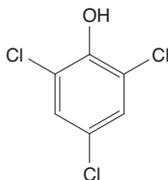


2,4,6-Trichlorophenol

CAS No. 88-06-2

Reasonably anticipated to be a human carcinogen

First listed in the *Third Annual Report on Carcinogens* (1983)



Carcinogenicity

2,4,6-Trichlorophenol is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Oral exposure to 2,4,6-trichlorophenol caused tumors in two rodent species and at several different tissue sites. Administered in the diet, 2,4,6-trichlorophenol caused benign or malignant liver tumors (hepatocellular adenoma or carcinoma) in mice of both sexes and lymphoma or mononuclear-cell leukemia in male rats (NCI 1979, IARC 1982).

Cancer Studies in Humans

No studies were identified that evaluated the relationship between human cancer and exposure specifically to 2,4,6-trichlorophenol.

Properties

2,4,6-Trichlorophenol is a chlorinated phenolic compound that exists at room temperature as colorless to yellow crystals with a strong phenolic odor (IARC 1979, 1999, HSDB 2009). It is practically insoluble in water but soluble in ethanol, diethyl ether, hot acetic acid, benzene, carbon tetrachloride, methanol, Stoddard solvent, toluene, and turpentine. It is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of 2,4,6-trichlorophenol are listed in the following table.

Property	Information
Molecular weight	197.5
Specific gravity	1.4901
Melting point	69°C
Boiling point	246°C
Log K_{ow}	3.69
Water solubility	0.800 g/L at 25°C
Vapor pressure	0.008 mm Hg at 25°C
Dissociation constant (pK_a)	6.23 at 25°C

Source: HSDB 2009.

Use

2,4,6-Trichlorophenol has been used primarily in various pesticide formulations and as a wood preservative. It has been used as a fungicide, glue preservative, insecticide, bactericide, defoliant, herbicide, and anti-mildew agent for textiles (IARC 1979, HSDB 2009). Most uses of 2,4,6-trichlorophenol were canceled in the United States; however, it continues to be used in the synthesis of some fungicides (HSDB 2009). Trichlorophenol has been reported to be used in a mixture as a disinfectant and antiseptic in the treatment of Guinea worm ulcers in Africa, but the information reported did not indi-

cate whether the product contained the 2,4,6-trichlorophenol isomer (Ogunniyi *et al.* 2000).

Production

Commercial production of 2,4,6-trichlorophenol in the United States was first reported in 1950 (IARC 1979). In 1975, production was discontinued by the only U.S. manufacturer because of the high cost of removing chlorinated dibenzo-*p*-dioxins, which occurred as toxic impurities (HSDB 2009). In 2009, 2,4,6-trichlorophenol was produced by one manufacturer each in China, India, and Europe (SRI 2009) and was available from 27 suppliers worldwide, including 16 U.S. suppliers (ChemSources 2009). U.S. imports of 2,4,6-trichlorophenol totaled 2,200 lb in 1976, 600 lb in 1978, and 550 lb in 1980 (IARC 1979, HSDB 2009).

Exposure

The routes of potential human exposure to 2,4,6-trichlorophenol are inhalation, ingestion, and dermal contact. The general population may be exposed to 2,4,6-trichlorophenol through ingestion of contaminated food or water or inhalation of contaminated air (IARC 1979, HSDB 2009). According to the National Cancer Institute (NCI 1979), substantial exposure of the general population was questionable; however, residues may be present throughout the environment, because 2,4,6-trichlorophenol was widely used as a pesticide. 2,4,6-Trichlorophenol can also form when industrial wastewater containing phenol or certain aromatic acids is treated with hypochlorite or during the disinfection of drinking-water sources. Trichlorophenol (unspecified isomers) has been detected in ambient air and in samples of river water, landfill leachate, chemical plant effluent water, sewage treatment plant effluent, and tap water (ATSDR 1999, HSDB 2009).

2,4,6-Trichlorophenol is a precursor of 2,4,6-trichloroanisole, which is believed to be a potential cause of "cork taint" in wine (Soleas *et al.* 2002). In one study, 80% of spoiled wines contained 2,4,6-trichloroanisole (Insa *et al.* 2006). 2,4,6-Trichlorophenol was measured in cork samples at mean concentrations of up to 26 ng/g (0.026 µg/g) and in oak barrels used for aging wine at up to 0.8 µg/g (Pizarro *et al.* 2006). The efficiency with which trichlorophenol is converted to trichloroanisole depends on the microorganisms present in the cork. Trichlorophenol may also cause off odors in potato chips, dried fruit, coffee, and drinking water (Alvarez-Rodriguez *et al.* 2002). It was measured in coffee at concentrations of up to 42 ppb (0.042 µg/g) (Spadone *et al.* 1990) and in semi-bleached-paper dishes and napkins at 0.075 µg/g (Ozaki *et al.* 2004).

According to the U.S. Environmental Protection Agency's Toxics Release Inventory, environmental releases of 2,4,6-trichlorophenol totaled 12,310 lb in 1988. Releases declined by nearly 99% from 1988 to 1990 and remained at about the same level from 1990 to 1999, but in 2005 returned to nearly the same level as in 1988. In 1988 and 2005, over 88% was released to underground injection wells. In 2007, four facilities released a total of 513 lb (TRI 2009). In air, 2,4,6-trichlorophenol is degraded by reaction with photochemically produced hydroxyl radicals, with a half-life of 26 days. In surface water, 2,4,6-trichlorophenol is expected to dissociate somewhat. It may adsorb to sediment and suspended particles or volatilize from water, with a half-life of 20 days in a river and 150 days in a lake model. It has a high potential for bioconcentration in aquatic organisms. When released to moist soil, 2,4,6-trichlorophenol is expected to somewhat dissociate. The portion that does not dissociate is expected to remain relatively immobile; however, 2,4,6-trichlorophenol is subject to some biodegradation in soil, with a half-life of 5 to 20 days (HSDB 2009).

In the United States, 2,4,6-trichlorophenol was measured in the atmosphere at a median concentration of 0.3 µg/m³. It was detected

Report on Carcinogens, Fourteenth Edition

in groundwater at concentrations of up to 91.3 ppb, in surface water in Canada at up to 30 ppb, in sediments of Canadian streams at up to 10 mg/kg (10,000 ppb), and in snow in Finland at 0.509 ppb (HSDB 2009). 2,4,6-Trichlorophenol was measured in runoff down-gradient from 43 Finnish waste sites at a median concentration of 0.11 µg/L (Assmuth 1996). It was found in finished drinking water in the United States, Finland, and Canada at concentrations of 14 to 700 ppt (0.014 to 0.7 ppb) and in goldfish in New Zealand at up to 40.5 ppb (HSDB 2009).

Average daily intake of 2,4,6-trichlorophenol in Finland was estimated to be 50 µg (HSDB 2009). In urine samples collected from 1,000 adults in the U.S. general population as a part of the Third National Health and Nutrition Examination Survey (conducted from 1988 to 1994), 2,4,6-trichlorophenol was detected in 9.5% of the samples, and the 90th-percentile concentration was 3.3 µg/L (Hill *et al.* 1995). The Centers for Disease Control and Prevention reported that 2,4,6-trichlorophenol was present in urine from 5 of 30 volunteers with no known occupational exposures to phenols, at a median concentration of 0.3 ng/mL (0.3 µg/L) (Ye *et al.* 2005) and in 5% of 20 samples of breast milk from women with no known exposure to 2,4,6-trichlorophenol (Ye *et al.* 2006). 2,4,6-Trichlorophenol was detected in the urine of 37% of the general population of Germany, at a mean concentration of 0.6 µg/g of creatinine (IARC 1979).

The potential for occupational exposure to 2,4,6-trichlorophenol is greatest for workers involved in wood preservation or the production of chlorophenols or chemicals made from chlorophenols and for workers in hospitals and in the leather tanning and finishing industry (ATSDR 1999, HSDB 2009). 2,4,6-Trichlorophenol was found in the urine of workers at a hazardous-waste incinerator in 1999–2000 at mean concentrations of up to 3.5 µg/g of creatinine (Schuhmacher *et al.* 2002); in more than half of the urine samples from harbor workers exposed to river silt aerosols in Hamburg, Germany, at mean concentrations of up to 0.39 µg/g of creatinine (Radon *et al.* 2004); and in the urine of sawmill workers at up to 2,000 µg/L. High urinary levels of trichlorophenol were also reported for lindane production workers and municipal waste incinerator workers (0.85 µg/g of creatinine) (IARC 1979, HSDB 2009). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 851 workers (chemists), including 187 women, potentially were exposed to 2,4,6-trichlorophenol (NIOSH 1990).

Regulations

Department of Transportation (DOT)

2,4,6-Trichlorophenol is considered a hazardous material, and special requirements have been set for transporting this material in tank cars.

Environmental Protection Agency (EPA)

Clean Air Act

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

Clean Water Act

Designated a hazardous substance.

Effluent Guidelines: Chlorinated phenols are listed as a toxic pollutant.

Water Quality Criteria: Based on fish or shellfish and water consumption = 1.5 µg/L; based on fish or shellfish consumption only = 2.8 µg/L; based on organoleptic-effect criteria = 2.0 µg/L.

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.

Resource Conservation and Recovery Act

Characteristic Hazardous Waste: Toxicity characteristic leaching procedure (TCLP) threshold = 2.0 mg/L.

Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of 2,4,6-trichlorophenol = F027, K043, K099, K105.

Listed as a hazardous constituent of waste.

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: 8/19/09.
- Alvarez-Rodriguez ML, Lopez-Ocana L, Lopez-Coronado JM, Rodriguez E, Martinez MJ, Larriva G, Coque JJ. 2002. Cork taint of wines: role of the filamentous fungi isolated from cork in the formation of 2,4,6-trichloroanisole by O-methylation of 2,4,6-trichlorophenol. *Appl Environ Microbiol* 68(12): 5860-5869.
- Assmuth TW. 1996. Comparative risk analysis of waste site toxicants by indices based on concentration distributions, fluxes, environmental fate and critical effects. *J Hazard Mater* 48(1-3): 121-135.
- ATSDR. 1999. *Toxicological Profile for Chlorophenols*. Agency for Toxic Substances and Disease Registry. <http://www.atsdr.cdc.gov/toxprofiles/tp107.pdf>.
- ChemSources. 2009. *Chem Sources - Chemical Search*. Chemical Sources International. <http://www.chemsources.com/chemonline.html> and search on trichlorophenol. Last accessed: 6/22/09.
- Hill RH Jr, Head SL, Baker S, Gregg M, Shealy DB, Bailey SL, Williams CC, Sampson EJ, Needham LL. 1995. Pesticide residues in urine of adults living in the United States: reference range concentrations. *Environ Res* 71(2): 99-108.
- 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: 6/18/09.
- IARC. 1979. 2,4,5- and 2,4,6-Trichlorophenols. 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. 349-367.
- IARC. 1982. 2,4,5-Trichlorophenol and 2,4,6-trichlorophenol. In *Chemicals, Industrial Processes and Industries Associated with Cancer in Humans*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, suppl. 4. Lyon, France: International Agency for Research on Cancer. pp. 249-250.
- IARC. 1999. Polychlorophenols and their sodium salts. 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. 769-816.
- Insa S, Salvado V, Antico E. 2006. Assays on the simultaneous determination and elimination of chloroanisoles and chlorophenols from contaminated cork samples. *J Chromatogr A* 1122(1-2): 215-221.
- NCI. 1979. *Bioassay of 2,4,6-Trichlorophenol for Possible Carcinogenicity*. National Cancer Institute Technical Report Series no. 155. DHEW (NIH) Publication no. 79-1711. 128 pp.
- 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/noes1/84393sic.html>.
- Ogunniyi TA, Oni PO, Juba A, Asaolu SO, Kolawole DO. 2000. Disinfectants/antiseptics in the management of guinea worm ulcers in the rural areas. *Acta Trop* 74(1): 33-38.
- Ozaki A, Yamaguchi Y, Fujita T, Kuroda K, Endo G. 2004. Chemical analysis and genotoxicological safety assessment of paper and paperboard used for food packaging. *Food Chem Toxicol* 42(8): 1323-1337.
- Pizarro C, Gonzalez-Saiz JM, Perez-del-Notario N. 2006. Multiple response optimisation based on desirability functions of a microwave-assisted extraction method for the simultaneous determination of chloroanisoles and chlorophenols in oak barrel sawdust. *J Chromatogr A* 1132(1-2): 8-14.
- Radon K, Wegner R, Heinrich-Ramm R, Baur X, Poschadel B, Szadkowski D. 2004. Chlorophenol exposure in harbor workers exposed to river silt aerosols. *Am J Ind Med* 45(5): 440-445.
- Schuhmacher M, Domingo JL, Agramunt MC, Bocio A, Muller L. 2002. Biological monitoring of metals and organic substances in hazardous-waste incineration workers. *Int Arch Occup Environ Health* 75(7): 500-506.
- Soleas GJ, Yan J, Seaver T, Goldberg DM. 2002. Method for the gas chromatographic assay with mass selective detection of trichloro compounds in corks and wines applied to elucidate the potential cause of cork taint. *J Agric Food Chem* 50(5): 1032-1039.
- Spadone JC, Takeoka G, Liardon R. 1990. Analytical investigation of Rio off-flavor in green coffee. *J Agric Food Chem* 38(1): 226-233.
- SRI. 2009. *Directory of Chemical Producers*. Menlo Park, CA: SRI Consulting. Database edition. Last accessed: 2009.
- TRI. 2009. *TRI Explorer Chemical Report*. U.S. Environmental Protection Agency. Last updated: 3/19/09. <http://www.epa.gov/triexplorer> and select 2,4,6-Trichlorophenol.
- Ye X, Kuklennyk Z, Needham LL, Calafat AM. 2005. Automated on-line column-switching HPLC-MS/MS method with peak focusing for the determination of nine environmental phenols in urine. *Anal Chem* 77(16): 5407-5413.
- Ye X, Kuklennyk Z, Needham LL, Calafat AM. 2006. Measuring environmental phenols and chlorinated organic chemicals in breast milk using automated on-line column-switching-high performance liquid chromatography-isotope dilution tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci* 831(1-2): 110-115.