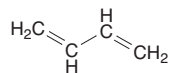


1,3-Butadiene

CAS No. 106-99-0

Known to be a human carcinogen

First listed in the *Fifth Annual Report on Carcinogens* (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 studies. 1,3-Butadiene was first listed in the *Fifth Annual Report on Carcinogens* in 1989 as *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals. The listing was revised to *known to be a human carcinogen* in the *Ninth Report on Carcinogens* in 2000.

Cancer Studies in Humans

A number of epidemiological studies have shown an association between occupational exposure to 1,3-butadiene and excess mortality from cancer of the lymphatic and hematopoietic systems. These include (1) a cohort study showing increased risk of lymphosarcoma and reticulosarcoma in workers who manufactured 1,3-butadiene monomer, (2) a study of styrene-butadiene rubber workers in eight plants in the United States and Canada showing increased risk of leukemia among production workers, and (3) a case-control study within the cohort of styrene-butadiene rubber workers showing a large excess of leukemia associated with exposure to 1,3-butadiene and not to styrene (IARC 1992). In addition, an excess of lymphosarcoma and reticulosarcoma was found among 1,3-butadiene production workers in a previously unstudied chemical plant (Ward *et al.* 1996). Excess deaths from leukemia were observed among long-term workers who were hired before 1960 and had worked in the three (of eight studied) styrene-butadiene rubber plants with the highest exposure to butadiene (standardized mortality ratio = 1.8 in comparison with the U.S. population). A second case-control study of styrene-butadiene rubber workers with lymphopoietic cancer (with a new set of controls for each case) confirmed the strong association and significant dose-response relationship between 1,3-butadiene exposure score and risk of leukemia (Matanoski *et al.* 1993). Finally, a follow-up study of styrene-butadiene rubber workers in the synthetic rubber industry also found a dose-response relationship between 1,3-butadiene exposure level and the occurrence of leukemia (Dellzell *et al.* 1996, 2006, Macaluso *et al.* 1996).

Studies on Mechanisms of Carcinogenesis

1,3-Butadiene appears to cause tumors in humans and rodents through its metabolism to DNA-reactive epoxide intermediates, which cause genetic alterations in proto-oncogenes or tumor-suppressor genes (Melnick and Kohn 1995). 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 in the urine of a worker exposed to 1,3-butadiene. Activated *K-ras* oncogenes 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 for ethylene oxide, an alkylating agent listed in the Report on Carcinogens as *known to be a human carcinogen*.

Cancer Studies in Experimental Animals

There is sufficient evidence for the carcinogenicity of 1,3-butadiene from studies in experimental animals. Inhalation exposure to 1,3-butadiene caused benign or malignant tumors at several different tissue sites in rodents, including the hematopoietic system, heart (hemangiosarcoma), lung, forestomach, Harderian gland, preputial gland, liver, mammary gland, ovary, and kidney in mice (NTP 1984, Huff *et al.* 1985, Melnick *et al.* 1990) and the pancreas, testis, thyroid gland, mammary gland, uterus, and Zymbal gland in rats (Owen *et al.* 1987).

Properties

1,3-Butadiene is an olefin which at room temperature is a colorless gas with a mild aromatic or gasoline odor. It is insoluble in water but soluble in ether, ethanol, acetone, and other organic solvents. It polymerizes readily, especially in the presence of oxygen; therefore, it is shipped and stored with an inhibitor to prevent this reaction (Akron 2009). It is also a dangerous fire hazard. Physical and chemical properties of 1,3-butadiene are listed in the following table.

Property	Information
Molecular weight	54.1 ^a
Density	0.6149 g/cm ³ at 25°C ^a
Melting point	-108.966°C ^a
Boiling point	-4.5°C at 760 mm Hg ^a
Log <i>K_{ow}</i>	1.99 ^b
Water solubility	0.735 g/L at 20°C ^a
Vapor pressure	2,110 mm Hg at 25°C ^a
Vapor density relative to air	1.87 ^a

Sources: ^aHSDB 2009, ^bChemIDplus 2009.

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 production of 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%), and nitrile rubber (3%), exports (4%), and other uses, including production of specialty polymers (2% to 8%) (IARC 1992, ATSDR 1993). The major end-use products containing styrene-butadiene and polybutadiene are tires. Other products 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 in the manufacture of adiponitrile, a nylon intermediate. Butadiene is also 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). In 2009, 11 U.S. producers and 12 U.S. suppliers of 1,3-butadiene were identified

(ChemSources 2009, SRI 2009). In 2015, the U.S. Environmental Protection Agency (EPA) estimated that combined production and imports of butadiene were in the range of 1 to 5 billion pounds (EPA 2016), similar to annual production reported since the 1980s (ranging from 1.9 to 4.4 billion pounds) (IARC 1992, CEN 1999, 2003). Because U.S. demand for 1,3-butadiene has generally exceeded the domestic supply, imports have greatly exceeded exports (as shown in the following table).

Category	Year	Quantity (lb)
Production + imports ^a	2015	1 to 5 billion
U.S. imports ^b	2017	629.2 million
U.S. exports ^b	2017	87.9 million

Sources: ^aEPA 2016. ^bUSITC 2018 (imports category reported as "buta-1,3-diene and isomer thereof").

Exposure

Occupational exposure to 1,3-butadiene may occur through inhalation and, to a lesser extent, dermal contact (NTP 1984). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that about 52,000 workers at 2,201 facilities, including 1,410 women, potentially were exposed to 1,3-butadiene (NIOSH 1990). This estimate does not include workers exposed to butadiene polymers and copolymers and is consistent with an earlier estimate of about 66,000 to 70,000 workers at 3,086 facilities reported in the National Occupational Hazard Survey (conducted from 1972 to 1974) (NIOSH 1976). Health hazard evaluation surveys conducted by the National Institute for Occupational Safety and Health at six facilities found air concentrations of 1,3-butadiene ranging 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/m³). In most cases, 8-hour time-weighted-average concentrations were less than 10 ppm (< 22 mg/m³) (IARC 1992, ATSDR 1993). For the monomer industry as a whole, 1,3-butadiene concentrations were greater than 10 ppm (> 22 mg/m³) in 7.1% of the samples, 2 to 10 ppm (4 to 22 mg/m³) in 12.8%, 1 to 2 ppm (2 to 4 mg/m³) in 12.3% and less than 1 ppm (< 2 mg/m³) in 67.8%. The Occupational Safety and Health Administration permissible exposure 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/m³) (Fajen *et al.* 1993).

The primary route of potential exposure to 1,3-butadiene for the general population is inhalation. Some exposure may occur through ingestion of contaminated food or water or dermal contact; however, these routes of exposure are unlikely under most circumstances. 1,3-Butadiene is not a common contaminant of water supplies. 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 rapeseed 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 petroleum refineries and from furnaces at secondary lead smelting facilities handling automotive lead-acid batteries that contain plastic battery separators or that have hard rubber casings (EPA 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 mo-

tor-vehicle exhaust emissions as a product of incomplete combustion of gasoline and diesel oil and from the thermal breakdown of plastics (ATSDR 1993, EPA 1996). Through modeling of dispersion from a typical freeway source in California, it was estimated that gasoline-fueled vehicles emit 0.011 g of 1,3-butadiene per mile (Cooper and Reisman 1992). 1,3-Butadiene also is formed naturally as a by-product of forest fires (HSDB 2009). Releases of 1,3-butadiene in side-stream cigarette smoke into the air have been variously estimated at 152 to 400 µg per cigarette (Ligocki *et al.* 1995). Calculations based on 400 µg per cigarette indicate that 1,3-butadiene concentrations in the homes of smokers would be increased by approximately 4 µg/m³, and concentrations in air at workplaces allowing smoking would be increased by 13 µg/m³ (Wallace 1991).

According to EPA's Toxics Release Inventory, total industrial environmental releases of 1,3-butadiene declined from more than 7.7 million pounds in 1988 to about 1.8 million pounds in 2007, of which over 90% was released to air (TRI 2009). 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 EPA's estimate of about 5.2 million pounds (2.4 million kilograms) for industrial emissions in the same year.

The median daily concentrations of 1,3-butadiene in U.S. ambient air samples collected 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). The maximum 24-hour average concentrations of 1,3-butadiene reported for four U.S. cities in 2004 were 0.3 ppb for St. Louis, Missouri, 0.5 ppb for Chicago, Illinois, and Los Angeles, California, and 37.4 ppb for Houston, Texas (Clements *et al.* 2006). However, reported average daily concentrations of 1,3-butadiene in ambient air 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 has been calculated to be 21 tons per year (EPA 1996).

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full-shift exposures in the polymer plants was 1.14 ppm (2.57 mg/m³) (Fajen *et al.* 1993).

Regulations

Department of Transportation (DOT)

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

Environmental Protection Agency (EPA)

Clean Air Act

Mobile Source Air Toxics: Listed as a mobile source air toxic for which regulations are to be developed. *National Emission Standards for Hazardous Air Pollutants*: Listed as a hazardous air pollutant.

New Source Performance Standards: Manufacture of 1,3-butadiene is subject to certain provisions for the control of volatile organic compound emissions.

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

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

Standards have been established for emissions of 1,3-butadiene from reformulated gasoline and motor vehicles.

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.

Occupational Safety and Health Administration (OSHA)

While this section accurately identifies OSHA's legally enforceable PELs for this substance in 2018, specific PELs may not reflect the more current studies and may not adequately protect workers.

Permissible exposure limit (PEL) = 1 ppm.

Short-term exposure limit (STEL) = 5 ppm.

Comprehensive standards for occupational exposure to 1,3-butadiene have been developed.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 2 ppm.

Biological exposure index (BEI) (end of shift) = 2.5 mg/L for 1,2-dihydroxy-4-(*N*-acetylcysteinyl)-butane in urine; (timing not critical) = 2.5 pmol/g of hemoglobin for a mixture of *N*-(1-hydroxybutenyl)- and *N*-(2-hydroxybutenyl)-valine hemoglobin adducts in blood.

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

Immediately dangerous to life and health (IDLH) limit = 2,000 ppm.

Listed as a potential occupational carcinogen.

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