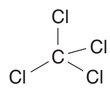
Carbon Tetrachloride

CAS No. 56-23-5

Reasonably anticipated to be a human carcinogen

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

Also known as tetrachloromethane



Carcinogenicity

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

Cancer Studies in Experimental Animals

Carbon tetrachloride caused tumors in several species of experimental animals, at two different tissue sites, and by several different routes of exposure. It caused benign or malignant liver tumors when administered (1) orally in mice and rats of both sexes, in hamsters, and in trout, (2) by subcutaneous injection in male rats, and (3) by inhalation in rats (of unspecified sex) (IARC 1972, 1979). Subcutaneous injection of carbon tetrachloride caused benign and malignant mammary-gland tumors (fibroadenoma and adenocarcinoma) in female rats.

Since carbon tetrachloride was listed in the *Second Annual Report on Carcinogens,* additional studies in mice have been identified. Inhalation exposure to carbon tetrachloride caused benign and malignant liver tumors (hepatocellular adenoma and carcinoma) and benign adrenal-gland tumors (pheochromocytoma) in mice of both sexes (Nagano *et al.* 1998, 2007, IARC 1999).

Cancer Studies in Humans

The data available from epidemiological studies were inadequate to evaluate the relationship between human cancer and exposure specifically to carbon tetrachloride. Three cases of liver cancer were reported in humans with cirrhosis of the liver who had been exposed to carbon tetrachloride (IARC 1979).

After carbon tetrachloride was listed in the *Second Annual Report on Carcinogens,* additional epidemiological studies were identified and reviewed by the International Agency for Research on Cancer. IARC (1999) concluded that there was inadequate evidence in humans for the carcinogenicity of carbon tetrachloride. Statistically nonsignificant increased risks for non-Hodgkin lymphoma (NHL) in association with potential exposure to carbon tetrachloride were found among female aircraft-maintenance workers (Blair *et al.* 1998) and in a nested case-control study of rubber workers (Checkoway *et al.* 1984, Wilcosky *et al.* 1984). The latter study also found an increased risk of leukemia. Studies on drycleaning workers were not specific for exposure to carbon tetrachloride (Blair *et al.* 1990, 1993), and IARC considered the population-based case-control studies to be uninformative (IARC 1999).

Since the 1999 IARC review, additional studies have been identified that evaluated the relationship between (NHL) and carbon tetrachloride exposure. Statistically significant risks of NHL were reported among individuals with potential exposure to carbon tetrachloride used as a pesticide (McDuffie *et al.* 2001) and among women occupationally exposed to carbon tetrachloride (Wang *et al.* 2009). A small, statistically nonsignificant excess of NHL was also found among laboratory workers potentially exposed to carbon tetrachloride and other agents (Kauppinen *et al.* 2003). In an extended follow-up of the cohort of female aircraft-maintenance workers exposed to carbon tetrachloride, the risk of NHL was lower than in the earlier study, although still (nonsignificantly) elevated (Radican *et al*. 2008).

Properties

Carbon tetrachloride is a halomethane that exists at room temperature as a clear, colorless, heavy liquid with a sweetish, aromatic, moderately strong ethereal odor. It is very slightly soluble in water, soluble in ethanol and acetone, and miscible with benzene, chloroform, ether, carbon disulfide, petroleum ether, and oils. It is nonflammable and is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of carbon tetrachloride are listed in the following table.

Property	Information
Molecular weight	153.8
Specific gravity	1.594 at 20°C/4°C
Melting point	–23°C
Boiling point	76.8°C
Log K_{ow}	2.83
Water solubility	793 mg/L at 25°C
Vapor pressure	115 mm Hg at 25°C
Vapor density relative to air	5.32

Source: HSDB 2009.

Use

Carbon tetrachloride is used as a chemical intermediate and as a feedstock in the production of chlorofluorocarbons, such as the Freons dichlorodifluoromethane (F-12) and trichlorofluromethane (F-11), which are used primarily as refrigerants. It is also used in petroleum refining, in pharmaceutical manufacturing, as an industrial solvent, in the processing of fats, oils, and rubber, and in laboratory applications (IARC 1999, ATSDR 2005, HSDB 2009). It currently is not permitted in products intended for home use (HSDB 2009). Until the mid 1960s, carbon tetrachloride was used as a cleaning fluid both in industry and in the home (in spot removers) and in fire extinguishers (ATSDR 2005). It was also used as a grain fumigant until 1986, when its use for this purpose was cancelled by the U.S. Environmental Protection Agency. Other previous uses include as a rodenticide, as a solvent in some household products, in the formulation of gasoline additives, and in metal recovery and catalyst regeneration (ATSDR 2005, HSDB 2009). In the early 1900s, it was used in human medicine to destroy intestinal parasitic worms, and it was used for a short period as an anesthetic (IARC 1972, ATSDR 2005).

Production

Large-scale U.S. production of carbon tetrachloride began in 1907 (IARC 1979). In 2009, carbon tetrachloride was produced by 26 manufacturers worldwide, including 3 in the United States (SRI 2009), and was available from 69 suppliers, including 19 U.S. suppliers (ChemSources 2009). U.S. imports of carbon tetrachloride totaled 110 million kilograms (242 million pounds) in 1989, decreasing to zero 1996; since 1996, only 41 kilograms (90 lb) has been imported. U.S. exports of carbon tetrachloride decreased from 52.7 million kilograms (116 million pounds) in 1989 to 1.7 million kilograms (3.8 million pounds) in 2008 (USITC 2009).

Exposure

The primary routes of potential human exposure to carbon tetrachloride are inhalation, ingestion, and dermal contact. The general population is most likely to be exposed to carbon tetrachloride through air and drinking water. In 1988, EPA's Toxics Release Inventory listed 95 industrial facilities that produced, processed, or otherwise used carbon tetrachloride and reported environmental releases of carbon tetrachloride totaling 3.9 million pounds (TRI 2009). In 1990, 1.7 million pounds was released to air, 36,201 lb to water, and a little over 1,000 lb to soil (ATSDR 2005). In 1999, on-site releases totaled 268,140 lb, and in 2007, 308,633 lb was released by 44 facilities, mostly to underground injection wells or to air (TRI 2009).

Carbon tetrachloride is also formed in the troposphere by solar-induced photochemical reactions of chlorinated alkenes. Because it is readily volatile at ambient temperature and degrades very slowly, it has gradually accumulated in the environment. It is broken down by chemical reactions in air, but so slowly that its estimated atmospheric lifetime is between 30 and 100 years, with 50 years generally regarded as the probable value. In 1988, the average concentration of carbon tetrachloride in air in the United States was reported to be 0.168 ppb, and other studies have observed a steady increase in global atmospheric levels at an annual rate of about 1.3% (IARC 1979). EPA estimated that 8 million people living within 12.5 miles of manufacturing sites were possibly exposed to carbon tetrachloride at an average concentration of 0.5 μg/m^3 and a peak concentration of 1,580 μg/m^3. Point sources of carbon tetrachloride from industry and wind direction are responsible for localized increases in air concentration (ATSDR 2005). A recent study found that during the use of chlorine bleach in cleaning bathrooms and kitchen surfaces, the indoor air concentration of carbon tetrachloride reached 55 μg/m^3; even after 30 minutes, it was measured at 23 μg/m^3 (Odabasi 2008). Based on a typical carbon tetrachloride concentration in ambient air of about 1 μg/m^3 and assuming inhalation of 20 m^3 of air per day by a 70-kg adult and 40% absorption of carbon tetrachloride across the lung, daily inhalation exposure has been estimated at 0.1 μg/kg of body weight (ATSDR 2005).

Exposure to carbon tetrachloride may also occur by dermal contact with tap water (e.g., during bathing) (ATSDR 2005). Surveys have found that about 99% of all groundwater supplies and 95% of all surface-water supplies contain carbon tetrachloride at a concentration of less than 0.5 μg/L. Exposure to carbon tetrachloride by ingestion may occur through consumption of contaminated drinking water or food. In a study of New Jersey tap water, the maximum monthly estimated concentration of carbon tetrachloride was 7 μg/L, based on measurements by utilities (Bove *et al.* 1995). Based on a typical carbon tetrachloride concentration of 0.5 μg/L in drinking water, daily consumption of 2 L of water by a 70-kg adult yields an estimated daily intake of about 0.01 μg/kg of body weight (ATSDR 2005). Exposure from contaminated food is possible, but it is not likely to be of much significance, because levels of carbon tetrachloride in most foods are below the limit of detection. In the U.S. Food and Drug Administration's Total Diet Study, carbon tetrachloride was detected in 41 of 1,331 samples (3%) of 37 food items (FDA 2006). The highest measured concentration was 0.031 mg/kg in one sample of smooth peanut butter, and carbon tetrachloride was detected in two samples of boiled beef frankfurters. Carbon tetrachloride might have been ingested as a contaminant of foods treated before its use as a grain fumigant was banned; in treated stored grain, it was detected at concentrations ranging from 1 to 100 mg/kg (ATSDR 2005).

The greatest risk of occupational exposure to carbon tetrachloride most likely occurred during its use as a fumigant. According to the National Institute for Occupational Safety and Health, the workers most likely to be exposed to carbon tetrachloride are employed at blast furnaces and steel mills, in the air transportation industry, and in motor vehicle and telephone and telegraph equipment manufacturing. It was estimated that 4,500 workers potentially were exposed during production of carbon tetrachloride and 52,000 during its industrial use. The Occupational Safety and Health Administration estimated that 3.4 million workers potentially were exposed to carbon tetrachloride directly or indirectly. Exposure to carbon tetrachloride may occur in drycleaning establishments, where its concentration in ambient air was found to average between 20 and 70 ppm. Average exposures of 206 and 338 ppm, with excursions to 1,252 and 7,100 ppm, were reported during operation of drycleaning machines. Occupational exposure may also occur during its use in the manufacture of F-11 and F-12. Exposure during fluorocarbon production is most likely for tank-farm and process operators, who may be exposed to emissions from storage-tank vents, from process-equipment leaks or spills, or resulting from transfer of the chemical (NCI 1985). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 77,315 workers, including 12,605 women, potentially were exposed to carbon tetrachloride (NIOSH 1990).

Regulations

Coast Guard, Department of Homeland Security

Minimum requirements have been established for safe transport of carbon tetrachloride on ships and barges.

Consumer Product Safety Commission (CPSC)

Carbon tetrachloride and mixtures containing it (with the exception of chemicals containing unavoidable residues of carbon tetrachloride that do not result in atmospheric concentrations of carbon tetrachloride greater than 10 ppm) are banned from consumer products.

Department of Transportation (DOT)

Carbon tetrachloride is considered a hazardous material and marine pollutant, 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.
New Source Performance Standards: Manufacture of carbon tetrachloride is subject to certain provisions for the control of volatile organic compound emissions.
Urban Air Toxics Strategy: Identified as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas.
Carbon tetrachloride is regulated as a Class I substance for stratospheric ozone protection.

Clean Water Act

Effluent Guidelines: Listed as a toxic pollutant.
Water Quality Criteria: Based on fish or shellfish and water consumption = 0.4 μg/L; based on fish or shellfish consumption only = 5 μg/L.
Designated a hazardous substance.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 10 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.

Federal Insecticide, Fungicide, and Rodenticide Act

All registrations for use as a pesticide have been cancelled.

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 carbon tetrachloride = U211, F001, F024, F025, K016, K019, K020, K021, K073, K116, K150, K151, K157.
Listed as a hazardous constituent of waste.

Safe Drinking Water Act

Maximum contaminant level (MCL) = 0.005 mg/L.

Food and Drug Administration (FDA)

Maximum permissible level in bottled water = 0.005 mg/L.
All medical devices containing or manufactured with carbon tetrachloride must contain a warning statement that the compound may destroy ozone in the atmosphere.

Mine Safety and Health Administration

Carbon tetrachloride use is banned in metal and non-metal surface and underground mines.

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) = 10 ppm.
Ceiling concentration = 25 ppm.
Acceptable peak exposure = 200 ppm (maximum duration = 5 min in any 4 h).
Carbon tetrachloride can not be used as a fire extinguishing agent where employees may be exposed.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 5 ppm.
Threshold limit value – short-term exposure limit (TLV-STEL) = 10 ppm.
Potential for dermal absorption.

National Institute for Occupational Safety and Health (NIOSH)

Short-term exposure limit (STEL) = 2 ppm (12.6 mg/m^3) (60-min exposure).
Immediately dangerous to life and health (IDLH) limit = 200 ppm.
Listed as a potential occupational carcinogen.

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: 12/14/09.

ATSDR. 2005. *Toxicological Profile for Carbon Tetrachloride*. Agency for Toxic Substances and Disease Registry. http://www.atsdr.cdc.gov/toxprofiles/tp30.pdf.

Blair A, Stewart PA, Tolbert PE, Grauman D, Moran FX, Vaught J, Rayner J. 1990. Cancer and other causes of death among a cohort of dry cleaners. *Br J Ind Med* 47(3): 162-168.

Blair A, Hartge P, Stewart PA, McAdams M, Lubin J. 1998. Mortality and cancer incidence of aircraft maintenance workers exposed to trichloroethylene and other organic solvents and chemicals: extended follow up. *Occup Environ Med* 55(3): 161-171.

Bove FJ, Fulcomer MC, Klotz JB, Esmart J, Dufficy EM, Savrin JE. 1995. Public drinking-water contamination and birth outcomes. *Am J Epidemiol* 141(9): 850-862.

Checkoway H, Wilcosky T, Wolf P, Tyroler H. 1984. An evaluation of the associations of leukemia and rubber industry solvent exposures. *Am J Ind Med* 5(3): 239-249.

ChemSources. 2009. *Chem Sources - Chemical Search*. Chemical Sources International. http://www.chemsources.com/chemonline.html and search on carbon tetrachloride. Last accessed: 8/20/09.

FDA. 2006. *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.

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: 8/20/09.

IARC. 1972. Carbon tetrachloride. In *Some Inorganic Substances, Chlorinated Hydrocarbons, Aromatic Amines, N-Nitroso Compounds and Natural Products*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 1. Lyon, France: International Agency for Research on Cancer. pp. 53-60.

IARC. 1979. Carbon tetrachloride. 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. 371-398.

IARC. 1999. Carbon tetrachloride. In *Re-evaluation of Some Organic Chemicals, Hydrazine, and Hydrogen Peroxide.* IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 71. Lyon, France: International Agency for Research on Cancer. pp. 401-432.

Kauppinen T, Pukkala E, Saalo A, Sasco AJ. 2003. Exposure to chemical carcinogens and risk of cancer among Finnish laboratory workers. *Am J Ind Med* 44(4): 343-350.

McDuffie HH, Pahwa P, McLaughlin JR, Spinelli JJ, Fincham S, Dosman JA, Robson D, Skinnider LF, Choi NW. 2001. Non-Hodgkin's lymphoma and specific pesticide exposures in men: cross-Canada study of pesticides and health. *Cancer Epidemiol Biomarkers Prev* 10(11): 1155-1163.

Nagano K, Nishizawa T, Yamamoto S, Matsushima T. 1998. Inhalation carcinogenesis studies of six halogenated hydrocarbons in rats and mice. In *Advances in the Prevention of Occupational Respiratory Diseases*. Chiyotani K, Hosoda Y, Aizawa Y, eds. Amsterdam: Elsevier Science. pp. 741-746.

Nagano K, Sasaki T, Umeda Y, Nishizawa T, Ikawa N, Ohbayashi H, Arito H, Yamamoto S, Fukushima S. 2007. Inhalation carcinogenicity and chronic toxicity of carbon tetrachloride in rats and mice. *Inhal Toxicol* 19(13): 1089-1103.

NCI. 1985. *Monograph on Human Exposure to Chemicals in the Workplace: Carbon Tetrachloride*. Technical Report No. 84-1123. Bethesda, MD: Department of Health and Human Services.

NIOSH. 1990. *National Occupational Exposure Survey (1981-83).* National Institute for Occupational Safety and Health. Last updated: 7/1/90. http://www.cdc.gov/noes/noes1/17490sic.html.

Odabasi M. 2008. Halogenated volatile organic compounds from the use of chlorine-bleach-containing household products. *Environ Sci Technol* 42(5): 1445-1451.

Radican L, Blair A, Stewart P, Wartenberg D. 2008. Mortality of aircraft maintenance workers exposed to trichloroethylene and other hydrocarbons and chemicals: extended follow-up. *J Occup Environ Med* 50(11): 1306-1319.

SRI. 2009. *Directory of Chemical Producers*. Menlo Park, CA: SRI Consulting. Database edition. Last accessed:8/20/09.

TRI. 2009. *TRI Explorer Chemical Report.* U.S. Environmental Protection Agency. Last updated: 3/19/09. http://www.epa.gov/triexplorer and select Carbon Tetrachloride.

USITC. 2009. *USITC Interactive Tariff and Trade DataWeb.* United States International Trade Commission. http://dataweb.usitc.gov/scripts/user_set.asp and search on HTS no. 290314. Last accessed: 8/20/09.

Wang R, Zhang Y, Lan Q, Holford TR, Leaderer B, Zahm SH, *et al*. 2009. Occupational exposure to solvents and risk of non-Hodgkin's lymphoma in Connecticut women. *Am J Epidemiol* 169(2): 176-185.

Wilcosky TC, Checkoway H, Marshall EG, Tyroler HA. 1984. Cancer mortality and solvent exposures in the rubber industry. *Am Ind Hyg Assoc J* 45(12): 809-811.