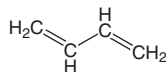


1,3-Butadiene

CAS No. 106-99-0

Known to be a human carcinogen

First Listed in the *Fifth Annual Report on Carcinogens* as (1989)



Carcinogenicity

1,3-Butadiene is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans, including epidemiological and mechanistic information, which indicate a causal relationship between occupational exposure to 1,3-butadiene and excess mortality from lymphatic and/or hematopoietic cancers. 1,3-Butadiene was first listed in the *Fifth Annual Report on Carcinogens* as *reasonably anticipated to be a human carcinogen* based on evidence of its carcinogenicity in experimental animals; however, the listing was revised to *known to be a human carcinogen* in the *Ninth Report on Carcinogens* in 2000. Subsequent to the initial animal cancer findings, 1,3-butadiene was shown to be metabolized to mutagenic and carcinogenic epoxides (epoxybutene and diepoxybutane) in all mammalian species studied, including humans. A number of human epidemiology studies have been published, including (1) a cohort study showing excess risk for lymphosarcoma and reticulosarcoma in workers who manufactured 1,3-butadiene monomer, (2) a significantly increased risk for leukemia among production workers in a study of styrene-butadiene rubber workers in eight plants in the United States and Canada, and (3) a large excess of leukemia that was associated with exposure to 1,3-butadiene and not to styrene in a case-control study within the cohort of styrene-butadiene rubber workers (IARC 1992). In addition, Ward *et al.* (1996) found an excess of lymphosarcoma and reticulosarcoma among 1,3-butadiene production workers in a previously unstudied chemical plant. Matanoski *et al.* (1993) reported that the standardized mortality ratio for leukemia in comparison with the U.S. population was 1.8 times higher in long-term workers who were hired before 1960 and who had worked in the three (of eight studied) styrene-butadiene rubber plants with the highest exposure to butadiene. A second case-control study of the lymphopoietic cancers among styrene-butadiene rubber workers (new set of controls per case) confirmed the strong association and significant dose-response effect between increasing 1,3-butadiene exposure score and increasing risk for leukemia (Matanoski *et al.* 1993). Finally, a follow-up study of styrene-butadiene rubber workers concluded that exposure to 1,3-butadiene in the synthetic rubber industry produced a dose-related increase in the occurrence of leukemia (Delzell *et al.* 1996, Macaluso *et al.* 1996).

The evidence that butadiene is a human carcinogen is supported by experimental animal studies, which have shown that 1,3-butadiene causes both benign and malignant neoplasms at multiple tissue sites in multiple species, and supporting mechanistic data. Sites of tumor induction in mice included the hematopoietic system, heart (hemangiosarcomas), lung, forestomach, harderian gland, preputial gland, liver, mammary gland, ovary, and kidney (NTP 1984, Huff *et al.* 1985, Melnick *et al.* 1990). Sites of tumor induction in rats included the pancreas, testis, thyroid gland, mammary gland, uterus, and Zymbal gland (Owen *et al.* 1987).

Additional Information Relevant to Carcinogenicity

Mouse, rat, and human liver microsomes have been shown to oxidize 1,3-butadiene to epoxybutene (Csadany *et al.* 1992) and to further oxidize the monoepoxide to diepoxybutane (Seaton *et al.* 1995). These metabolites form *N'*-alkylguanine adducts that have been detected in liver DNA of mice exposed to 1,3-butadiene and identified in the urine

of a worker exposed to 1,3-butadiene. Activated *K-ras* genes and inactivated tumor suppressor genes observed in 1,3-butadiene-induced tumors in mice are analogous to genetic alterations frequently observed in a wide variety of human cancers. Dose-related increases in *hprt* mutations have been observed in lymphocytes isolated from mice exposed to 1,3-butadiene or its epoxide metabolites and in occupationally exposed workers. The mutational spectra for 1,3-butadiene and its epoxide metabolites at the *hprt* locus in mouse lymphocytes are similar to the mutational spectrum of ethylene oxide, an alkylating agent listed as *known to be a human carcinogen* (See Ethylene Oxide profile). The mechanism of tumor induction by 1,3-butadiene in rodents and humans appears to be due to its metabolism to DNA-reactive intermediates resulting in genetic alterations in protooncogenes and/or tumor suppressor genes (Melnick and Kohn 1995).

Properties

1,3-Butadiene, an aliphatic hydrocarbon, is a colorless, non-corrosive gas with a mild aromatic or gasoline-like odor and a molecular weight of 54. The boiling point is -4.4°C and the melting point is -108.9°C . The vapor pressure is 1,790 mm Hg at 20°C , and the vapor is heavier than air with a vapor density of 1.87 (IARC 1992). When heated, 1,3-butadiene emits acrid fumes and is flammable. When exposed to air, it also will form explosive peroxides that are sensitive to shock or heating above 27°C . 1,3-Butadiene has a log octanol-water partition coefficient of 1.99 and is sparingly soluble in water, slightly soluble in methanol and ethanol, and soluble in most common organic solvents such as acetone, diethyl ether, benzene, and cyclohexane. It polymerizes readily in the presence of sodium or oxygen (Lewis 1992, Budavari *et al.* 1996, HSDB 2003). The commercial product is 99% pure. It may contain parts-per-million (ppm) levels of butadiene dimer (NTP 1993). 1,3-Butadiene is transported as a liquified gas under pressure (Morrow 1990).

Use

1,3-Butadiene is used primarily as a monomer to manufacture many different types of polymers and copolymers and as a chemical intermediate to produce a number of important industrial chemicals. More than 75% of the 1,3-butadiene produced goes into synthetic rubber products (CEN 1986). The major uses include styrene-butadiene rubber (30% to 35%), polybutadiene rubber (20% to 22%), adiponitrile (12% to 15%), styrene-butadiene latex (10%), neoprene rubber (5% to 6%), acrylonitrile-butadiene-styrene resins (5% to 6%), exports (4%), nitrile rubber (3%), and other uses, including specialty polymers (2% to 8%) (IARC 1992, ATSDR 1993). The major end-use products for styrene-butadiene and polybutadiene are tires. Other uses include latex adhesives, seals, hoses, gaskets, various rubber products, nylon carpet backings, paper coatings, paints, pipes, conduits, appliance and electrical equipment components, automotive parts, and luggage. The only major nonpolymer use is to manufacture adiponitrile, a nylon intermediate. Butadiene also is used in the manufacture of the fungicides, captan and captafol (Morrow 1990, IARC 1992, Kirschner 1996).

Production

1,3-Butadiene is isolated by distillation or extraction from crude butadiene, which is a by-product of ethylene production. Commercial production began in the 1930s (IARC 1992). Between 1980 and 2002, annual U.S. production of rubber-grade 1,3-butadiene ranged from a low of about 869,000 metric tons (1.9 billion pounds) in 1982 to a high of 2,009,000 metric tons (4.4 billion pounds) in 2000 (IARC 1992, CEN 1999, 2003). The average annual change was about 2.5% from 1992 to 2002 compared to about 1.2% from 1980 to 1990. In 1987, 1,3-butadiene ranked 34th among the top 50 chemical commodities produced in the United States and fell slightly to 36th by the mid 1990s (Morrow 1990, Kirschner 1996, CEN

1997). In 1990, 30 ethylene plants in the United States produced crude butadiene streams that were processed in 11 extraction plants (Morrow 1990). Ten U.S. producing companies and 17 U.S. suppliers were identified in 2003 (ChemSources 2003, SRI 2003).

U.S. demand exceeds the domestic supply in most years; therefore, imports greatly exceed exports. Imports ranged from about 500 to 900 million pounds (227,000 to 408,000 metric tons) annually from the late 1970s to the mid 1980s. 1,3-Butadiene imports were approximately 1.2 to 1.4 billion pounds (544,000 to 635,000 metric tons) from 1998 to 2000 but decreased to 200 million pounds (91,000 metric tons) in 2002. Exports ranged from about 94 million to 145 million pounds (43,000 to 66,000 metric tons) annually in the late 1970s through the mid 1980s but decreased to about 37.6 million pounds (17,000 metric tons) in 2000 and 15.2 million pounds (6,900 metric tons) in 2002 (ATSDR 1993, ITA 2001, 2003).

Exposure

The primary route of potential exposure to 1,3-butadiene for the general population is inhalation. Some exposure may occur from ingesting contaminated food or water or dermal (skin) contact; however, these types of exposures are unlikely in most circumstances. This chemical is not a common contaminant of water supplies, and, although some food packaging contains residual 1,3-butadiene, the available data indicate that it does not usually migrate to the food. Certain cooking oils, such as rape oil (canola) release 1,3-butadiene when heated (Shields *et al.* 1995).

Most people are exposed to low levels of 1,3-butadiene in the air because it is released to the environment during its production, use, storage, and disposal and is present in gasoline, automobile exhausts, and cigarette smoke. 1,3-Butadiene is emitted from furnaces at secondary lead smelting facilities handling automotive lead-acid batteries that contain plastic battery separators or that have hard rubber casings and from petroleum refineries (EasternResearchGroupUSA 1996). Incomplete combustion of a variety of fuels forms 1,3-butadiene as a product. 1,3-Butadiene makes up 0.5 to 2% of the total organic gas emissions from most types of combustion (Ligocki *et al.* 1994). It can also be found in exhaust emissions from motor vehicles as a product of incomplete combustion of gasoline and diesel oil and from the thermal breakdown of plastics (ATSDR 1993, Eastern Research Group USA 1996). California has run dispersion modeling from a typical freeway source and has estimated that gasoline-fueled vehicles emit 0.011 grams per mile (Cooper and Reisman 1992). 1,3-butadiene also is formed naturally as a byproduct of forest fires (HSDB 2003).

Cigarette smoke is also an environmental source of 1,3-butadiene. Releases into the air in sidestream smoke have been variously estimated at 152 to 400 μg 1,3-butadiene per cigarette (Ligocki *et al.* 1995). Calculations based on 400 μg /cigarette indicate that 1,3-butadiene concentrations in the homes of smokers would be increased by approximately 4 $\mu\text{g}/\text{m}^3$, and concentrations in air at workplaces allowing smoking would increase by 13 $\mu\text{g}/\text{m}^3$ (Wallace 1991).

1,3-Butadiene has been detected in air samples collected from urban, suburban, and rural areas. The median daily concentrations compiled from ambient air samples collected in the United States from 1970 to 1987 were 0.29 ppb in urban areas (385 samples), 0.32 ppb in suburban areas (196 samples), and 0.1 ppb in rural areas (2 samples). However, reported average daily ambient air concentrations within a mile of petrochemical facilities have exceeded 100 ppb, and the highest hourly average concentrations have exceeded 900 ppb (ATSDR 1993). Volatilization of 1,3-butadiene from wastewaters of styrene-1,3-butadiene copolymer production at publicly owned treatment works (POTW) has been calculated to be 21 tons/yr (19,000 kg/yr) (EasternResearchGroupUSA 1996).

Occupational exposure to 1,3-butadiene may occur through inhalation and, to a lesser extent, skin contact (NTP 1984). According to the National Occupational Exposure Survey (NOES) conducted from 1981 to 1983, about 52,000 workers, including 1,410 women, at 2,201 facilities were potentially exposed to 1,3-butadiene (NIOSH 1984, 1990). This number does not include workers exposed to butadiene polymers and copolymers and is consistent with earlier estimates of about 66,000 to 70,000 workers at 3,086 facilities reported in the National Occupational Hazard Survey (NOHS) conducted from 1972 to 1974 (NIOSH 1976). Health Hazard Evaluation surveys conducted by NIOSH at six facilities indicated that air concentrations of 1,3-butadiene ranged from 0.06 to 39 ppm. Surveys conducted at many monomer, polymer, and end-user plants have reported concentrations ranging from below detection to 374 ppm (827 mg/m^3). In most cases, 8-hour time weighted average concentrations were less than 10 ppm (22 mg/m^3) (IARC 1992, ATSDR 1993). For the monomer industry as a whole, 1,3-butadiene concentrations were > 10 ppm (22 mg/m^3) in 7.1% of the samples, 2 to 10 ppm (4 to 22 mg/m^3) in 12.8%, 1 to 2 ppm (2 to 4 mg/m^3) in 12.3% and < 1 ppm in 67.8%. The present OSHA permissible limit is 1 ppm. For the polymer industry as a whole, the corresponding percentages for these four ranges were 3.3%, 7.7%, 3.3%, and 85.8%, respectively. The arithmetic mean exposure for personal full-shift exposures in the polymer plants was 1.14 ppm (2.57 mg/m^3) (Fajen *et al.* 1993).

According to U.S. Environmental Protection Agency's Toxics Release Inventory (TRI), total annual on- and off-site releases of 1,3-butadiene from industrial facilities have declined from more than 7.7 million pounds (3.5 million kilograms) in 1988 to about 2.3 million pounds (1.0 million kilograms) in 2001. More than 90% was released to the air (TRI01 2003). However, a nationwide 1,3-butadiene inventory (including vehicle emissions and emissions from manufacturing and producing facilities) calculated annual butadiene emissions to air to be 102 million kilograms (225 million pounds) in 1990 (Ligocki *et al.* 1994), considerably higher than the TRI estimate of about 5.2 million pounds (2.4 million kilograms) for industrial emissions for the same year.

Regulations

DOT

Butadienes are considered hazardous materials and special requirements have been set for marking, labeling, and transporting these materials

EPA

Clean Air Act

Mobile Source Air Toxics: Listed as a Mobile Source Air Toxic for which regulations are to be developed

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

Prevention of Accidental Release: Threshold Quantity (TQ) = 10,000 lb

Urban Air Toxics Strategy: Identified as one of 33 HAPs that present the greatest threat to public health in urban areas

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

OSHA

Permissible Exposure Limit (PEL) = 1 ppm

Short-Term Exposure Limit = 5 ppm

"Comprehensive Standards" for occupational exposure to this substance have been developed

Guidelines

ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = 2 ppm

NIOSH

Immediately Dangerous to Life and Health (IDLH) = 2000 ppm

Listed as a potential occupational carcinogen

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