Chloroform

67-66-3

Hazard Summary

Chloroform may be released to the air as a result of its formation in the chlorination of drinking water, wastewater and swimming pools. Other sources include pulp and paper mills, hazardous waste sites, and sanitary landfills. The major effect from acute (short-term) inhalation exposure to chloroform is central nervous system depression. Chronic (long-term) exposure to chloroform by inhalation in humans has resulted in effects on the liver, including hepatitis and jaundice, and central nervous system effects, such as depression and irritability. Chloroform has been shown to be carcinogenic in animals after oral exposure, resulting in an increase in kidney and liver tumors. EPA has classified chloroform as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS) (4), which contains information on oral chronic toxicity and the RfD, and the carcinogenic effects of chloroform including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Chloroform (1).

Uses

- The vast majority of the chloroform produced in the United States is used to make HCFC-22. The rest is produced for export and for miscellaneous uses. (1)
- Chloroform was used in the past as an extraction solvent for fats, oils, greases, and other products; as a dry cleaning spot remover; in fire extinguishers; as a fumigant; and as an anesthetic. However, chloroform is no longer used in these products. (1)

Sources and Potential Exposure

- Chloroform may be released to the air from a large number of sources related to its manufacture and use, as well as its formation in the chlorination of drinking water, wastewater, and swimming pools. Pulp and paper mills, hazardous waste sites, and sanitary landfills are also sources of air emissions. The background level of chloroform in ambient air in the early 1990s was estimated at 0.00004 parts per million (ppm). (1)
- Human exposure to chloroform may occur through drinking water, where chloroform is formed as a result of the chlorination of naturally occurring organic materials found in raw water supplies. Measurements of chloroform in drinking water during the 1970s and 1980s ranged from 0.022 to 0.068 ppm. (1)
- Chloroform may also be found in some foods and beverages, largely from the use of tap water during production processes. (1)

Assessing Personal Exposure

- Chloroform can be detected in blood, urine, and body tissues. However, these methods are not very reliable because chloroform is rapidly eliminated from the body, and the tests are not specific for chloroform. (1)

Health Hazard Information

Acute Effects:

- The major effect from acute inhalation exposure to chloroform in humans is central nervous system depression. At very high levels (40,000 ppm), chloroform exposure may result in death, with concentrations in the range of 1,500 to 30,000 ppm producing anesthesia, and lower concentrations (<1,500 ppm) resulting in dizziness, headache, tiredness, and other effects. (1,2)
- Effects noted in humans exposed to chloroform via anesthesia include changes in respiratory rate, cardiac effects, gastrointestinal effects, such as nausea and vomiting, and effects on the liver and kidney. Chloroform is not currently used as a surgical anesthetic. (1,2)
- In humans, a fatal oral dose of chloroform may be as low as 10 mL (14.8 g), with death due to respiratory or cardiac arrest. (1,2)
- Tests involving acute exposure of animals have shown chloroform to have low acute toxicity from inhalation exposure and moderate acute toxicity from oral exposure. (3)

Chronic Effects (Noncancer):

- Chronic exposure to chloroform by inhalation in humans is associated with effects on the liver, including hepatitis and jaundice, and central nervous system effects, such as depression and irritability. Inhalation exposures of animals have also resulted in effects on the kidney. (1,2)
- Chronic oral exposure to chloroform in humans has resulted in effects on the blood, liver, and kidney. (1,2)
- EPA has not established a Reference Concentration (RfC) for chloroform. (4)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.3 milligrams per cubic meter (mg/m^3) for chloroform based on exposures resulting in kidney and liver effects in rats. 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. (5)
- ATSDR has established an acute inhalation minimal risk level (MRL) of 0.5 mg/m^3 (0.1 ppm) based on exposures resulting in liver effects in mice, an intermediate inhalation MRL of 0.2 mg/m^3 (0.05 ppm) based on worker exposures resulting in liver effects in humans, and a chronic inhalation MRL of 0.1 mg/m^3 (0.02 ppm) also based on liver effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)
- The Reference Dose (RfD) for chloroform is 0.01 milligrams per kilogram per day (mg/kg/d) based on exposures resulting in fatty cyst formation in the livers of dogs. 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. (4)
- EPA has medium to low confidence in the RfD due to: medium confidence in the critical study on which the RfD was based because only two treatment doses were used, and a no-observed-effect level (NOEL) was not determined; and medium to low confidence in the database because several studies support the choice of a lowest-observed-adverse-effect level (LOAEL), but a NOEL was not found. (4)

Reproductive/Developmental Effects:

- Little information is available on the reproductive or developmental effects of chloroform in humans, via any route of exposure. A possible association between certain birth outcomes (e.g., low birth weight, cleft palate) and consumption of contaminated drinking water was reported. However, because multiple contaminants were present, the role of chloroform is unclear. (1)
- Animal studies have demonstrated developmental effects, such as decreased fetal body weight, fetal resorptions, and malformations in the offspring of animals exposed to chloroform via inhalation. (1)
- Reproductive effects, such as decreased conception rates, decreased ability to maintain pregnancy, and an increase in the percentage of abnormal sperm were observed in animals exposed to chloroform through inhalation. (1)

- Animal studies have noted decreased fetal weight, increased fetal resorptions, but no evidence of birth defects, in animals orally exposed to chloroform. (1)

Cancer Risk:

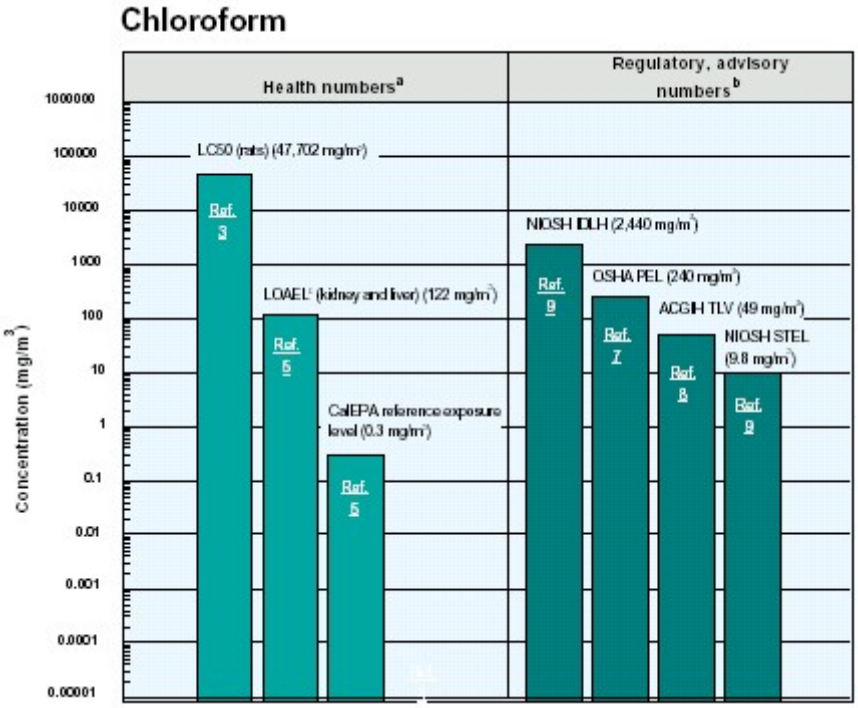
- No information is available regarding cancer in humans or animals after inhalation exposure to chloroform. (1)
- Epidemiologic studies suggest an association between cancer of the large intestine, rectum, and/or bladder and the constituents of chlorinated drinking water, including chloroform. However, there are no epidemiologic studies of water containing only chloroform. (1)
- Chloroform has been shown to be carcinogenic in animals after oral exposure, resulting in an increase in kidney and liver tumors. (1)
- EPA considers chloroform to be a probable human carcinogen and has ranked it in EPA's Group B2. (4)
- EPA has determined that although chloroform is likely to be carcinogenic to humans by all routes of exposure under high-exposure conditions that lead to cell death and regrowth in susceptible tissues, chloroform is not likely to cause cancer in humans by any route of exposure under exposure conditions that do not cause cell death and regrowth. Therefore, EPA has not derived either an oral carcinogenic potency slope or an inhalation unit risk for chloroform.

Physical Properties

- Chloroform is a colorless liquid that is not very soluble in water and is very volatile. (1,6)
- Chloroform has a pleasant, nonirritating odor; the odor threshold is 85 ppm. (1)
- The chemical formula for chloroform is $CHCl_3$, and it has a molecular weight of 119.38 g/mol. (1)
- The vapor pressure for chloroform is 159 mm Hg at 20 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 1.97. (1)

Conversion Factors:
To convert concentrations in air (at 25°C) from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For chloroform: 1 ppm = 4.88 mg/m^3. To convert concentrations in air 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



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_{50} (Lethal Concentration$_{50}$)--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.

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.

[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 and ACGIH numbers are advisory.

[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.

[d] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

Summary created in April 1992, updated in January 2000.

References

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Hazard Assessment, Berkeley, CA. 1997.
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