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 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 1982, 1987).

Since benzene was reviewed for listing in the *First Annual Report on Carcinogens* and by the International Agency for Research on Cancer, numerous epidemiological studies of benzene exposure have been published. Some studies found that the risk of leukemia increased with increasing benzene exposure; increased risk of death from leukemia was very high in the groups with the highest exposure (IPCS 1993). Savitz and Andrews (1997) reviewed 18 community-based and 16 industry-based studies of benzene exposure and suggested that the evidence supported an association between benzene exposure and leukemia in general, rather than specifically with acute myelogenous leukemia. Most studies found that benzene exposure increased the risks of total lymphatic and hematopoietic cancer (i.e., cancers of the lymphatic system and of organs and tissues involved in production of blood), total leukemia, and specific histologic types of leukemia, including chronic lymphocytic leukemia, as well as acute myelogenous leukemia. Little evidence was found for an association between benzene exposure and multiple myeloma or non-Hodgkin's lymphoma.

The evidence in humans is supported by studies in experimental animals, including many published after benzene was first reviewed for listing, demonstrating that benzene causes cancer at multiple tissues sites in rodents. Benzene was tested for carcinogenicity in mice and rats exposed by several routes, including oral administration, inhalation, injection, and dermal application. When administered orally, benzene caused Zymbal-gland carcinoma and oral-cavity tumors in rats of both sexes; skin carcinoma in male rats; Zymbal-gland carcinoma, malignant lymphoma, and lung tumors in mice of both sexes; harderian-gland adenoma and preputial-gland carcinoma in male mice; and ovarian tumors and mammary-gland carcinoma and carcinosarcoma in female mice (NTP 1986). When administered by inhalation, benzene caused tumors at many tissue sites in rats and a tendency towards lymphoid tumor induction in mice. Benzene administered by intraperitoneal injection caused benign lung tumors in male mice. No tumors were observed in mice administered benzene by subcutaneous injection or dermal application (IARC 1982, 1987). However, 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). Later studies reported that when administered benzene by gavage, heterozygous *p53*-deficient mice (with only one functional copy of the *p53* tumor-suppressor gene) developed head and neck, thoracic cavity, and subcutaneous sarcomas (French *et al.* 2001, Hulla *et al.* 2001).

Properties

Benzene is an aromatic hydrocarbon with molecular weight of 78.1. It occurs as a clear or colorless to light-yellow liquid with a gasoline-like odor. Benzene has a boiling point of 80.1°C, a melting point of 5.5°C, a vapor pressure of 95 mm Hg at 25°C, a specific gravity of 0.88 at 15°C/4°C, and an octanol-water partition coefficient of 2.13. It is slightly soluble in water and is miscible with alcohol, ether, chloroform, acetone, carbon tetrachloride, carbon disulfide, oils, and glacial acetic acid (HSDB 2003).

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 2003).

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 1994, benzene ranked 17th in production volume among chemicals produced in the United States. U.S. production of benzene increased from 5.4 million metric tons (12.0 billion pounds) in 1992 to 7.2 million metric tons (15.8 billion pounds) in 2002, an average increase of 2.8% per year (CEN 2003). Annual production during this period was highest in 2000, at 8.1 million metric tons (17.8 billion pounds). In 2003, 65 U.S. manufacturers of benzene were identified (SRI 2003).

In 2002, U.S. imports of benzene totaled over 4 billion liters (1.1 billion gallons), which greatly exceeded exports of 6 million liters (1.6 million gallons) (ITA 2003). This trend continued in 2003, during which 4.5 billion liters (1.2 billion gallons) were imported and 110 million liters (29 million gallons) were exported (ITA 2004). In 2003, 32 U.S. suppliers of benzene were identified (ChemSources 2003).

Exposure

The primary route of human exposure to benzene is inhalation of ambient air. 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). 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 an 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).

The general population also can be exposed to benzene by inhaling air containing tobacco smoke, drinking contaminated water, or eating contaminated food. Approximately half of the total national exposure to benzene comes from cigarette smoke. The median level of benzene 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 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). 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/m^3) (ATSDR, 1997).

Occupational exposure may occur during production of benzene or use of substances containing it. The National Occupational Health Survey (1972–1974) estimated that 147,600 U.S. workers were exposed to benzene (NIOSH 2003), and the National Occupational Exposure Survey (1981–1983) estimated that approximately 272,000 workers, including 143,000 women, potentially were exposed to benzene (NIOSH 1984).

The U.S. Environmental Protection Agency's Toxics Release Inventory listed 1,008 industrial facilities that released benzene into the environment in 2001. Reported benzene releases decreased from 34 million pounds (15,400 metric tons) in 1988 to 6 million pounds (2,700 metric tons) in 2001. In 2001, reported emissions to the air totaled 5 million pounds (2,300 metric tons), and reported discharges to surface water totaled 19,000 lb (8.6 metric tons) (TRI99 2001).

Regulations

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

DOT

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

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

Clean Water Act

- Effluent Guidelines: Listed as a Toxic Pollutant
- Water Quality Criteria: Based on fish/shellfish and water consumption = 0.61-2.2 µg/L; based on fish/shellfish consumption only = 14-51 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 Toxic Hazardous Waste: TCLP Threshold = 0.5 mg/L
- Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - 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

FDA

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

OSHA

Acceptable Peak Exposure = 50 ppm (maximum duration = 10 minutes)

Ceiling Concentration = 25 ppm (for select industries)

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 - Short Term Exposure Limit (TLV-STEL) = 2.5 ppm

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = 0.5 ppm

NIOSH

Immediately Dangerous to Life and Health (IDLH) = 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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