Level in drinking water = 3E-08 mg/L
- Water Quality Criteria:
  - Human health (ingesting water and organisms) = 1.3E-08 µg/L
  - Human health (ingesting organisms only) = 1.4E-08 µg/L
- Listed as a hazardous air pollutant under Section 112 of the Clean Air Act
- Reportable quantity = 1 lb
- Listed as a hazardous substance

Sources of Information

ATSDR (Agency for Toxic Substances and Disease Registry). 1998. *Toxicological Profile for Chlorinated Dibenzo-p-dioxins.* U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA.

U.S. EPA (Environmental Protection Agency). 1992. *National Study of Chemical Residues in Fish, Volume I.* Office of Science and Technology, Washington, DC. EPA 823-R-92-008a.

U.S. EPA (Environmental Protection Agency). 1994. *Health Assessment Document for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCPD) and Related Compounds* (External Review Draft) (3 volumes). Office of Research and Development, Washington, DC. (EPA/600/BP-92100/c).

U.S. EPA (Environmental Protection Agency). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Office of Research and Development, Office of Emergency and Remedial Response, Washington, DC. EPA-540-R-97-036.

U.S. EPA (Environmental Protection Agency). 1999. Fact Sheet: Update: National Listing of Fish and Wildlife Advisories. Office of Water. Washington, DC. EPA-823-F-99-005.

U.S. EPA (Environmental Protection Agency). 1999. *Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories. Volume 2, 3rd Edition,* Risk Assessment and Fish Consumption Limits. Office of Water. Washington, DC. EPA 823-B-97-009.

Zabik, M.E. and M.J. Zabik. 1995. Tetra-chlorodibenzo-p-dioxin residue reduction by cooking/processing of fish fillets harvested from the Great Lakes. *Bulletin of Environmental Contamination and Toxicology.* 55:264-269.

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The 1998 update of the database *National Listing of Fish and Wildlife Advisories* is available for downloading from the following Internet site: http://www.epa.gov/OST