

## Toxaphene

### CAS No. 8001-35-2

Reasonably anticipated to be a human carcinogen

First listed in the *Second Annual Report on Carcinogens* (1981)

### Carcinogenicity

Toxaphene is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

#### Cancer Studies in Experimental Animals

Dietary exposure to toxaphene caused tumors in two rodent species and at two different tissue sites. In mice of both sexes, it increased the combined incidence of benign and malignant liver tumors (hepatocellular adenoma and carcinoma), and in rats of both sexes, it caused benign tumors of the thyroid gland (follicular-cell adenoma) (IARC 1979, 2001, NCI 1979).

#### Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to toxaphene. Since toxaphene was listed in the *Second Annual Report on Carcinogens*, additional epidemiological studies have been identified. Two case-control studies, one for non-Hodgkin lymphoma and one for leukemia, found no association with toxaphene exposure (IARC 2001).

### Properties

Toxaphene is a manufactured insecticide containing a complex mixture of at least 670 chemicals, including chlorobornanes, chlorocamphenes, and other bicyclic chloroorganic compounds (ATSDR 1996). The relative proportions of the major components of the pesticide are essentially the same in different formulations. Toxaphene exists at room temperature as a yellow-to-amber waxy solid with a pleasant, piney odor (HSDB 2010). It is practically insoluble in water but is freely soluble in aromatic hydrocarbons, such as benzene and xylene, and is readily soluble in aliphatic organic solvents, such as carbon tetrachloride, ethylene dichloride, kerosene, or mineral oil (ATSDR 1996). Toxaphene is stable under normal room temperatures and pressures (Akron 2010). Physical and chemical properties of toxaphene are listed in the following table.

Property	Information
Molecular weight	414 (average) <sup>a</sup>
Specific gravity	1.65 at 25°C <sup>a</sup>
Melting point	65°C to 90°C <sup>a</sup>
Boiling point	decomposes <sup>a</sup>
Log $K_{ow}$	5.9 (median) <sup>b</sup>
Water solubility	0.00055 g/L at 20°C <sup>a</sup>
Vapor pressure	$6.69 \times 10^{-6}$ mm Hg at 20°C <sup>b</sup>
Vapor density relative to air	14.3 <sup>a</sup>

Sources: <sup>a</sup>HSDB 2010, <sup>b</sup>ChemIDplus 2010.

### Use

Toxaphene was used primarily as an insecticide for cotton; therefore, most of it was used in the southern United States from Texas to Georgia (HSDB 2010). It was also used to a lesser extent on other crops (e.g., corn, small grains, fruits, vegetables, and soybeans), to control ectoparasites (e.g., lice, flies, ticks, mange, and scab mites) on livestock, and to kill undesirable fish species in lakes and streams (ATSDR 1996). Use of toxaphene in the United States has been re-

corded since 1966 (HSDB 2010); during the early to mid 1970s, toxaphene became the most heavily used pesticide in the United States. The U.S. Environmental Protection Agency cancelled most of the pesticide registrations for toxaphene in 1982, and all uses were banned in 1990 (ATSDR 1996). After 1982, existing stocks of toxaphene could be used only in selected markets or on a case-by-case emergency basis as determined by EPA, and after 1990, remaining stocks could not be sold or used in the United States.

Annual use of toxaphene in the United States was over 34 million pounds from 1966 to 1976 (HSDB 2010), declining to 6.6 million pounds in 1982. By 1989, toxaphene was no longer used in the United States. During the peak years, approximately 85% of all toxaphene was used on cotton, 7% was used to control insect pests on livestock and poultry, 5% was used on other field crops, 3% was used on soybeans, and less than 1% was used on sorghum (IARC 1979). Toxaphene use continues in some countries, and it may be manufactured in the United States for export to those countries (ATSDR 1996). Cumulative global usage of toxaphene was interpolated to be 670 million kilograms (1.5 billion pounds) between 1970 and 1995 (Voldner and Li 1995).

### Production

Commercial production of toxaphene in the United States began in 1947, and four U.S. companies have produced toxaphene commercially (IARC 1979, ATSDR 1996, HSDB 2010). Technical toxaphene can be produced commercially by reacting chlorine gas with technical camphene in the presence of ultraviolet radiation and catalysts, yielding chlorinated camphene containing 67% to 69% chlorine by weight. Between 1964 and 1982, an estimated 234,000 metric tons (over 500 million pounds) of toxaphene was produced in the United States (HSDB 2010). Between 25% and 35% of the annual production was exported. Production peaked in 1975 at 59.4 million pounds, declining more than 90% by 1982 (ATSDR 1996). In 2010, toxaphene was available from 11 suppliers worldwide, including 7 U.S. suppliers (Chem Sources 2010).

It also appears that some polychlorinated camphenes like toxaphene may be generated unintentionally by other manufacturing processes that include chlorination, for example, in the pulp and paper industry (ATSDR 1996).

### Exposure

The routes of potential human exposure to toxaphene are ingestion, dermal contact, and inhalation (HSDB 2010). Toxaphene was the most widely used pesticide in the United States in the 1970s (Bidleman *et al.* 1998). Because toxaphene is no longer used in the United States, current exposure is due mainly to its persistence of the environment (ATSDR 1996).

The U.S. Food and Drug Administration estimated the average daily intake of toxaphene at 0.003 µg/kg of body weight from 1986 to 1991 and 0.007 to 0.02 µg/kg from 1986 to 1991. The highest estimated intakes were for children aged 2 years. In other studies conducted between 1981 and 1986, toxaphene was detected in fewer than half of 14,492 samples of foods either domestically produced or imported from 79 countries, but less than 1% of those samples contained toxaphene at levels exceeding regulatory limits (HSDB 2010). In the FDA Total Diet Study, conducted from 1991–93 through 2003–04, toxaphene was detected in 14 foods. It was found most frequently and at the highest mean concentrations in peanut butter (0.02018 ppm) and dry-roasted peanuts (0.02609 ppm) (FDA 2003). Specific toxaphene congeners have been measured in pooled human serum from three cities in the United States: Atlanta, Georgia, Chicago, Illinois, and Cincinnati, Ohio (Barr *et al.* 2004). In northernmost Canada, toxa-

phene levels in maternal and cord blood plasma were highest among the Inuit population who consumed marine mammals as a part of their regular diet (Butler Walker *et al.* 2003).

According to EPA's Toxics Release Inventory, environmental releases of toxaphene from 1990 to 2007 ranged from zero to a high of 25,602 lb in 1998. From 2000 to 2007, releases ranged from a high of 6,787 lb in 2005 to a low of 1,217 lb in 2007. In 2008, 11 facilities released a total of 418,525 lb of toxaphene, nearly all of which (415,473 lb) was released to an on-site hazardous-waste landfill by a single facility (TRI 2010). Toxaphene is persistent in soil; in one study, 45% of the toxaphene applied to a sandy loam soil in 1951 was still present 20 years later (IARC 1979). The mean concentration of toxaphene in soil in 1999–2000 was 688 ng/g of dry soil in Alabama, Louisiana, and Texas and 2,500 ng/g in South Carolina (Kannan *et al.* 2003, Bidleman and Leone 2004). Toxaphene is biotransformed under anaerobic conditions in soil and sediment, with a half-life in the range of weeks or months. Under aerobic conditions, its half-life is in the range of years. Toxaphene bioaccumulates in the environment and is biomagnified through the aquatic food chain.

In the 1990s, toxaphene was found to be widely distributed throughout the atmosphere as a result of air dispersion and deposition (Alegria *et al.* 2006). In 1994–95, the air concentration of toxaphene in Columbia, South Carolina, was much lower than it had been in 1977 to 1985, but much higher than near the Great Lakes (Bidleman *et al.* 1998). Toxaphene was measured in precipitation over Lake Ontario from 1994 to 1998, indicating loading of toxaphene to the lake by wet deposition (Burniston *et al.* 2005). In 2000, it was estimated that 15 million kilograms (33 million pounds) of toxaphene was still present in North American air, water, and soil (MacLeod *et al.* 2002) and that over 25% of the remaining toxaphene had moved through long-range atmospheric transport to the Great Lakes region. A systematic air-sampling study conducted in 2002–03 supported the premise that most toxaphene in the atmosphere in the northern United States had volatilized from southern cotton fields, where it had been heavily applied before 1982, and had been transported in the atmosphere to Indiana and the upper Great Lakes (James and Hites 2002, Jantunen and Bidleman 2003, Hoh and Hites 2004).

Toxaphene was measured in fish in the Great Lakes and in Lake Tahoe; the highest concentrations were found in lake trout (a species with high lipid content) in Lake Superior (Andrews *et al.* 1993, Datta *et al.* 1999, Carlson and Swackhamer 2006). Toxaphene was also found in other locations and in other species, including farm-raised and wild salmon. Fish in subarctic lakes were found to contain toxaphene at levels of concern for human health (Kidd *et al.* 1995). Toxaphene was also detected in fish from Alaska's Yukon River Basin (Hinck *et al.* 2006) and in marine mammals in the Alaskan Arctic at levels similar to those found in Northern Canada and Greenland. The native Arctic Alaskan population thus may be exposed to toxaphene through subsistence consumption of marine mammals (Becker *et al.* 1997, Becker 2000, Hoekstra *et al.* 2002).

In the past, the risk of occupational exposure to toxaphene was greatest for manufacturers of toxaphene, cotton farmers, and pesticide applicators (HSDB 2010). No estimates are available of the number of people potentially exposed through past agricultural use and handling, but the number may be substantial, because of toxaphene's importance as an agricultural pesticide in the 1970s (ATSDR 1996).

## Regulations

### Department of Transportation (DOT)

Toxaphene is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

### Environmental Protection Agency (EPA)

#### Clean Air Act

*National Emission Standards for Hazardous Air Pollutants:* Listed as a hazardous air pollutant.

#### Clean Water Act

*Effluent Guidelines:* Listed as a toxic pollutant.

Designated a hazardous substance.

*Water Quality Criteria:* Based on fish or shellfish and water consumption = 0.00070 µg/L; based on fish or shellfish consumption only = 0.00071 µg/L.

#### Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 1 lb.

#### Emergency Planning and Community Right-To-Know Act

*Toxics Release Inventory:* Listed substance subject to reporting requirements.

Reportable quantity (RQ) = 1 lb.

Threshold planning quantity (TPQ) = 500 lb for the solid in powder form of particle size < 100 µm or in solution or molten form; = 10,000 lb for all other forms.

#### Federal Insecticide, Fungicide, and Rodenticide Act

Registrations for all uses of toxaphene have been canceled.

#### Resource Conservation and Recovery Act

*Characteristic Hazardous Waste:* Toxicity characteristic leaching procedure (TCLP) threshold = 0.5 mg/L.

*Listed Hazardous Waste:* Waste codes for which the listing is based wholly or partly on the presence of toxaphene = P123, K041, K098.

Listed as a hazardous constituent of waste.

#### Safe Drinking Water Act

Maximum contaminant level (MCL) = 0.003 mg/L.

#### Food and Drug Administration (FDA)

Maximum permissible level in bottled water = 0.003 mg/L.

#### Occupational Safety and Health Administration (OSHA)

While this section accurately identifies OSHA's legally enforceable PELs for this substance in 2010, specific PELs may not reflect the more current studies and may not adequately protect workers.

Permissible exposure limit (PEL) = 0.5 mg/m<sup>3</sup>.

Potential for dermal absorption.

## Guidelines

### National Institute for Occupational Safety and Health (NIOSH)

Immediately dangerous to life and health (IDLH) limit = 200 mg/m<sup>3</sup>.

Potential for dermal absorption.

Listed as a potential occupational carcinogen.

## References

- Akron. 2010. *The Chemical Database*. The Department of Chemistry at the University of Akron. <http://ull.chemistry.uakron.edu/erd> and search on CAS number. Last accessed: 2/15/10.
- Alegria H, Bidleman TF, Figueroa MS. 2006. Organochlorine pesticides in the ambient air of Chiapas, Mexico. *Environ Pollut* 140(3): 483-491.
- Andrews P, Newsome WH, Boyle M, Collins P. 1993. High-resolution selective ion monitoring GC-MS determination of toxaphene in Great Lakes fish. *Chemosphere* 27(10): 1865-1872.
- ATSDR. 1996. *Toxicological Profile for Toxaphene*. Agency for Toxic Substances and Disease Registry. <http://www.atsdr.cdc.gov/toxprofiles/tp94.pdf>.
- Barr JR, Woolfitt AR, Maggio VL, Patterson DG Jr. 2004. Measurement of toxaphene congeners in pooled human serum collected in three U.S. cities using high-resolution mass spectrometry. *Arch of Environ Contam Toxicol* 46(4): 551-556.
- Becker PR, Mackey EA, Demiralp R, Schantz MM, Koster BJ, Wise SA. 1997. Concentrations of chlorinated hydrocarbons and trace elements in marine mammal tissues archived in the U.S. National Biomonitoring Specimen Bank. *Chemosphere* 34(9-10): 2067-2098.
- Becker PR. 2000. Concentration of chlorinated hydrocarbons and heavy metals in Alaska Arctic marine mammals. *Mar Pollut Bull* 40(10): 819-829.
- Bidleman TF, Alegria H, Ngabe B, Green C. 1998. Trends of chlordane and toxaphene in ambient air of Columbia, South Carolina. *Atmos Environ* 32(11): 1849-1856.
- Bidleman TF, Leone AD. 2004. Soil-air exchange of organochlorine pesticides in the Southern United States. *Environ Pollut* 128(1-2): 49-57.
- Burniston DA, Strachan WMJ, Wilkinson RJ. 2005. Toxaphene deposition to Lake Ontario via precipitation, 1994-1998. *Environ Sci Technol* 39(18): 7005-7011.
- Butler Walker J, Seddon L, McMullen E, Houseman J, Tofflemire K, Corriveau A, *et al.* 2003. Organochlorine levels in maternal and umbilical cord blood plasma in Arctic Canada. *Sci Total Environ* 302(1-3): 27-52.
- Carlson DL, Swackhamer DL. 2006. Results from the U.S. Great Lakes fish monitoring program and effects of lake processes on bioaccumulative contaminant concentrations. *J Great Lakes Res* 32(2): 370-385.

## Report on Carcinogens, Fourteenth Edition

- ChemIDplus. 2010. *ChemIDplus Advanced*. National Library of Medicine. <http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp> and select Registry Number and search on CAS number. Last accessed: 2/15/10.
- ChemSources. 2010. *Chem Sources - Chemical Search*. Chemical Sources International. <http://www.chemsources.com/chemonline.html> and search on toxaphene. Last accessed: 2/15/10.
- Datta S, Ohyama K, Dunlap DY, Matsumura F. 1999. Evidence for organochlorine contamination in tissues of salmonids in Lake Tahoe. *Ecotoxicol Environ Saf* 42(1): 94-101.
- FDA. 2003. *Total Diet Study Market Baskets 1991-3 through 2003-4*. U.S. Food and Drug Administration. <http://www.fda.gov/downloads/Food/FoodSafety/FoodContaminantsAdulteration/TotalDietStudy/UCM184304.pdf>.
- Hinck JE, Schmitt CJ, Echols KR, May TW, Orazio CE, Tillitt DE. 2006. Environmental contaminants in fish and their associated risk to piscivorous wildlife in the Yukon River Basin, Alaska. *Arch Environ Contam Toxicol* 51(4): 661-672.
- Hoekstra PF, O'Hara TM, Teixeira C, Backus S, Fisk AT, Muir DCG. 2002. Spatial trends and bioaccumulation of organochlorine pollutants in marine zooplankton from the Alaskan and Canadian Arctic. *Environ Toxicol Chem* 21(3): 575-583.
- Hoh E, Hites RA. 2004. Sources of toxaphene and other organochlorine pesticides in North America as determined by air measurements and potential source contribution function analyses. *Environ Sci Technol* 38(15): 4187-4194.
- HSDB. 2010. *Hazardous Substances Data Bank*. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB> and search on CAS number. Last accessed: 2/15/10.
- IARC. 1979. Toxaphene (polychlorinated camphenes). In *Some Halogenated Hydrocarbons*. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol. 20. Lyon, France: International Agency for Research on Cancer. pp. 327-348.
- IARC. 2001. Toxaphene. In *Some Thyrotropic Agents*. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol. 79. Lyon, France: International Agency for Research on Cancer. pp. 569-604.
- James RR, Hites RA. 2002. Atmospheric transport of toxaphene from the southern United States to the Great Lakes Region. *Environ Sci Technol* 36(16): 3474-3481.
- Jantunen LM, Bidleman TF. 2003. Air-water gas exchange of toxaphene in Lake Superior. *Environ Toxicol Chem* 22(6): 1229-1237.
- Kannan K, Battula S, Loganathan BG, Hong CS, Lato WH, Villeneuve DL, Sajwan K, Giesy JP, Aldous KM. 2003. Trace organic contaminants, including toxaphene and trifluralin, in cotton field soils from Georgia and South Carolina, USA. *Arch Environ Contam Toxicol* 45(1): 30-36.
- Kidd KA, Schindler DW, Muir DC, Lockhart WL, Hesslein RH. 1995. High concentrations of toxaphene in fishes from a subarctic lake. *Science* 269(5221): 240-242.
- MacLeod M, Woodfine D, Brimacombe J, Toose L, Mackay D. 2002. A dynamic mass budget for toxaphene in North America. *Environ Toxicol Chem* 21(8): 1628-1637.
- NCI. 1979. *Bioassay of Toxaphene for Possible Carcinogenicity*. Technical Report Series no. 37. DHEW (NIH) Publication No. 79-837. Bethesda, MD: National Institutes of Health. 104 pp.
- TRI. 2010. *TRI Explorer Chemical Report*. U.S. Environmental Protection Agency. <http://www.epa.gov/triexplorer> and select Toxaphene. Last accessed: 2/15/10.
- Voldner EC, Li YF. 1995. Global usage of selected persistent organochlorines. *Sci Total Environ* 161: 201-210