BENZENE- TOXGUIDE™

CHEMICAL AND PHYSICAL INFORMATION

Benzene (CASRN 71-43-2) is a colorless liquid with a petroleum-like odor. It easily evaporates into the air and is soluble in water. Benzene is highly flammable.

Benzene has been used extensively as a solvent in the chemical and drug industries and as a starting material and intermediate in the synthesis of numerous chemicals The major uses of benzene are in the production of ethylbenzene, cumene, and cyclohexane used to make plastics, nylon resins, detergents, paint removers, and rubber goods. Benzene is used as a gasoline additive, and it is especially important for unleaded gasoline because of its anti-knock characteristics.

Benzene is released to the environment by both natural and industrial sources. Natural sources include crude oil seeps, forest fires, and plant volatiles. Major anthropogenic sources of benzene include industrial emissions, automobile exhaust, automobile refueling operations, and tobacco smoke.

ENVIRONMENTAL FATE AND DETECTED LEVELS

Air: The average ambient air concentration across 117 U.S. locations in 2023 was 0.176 ppbv.

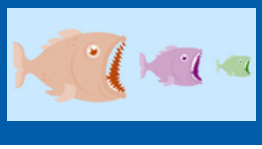
Chemical degradation reactions, primarily reaction with hydroxyl radicals, limit the atmospheric residence time of benzene to only a few days, and possibly to only a few hours. Since benzene is soluble in water, removal from the atmosphere via wet deposition may occur.

Water: The average surface water concentration from 86 U.S. samples in 2023 was 0.038 ppb as reported in the U.S. Environmental Protection Agency (EPA) Water Quality Portal (WQP) database.

Benzene readily volatilizes to air from water. Benzene released to waterways is also subject to photooxidation and biodegradation. Benzene is readily biodegraded in aerobic conditions (e.g., surface water) and is not readily degraded under anaerobic conditions (e.g., groundwater).

Sediment and Soil: Benzene was not detected in sediment (n=52) samples and an average soil (n=14) concentration could not be obtained from samples reported between 2019 and 2023 in the EPA WQP database.

Benzene is mobile in soils and will migrate to groundwater. Benzene released to soil is also subject to volatilization, photooxidation, and biodegradation. It is readily biodegraded in aerobic conditions (e.g., surface soil) and is not readily degraded under anaerobic conditions (e.g., subsurface sediments).



Bioconcentration: Bioaccumulation in biota is not expected to occur to a significant degree.

GENERAL POPULATION EXPOSURE

Benzene is ubiquitous in the atmosphere, but concentrations have decreased in the past decades.

Primary route of potential exposure: Inhalation

- The major source of exposure to benzene in the general population is cigarette smoke.
- The general population is most likely to be exposed to trace levels of benzene in air.
- Benzene levels in indoor air have been shown to be higher in homes with attached garages, where the inhabitants smoke inside the house, or where gas stoves or ovens are used.
- Activities such as pumping gasoline and smoking increase benzene inhalation exposure.

BENZENE

POPULATIONS WITH POTENTIALLY HIGH EXPOSURE

Individuals employed in industries that make or use benzene or products containing benzene are probably exposed to the highest concentrations of benzene. The potential for benzene exposure is also high for workers in other jobs, such as gasoline station workers and drycleaners. Benzene is a common combustion product, providing the potential for high inhalation exposure in firefighters. Occupational exposure may occur via:

- Inhalation of contaminated workplace air (predominant route of exposure)
- Direct skin contact with benzene

Compared to the general population, the following groups may also have increased risk of exposure:

- Populations living near industrial releases, contaminated hazardous waste sites, or leaking underground fuel tanks (via ambient or indoor air and/or groundwater contamination).

BIOMARKERS

- Unmetabolized benzene can be detected in the expired air and urine of humans.
- Urinary metabolites of benzene, including phenol, trans,trans-muconic acid, and S-phenyl mercapturic acid, are commonly used as biomarkers of exposure.
- Urinary phenol and trans,trans-muconic are not specific for benzene exposure.

BIOMONITORING LEVELS

Geometric mean blood benzene levels (NHANES 2015–2016):

Nonsmoking adults:
below the level of detection

Smoking adults:
0.123 mg/mL

TOXICOKINETICS

Absorption: Benzene is readily absorbed following inhalation or oral exposure. Although benzene is also readily absorbed from the skin, a significant amount of a dermal application evaporates from the skin surface.

Distribution: Absorbed benzene is rapidly distributed throughout the body and tends to accumulate in fatty tissues.

Metabolism: Benzene is metabolized in liver and other tissues, including lymphocyte progenitor cells in bone marrow. Benzene metabolism results in the production of several reactive metabolites that contribute to benzene toxicity.

Excretion:

- At low exposure levels, benzene is rapidly metabolized and excreted predominantly as conjugated urinary metabolites.
- At higher exposure levels, metabolic pathways appear to become saturated and a large portion of an absorbed dose of benzene is excreted as parent compound in exhaled air.

HEALTH EFFECTS

The primary effect of benzene via all routes is on the hematological system, and involves disruption of hematopoiesis (production of blood cells and platelets).

Hematological effects observed in humans and animals after exposure to benzene include decreased numbers of peripheral blood cells, hematopoietic stem cells and progenitor cells in hematopoietic tissues, and histopathological changes to hematopoietic tissues.

Health effects are determined by the dose (how much), the duration (how long), and the route of exposure.

The discussion of health effects is continued on Page 3.

BENZENE

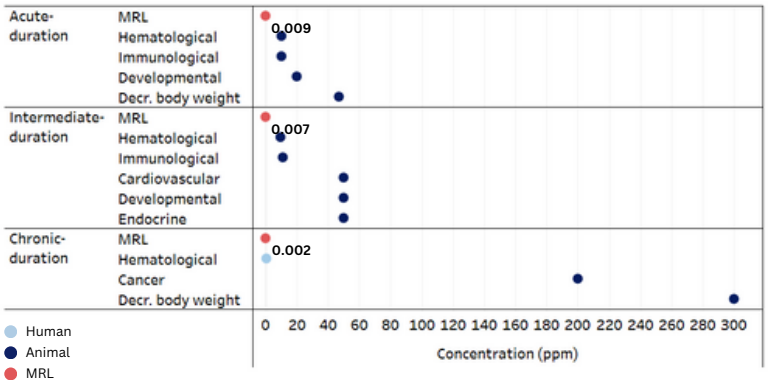
HEALTH EFFECTS (CONTINUED)

Altered immune responses to antigens, function of peripheral lymphocytes, and levels of circulating antibodies were seen in animals following exposure.

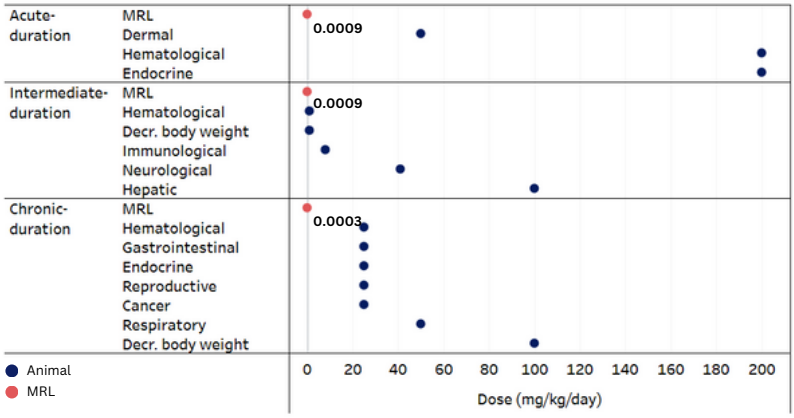
Developmental effects (decreased fetal weight, increased skeletal variations, changes in hematological parameters, and neurodevelopmental effects) have been reported in animals exposed in utero.

In workers, studies have shown that exposure to benzene is associated with increased risk of myelodysplastic syndromes and acute myelogenous leukemia. Benzene exposure induced tumors at multiple sites in rats and mice, with a tendency towards induction of lymphomas in mice.

Sensitive Effects of Inhalation Exposure to Benzene



Sensitive Effects of Oral Exposure to Benzene



MINIMAL RISK LEVELS (MRLs)

Acute: ≤14 days; Intermediate: 15–364 days; Chronic: ≥365 days

Inhalation

- **Acute:** A provisional acute-duration inhalation MRL of 0.009 ppm (0.029 mg/m^3) was derived based on hematological and immunological effects in mice.
- **Intermediate:** A provisional intermediate-duration inhalation MRL of 0.007 ppm (0.019 mg/m^3) was derived based on immunological effects in mice.
- **Chronic:** A provisional chronic-duration inhalation MRL of 0.002 ppm (6.4×10^{-3} mg/m^3) was derived based on hematological effects in humans.

Oral:

- **Acute:** The provisional intermediate-duration oral MRL of 9×10^{-4} mg/kg/day derived based on hematological effects in mice was adopted as the provisional acute-duration oral MRL.
- **Intermediate:** A provisional intermediate-duration oral MRL of 9×10^{-4} mg/kg/day was derived based on hematological effects in mice.
- **Chronic:** A provisional chronic-duration oral MRL of 3×10^{-4} mg/kg/day was derived based on hematological effects in humans (using route-to-route extrapolation from an inhalation exposure study).

CANCER

The Department of Health and Human Services (HHS) has determined that benzene is a known human carcinogen. The EPA has classified benzene as a Group A carcinogen (known human carcinogen) and the International Agency Research on Cancer has placed benzene in Group 1 (carcinogenic to humans).

REFERENCE

Agency for Toxic Substances and Disease Registry (ATSDR). 2024. Toxicological profile for benzene (draft for public comment). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Services. https://wwwn.cdc.gov/TSP/ToxProfiles/ToxProfiles.aspx?id=40&tid=14.