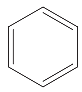
Benzene

CAS No. 71-43-2

Known to be a human carcinogen

First listed in the *First Annual Report on Carcinogens* (1980)



Carcinogenicity

Benzene is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans.

Cancer Studies in Humans

Case reports and case series have reported leukemia (mostly acute myelogenous leukemia, also known as acute myeloid or myelocytic leukemia) in individuals exposed to benzene. The strongest epidemiological evidence that benzene causes cancer is from several cohort studies in various industries and geographical locations, which found that occupational exposure to benzene increased the risk of mortality from leukemia (mainly acute myelogenous leukemia). Case-control studies also reported that exposure to benzene increased the risk of leukemia, but the usefulness of these studies was limited by poorly defined exposures and mixed exposure patterns (IARC 1974, 1982, 1987).

Since benzene was reviewed for listing in the *First Annual Report on Carcinogens,* numerous epidemiological studies of benzene exposure and cancer have been published. The International Agency for Research on Cancer (IARC) evaluated benzene in 2012 and concluded that there was sufficient evidence for the carcinogenicity of benzene in humans, based on a causal relationship with myeloid leukemia/acute nonlymphocytic leukemia (IARC 2012). IARC also concluded that there was limited evidence of carcinogenicity based on a positive association between exposure to benzene and acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, and non-Hodgkin lymphoma.

Cancer Studies in Experimental Animals

Studies in experimental animals, including many published after benzene was listed in the *First Annual Report on Carcinogens,* have demonstrated that benzene causes cancer at numerous tissue sites in rodents. Oral exposure to benzene caused cancer of the Zymbal gland (carcinoma) in rats and mice of both sexes, cancer of the oral cavity (squamous-cell carcinoma) in rats of both sexes, malignant lymphoma and lung cancer (alveolar/bronchiolar carcinoma) in mice of both sexes, skin cancer (squamous-cell carcinoma) in male rats, benign tumors of the Harderian gland (adenoma) and cancer of the preputial gland (carcinoma) in male mice, and benign ovarian tumors and cancer of the mammary gland (carcinoma and carcinosarcoma) in female mice (NTP 1986, Huff *et al.* 1989). Inhalation exposure to benzene caused tumors at many tissue sites in rats and a tendency towards induction of lymphoid tumors in mice. Benzene administered by intraperitoneal injection caused benign lung tumors in male mice (IARC 1982, 1987). Dermal application of benzene caused benign skin tumors in transgenic mice carrying the v-Ha-*ras* oncogene, which increases their susceptibility to carcinogens (Blanchard *et al.* 1998, Spalding *et al.* 1999, French and Saulnier 2000). In heterozygous p53-deficient mice (with only one functional copy of the *p53* tumor-suppressor gene), benzene administered by stomach tube caused cancer (sarcoma) of head and neck, thoracic cavity, and subcutaneous tissue (French *et al.* 2001, Hulla *et al.* 2001).

Properties

Benzene is the primary aromatic compound. It exists at room temperature as a clear, colorless-to-yellow liquid with an aromatic odor. It is only slightly soluble in water, but it is miscible with alcohol, ether, chloroform, carbon disulfide, acetone, oils, carbon tetrachloride, glacial acetic acid, and most other organic solvents. Benzene is highly flammable (Akron 2009). Physical and chemical properties of benzene are listed in the following table.

Property	Information
Molecular weight	78.1
Specific gravity	0.8787 at 15°C/4°C
Melting point	5.5°C
Boiling point	80.1°C
Log K_{ow}	2.13
Water solubility	1.79 g/L at 25°C
Vapor pressure	94.8 mm Hg at 25°C
Vapor density relative to air	2.8

Source: HSDB 2009.

Use

Benzene is used primarily as a solvent in the chemical and pharmaceutical industries, as a starting material and intermediate in the synthesis of numerous chemicals, and in gasoline. As a raw material, it is used in the synthesis of ethylbenzene (used to produce styrene) (53%), cumene (used to produce phenol and acetone) (22%), cyclohexane (12%), nitrobenzene (used to produce aniline and other chemicals) (5%), detergent alkylate (linear alkylbenzene sulfonates) (3%), and chlorobenzenes and other products (5%). Benzene is used as an additive in gasoline, but it also is present naturally in gasoline, because it occurs naturally in crude oil and is a by-product of oil-refining processes. The percentage of benzene in unleaded gasoline is approximately 1% to 2% by volume (ATSDR 1997, HSDB 2009).

Production

Benzene has been produced commercially from coal since 1849 and from petroleum since 1941. Since 1959, the major U.S. source of benzene has been petroleum (IARC 1989). In 2009, 59 U.S. manufacturers (SRI 2009) and 24 U.S. suppliers of benzene were identified (ChemSources 2009). In 2015, the U.S. Environmental Protection Agency (EPA) estimated that combined production and imports of benzene were in the range of 10 to 20 billion pounds, similar to the 12.0 to 17.8 billion pounds reported for production only from 1990 to 2000 (CEN 2003). In 2017, U.S. imports of benzene were substantially higher than exports (as shown in the following table).

Category	Year	Quantity (lb)
Production + imports[a]	2015	10 billion to 20 billion
U.S. imports[b]	2017	6.5 billion
U.S. exports[b]	2017	372.5 million

Sources: [a]EPA 2016. [b]USITC 2018 (imports reported as "benzene of a purity of 95% or more by weight").

Exposure

People are exposed to benzene in the workplace and in their everyday lives. Occupational exposure may occur during production of benzene or use of substances containing it. In the vulcanization step of tire manufacturing, benzene was measured at concentrations of up to 27.2 mg/m^3, resulting in an estimated daily intake of 0.0045 mg/kg of body weight for workers (Durmusoglu 2007). The National Occupational Health Survey (conducted from 1972 to 1974) estimated that 147,600 U.S. workers potentially were exposed to benzene (NIOSH

1976), and the National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that about 272,000 workers, including 143,000 women, potentially were exposed to benzene (NIOSH 1990).

Evidence that the U.S. general population is exposed to benzene comes from the 2013–2014 National Health and Nutrition Examination Survey (NHANES), which found that the 95th-percentile concentration of benzene in whole blood was 0.285 ng/mL (0.285 μg/L), based on a sample of 3,094 individuals of all ages, both genders, and all race and ethnicity groups (CDC 2018a). The primary route of human exposure to benzene is inhalation of ambient air. The general population can also be exposed to benzene by inhaling air containing tobacco smoke, drinking contaminated water, or eating contaminated food. About half of the total national exposure to benzene comes from cigarette smoke. In the NHANES study, benzene levels in blood were much higher in smokers (95th percentile = 0.500 ng/mL [0.500 μg/L], 915 samples) than in nonsmokers (0.081 ng/mL [0.081 μg/L], 2,049 samples) (CDC 2018b). In a study of benzene levels in homes, the median level was 2.2 ppb (7 μg/m^3) in 185 homes without smokers and 3.3 ppb (10.5 μg/m^3) in 343 homes with one or more smokers. Amounts of benzene measured per cigarette ranged from 5.9 to 75 μg in mainstream smoke and from 345 to 653 μg in sidestream smoke.

Benzene has also been found in some consumer products, including hand sanitizers and sun-care products. In 2021, an independent testing laboratory reported benzene contamination at levels ranging from 0.1 to 16.1 ppm in 44 (17%) of 260 unique batches of liquid and non-liquid hand sanitizers and at levels ranging from < 0.1 to 6.26 ppm in 78 (27%) of 294 unique batches of sunscreen and after-sun products (sprays, gels, and lotions with chemical- and mineral-based formulations) (Valisure 2021a,b). Benzene has been detected in fruits, vegetables, nuts, dairy products, eggs, and fish. In a 1992 survey of more than 50 foods, benzene concentrations in foods containing both benzoate and ascorbate food additives ranged from less than 1 to 38 ppb (< 3 to 120 μg/m3) (ATSDR 1997).

Benzene is present in the atmosphere both from natural sources, which include forest fires and oil seeps, and from industrial sources, which include automobile exhaust, industrial emissions, and fuel evaporation from gasoline filling stations. Benzene has been measured in outdoor air at various U.S. locations at concentrations ranging from 0.02 ppb (0.06 μg/m^3) in a rural area to 112 ppb (356 μg/m^3) in an urban area. The maximum 24-hour average concentrations of benzene reported for four U.S. cities in 2004 were 1.1 ppb (3.5 μg/m^3) for St. Louis, Missouri, 2.7 ppb (8.6 μg/m^3) for Chicago, Illinois, 2.9 ppb (9.3 μg/m^3) for Los Angeles, California, and 73.5 ppb (234.8 μg/m^3) for Houston, Texas (Clements *et al.* 2006). Exposure to benzene is highest in areas of heavy motor vehicle traffic and around gasoline filling stations. Based on an average benzene concentration of 12.5 ppb (40 μg/m^3) in the air and exposure of 1 hour per day, daily benzene intake from driving or riding in a motor vehicle is estimated to be 40 μg. Exposure is greater among people who spend significant time in motor vehicles in areas of congested traffic. In addition, pumping of gasoline can be a significant source of benzene exposure; for an individual spending 70 minutes per year pumping gasoline, daily benzene intake is estimated to be 10 μg (ATSDR 1997). According to EPA's Toxics Release Inventory, environmental releases of benzene decreased from 34 million pounds in 1988 to 6 million pounds in 2001, when 5 million pounds was released to air and 19,000 lb to water. In 2007, 775 facilities released 6.3 million pounds of benzene (TRI 2009). Benzene levels in water in the vicinity of four manufacturing facilities using or producing benzene ranged from less than 1 to 179 ppb (< 3 to 569 μg/m^3) (ATSDR 1997).

Regulations

Coast Guard, Dept. of Homeland Security

Comprehensive regulations have been established for safe transport of benzene on ships and barges.

Consumer Product Safety Commission (CPSC)

Products containing 5% or more by weight of benzene are considered hazardous and require special labeling.

Solvents for paints or other surface-coating materials containing 10% or more by weight of benzene require special packaging.

Department of Transportation (DOT)

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

Environmental Protection Agency (EPA)

Clean Air Act

Comprehensive regulations have been developed to control benzene levels in gasoline and benzene emissions from motor vehicles.

Mobile Source Air Toxics: Beginning in 2011, refiners must meet an annual average gasoline benzene content standard of 0.62% by volume (vol%) on all gasoline; by 2012, a maximum benzene content of 1.3 vol% may not be exceeded.

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

New Source Performance Standards: Manufacture 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.

Clean Water Act

Designated a hazardous substance.

Effluent Guidelines: Listed as a toxic pollutant.

Water Quality Criteria: Based on fish or shellfish and water consumption = 0.58 to 2.1 μg/L; based on fish or shellfish consumption only = 16 to 58 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 = 0.5 mg/L.

Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of benzene = U019, F005, F024, F025, F037, F038, K085, K104, K105, K141, K142, K143, K144, K145, K147, K151, K159, K169, K171, K172.

Listed as a hazardous constituent of waste.

Safe Drinking Water Act

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

Food and Drug Administration (FDA, an HHS agency)

Maximum permissible level in bottled water = 0.005 mg/L.

Residues of benzene used as a solvent in producing modified hop extract shall not exceed 1.0 ppm.

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

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.

Acceptable peak exposure = 50 ppm (maximum duration = 10 min) for select industries.

Ceiling concentration = 25 ppm for select industries.

Permissible exposure limit (PEL) = 1 ppm; = 10 ppm for select industries.

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

Comprehensive standards for occupational exposure to benzene have been developed.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 0.5 ppm.

Threshold limit value – short-term exposure limit (TLV-STEL) = 2.5 ppm.

Potential for dermal absorption.

Biological exposure index (BEI) (end of shift) = 25 μg/g of creatinine for *S*-phenylmercapturic acid in urine; = 500 μg/g of creatinine for *t,t*-muconic acid in urine.

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

Immediately dangerous to life and health (IDLH) limit = 500 ppm.

Short-term exposure limit (STEL) = 1 ppm.

Recommended exposure limit (time-weighted-average workday) = 0.1 ppm.

Listed as a potential occupational carcinogen.

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