

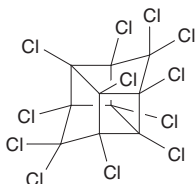
Mirex

CAS No. 2385-85-5

Reasonably anticipated to be a human carcinogen

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

Also known as 1,1a,2,2,3,3a,4,5,5a,5b,6-dodecachlorooctahydro-1,3,4-metheno-1H-cyclobuta[cd]pentalene



Carcinogenicity

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

Cancer Studies in Experimental Animals

Mirex caused tumors in mice and rats by two different routes of exposure. It caused benign or malignant liver tumors after (1) administration to infant mice of both sexes by stomach tube for three weeks, followed by dietary exposure, (2) dietary administration to rats of both sexes, and (3) a single subcutaneous injection in male mice. An excess of lymphoma (reticulum-cell sarcoma) observed in male mice exposed by subcutaneous injection also may have been related to mirex exposure (IARC 1974, 1979).

Since mirex was listed in the *Second Annual Report on Carcinogens*, additional studies in rats have been identified. Dietary administration of mirex caused benign liver tumors (adenoma) in both sexes, benign tumors of the adrenal glands (pheochromocytoma) and kidney (transitional-cell papilloma) in males, and mononuclear-cell leukemia in females (NTP 1990).

Cancer Studies in Humans

The data available from epidemiological studies were inadequate to evaluate the relationship between human cancer and exposure specifically to mirex.

Properties

Mirex is a chlorinated insecticide that is an odorless snow-white crystal at room temperature (HSDB 2009). Mirex is practically insoluble in water, but is soluble in dioxane, xylene, benzene, carbon tetrachloride, and methyl ethyl ketone. It is very stable at normal temperatures and pressures (Akron 2009). Physical and chemical properties of mirex are listed in the following table.

Property	Information
Molecular weight	545.6 ^a
Melting point	485°C ^a
Log K_{ow}	5.28 ^a
Water solubility	0.085 mg/L at 25°C ^b
Vapor pressure	8×10^{-7} mm Hg at 25°C ^b
Vapor density relative to air	18.8 ^a

Sources: ^aHSDB 2009, ^bChemIDplus 2009.

Use

Mirex was used in the United States from 1959 until 1972 as a fire-retardant additive and as an insecticide to control fire ants in southeastern states; the latter use continued until 1978 (IARC 1979, ATSDR

1995). From 1962 to 1976, 132 million acres in nine states were treated for fire-ant control with about 500,000 lb of mirex bait, primarily by aerial application. Mirex was also used to control other species of ants, yellow jackets, and mealy bugs in pineapples (IARC 1979). The U.S. Environmental Protection Agency canceled all registered uses of mirex in December 1977; however, selected applications were allowed until existing stocks were exhausted in June 1978.

Production

Mirex was first synthesized in the mid 1940s, but it did not become commercially available in the United States until 1958 (IARC 1979). Technical-grade mirex was produced commercially by one company in the United States until 1967. The insecticidal baits were produced until 1975, when all registrations and the rights to produce and sell baits containing mirex were transferred to the Mississippi Department of Agriculture until the supply of mirex was exhausted. One company produced an estimated 3.3 million pounds of mirex between 1959 and 1975 and purchased an additional 1.5 million pounds from another company (ATSDR 1995). Peak production occurred from 1963 to 1968. U.S. production was 41,500 lb in 1972 and less than 1,000 lb in 1975 (HSDB 2009). Mirex is available in small quantities for laboratory use from seven U.S. suppliers and four other suppliers worldwide (ChemSources 2009). Before cancellation of its registrations for technical products, mirex was imported from Brazil; however, no data on U.S. import volumes were found (ATSDR 1995). Over 90% of the mirex produced in the United States between 1950 and 1975 was exported.

Exposure

Although mirex is no longer produced or used in the United States, it is very persistent in the environment and is highly resistant to degradation. Because mirex remains in the environment for a long time, the general population may continue to be exposed at low concentrations (ATSDR 1995). Populations with the greatest potential for exposure include those who eat fish from contaminated water bodies, reside near a former mirex manufacturing or waste-disposal site, or live in areas where mirex was extensively used to control fire ants.

Mirex has a half-life of up to 10 years in the environment. It is very soluble in fat and bioaccumulates in animals. Mirex has been found in Antarctic species, indicating that it is transported over long distances (Bustnes *et al.* 2006). It has been measured in top avian predators at both poles; however, concentrations were much higher in the Antarctic species. The one U.S. plant that manufactured mirex was located on the Niagara River upstream from Lake Ontario. It was estimated that almost 6,000 lb of mirex entered Lake Ontario from that facility. From 1977 to 1999, concentrations of mirex in salmon fillets collected from Lake Ontario declined by more than tenfold, to less than 0.1 mg/kg; the decline was attributed to clean-up of the groundwater discharge from the former manufacturing site, resulting in less mirex available in Lake Ontario for biomagnification in the food chain (Makarewicz *et al.* 2003). In another study, mirex was found at concentrations of up to 360 ng/g in lake trout taken near the former manufacturing site; in lake trout in the other Great Lakes, it was found at much lower concentrations or was below the limit of detection (2 ng/g) (Hickey *et al.* 2006). In Arctic Greenland populations, the daily intake of mirex increased from 0.002 µg/kg of body weight in 1976 to 0.0044 µg/kg in 2004, even though the consumption of traditional foods declined (Deutch *et al.* 2004).

Mirex has been found in the blood of numerous human populations, especially in indigenous people of northern regions (Van Oostdam *et al.* 2004). A survey of organochlorine pesticides in maternal blood found mirex at concentrations up to 12 µg/kg of serum lipids

Report on Carcinogens, Fourteenth Edition

in Arctic populations in Greenland, Canada, Alaska, Norway, Sweden, Iceland, Finland, and Russia. The blood levels of mirex in Greenland arctic populations ranged from 34.1 to 88.1 µg/kg of lipid and correlated with Inuit consumption of seal and fish (Deutch *et al.* 2004). In Arctic Canada, mirex was detected in 84% of Inuit maternal blood samples at a mean concentration of 0.07 µg/L, but in less than 45% of samples from other ethnic groups, at a median concentration of only 0.02 µg/L. However, it was detected in only 8.5% of the corresponding cord blood plasma samples from all ethnic groups, at a mean concentration of 0.01 µg/L (Butler Walker *et al.* 2003).

Mirex was found in 46% of the blood samples collected from Akwesasne Mohawk youth living along the St. Lawrence River in New York and Quebec, at a mean concentration of 0.036 ppb. Levels were somewhat higher in youths who had been breastfed as infants, but the difference was not statistically significant (Schell *et al.* 2003). In Montreal, mirex was found in the blood of ethnic Bangladeshi and Vietnamese fishermen and in majority-community sport fishers; concentrations were highest among the majority sport fishers, because they caught and ate larger fish (Kosatsky *et al.* 1999). In a study of male sport fishers in New York State, their mean blood mirex concentration was 18.4 ng/g of lipid, significantly higher than in non-consumers of sport fish (Bloom *et al.* 2005). A study in the Great Lakes also found higher blood concentrations of mirex among men and women who consumed fish than in non-consumers (Kearney *et al.* 1999). Mirex was found in 86% of the blood samples collected from pregnant women in an agricultural community in California, at a median concentration of 0.29 ng/g of lipid (Fenster *et al.* 2006). A study in southern Spain measured organochlorine pesticides in 150 placentas and detected mirex in 40% of the samples, at a mean concentration of 0.38 ng/g of placenta (Lopez-Espinosa *et al.* 2006).

Mirex was found in all adipose-tissue samples collected at autopsy from Greenlanders; the highest mean concentration, 126 µg/kg of lipid, was found in omental fat. This was lower than found in a previous study of Greenlanders, but much higher than in studies conducted in other locations (Deutch *et al.* 2006). Breast-milk concentrations of mirex also were elevated in populations of women in New York State who had eaten contaminated local fish (Greizerstein *et al.* 1999, Fitzgerald *et al.* 2001).

The National Occupational Hazard Survey (conducted from 1972 to 1974) estimated that 932 workers potentially were exposed to mirex (HSDB 2009). However, occupational exposure is now limited to workers employed at hazardous-waste sites or those involved in remediation of sites contaminated with mirex (ATSDR 1995).

Regulations

Department of Transportation (DOT)

Mirex is considered a marine pollutant, and special requirements have been set for marking, labeling, and transporting this material.

Environmental Protection Agency (EPA)

Federal Insecticide, Fungicide, and Rodenticide Act

Registrations for all uses have been canceled.

Food and Drug Administration (FDA)

Action level in the edible portion of fish = 0.1 ppm.

References

Akron. 2009. *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: 8/11/09.

ATSDR. 1995. *Toxicological Profile for Mirex and Chlordane*. Agency for Toxic Substances and Disease Registry. <http://www.atsdr.cdc.gov/toxprofiles/tp66.pdf>.

Bloom MS, Vena JE, Swanson MK, Moysich KB, Olson JR. 2005. Profiles of ortho-polychlorinated biphenyl congeners, dichlorodiphenyldichloroethylene, hexachlorobenzene, and mirex among male Lake Ontario sportfish consumers: The New York State Angler cohort study. *Environ Res* 97(2): 178-194.

Bustnes JO, Tveraa T, Henden JA, Varpe O, Janssen K, Skaare JU. 2006. Organochlorines in antarctic and arctic avian top predators: A comparison between the South Polar skua and two species of northern hemisphere gulls. *Environ Sci Technol* 40(8): 2826-2831.

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.

ChemIDplus. 2009. *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: 8/11/09.

ChemSources. 2009. *Chem Sources - Chemical Search*. Chemical Sources International. <http://www.chemsources.com/chemonline.html> and search on mirex. Last accessed: 8/11/09.

Deutch B, Pedersen HS, Hansen JC. 2004. Dietary composition in Greenland 2000, plasma fatty acids and persistent organic pollutants. *Sci Total Environ* 331(1-3): 177-188.

Deutch B, Dyerberg J, Pedersen HS, Asmund G, Moller P, Hansen JC. 2006. Dietary composition and contaminants in north Greenland, in the 1970s and 2004. *Sci Total Environ* 370(2-3): 372-381.

Fenster L, Eskenazi B, Anderson M, Bradman A, Harley K, Hernandez H, Hubbard A, Barr DB. 2006. Association of *in utero* organochlorine pesticide exposure and fetal growth and length of gestation in an agricultural population. *Environ Health Perspect* 114(4): 597-602.

Fitzgerald EF, Hwang SA, Deres DA, Bush B, Cook K, Worswick P. 2001. The association between local fish consumption and DDE, mirex, and HCB concentrations in the breast milk of Mohawk women at Akwesasne. *J Expo Anal Environ Epidemiol* 11(5): 381-388.

Greizerstein HB, Stinson C, Mendola P, Buck GM, Kostyniak PJ, Vena JE. 1999. Comparison of PCB congeners and pesticide levels between serum and milk from lactating women. *Environ Res* 80(3): 280-286.

Hickey JP, Batterman SA, Chernyak SM. 2006. Trends of chlorinated organic contaminants in Great Lakes trout and walleye from 1970 to 1998. *Arch Environ Contam Toxicol* 50(1): 97-110.

HSDB. 2009. *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: 8/11/09.

IARC. 1974. Mirex. In *Some Organochlorine Pesticides*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 5. Lyon, France: International Agency for Research on Cancer. pp. 203-210.

IARC. 1979. Mirex. In *Some Halogenated Hydrocarbons*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 20. Lyon, France: International Agency for Research on Cancer. pp. 283-301.

Kearney JP, Cole DC, Ferron LA, Weber JP. 1999. Blood PCB, *p,p'*-DDE, and mirex levels in Great Lakes fish and waterfowl consumers in two Ontario communities. *Environ Res* 80(2 Pt 2): S138-S149.

Kosatsky T, Przybysz R, Shatenstein B, Weber JP, Armstrong B. 1999. Contaminant exposure in Montrealers of Asian origin fishing the St. Lawrence River: Exploratory assessment. *Environ Res* 80(2 Pt 2): S159-S165.

Lopez-Espinosa MJ, Granada A, Carreno J, Salvatierra M, Olea-Serrano F, Olea N. 2006. Organochlorine pesticides in placentas from southern Spain and some related factors. *Placenta*: 631-638.

Makarewicz JC, Damaske E, Lewis TW, Merner M. 2003. Trend analysis reveals a recent reduction in mirex concentrations in coho (*Oncorhynchus kisutch*) and chinook (*O. tshawytscha*) salmon from Lake Ontario. *Environ Sci Technol* 37(8): 1521-1527.

NTP. 1990. *Toxicology and Carcinogenesis Studies of Mirex (1,1a,2,2,3,3a,4,5,5,5a,5b,6-Dodecachloro-octahydro-1,3,4-metheno-1H-cyclobuta[cd]pentalene) (CAS No. 2385-85-5) in F344/N Rats (Feed Studies)*. Technical Report Series no. 313. NIH Publication No. 90-2569. Research Triangle Park, NC: National Toxicology Program. 140 pp.

Schell LM, Hubicki LA, DeCaprio AP, Gallo MV, Ravenscroft J, Tarbell A, Jacobs A, David D, Worswick P. 2003. Organochlorines, lead, and mercury in Akwesasne Mohawk youth. *Environ Health Perspect* 111(7): 954-961.

Van Oostdam JC, Dewailly E, Gilman A, Hansen JC, Odland JO, Chashchin V, *et al.* 2004. Circumpolar maternal blood contaminant survey, 1994-1997 organochlorine compounds. *Sci Total Environ* 330(1-3): 55-70.