

US EPA, Health Effects Notebook for Hazardous Air Pollutants, Benzene

(Publicly available at <https://www.epa.gov/sites/default/files/2016-09/documents/benzene.pdf>)

Benzene

71-43-2

Hazard Summary

Benzene is found in the air from emissions from burning coal and oil, gasoline service stations, and motor vehicle exhaust. Acute (short-term) inhalation exposure of humans to benzene may cause drowsiness, dizziness, headaches, as well as eye, skin, and respiratory tract irritation, and, at high levels, unconsciousness. Chronic (long-term) inhalation exposure has caused various disorders in the blood, including reduced numbers of red blood cells and aplastic anemia, in occupational settings. Reproductive effects have been reported for women exposed by inhalation to high levels, and adverse effects on the developing fetus have been observed in animal tests. Increased incidence of leukemia (cancer of the tissues that form white blood cells) have been observed in humans occupationally exposed to benzene. EPA has classified benzene as known human carcinogen for all routes of exposure.

Please Note: The main sources of information for this fact sheet are the Agency for Toxic Substances and Disease Registry's (ATSDR's) [Toxicological Profile for Benzene \(1\)](#) and EPA's [Integrated Risk Information System \(IRIS\) \(4\)](#), which contains information on the health effects of benzene including the unit cancer risk for inhalation exposure.

Uses

- Benzene is used as a constituent in motor fuels; as a solvent for fats, waxes, resins, oils, inks, paints, plastics, and rubber; in the extraction of oils from seeds and nuts; and in photogravure printing. It is also used as a chemical intermediate. Benzene is also used in the manufacture of detergents, explosives, pharmaceuticals, and dyestuffs. (1,2,6)

Sources and Potential Exposure

- Individuals employed in industries that manufacture or use benzene may be exposed to the highest levels of benzene. (1)
- Benzene is found in emissions from burning coal and oil, motor vehicle exhaust, and evaporation from gasoline service stations and in industrial solvents. These sources contribute to elevated levels of benzene in the ambient air, which may subsequently be breathed by the public. (1)
- Tobacco smoke contains benzene and accounts for nearly half the national exposure to benzene. (1)
- Individuals may also be exposed to benzene by consuming contaminated water. (1)

Assessing Personal Exposure

- Measurement of benzene in an individual's breath or blood or the measurement of breakdown products in the urine (phenol) can estimate personal exposure. However, the tests must be done shortly after exposure and are not helpful for measuring low levels of benzene. (1)

Health Hazard Information

Acute Effects:

- Coexposure to benzene with ethanol (e.g., alcoholic beverages) can increase benzene toxicity in humans. (1)

- Neurological symptoms of inhalation exposure to benzene include drowsiness, dizziness, headaches, and unconsciousness in humans. Ingestion of large amounts of benzene may result in vomiting, dizziness, and convulsions in humans. (1)
- Exposure to liquid and vapor may irritate the skin, eyes, and upper respiratory tract in humans. Redness and blisters may result from dermal exposure to benzene. (1,2)
- Animal studies show neurologic, immunologic, and hematologic effects from inhalation and oral exposure to benzene. (1)
- Tests involving acute exposure of rats, mice, rabbits, and guinea pigs have demonstrated benzene to have **low** acute toxicity from inhalation, **moderate** acute toxicity from ingestion, and **low** or **moderate** acute toxicity from dermal exposure. (3)
- The reference concentration for benzene is 0.03 mg/m³ based on hematological effects in humans. The **RfC** is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive groups) that is likely to be without appreciable risk deleterious noncancer effects over a lifetime. (4)

Chronic Effects (Noncancer):

- Chronic inhalation of certain levels of benzene causes disorders in the blood in humans. Benzene specifically affects bone marrow (the tissues that produce blood cells). Aplastic anemia (a risk factor for acute nonlymphocytic leukemia), excessive bleeding, and damage to the immune system (by changes in blood levels of antibodies and loss of white blood cells) may develop. (1)
- In animals, chronic inhalation and oral exposure to benzene produces the same effects as seen in humans. (1)
- Benzene causes both structural and numerical chromosomal aberrations in humans. (1)
- EPA has established an oral Reference Dose (**RfD**) for benzene of 0.004 milligrams per kilogram per day (mg/kg/d) based on hematological effects in humans. The **RfD** is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential for effects. At exposures increasingly greater than the **RfD**, the potential for adverse health effects increases. Lifetime exposure above the **RfD** does not imply that an adverse health effect would necessarily occur. (4)
- EPA has established a Reference Concentration (**RfC**) of 0.03 milligrams per cubic meter (0.03 mg/m³) for benzene based on hematological effects in humans. The **RfC** is an inhalation exposure concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential for effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (4)

Reproductive/Developmental Effects:

- There is some evidence from human epidemiological studies of reproductive and developmental toxicity of benzene, however the data do not provide conclusive evidence of a link between exposure and effect. (4) Animal studies have provided limited evidence that exposure to benzene may affect reproductive organs, however these effects were only observed at exposure levels over the maximum tolerated dose. (4)
- Adverse effects on the fetus, including low birth weight, delayed bone formation, and bone marrow damage, have been observed where pregnant animals were exposed to benzene by inhalation.(4)

Cancer Risk:

- Increased incidence of leukemia (cancer of the tissues that form white blood cells) has been observed in humans occupationally exposed to benzene. (1,4)
- EPA has classified benzene as a Group A, known human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated a range of 2.2×10^{-6} to 7.8×10^{-6} as the increase in the lifetime risk of an individual who is continuously exposed to 1 µg/m³ of benzene in the air over their lifetime.

- EPA estimates that, if an individual were to continuously breathe the air containing benzene at an average of 0.13 to 0.45 $\mu\text{g}/\text{m}^3$ (1.3×10^{-4} to 4.5×10^{-4} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of continuously breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 1.3 to 4.5 $\mu\text{g}/\text{m}^3$ (1.3×10^{-3} to 4.5×10^{-3} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 13 to 45 $\mu\text{g}/\text{m}^3$ (1.3×10^{-2} to 4.5×10^{-2} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS.(4)
- EPA has calculated an oral cancer slope factor ranging from 1.5×10^{-2} to 5.5×10^{-2} ($\text{mg}/\text{kg}/\text{d}$)⁻¹ that is an extrapolation from inhalation dose-response data. (4)

Physical Properties

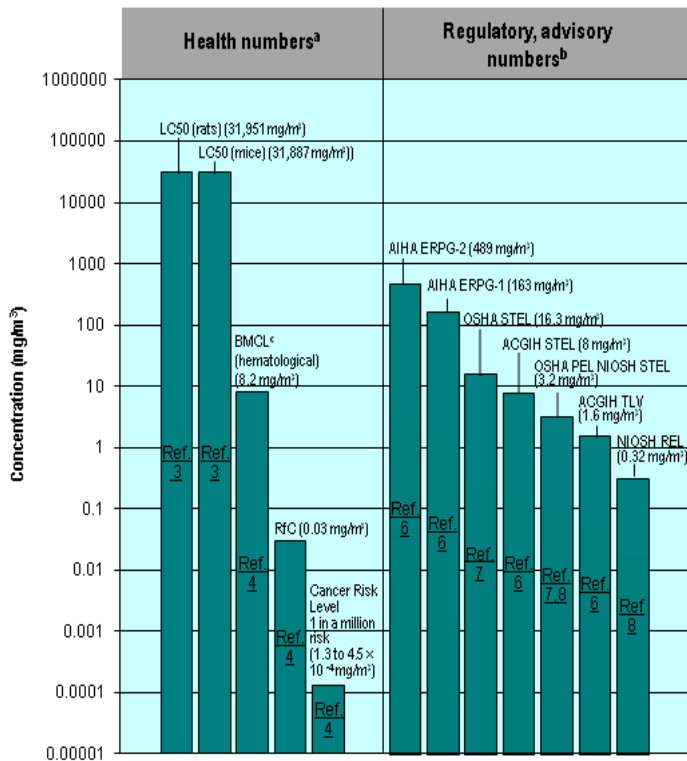
- The chemical formula for benzene is C_6H_6 , and it has a molecular weight of 78.11 g/mol. (4) Benzene occurs as a volatile, colorless, highly flammable liquid that dissolves easily in water. (1,7)
- Benzene has a sweet odor with an ASTDR reported odor threshold of 1.5 ppm (5 mg/m^3).
- The vapor pressure for benzene is 95.2 mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log Kow) of 2.13. (1)

Conversion Factors (only for the gaseous form):

To convert concentrations in air (at 25°C) from ppm to mg/m^3 : $\text{mg}/\text{m}^3 = (\text{ppm}) \times (\text{molecular weight of the compound}) / (24.45)$. For benzene: 1 ppm = 3.19 mg/m^3 . To convert concentrations in air from $\mu\text{g}/\text{m}^3$ to mg/m^3 : $\text{mg}/\text{m}^3 = (\mu\text{g}/\text{m}^3) \times (1 \text{ mg}/1,000 \mu\text{g})$.

Health Data from Inhalation Exposure

Benzene



ACGIH STEL--American Conference of Governmental and Industrial Hygienists' short-term exposure limit.

ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

AIHA ERPG--American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action. The American Industrial Hygiene Association's detection and recognition odor thresholds for benzene are 61 ppm and 97 ppm, respectively.

LC₅₀ (Lethal Concentration₅₀)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

NIOSH REL--National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH--recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH STEL--NIOSH's short term exposure limit; NIOSH recommended exposure limit for a 15-minute period.

OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

OSHA STEL--Occupational Safety and Health Administration's short-term exposure limit.

The health and regulatory values cited in this graph were obtained in April 2009.

^a Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.

^b Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers

are nonregulatory values provided by the Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH, ACGIH, and AIHA numbers are advisory.

^c The BMCL (statistical lower confidence limit on the concentration at the benchmark concentration, which is the concentration producing a specified change in a response rate that is considered a critical effect) was used as the point of departure for the RfC derivation. The BMCL for benzene is for hematological effects (reduction in absolute lymphocyte count) in humans (4).

Summary created in April 1992, updated in January 2000 and January 2012.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Benzene. U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 2007.
 2. M. Sittig. Handbook of Toxic and Hazardous Chemicals and Carcinogens. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.
 3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
 4. U.S. Environmental Protection Agency. [Integrated Risk Information System \(IRIS\) on Benzene](#). National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 2009.
 5. [California Environmental Protection Agency \(CalEPA\)](#). Air Toxics Hot Spots Program Risk Assessment Guidelines: Part III. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. SRP Draft. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1999.
 6. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.
 7. American Conference of Governmental Industrial Hygienists (ACGIH). 1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices. Cincinnati, OH. 1999.
 8. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. Code of Federal Regulations. 29 CFR 1910.1000. 1998.
 9. National Institute for Occupational Safety and Health (NIOSH). [Pocket Guide to Chemical Hazards](#). U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.
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