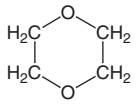
1,4-Dioxane
CAS No. 123-91-1

Reasonably anticipated to be a human carcinogen
First Listed in the *Second Annual Report on Carcinogens* (1981)



Carcinogenicity

1,4-Dioxane is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1976, 1982, 1999, NCI 1978). When administered in drinking water, 1,4-dioxane increased the incidences of squamous cell carcinomas of the nasal turbinates in rats of both sexes and hepatocellular adenomas in female rats. When administered in the drinking water in another study, 1,4-dioxane induced hepatocellular carcinomas in rats of both sexes. When administered in the drinking water, the compound induced hepatomas and carcinomas of the gallbladder in male guinea pigs. When administered in drinking water, 1,4-dioxane increased the incidence of hepatocellular carcinomas in mice of both sexes. As a promoter in a two-stage skin carcinogenesis study, the compound caused increased incidences of skin tumors (papillomas and squamous cell carcinomas and sarcomas) in mice of both sexes. When administered by intraperitoneal injection, 1,4-dioxane increased the incidence of lung tumors in male mice.

There is inadequate evidence for the carcinogenicity of 1,4-dioxane in humans (IARC 1999). In a mortality study of 165 workers potentially exposed to 1,4-dioxane since 1954, two workers died from cancer (IARC 1987, 1999).

Properties

1,4-Dioxane is a volatile, colorless liquid with a mild, ethereal odor. It is miscible with water, most organic solvents, aromatic hydrocarbons, and oils. 1,4-Dioxane is flammable and is available in reagent, technical (more than 99.9% pure), spectrophotometric, and scintillation grades (HSDB 2001).

Use

1,4-Dioxane is used primarily as a stabilizer in chlorinated solvents, particularly 1,1,1-trichloroethane (approximately 90% of the 1,4-dioxane produced). It is also used as a solvent for cellulose acetate, ethyl cellulose, benzyl cellulose, lacquers, plastics, varnishes, paints, dyes, resins, oils, fats, waxes, greases, and polyvinyl polymers. 1,4-Dioxane is used as a reaction medium solvent in organic chemical manufacture, as a wetting agent and dispersing agent in textile processing, as a solvent for specific applications in biological procedures, as a liquid scintillation counting medium, as a reagent for laboratory research and testing, in the preparation of histological sections for microscopic examination, in paint and varnish strippers, and in stain and printing compositions. 1,4-Dioxane may also have been used as a solvent in coatings, sealants, adhesives, cosmetics, and pharmaceuticals (HSDB 2001).

Production

Chem Sources (2001) identified 22 domestic suppliers of 1,4-dioxane. The 1998 *Chemical Buyers Directory* identified seven domestic suppliers of 1,4-dioxane, and *Chemcyclopedia 98* named five (Tilton 1997, Rodnan 1997). The 1997 *Directory of Chemical Producers* listed two producers of the compound with undisclosed amounts (SRI 1997). The USITC has identified one U.S. producer of 1,4-dioxane since 1987, also without production volumes (USITC 1988-1995). In 1986, the USITC identified two domestic producers of 1,4-dioxane. No import data were available. In 1985, four companies produced approximately 25 million lb of 1,4-dioxane, and none was imported into the United States (ICF 1986, SRI 1986). There were three producers in 1984 and 1983, but U.S. production for these years was not reported (USITC 1984, 1985). In 1982, nearly 15 million lb of 1,4-dioxane were produced by three companies in the United States (USITC 1983). There were three producers in 1981, but no production figure was reported. Sales of 1,4-dioxane in the United States were reported to be 7.4 million lb in 1981 (USITC 1982). The 1979 TSCA Inventory identified seven U.S. companies producing approximately 11.6 million lb and three companies importing 1.1 million lb of 1,4-dioxane in 1977 (TSCA 1979). Commercial production of 1,4-dioxane in the United States was first reported in 1951, but commercial quantities were produced before that time (NCI 1985).

Exposure

The primary routes of potential human exposure to 1,4-dioxane are inhalation, ingestion, and dermal contact. 1,4-Dioxane may be formed as a by-product of reactions based on condensing ethylene oxide or ethylene glycol during the production of certain consumer products. Exposure of the general population to 1,4-dioxane could possibly occur from contact with products containing residues of the compound. According to the Consumer Product Safety Commission (CPSC), consumers may possibly be exposed to residual levels of 1,4-dioxane formed during the manufacture of detergents, shampoos, surfactants, and certain pharmaceuticals. CPSC reported that the presence of 1,4-dioxane, even as a trace contaminant, is cause for concern and the Commission continues to monitor its use in consumer products. Residues may be present in food packaged in 1,4-dioxane-containing materials, or on food crops treated with 1,4-dioxane-containing pesticides. Potential occupational exposure to 1,4-dioxane could occur during its production and use as a stabilizer or solvent.

Potential exposure of workers involved in transporting 1,4-dioxane (rail and truck) may occur due to leakage from bulk loading lines. The National Occupational Exposure Survey (1981-1983) indicated that 86,489 workers, including 30,542 women, potentially were exposed to 1,4-dioxane (NIOSH 1984). This estimate was derived from observations of the actual use of the compound (25% of total observations) and the use of trade name products known to contain the compound (75%). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 334,000 workers were potentially exposed to 1,4-dioxane, including 100,000 workers possibly exposed as a result of 1,4-dioxane contamination of 1,1,1-trichloroethane (NIOSH 1976). In 1977, NIOSH estimated that 2,500 workers were potentially exposed to 1,4-dioxane in the workplace, in addition to the 100,000 workers possibly exposed to both 1,1,1-trichloroethane and 1,4-dioxane (NIOSH 1979). OSHA reported that as many as 466,000 workers may possibly be exposed to 1,4-dioxane in the workplace. Jobs involving transfer and handling of 1,4-dioxane in a production facility involve the greatest potential for exposure, with concentrations of up to 32 ppm. Samples taken near points of 1,4-dioxane emission in production facilities indicated concentrations of up to 108 ppm, and in the vicinity of storage tanks the concentration of 1,4-dioxane was as high as 800 ppm (NCI 1985).

1,4-Dioxane has a high potential for entering the environment due to its volatility and solubility in water. Emissions to the atmosphere can occur at the sites of manufacture and use of 1,4-dioxane. EPA's Toxic Chemical Release Inventory (TRI) estimated that 977,447 lb of 1,4-dioxane were released to the environment (on- and off-site releases) from 64 facilities that produced, processed, or used the chemical in the United States in 1996. Of that total, 66% was released

off-site; 17% of the total release was to air and 17% was in surface water discharges (TRI99 2001). Spent solvents disposed of improperly can contaminate ground and surface waters, and 1,4-dioxane has been detected in surface waters in the United States (CHIP 1979).

Regulations

DOT

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

EPA

Clean Air Act

NESHAP: Listed as a Hazardous Air Pollutant (HAP)

NSPS: Manufacture of substance is subject to certain provisions for the control of Volatile Organic Compound (VOC) emissions

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable Quantity (RQ) = 100 lb

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - U108

Listed as a Hazardous Constituent of Waste

OSHA

Permissible Exposure Limit (PEL) = 100 ppm (360 mg/m^3)

Guidelines

ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = 20 ppm

NIOSH

Ceiling Recommended Exposure Limit = 1 ppm (3.6 mg/m^3) (30 minute exposure)
Immediately Dangerous to Life and Health (IDLH) = 500 ppm
Listed as a potential occupational carcinogen

REFERENCES

ChemSources. 2001. Chemical Sources International, Inc. http://www.chemsources.com.

CHIP. 1979. Chemical Hazard Information Profile. Dioxane. Washington, D.C.: U.S. Environmental Protection Agency, Office of Pesticide Programs and Toxic Substances.

HSDB. 2001. Hazardous Substances Data Base. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

IARC. 1976. Cadmium, Nickel Some Epoxides, Miscellaneous Industrial Chemicals and General Considerations on Volatile Anaesthetics. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 11. Lyon, France: International Agency for Research on Cancer. 306 pp.

IARC. 1982. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 4. Lyon, France: International Agency for Research on Cancer. 292 pp.

IARC. 1987. Overall Evaluations of Carcinogenicity. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 7. Lyon, France: International Agency for Research on Cancer. 440 pp.

IARC. 1999. 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. 1589 pp.

ICF. 1986. Use and Substitute Analysis for 1,3-Dioxolane. ICF, Incorporated.

NCI. 1978. Bioassay of 1,4-Dioxane (CAS No. 123-91-1) for Possible Carcinogenicity. Technical Report Series No 80. DHEW (NIH) Publication No. 78-1330. Bethesda, MD: National Institute of Health. 108 pp.

NCI. 1985. Monograph on Human Exposure to Chemicals in the Workplace: 1,4-Dioxane. Technical Report No. 86-131414. Bethesda, MD: Department of Health and Human Services. 31 pp.

NIOSH. 1976. National Occupational Hazard Survey (1972-74). Cincinnati, OH: Department of Health, Education and Welfare.

NIOSH. 1979. A Recommended Standard for Occupational Exposure to Dioxane. Cincinnati, OH: Department of Health, Education and Welfare. 7.

NIOSH. 1984. National Occupational Exposure Survey (1981-83). Cincinnati, OH: U. S. Department of Health and Human Services. http://www.cdc.gov/noes/noes3/empl0003.html.

Rodnan, N., ed. 1997. Chemcyclopedia '98. The Manual of Commercially Available Chemicals, vol. 16. Washington, D.C., American Chemical Society. p. 33-214.

SRI. 1986. Directory of Chemical Producers, United States, 1985. Stanford Research Institute, Menlo Park, CA: SRI International.

SRI. 1997. Directory of Chemical Producers, United States, 1997. Stanford Research Institute, Menlo Park, CA: SRI International.

Tilton, H., ed. 1997. OPD Chemical Buyers Directory 1998. The Green Book. 85th ed. New York, NY, Schnell Publishing.

TRI99. 2001. Toxic Chemical Release Inventory 1999. Data contained in the Toxic Chemical Release Inventory (TRI). National Library of Medicine. http://www.epa.gov/triexplorer/.

TSCA. 1979. Toxic Substances Control Act, Chemical Substances Inventory.

USITC. 1982. Synthetic Organic Chemicals, United States Production and Sales, 1981. USITC Publication No 1292. Washington, D.C.: U.S. Government Printing Office.

USITC. 1983. Synthetic Organic Chemicals, United States Production and Sales, 1982. USITC Publication No 1422. Washington, D.C.: U.S. Government Printing Office.

USITC. 1984. Synthetic Organic Chemicals, United States Production and Sales, 1983. USITC Publication No 1588. Washington, D.C.: U.S. Government Printing Office.

USITC. 1985. Synthetic Organic Chemicals, United States Production and Sales, 1984. USITC Publication No 1745. Washington, D.C.: U.S. Government Printing Office.

USITC. 1988. Synthetic Organic Chemicals, United States Production and Sales, 1987. USITC Publication No 2118. Washington, D.C.: U.S. Government Printing Office.

USITC. 1989. Synthetic Organic Chemicals, United States Production and Sales, 1988. USITC Publication No 2219. Washington, D.C.: U.S. Government Printing Office.

USITC. 1990. Synthetic Organic Chemicals, United States Production and Sales, 1989. USITC Publication No 2338. Washington, D.C.: U.S. Government Printing Office.

USITC. 1991. Synthetic Organic Chemicals, United States Production and Sales, 1990. USITC Publication No 2470. Washington, D.C.: U.S. Government Printing Office.

USITC. 1993. Synthetic Organic Chemicals, United States Production and Sales, 1991. USITC Publication No 2607. Washington, D.C.: U.S. Government Printing Office.

USITC. 1994. Synthetic Organic Chemicals, United States Production and Sales, 1992. USITC Publication No 2720. Washington, D.C.: U.S. Government Printing Office.

USITC. 1995. Synthetic Organic Chemicals, United States Production and Sales, 1994. USITC Publication No 2933. Washington, D.C.: U.S. Government Printing Office.