Benzidine

92-87-5

Hazard Summary

Benzidine is no longer produced in the United States, although benzidine-based dyes may be imported into this country. No information is available on the acute (short-term) effects of benzidine in humans by inhalation exposure but benzidine is considered to be very acutely toxic to humans by ingestion. Chronic (long-term) exposure to benzidine in humans may result in injury to the bladder. Epidemiological studies have shown occupational exposure to benzidine to result in an increased risk of bladder cancer. Animal studies have reported various tumor types at multiple sites from benzidine exposure via oral, inhalation, and injection exposure. EPA has classified benzidine as a Group A, known human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS) (3), which contains information on oral chronic toxicity of benzidine and the RfD, and the carcinogenic effects of benzidine including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Benzidine. (1)

Uses

- The predominant use for benzidine is in the production of dyes, especially azo dyes in the leather, textile, and paper industries. (1)
- Benzidine is no longer produced for commercial sale in the United States. In 1973, Occupational Safety and Health Association (OSHA) regulations banned United States production of benzidine. In addition, benzidine is no longer imported into the United States; however, benzidine-based dyes may be imported into this country. (1)

Sources and Potential Exposure

- No data are available on the concentrations of benzidine in air. (1)
- Benzidine has been detected in soil and water near industrial sources, especially those that have disposed of benzidine solid wastes improperly. (1)

Assessing Personal Exposure

- Tests are available that measure the breakdown products of benzidine in urine. (1)

Health Hazard Information

Acute Effects:

- No information is available on the acute effects of benzidine in humans via inhalation exposure. Benzidine is considered to be very acutely toxic to humans by ingestion. Symptoms of acute ingestion exposure include cyanosis, headache, mental confusion, nausea, and vertigo. Dermal exposure may cause skin rashes and irritation. (1,2)
- Tests involving acute exposure of rats and mice have shown benzidine to have high toxicity from oral exposure. (2)

Chronic Effects (Noncancer):

- Chronic exposure to benzidine in humans may result in bladder injury. (1)
- Animal studies have reported effects on the blood, liver, kidney, and central nervous system from oral exposure to benzidine. (1)
- The Reference Dose (RfD) for benzidine is 0.003 milligram per kilogram body weight per day (mg/kg/d) based on brain cell vacuolization in mice and liver cell alterations in female mice. 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 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. (3)
- EPA has medium confidence in the study on which the RfD was based because it used adequate numbers of both sexes of two strains of mice and several other chronic studies support the RfD; medium confidence in the database because teratogenicity and reproductive studies are lacking; and, consequently, confidence in the RfD is medium. (3)
- EPA has not established a Reference Concentration (RfC) for benzidine. (3)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.01 milligrams per cubic meter (mg/m^3) for benzidine based on neurological, liver, and spleen effects in mice. (4)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of benzidine in humans and animals. (1)

Cancer Risk:

- Numerous epidemiologic studies have shown occupational exposure to benzidine to result in an increased risk of bladder cancer. (1,3)
- Animal studies have reported various tumor types at multiple sites from benzidine exposure via oral, inhalation, and injection exposure. (1,3)
- EPA has classified benzidine as a Group A, human carcinogen. (3)
- 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 has calculated an inhalation unit risk estimate of 6.7×10^{-2} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing benzidine at an average of 0.00002 $\mu g/m^3$ (2×10^{-8} 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 breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.0002 $\mu g/m^3$ (2×10^{-7} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.002 $\mu g/m^3$ (2×10^{-6} mg/m^3) would result in not greater than a one-in-ten-thousand increased chance of developing cancer. (3)
- EPA has calculated an oral cancer slope factor of 230 $(mg/kg/d)^{-1}$. (3)

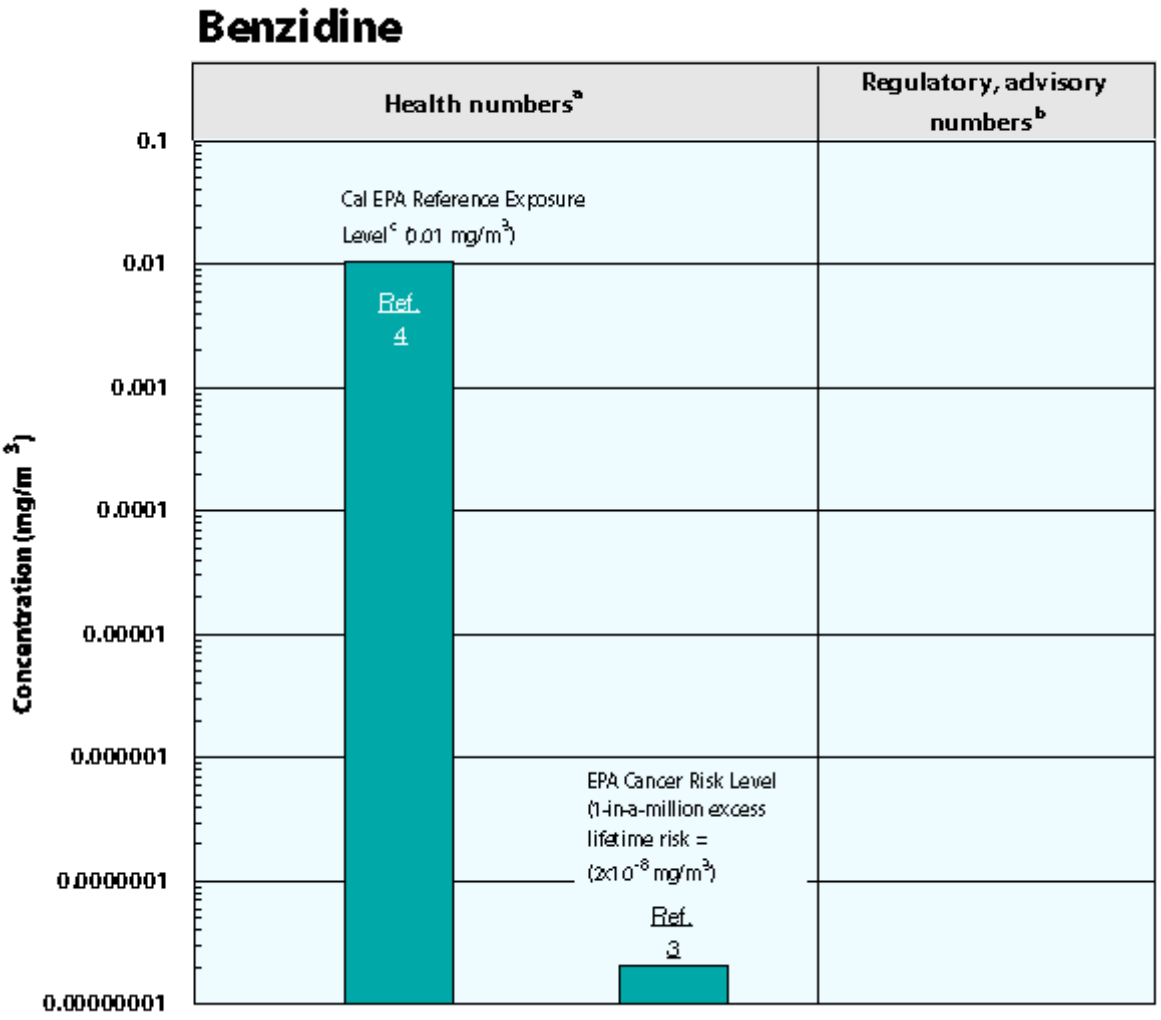
Physical Properties

- Benzidine is a white, grayish-yellow, or slightly reddish crystalline solid or powder. (1)
- Benzidine is usually present as benzidine hydrochloride or benzidine sulfate. (1)
- The odor threshold for benzidine has not been established. (1)
- The chemical formula for benzidine is $C_{12}H_{12}N_2$, and the molecular weight is 184.2 g/mol. (1)
- The vapor pressure for benzidine is 5×10^{-4} mm Hg at 25 °C, and it has an octanol/water partition

coefficient (log K_{ow}) of 1.58. (1)

Conversion Factors (only for the gaseous form):
To convert concentrations in air (at 25*E*C) from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For benzidine: 1 ppm = 7.53 mg/m^3. To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) × (1 mg/1,000 µg).

Health Data from Inhalation Exposure



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

[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.

[c] The CalEPA Reference Exposure level (REL) was derived from oral data.

Summary created in April 1992, updated in January 2000.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Benzidine. U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1995.
2. 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.

3. U.S. Environmental Protection Agency. Integrated Risk Information System (IRIS) on Benzidine. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.
4. 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.