

# Hexachlorobenzene

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## Hazard Summary

Hexachlorobenzene is formed as a byproduct during the manufacture of other chemicals. It was widely used as a pesticide until 1965. Chronic (long-term) oral exposure to hexachlorobenzene in humans results in a liver disease with associated skin lesions. Epidemiologic studies of persons orally exposed to hexachlorobenzene have not shown an increased cancer incidence. However, based on animal studies that have reported cancer of the liver, thyroid, and kidney from oral exposure to hexachlorobenzene, EPA has classified hexachlorobenzene as a probable human carcinogen (Group B2). Very little inhalation data are available.

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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 Reference Dose (RfD), and the carcinogenic effects of hexachlorobenzene including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Hexachlorobenzene. (1)

## Uses

- There are currently no commercial uses of hexachlorobenzene in the United States. (1)
- Hexachlorobenzene was used as a pesticide until 1965 and was also used in the production of rubber, aluminum, and dyes and in wood preservation. (1)
- Hexachlorobenzene is currently formed as a byproduct during the manufacture of other chemicals (mainly solvents) and pesticides. (1)

## Sources and Potential Exposure

- Inhalation exposure to hexachlorobenzene may occur through proximity to industrial sites where it is formed as a byproduct or to waste facilities where it is disposed. (1)
- Occupational exposure, via inhalation and dermally, can occur at industries where hexachlorobenzene is produced as a byproduct. (1)
- Exposure to hexachlorobenzene can also occur through consuming foods tainted with hexachlorobenzene. (1)
- Hexachlorobenzene has been listed as a pollutant of concern to EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment (2).

## Assessing Personal Exposure

- Medical tests can measure levels of hexachlorobenzene in the fat or blood. (1)

## Health Hazard Information

Acute Effects:

- No information is available on the acute (short-term) effects of hexachlorobenzene in humans. (1,3)

- Acute animal tests in rats and mice have shown hexachlorobenzene to have low-to-moderate acute toxicity from oral exposure. (4)

#### Chronic Effects (Noncancer):

- Humans who ingested hexachlorobenzene in heavily contaminated bread during a 4-year poisoning incident were sickened with a liver disease with associated skin lesions (porphyria cutanea tarda). (1)
- Very little data are available on the health effects of hexachlorobenzene in humans or animals following inhalation exposure.
- Animal studies have reported effects on the liver, skin, immune system, kidneys, and blood from chronic oral exposure to hexachlorobenzene. (1,3)
- EPA has determined that there are inadequate data to establish a Reference Concentration (RfC) for hexachlorobenzene. (5)
- The California Environmental Protection Agency (CalEPA) has established a chronic inhalation reference exposure level of 0.003 milligrams per cubic meter (mg/m<sup>3</sup>) for hexachlorobenzene. The CalEPA reference exposure level is a 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 effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (6)
- The Reference Dose (RfD) for hexachlorobenzene is 0.0008 milligrams per kilogram body weight per day (mg/kg/d) based on liver effects in rats. 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. (5)
- EPA has medium confidence in the study used as the basis for the RfD because it had an unusual dosing scheme making it difficult to determine the true doses received by each experimental group; high confidence in the database due to the extensive number of quality research studies available; and consequently medium confidence in the RfD. (5)

#### Reproductive/Developmental Effects:

- One human study reported abnormal physical development in young children who ingested contaminated bread during a 4-year poisoning incident. (1)
- Hexachlorobenzene has been found to decrease the survival rates of newborn animals and to cross the placenta and accumulate in fetal tissue in several animal species. (3)
- Neurological, teratogenic, liver, and immune system effects have been reported in the offspring of animals orally exposed to hexachlorobenzene while they were pregnant. (1)

#### Cancer Risk:

- Human data regarding the carcinogenic effects of hexachlorobenzene are inadequate. (5)
- Hexachlorobenzene, when administered orally, has been shown to induce tumors of the liver, thyroid, and kidney in several animal species. (1,3,5)
- EPA has classified hexachlorobenzene as a Group B2, probable human carcinogen. (5)
- EPA uses mathematical models, based on animal studies to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of  $4.6 \times 10^{-4}$  ( $\mu\text{g}/\text{m}^3$ )<sup>-1</sup>. EPA estimates that, if an individual were to continuously breathe air containing hexachlorobenzene at an average of 0.002  $\mu\text{g}/\text{m}^3$  ( $2.0 \times 10^{-6}$  mg/m<sup>3</sup>) 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 breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.02  $\mu\text{g}/\text{m}^3$  ( $2.0 \times 10^{-5}$  mg/m<sup>3</sup>) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.2  $\mu\text{g}/\text{m}^3$  ( $2.0 \times 10^{-4}$  mg/m<sup>3</sup>) 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. (5)
- EPA has calculated an oral cancer slope factor of 1.6 (mg/kg/d)<sup>-1</sup>. (5)

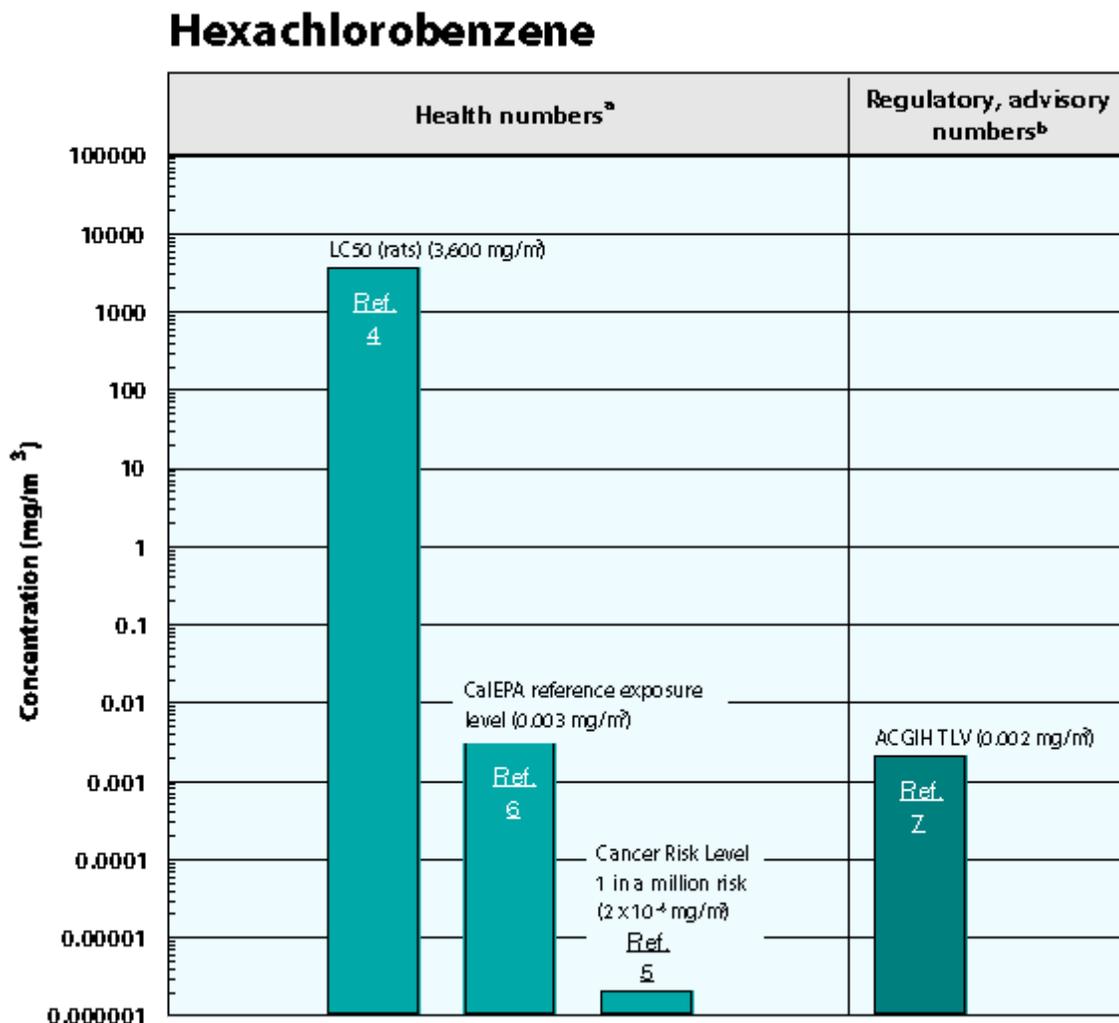
# Physical Properties

- Hexachlorobenzene is a white crystalline solid which is not very soluble in water. (1)
- The odor threshold for hexachlorobenzene is not available.
- The chemical formula for hexachlorobenzene is  $C_6Cl_6$ , and the molecular weight is 284.8 g/mol. (1)
- The vapor pressure for hexachlorobenzene is  $1.09 \times 10^{-5}$  mm Hg at 20 °C, and it has a log octanol/water partition coefficient ( $\log K_{ow}$ ) of 6.18. (1)

Conversion Factors:

To convert concentrations in air (at 25°C) from ppm to  $mg/m^3$ :  $mg/m^3 = (ppm) \times (\text{molecular weight of the compound}) / (24.45)$ . For hexachlorobenzene: 1 ppm = 11.6  $mg/m^3$ .

## Health Data from Inhalation Exposure



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>50</sub> (Lethal Concentration<sub>50</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.

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. ACGIH numbers are advisory.  
<sup>c</sup> These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.

Summary created in April 1992, updated January 2000

## References

1. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Hexachlorobenzene(Update). Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1996.
2. U.S. Environmental Protection Agency. Deposition of Air Pollutants to the Great Waters. First Report to Congress. EPA-453/R-93-055. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.
3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
4. 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.
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6. California Environmental Protection Agency (CalEPA). Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.
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.