Chlorobenzene

Hazard Summary

Chlorobenzene is used primarily as a solvent, a degreasing agent, and a chemical intermediate. Limited information is available on the acute (short-term) effects of chlorobenzene. Acute inhalation exposure of animals to chlorobenzene produced narcosis, restlessness, tremors, and muscle spasms. Chronic (long-term) exposure of humans to chlorobenzene affects the central nervous system (CNS). Signs of neurotoxicity in humans include numbness, cyanosis, hyperesthesia (increased sensation), and muscle spasms. No information is available on the carcinogenic effects of chlorobenzene in humans. EPA has classified chlorobenzene as a Group D, not classifiable as to human carcinogenicity.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS) (5), which contains information on oral chronic toxicity and the RfD, and the carcinogenic effects of chlorobenzene, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Chlorobenzene (1).

Uses

- The primary uses of chlorobenzene are as a solvent for pesticide formulations, diisocyanate manufacture, and degreasing automobile parts and for the production of nitrochlorobenzene. (1)
- In the past, chlorobenzene was used as an intermediate in phenol and DDT production. (1)

Sources and Potential Exposure

- Human exposure to chlorobenzene appears to be primarily occupational. (1)
- In urban areas, chlorobenzene may be released to the ambient air during its manufacture and use. (1)

Assessing Personal Exposure

- Chlorobenzene or its breakdown products can be detected in urine, exhaled breath, blood, and body fat to determine whether or not exposure has occurred. (1)

Health Hazard Information

Acute Effects:

- A child who ingested chlorobenzene became unconscious and cyanotic and had muscle spasms but recovered completely. (1)
- Acute inhalation exposure of animals to chlorobenzene produced narcosis, restlessness, tremors, and muscle spasms. (1,2)
- Acute animal tests in rats, mice, rabbits, and guinea pigs have demonstrated chlorobenzene to have low acute toxicity by inhalation and moderate acute toxicity from oral exposure. (1,3)

Chronic Effects (Noncancer):

- Chronic exposure of humans to chlorobenzene affects the CNS. Signs of neurotoxicity include numbness, cyanosis, hyperesthesia (increased sensation), and muscle spasms. (1,4)
- Headaches and irritation of the mucosa of the upper respiratory tract and eyes have also been reported in
humans chronically exposed via inhalation. (4)

- The CNS, liver, and kidneys have been affected in animals chronically exposed to chlorobenzene by inhalation. (1)
- Chronic ingestion of chlorobenzene has resulted in damage to the kidneys and liver in animals. (1,4)
- EPA has calculated a provisional Reference Concentration (RfC) of 0.02 milligrams per cubic meter (mg/m$^3$) for chlorobenzene based on kidney and liver effects in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation 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 effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. The provisional RfC is a value that has had some form of Agency review, but it does not appear on IRIS. (6)
- The Reference Dose (RfD) for chlorobenzene is 0.02 milligrams per kilogram body weight per day (mg/kg/d) based on histopathologic changes in the liver in dogs. (5)
- EPA has medium confidence in the study on which the RfD was based because it provided both a no-observed-adverse-effect level (NOAEL) and a lowest-observed-adverse-effect level (LOAEL) and incorporated several biochemical and biological endpoints; medium confidence in the database because several subchronic, chronic, developmental, and reproductive toxicity studies provide supportive data, but they did not give a complete assessment of toxicity; and, consequently, medium confidence in the RfD. (5)

Reproductive/Developmental Effects:
- No information is available on the reproductive or developmental effects of chlorobenzene in humans.
- Chronic inhalation exposure of rats to chlorobenzene did not adversely affect reproductive performance or fertility. However, a slight increase in the incidence of degenerative testicular changes was observed. (1,4)
- Chlorobenzene does not appear to be a developmental toxicant and did not produce structural malformations in rats and rabbits acutely exposed via inhalation. (1,4,5)

Cancer Risk:
- No information is available on the carcinogenic effects of chlorobenzene in humans.
- In a National Toxicology Program (NTP) study of rats and mice exposed to chlorobenzene via gavage (experimentally placing the chemical in the stomach), an increased incidence of neoplastic nodules of the liver in high dose male rats was observed, but not in female rats or male or female mice. (7)
- EPA has classified chlorobenzene as a Group D, not classifiable as to human carcinogenicity. (5)

Physical Properties

- The chemical formula for chlorobenzene is C$_6$H$_5$Cl, and its molecular weight is 112.56 g/mol. (1)
- Chlorobenzene occurs as a colorless flammable liquid, with low solubility in water. (1,4)
- Chlorobenzene has an aromatic, almond–like odor, with an odor threshold of 1 to 8 mg/m$^3$. (1)
- The vapor pressure for chlorobenzene is 8.8 mm Hg at 20 °C, and its log octanol/water partition coefficient (log K$_{ow}$) is 2.84. (1)

Conversion Factors:
To convert concentrations in air (at 25 °C) from ppm to mg/m$^3$: \( \text{mg/m}^3 = (\text{ppm}) \times (\text{molecular weight of the compound})/(24.45). \) For chlorobenzene: 1 ppm = 4.60 mg/m$^3$.  

Health Data from Inhalation Exposure
### Chlorobenzene

<table>
<thead>
<tr>
<th>Health numbers&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Regulatory, advisory numbers&lt;sup&gt;b&lt;/sup&gt;</th>
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<tr>
<td>LC&lt;sub&gt;50&lt;/sub&gt; (nilexa) (19,780 mg/m&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>NIOSH IDLH (4,600 mg/m&lt;sup&gt;3&lt;/sup&gt;)</td>
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<tr>
<td>Provisional RfC (0.02 mg/m&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>OSHA PEL (350 mg/m&lt;sup&gt;3&lt;/sup&gt;)</td>
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<td></td>
<td>ACGIH TLV (44 mg/m&lt;sup&gt;3&lt;/sup&gt;)</td>
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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.

LC<sub>n</sub> (Lethal Concentration <sub>n</sub>) -- 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 IDLH -- National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

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.

The health and regulatory values cited in this factsheet were obtained in December 1999.

<sup>a</sup> Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.

<sup>b</sup> 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 and ACGIH numbers are advisory.


**References**


