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Fact Sheet

Toxaphene Update: Impact on Fish Advisories

Toxaphene is the tradename for an organochlorine pesticide that is comprised of a mixture of at least 670 chlorinated camphenes. Toxaphene was first introduced in 1947 and was probably the most heavily used pesticide in the United States during the 1970s after DDT was banned. In the United States, toxaphene was banned for most uses in 1982 and all uses were banned in 1990. However, due to its relatively long half-life, toxaphene persists in the environment. The soil half-life is approximately 1 to 14 years. Toxaphene can enter waterbodies from soil runoff and can also volatilize and be transported to waterbodies via the atmosphere. Toxaphene absorbed by organisms accumulates in fatty tissues and has been shown to affect the central nervous system and the liver. EPA has classified toxaphene as a probable human carcinogen (Group B2). As of 1998, four states have issued a total of six fish advisories for toxaphene. These advisories inform the public that high concentrations of toxaphene 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 toxaphene. 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 dioxins/furans, mercury, and PCBs, are available at **http://www.epa.gov/OST/fish**. Future revisions will be posted on the web as they become available.

Sources of Toxaphene in the Environment

In the United States, all uses of toxaphene were banned in 1990. As a result, no entries for toxaphene are reported in EPA's Toxic Chemical Release Inventory (TRI). In the past, toxaphene entered the environment as an insecticide. Toxaphene entered surface waters through runoff from rain, by direct application to lakes as a pesticide, by wastewater release from manufacturing facilities, and through activities related to disposal of waste pesticides. Toxaphene adsorbs to soil particles, and may enter waterbodies in this form. Virtually all of the toxaphene in waterbodies is in the particulate and sediment fractions. Toxaphene was also applied directly to soil as an insecticide for agricultural crops.

Fate and Transport of Toxaphene

Once toxaphene enters the environment, it breaks down very slowly. Therefore, even though the use of toxaphene has been banned in the United States for more than 10 years, exposures may still occur. After releases to surface water or soils or application to crops, the more volatile components of toxaphene readily partition to the atmosphere where they persist. The atmosphere is the most important environmental medium for the transport of toxaphene and it can also be transported to surface water and soil by wet and dry deposition. As a result, toxaphene can be carried far from its original release site. In soil, toxaphene binds to soil particles; therefore, leaching to ground water is not of great concern. In surface water, the toxaphene that does not volatilize is eventually deposited in sediments.

Toxaphene can bioconcentrate in the tissues of aquatic organisms and may also be biomagnified in the aquatic food chain. In 1984 and 1985, the U.S. Fish and Wildlife Service collected 321 composite samples of whole fish from 112 stations nationwide as part of the National Contaminant Biomonitoring Program (NCBP). Toxaphene was detected in freshwater fish at 69% of 112 stations sampled in the NCBP study. Maximum and geometric mean tissue concentrations of toxaphene in 1984 were 8.2 and 0.14 ppm (wet weight), respectively. An analysis of all 1984-1985 data from the NCBP study on toxaphene in bottom-feeding and predatory fish species showed there was no significant difference in residues in these two trophic groups of fish. Mean tissue concentrations of toxaphene were 0.19 ± 0.63 and 0.17 ± 0.35 ppm, respectively, for bottom feeders and predator species. Results of a more recent study show the range of total toxaphene concentrations (wet weight) measured in various fish species in the Great Lakes from 1992-1994 (see Table 1).

Table 1. Mean Concentrations of Toxaphene Reported in Great Lakes Fish[a] (1992-1994)

Lake	Species	Mean Concentration[b] (ppm)	Standard Error of Mean (ppm)
Superior	Lake trout	4.9	1.4
Michigan	Lake trout	1.5	0.3
Huron	Lake trout	2.4	0.5
Ontario	Lake trout	0.54	0.2
Erie	Walleye	0.13	0.02
Superior	Smelt	0.16	0.04
Michigan	Smelt	0.059	0.006
Ontario	Smelt	0.067	0.02

[a] Species included only freshwater finfish.
[b] Concentrations are reported on a wet weight basis.
Source: Glassmeyer et al., 1997.

Potential Sources of Exposure and Occurrence in Human Tissues

Because the use of toxaphene was banned in the United States, potential sources of exposure are limited. Low-level exposures may occur in the general population through ingestion of contaminated food. Because toxaphene may accumulate in fish and shellfish, persons who consume large quantities of these foods may be at greater risk of higher level exposure than the general population. Additionally, persons who eat large quantities of wild game from areas where toxaphene was heavily used as a pesticide may also be at higher risk. An additional source of potential exposure is contact with toxaphene-contaminated media near toxaphene waste disposal sites. Before toxaphene was banned, major sources of exposure resulted during its manufacture and use as an insecticide. These exposures were primarily dermal or by inhalation.

Analytical methods can be used to measure toxaphene in blood, urine, breast milk, and body tissues. Similar to PCBs, toxaphene analysis can be conducted for specific congeners using high resolution spectrometry or gas chromatography with electron-capture negative ionization. However, there currently are no standard methods for these analyses. At this time, EPA's Office of Water recommends analysis of total toxaphene until further development of congener-specific analyses.

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 public that high concentrations of chemical contaminants, such as toxaphene, 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).

As of December 1998, toxaphene was the chemical contaminant responsible, at least in part, for the issuance of a total of six fish consumption advisories by four states: Arizona (3), Georgia (1), Oklahoma (1), and Texas (1) (see Figure 1). This contaminant accounts for less than 0.2 % of all advisories issued in the United States. The number of advisories for toxaphene has remained relatively unchanged from 1993 through 1998. Currently, no states have issued statewide or regionwide advisories for toxaphene in their freshwater lakes and/or rivers or in their coastal marine waters.

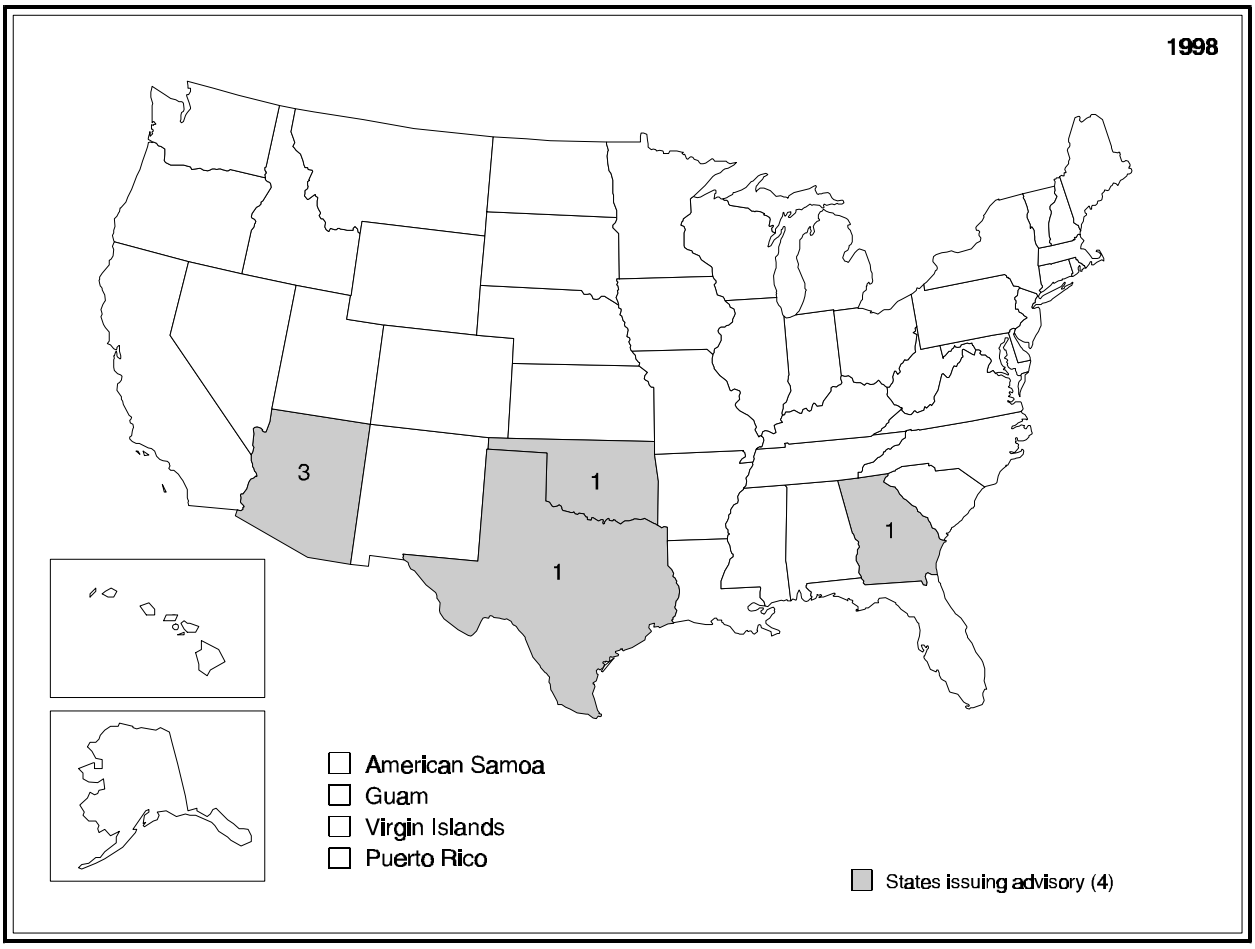
Fish Consumption Limits—Table 2 shows the recommended monthly fish consumption limits for toxaphene for fish consumers based on EPA's default

Table 2. Monthly Fish Consumption Limits for Toxaphene

Risk-Based Consumption Limit	Noncancer Health Endpoints	Cancer Health Endpoints
Fish Meals/Month	Fish Tissue Concentrations (*ppm*, wet weight)	Fish Tissue Concentrations (*ppm*, wet weight)
16	>0.075 - 0.15	>0.0027 - 0.0055
12	>0.15 - 0.2	>0.0055 - 0.0073
8	>0.2 - 0.3	>0.0073 - 0.011
4	>0.3 - 0.6	>0.011 - 0.022
3	>0.6 - 0.8	>0.022 - 0.029
2	>0.8 - 1.2	>0.029 - 0.044
1	>1.2 - 2.4	>0.044 - 0.088
0.5	>2.4 - 4.8	>0.088 - 0.18
None (<0.5)[a]	>4.8	>0.18

[a]None = No consumption recommended.
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 for methods to determine safe consumption limits.

Figure 1. Fish Advisories for Toxaphene.



values for risk assessment parameters. Consumption limits have been calculated as the number of allowable fish meals per month, based on the ranges of toxaphene 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 (30.44 d)
- EPA's reference dose for toxaphene (2.5×10^{-4} mg/kg-d) from EPA's Reference Dose Tracking Report (U.S. EPA, 1997)
- EPA's cancer slope factor for toxaphene (1.1 per mg/kg-d) from EPA's Integrated Risk Information System (U.S. EPA, 1999b)
- Maximum acceptable cancer risk level (10^{-5} over a 70-year lifetime).

For example, when toxaphene levels in fish tissue are 1 ppm, then sixteen 8-oz. meals per month (based on the noncancer health endpoint-EPA's reference dose) or a half an 8-oz. meal per month (based on the cancer health endpoint-EPA's cancer slope factor) can safely be consumed. EPA recommends using the more conservative of the two limits; for toxaphene, this is the consumption limit based on the cancer health endpoint. 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 toxaphene. Additional information on calculating specific limits for these sensitive populations is available in *EPAs Guidance for Assessing Chemical Contaminant Data for Use in Fish Advisories, Volume 2, Section 3.*

Toxicity of Toxaphene

Pharmacokinetics—Most of the components of toxaphene are rapidly degraded in mammals via dechlorination, dehydrodechlorination, and oxidation, primarily through the action of the mixed function oxidase system and other hepatic microsomal enzymes. Conjugation may occur but is not a major route of metabolism. Each component of toxaphene has its own rate of biotransformation, making the characterization of toxaphene pharmacokinetics complex. Some components of toxaphene are highly lipophilic and poorly metabolized; these components may accumulate in body fat.

Acute Toxicity—Acute high-level exposures to toxaphene and toxaphene-contaminated food have

resulted in death in adults and children with an estimated minimum lethal dose of 2 to 7 g, which is equivalent to 29 to 100 mg/kg for an adult male. LD_{50} values in rats were 80 mg/kg for females and 90 mg/kg for males. Transient liver and kidney effects and periods of memory loss have been observed in humans after single large oral exposures. In animals, the most sensitive organ is the liver. Toxicity to the central nervous system, kidneys, and adrenal glands has also been observed.

Chronic Toxicity—Chronic exposure to toxaphene may result in damage to the following organ systems: liver, kidney, adrenal, immunological, and neurological. Chronic exposure to toxaphene may cause hormonal alterations. A study on chronic exposure found increased levels of hepatic metabolism of the hormones estradiol and estrone and a decrease in their uterotropic action. Some adverse effects of toxaphene that do not occur with a single exposure may result from repeated exposure totaling a lower cumulative dose. Exposures at 0.06 mg/kg-d over 5 weeks caused adrenal hormone reductions, whereas a single dose of 16 mg/kg did not cause effects.

Developmental Toxicity—Women exposed to toxaphene after entering a field that had recently been sprayed with the chemical exhibited a higher incidence of chromosomal aberrations in cultured lymphocytes than did unexposed women. Dermal and inhalation uptake were the probable routes of exposure; however, the exposure was not quantified. Animal study results suggest that toxaphene does not interfere with fertility in experimental animals at the doses tested (up to 25 mg/kg-d).

Adverse developmental effects, including immunosuppressive and behavioral, were noted in experimental animals at levels below those required to induce maternal toxicity. Immunosuppression (reduction in macrophage levels, cell-mediated immunity, and humoral immunity) was observed in test animals exposed during gestation and nursing, as were alterations in kidney and liver enzymes and delayed bone development. Other adverse effects noted in offspring of maternally exposed animals included histological changes in the liver, thyroid, and kidney.

Toxaphene is known to be rapidly conveyed into breast milk after maternal exposure to the chemical. The half-life of toxaphene in milk has been estimated at 9 days.

As noted above, toxaphene accumulates in body tissue; consequently, exposure occurring prior to pregnancy can contribute to the overall maternal body burden and result in exposure to the developing individual. Therefore, it is necessary to reduce exposure to children and women with childbearing potential to reduce overall body burden. Depending on the timing and extent of an individual's prior exposure to toxophene, the outcome of that pregnancy may be affected even if exposure is reduced during pregnancy.

Children may be at greater risk for toxic effects caused by toxaphene because their immune systems are not fully developed until 10 to 12 years of age. Immunosuppressive effects have been demonstrated in animals after chronic exposure to toxaphene. These studies have also suggested that immature animals cannot detoxify a toxaphene mixture as efficiently as they can the single components of the mixture.

Mutagenicity—Changes in human genetic material have been noted in workers exposed to toxaphene. There are also numerous positive mutagenicity assays of toxaphene: the Ames test, sister chromatid exchange, chromosomal aberrations in toxaphene-exposed humans, and forward mutation assays. The implications of this for human germ cells are not known. One assay designed to assess the dominant lethal effects on implantations in mice yielded negative results. Some data suggest that the polar fraction of toxaphene may be more mutagenic than the nonpolar fraction.

Carcinogenicity—Toxaphene is classified as a probable human carcinogen (Group B2) by EPA based on oral studies in animals. No conclusive human epidemiological studies are available for toxaphene. Oral administration of toxaphene resulted in an increased incidence of hepatocellular carcinomas and neoplastic nodules in mice and thyroid tumors in rats.

Toxaphene has recently been observed to have estrogenic effects on human breast cancer estrogen-sensitive cells. Xenoestrogens have been hypothesized to have a role in human breast cancer. In addition to potential carcinogenic effects, toxaphene may also cause disruption of the endocrine system due to its estrogenic activity.

Summary of EPA Health Benchmarks

- Chronic Toxicity—Reference Dose: 2.5×10^{-4} mg/kg-d (U.S. EPA, 1997)
- Carcinogenicity: 1.1 per mg/kg-d (U.S. EPA, 1999b)

Special Susceptibilities—A protein-deficient diet may increase the toxicity of toxaphene approximately threefold based on an LD_{50} study in rats. Individuals with latent or clinical neurological diseases, such as

epilepsy or behavioral disorders, may be at higher risk for toxaphene toxicity. In addition, children may be especially susceptible to toxaphene-induced neurotoxicity based on early reports of acute ingestion toxicity.

Other individuals who may be at higher risk are those with diseases of the renal, nervous, cardiac, adrenal, and respiratory systems. Individuals using certain medications are also at potential risk due to the induction of hepatic microsomal enzymes by toxaphene (discussed further in the following section).

Interactive Effects —Metabolism of some drugs and alcohol may be affected by toxaphene's induction of hepatic microsomal enzymes. This was observed in a man using warfarin as an anticoagulant while he used toxaphene as an insecticide. The effectiveness of the drug was reduced because toxaphene's induction of microsomal enzymes increased the drug's metabolism.

Based on acute studies in animals and anecdotal reports of acute exposure in humans, exposure to chemicals that increase microsomal mixed-function oxidase systems (e.g., lindane) are likely to reduce the acute toxicity of other chemicals detoxified by the same system (e.g., toxaphene) because the system is functioning at a higher than normal level. Toxaphene, in turn, may reduce the acute toxicity of chemicals that require this system for detoxification.

Critical Data Gaps —The following data gaps have been identified for toxaphene.

- mammalian germ cell genotoxicity,
- studies that investigate sensitive developmental toxicity endpoints including behavioral effects,
- epidemiological and animal studies of immunotoxicity,
- long-term neurotoxicity studies in animals using sensitive functional and neuropathological tests and behavioral effects on prenatally exposed animals,
- epidemiological studies evaluating multiple organ systems, and pharmacokinetic studies.

EPA Regulations and Advisories

- Maximum Contaminant Level in drinking water = 0.003 mg/L
- Listed as a hazardous air pollutant under the Clean Air Act
- Reportable Quantity = 1 lb
- Toxaphene Effluent Standard = 0-15 µg/L discharge/day
- Effluent Guidelines and Standards: Electroplating—Definition of Total Toxic Organic = > 0.01 mg/L
- Effluent Guidelines and Standards: Metal Finishing—Definition of Total Toxic Organic = >0.01 mg/L
- Chemicals and chemical categories to which this part applies (Toxic Release Inventory) = 25,000 lb manufactured or processed, 10,000 lb otherwise used
- Extremely Hazardous Substances and Their Threshold Planning Quantities (Camphechlor) = 500/10,000 lb
- Municipal Solid Waste Landfills: Design Criteria—MCL for Upper Aquifer = 0.005 mg/L
- Municipal Solid Waste Landfills: Appendix II = 2 µg/L (Practical Quantitation Limit)

Sources of Information

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The 1997 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