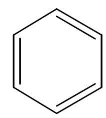
BENZENE
CAS No. 71-43-2
First Listed in the *First Annual Report on Carcinogens*



CARCINOGENICITY

Benzene is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity in humans (IARC 1982a,b). Many case reports and case series have described the association of leukemia with exposure to benzene, either alone or in combination with other chemicals. Most cases were acute myelogenous leukemia, although some were monocytic, erythroblastic or lymphocytic, and some lymphomas have been noted. Two follow-up studies showed high incidences of leukemia among individuals ascertained as cases of benzene hemopathy. A series of epidemiological studies, both cohort and case-control, showed statistically significant associations between leukemia (predominantly myelogenous) and occupational exposure to benzene and benzene-containing solvents. These results were replicated in a number of countries and different industries. In the epidemiological studies of people exposed primarily to benzene, statistically significant excesses of leukemia were observed.

There is sufficient evidence of carcinogenicity of benzene in experimental animals (IARC 1982a, 1987, NTP 1986). When administered by gavage, benzene increased the incidences of Zymbal gland carcinomas and oral cavity papillomas and carcinomas in rats of both sexes, as well as skin carcinomas in male rats. When administered by gavage, benzene increased the incidences of Zymbal gland carcinomas, malignant lymphomas, and alveolar/bronchiolar adenomas and carcinomas in mice of both sexes; harderian gland adenomas and carcinomas of the preputial gland in male mice; and ovarian granulosa cell tumors and benign mixed tumors and mammary gland carcinomas and carcinosarcomas in female mice (NTP 1986).

PROPERTIES

Benzene is a clear, colorless to light yellow, volatile, flammable liquid with an aromatic odor. It is hygroscopic and sensitive to heat. This chemical is slightly soluble in water and is miscible with alcohol, ether, chloroform, acetone, carbon tetrachloride, carbon disulfide, oils, and glacial acetic acid (NTP 2001).

USE

Benzene, an industrial chemical, is a major raw material used extensively as a solvent in the chemical and pharmaceutical industries, as a starting material and intermediate in the synthesis of numerous chemicals, and as a gasoline additive. As a raw material, it is used in the synthesis of. ethylbenzene/styrene (55%), cumene/phenol (21%), cyclohexane (14%), nitrobenzene/aniline (5%), detergent alkylate (3%), and chlorobenzenes, exports, and other products such as dyes and insecticide (2%). While its use as a gasoline additive has been largely reduced in the U.S., benzene continues to be used in the U.S. and more extensively in many other countries for the production of commercial gasoline (HSDB 2000).

PRODUCTION

The vast use of benzene has ranked the chemical in the top 20 highest volume chemicals produced in the United States for the past several years by *Chemical and Engineering News*. Although there have been a few decreases in output, the percent annual change has been positive. Production of benzene has increased from 1.6 billion gal in 1980 to 2.3 billion gal in 1997. In addition, the average yearly import of benzene was 0.3 billion gal during this time period. From 1987 to 1997, a 4% positive change has been reported (Chem. Eng. News 1998). The production figures from 1987 to 1997 do not reflect benzene obtained from the fractional distillation of the light oil formed as a by-product in the high-temperature destructive distillation of coal in coke production. Coke oven benzene has accounted for less than 5% of total U.S. output for several years (Chem. Prof. 1987, Chem. Eng. News 1998). Benzene is expected to remain one of industry's most important chemicals.

U.S. domestic exports of benzene for the year 2000 were 13,567,546 L; U.S domestic imports for the year 2000 were 4,794,533,678 L (ITA 2001). Chem Sources identified 32 U.S. suppliers in 2000 (Chem Sources 2001), while 24 manufacturers of benzene were identified (HSDB 2000).

EXPOSURE

The primary routes of potential human exposure to benzene are inhalation and dermal contact, with the former being the dominant pathway, accounting for more than 99% of the total daily intake. Exposure via inhalation occurs not only from contaminated air but also from tobacco smoke, both active and passive smoking. Approximately half of the total national exposure to benzene comes from cigarette smoke, with levels in mainstream smoke ranging from 5.9 to 73 µg/cigarette and those in sidestream smoke ranging from 345 to 653 µg/cigarette. Contaminated air occurs mainly in areas of heavy motor vehicle traffic and around gas stations, since benzene is a constituent of auto exhaust and fuel evaporation (ATSDR 1997). Outdoor environmental levels up to 349 $\mu g/m^3$ in industrial centers with a high density of automobile traffic have been measured; in remote rural areas levels up to 0.2 $\mu g/m^3$ have been recorded (IPCS 1993).

EPA estimates benzene emissions from pharmaceutical, plastics, resin, and rubber plants at 495 million tons per year. Its new, far more stringent standards for benzene call for reducing current benzene emissions by 97% at storage tanks and coke by-product recovery plants. EPA proposes that emissions from those sources be cut by 94 tons/year through the use of carbon absorbers and incinerators. The new rules will lower total industrial emissions of benzene by 90%. According to EPA, half the U.S. population is exposed to benzene from industrial sources, and virtually everyone in the country is exposed to benzene in gasoline. EPA now estimates that three people die annually from cancer caused by exposure to benzene emissions (Chem. Mktg. Rep. 1986). The Toxic Chemical Release Inventory (TRI) listed 975 industrial facilities that produced, processed, or otherwise used benzene in 1999 (TRI99 2001). A decrease in benzene release was reported by these facilities for the years 1988 to 1999; reported releases totaled 33.8 million lbs in 1988 and 8.1 million lbs in 1999. In the 1993 inventory, estimated atmospheric emissions from manufacturing and processing facilities were 10.2 million lb (ATSDR 1997). In 1989, EPA estimated that the largest industrial source was coke oven emissions (17,000 metric tons/year) (ATSDR 1997). Estimates indicate that possibly 800,000 persons may be exposed to benzene from coke oven emissions at levels greater than 0.1 ppm (see Coke Oven Emissions); 5 million persons may be exposed to benzene from petroleum refinery emissions at levels of 0.1 to 1.0 ppm. However, information on the levels of benzene in the atmosphere is limited. Ambient monitoring data indicate that levels of benzene range from 1 to 100 ppb. The highest values were reported in metropolitan areas (IARC 1982a).

Additionally, benzene has been identified in drinking water and in subsurface water at concentrations up to 10 ppm. Benzene occurs in fruits, fish, vegetables, nuts, dairy products, beverages, and eggs. The Public Health Service estimated that an individual may ingest up to 250 μg/day (OSH 1982). Therefore, water and food-borne benzene are a small contribution to the total daily intake in non-smoking adults (between approximately 3 and 24 μg/kg body weight per day) (IPCS 1993).

An estimated 3 million workers potentially may be exposed to benzene (IARC 1982a). Exposure may occur during the production of benzene or during the use of substances containing the chemical as an ingredient or contaminant. In the National Occupational Health Survey (NOHS), conducted by NIOSH from 1972 to 1974, an estimated 1,495,706 workers were exposed to benzene in the United States (NIOSH 1976). The National Occupational Exposure Survey (NOES), conducted by NIOSH from 1981 to 1983, estimated 272,300 workers potentially exposed to benzene (ATSDR 1997). Occupational exposure levels usually do not exceed a time-weighted average of 15 mg/m^3; they may be higher in some industrially developing countries (IPCS 1993).

Javelaud et al. (1998) compared benzene exposure in car mechanics and road tanker drivers. Each exposed worker was given a personal air sampler that was fixed at chest height to monitor inhalation exposure to benzene during a working day. Road tanker drivers had significantly higher inhalation exposures to benzene than mechanics. Benzene was detected in 60% (39 of 65) of the air samplers from the mechanics and in about 94% (31 of 33) of the samplers from road tanker drivers. The mean and median concentrations were 0.48 and 0.14 mg/m3, respecitively for mechanics and 1.88 and 0.68 mg/m3, respectively for road tanker drivers. Furthermore, 6.1% of car mechanics and 33% of road tanker drivers were found to be exposed to more than 0.3 ppm (~ 1 mg/m3) of atmospheric benzene. The road tanker drivers were primarily exposed to benzene through inhalation, whereas car mechanics had a higher risk of exposure via dermal contact. Average exposure to benzene during top loading is 6.1 mg/m^3 and during bottom loading is 1.4 mg/m^3 (IARC 1989). Car mechanics are primarily exposed to benzene during the adjustment of direct fuel injection systems (Nordlinder and Ramnas 1987). The benzene concentration in the breathing zone during this type of work has reached 1.1 ppm (3.5 mg/m^3) (Laitinen *et al*. 1994). The same results were found in a cross-sectional exposure survey conducted in Fairbanks, Alaska. All mechanics had higher post-shift blood benzene concentrations than did non-mechanics (drivers and other garage workers). The levels were significantly increased during the workshift for the former (during the suspension of the oxygenated fuel program) versus the latter, suggesting that the work activities of mechanics who were primarily exposed to raw gasoline and solvents resulted in greater benzene exposure than the activities of mechanics who were largely exposed to motor vehicle exhaust (Moolenaar *et al*. 1997).

General population exposures to benzene are not correlated with industrial or vehicular emissions. Emission sources comprise 82% cars, 14% industry, 3% personal and home, and 0.1% cigarettes; benzene exposures of the general population comprise 40% from cigarettes, 18% each from personal activities and car exhaust, 16% from home sources, 5% from environmental tobacco smoke, and 3% from industry. Average daily benzene air intake of urban and suburban residents is estimated to range from 180 to 1,300 μg. Intake from drinking water has been estimated at 0.2 μg/day (ATSDR 1997).

REGULATIONS

The U.S. Consumer Product Safety Commission (CPSC) has withdrawn its proposed ban of consumer products, except for gasoline and laboratory reagents, that contain benzene as an intentional ingredient or as a contaminant at 0.1% or greater by volume. The decision to withdraw the rulemaking was based on CPSC findings that benzene is no longer used as an intentional ingredient in consumer products and that the contaminant levels remaining in certain consumer products are unlikely to result in significant consumer exposure to benzene vapor. The CPSC has established labeling regulations for products containing more than 5% benzene and a safety packaging requirement for paint solvents and thinners containing 10% or more of petroleum distillates, such as benzene. The CPSC has prepared and distributed "School Science Laboratories - A Guide to Some Hazardous Substances" to high school laboratories throughout the states. This document indicates that benzene is a carcinogen and that the hazards posed by its use in the laboratories may be greater than its potential usefulness, therefore recommending that it not be used or stored in schools.

EPA regulates benzene under the Clean Air Act (CAA), Toxic Substances Control Act (TSCA), Clean Water Act (CWA), Superfund Amendments and Reauthorization Act (SARA), Food, Drug, and Cosmetic Act (FD&CA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), and Safe Drinking Water Act (SDWA). EPA has listed benzene as a hazardous air and water pollutant and a constituent of hazardous waste. EPA has assessed emission standards for ethylbenzene plants, benzene storage and fugitive emissions, and coke by-product plants. Under the SWDA, a maximum contaminant level (MCL) of 0.005 mg/L for benzene in drinking water has been set. Benzene is subject to reporting requirements under SARA and health and safety data reporting under TSCA. The SARA threshold planning quantity (TPQ) for benzene is 500/10,000 lb and the CERCLA RQ is 10 lb (4.54 kg).

FDA regulates benzene as an indirect food additive under FD&CA. FDA also limits the amount of benzene in bottled water (0.005 mg/L).

The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV) of 10 ppm (32 mg/m^3) for benzene as an 8-hr time weighted average (TWA). NIOSH recommends that exposure be reduced to 0.1 ppm as a 10-hr TWA, with a 1-ppm ceiling. OSHA has set the permissible exposure limit (PEL) for benzene at 1 ppm as an 8-hr TWA, and 5 ppm as a short-term exposure limit (STEL) averaged over any 15-minute period, except in certain industries (as explained in Table 19). OSHA also regulates benzene under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 19.

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