Isophorone

78-59-1

Hazard Summary

Isophorone is a widely used solvent and chemical intermediate. The acute (short-term) effects of isophorone in humans from inhalation exposure include eye, nose, and throat irritation. Chronic (long-term) exposure to isophorone in humans can cause dizziness, fatigue, and depression. Animal studies indicate that long-term inhalation of high concentrations of isophorone causes central nervous system effects. Limited evidence in animal studies suggests that isophorone may cause birth defects such as fetal malformations and growth retardation from inhalation exposure to isophorone during pregnancy. No information is available on the reproductive, developmental, or carcinogenic effects of isophorone in humans. EPA has classified isophorone as a Group C, possible human carcinogen.

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 isophorone including the unit cancer risk for oral exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Isophorone. (1)

Uses

- Isophorone is used mainly as a solvent for concentrated vinyl chloride/acetate-based coating systems for metal cans, other metal paints, nitrocellulose finishes, and printing inks for plastics. (1)
- Isophorone is also used in some herbicide and pesticide formulations and in adhesives for plastics, polyvinylchloride, and polystyrene materials. (1)
- Isophorone is an intermediate in the synthesis of 3,5-xylenol, 3,3,5-trimethylcyclohexanol, and plant growth retardants. (1)

Sources and Potential Exposure

- Major sources of airborne isophorone are the printing and the metal coating industries. Coal-fired power plants may also emit isophorone to the air. (1)
- Individuals may be exposed to isophorone through breathing contaminated air, especially people who work with inks, paints, lacquers, and adhesives. (1)
- Isophorone has been detected in the drinking water of several cities at very low concentrations. (1)

Assessing Personal Exposure

- No medical tests are currently available to determine human exposure to isophorone. (1,2)

Health Hazard Information

Acute Effects:

- The only acute effects of isophorone reported in humans are irritation of the skin, eyes, nose, and throat, headache, and dizziness. (1-3,6)
- Exposure to high concentration of isophorone via inhalation in animals causes inactivity and coma. (1-3)

- Tests involving acute exposure of rats and guinea pigs have shown isophorone to have moderate toxicity from oral and inhalation exposure. (4)

Chronic Effects (Noncancer):

- Dizziness, fatigue, and depression have been experienced by workers exposed to isophorone over a long-term period. (1-3)
- Animal studies indicate that long-term inhalation of high concentrations of isophorone causes central nervous system effects such as narcosis, staggering, depression, ataxia, lethargy, prostration, and coma. (1-3)
- The Reference Dose (RfD) for isophorone is 0.2 milligrams per kilogram body weight per day (mg/kg/d) based on no observed effects in 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. 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. (5)
- EPA has medium confidence in the study on which the RfD is based because it is of adequate quality; low confidence in the database because numerous data gaps exist for isophorone; and, consequently, low confidence in the RfD. (5)
- EPA has determined that there are inadequate data for establishing a Reference Concentration (RfC) for isophorone. (5)
- In the final listing rule for solvents, EPA calculated a provisional RfC of 0.012 milligrams per cubic meter (mg/m^3) based on body weight effect in rats. The provisional RfC is a value that has had some form of Agency review but is not on IRIS. (9)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level (REL) of 2 mg/m^3 for isophorone based on developmental effects in rats. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (6)

Reproductive/Developmental Effects:

- No studies were located regarding developmental or reproductive effects in humans. (1-3)
- Limited evidence in animal studies suggests that isophorone may cause birth defects such as fetal malformations and growth retardation from inhalation exposure to isophorone during pregnancy. (1,3,6)

Cancer Risk:

- No studies were found concerning the carcinogenicity of isophorone in humans. (1-3,5)
- One study demonstrated an increased incidence of kidney tumors and preputial gland (a male reproductive gland) tumors in male rats exposed to isophorone by gavage. However, the type of kidney tumor observed in male rats is of questionable relevance to humans. (1-3,5)
- EPA considers isophorone to be a possible human carcinogen (cancer-causing agent) and has ranked it in EPA's Group C. (5)
- EPA uses mathematical models, based on animal studies, to estimate the probability of a person developing cancer from ingesting water containing a specified concentration of a chemical. EPA calculated an oral cancer slope factor of 9.5×10^{-4} $(mg/kg/d)^{-1}$ and an oral unit risk estimate of 2.7×10^{-8} $(\mu g/L)^{-1}$. EPA estimates that, if an individual were to ingest water containing isophorone at 40 micrograms per liter (µg/L) (0.04 mg/L) 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 ingesting water containing this chemical. Similarly, EPA estimates that ingesting water containing 400 µg/L (0.4 mg/L) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and water containing 4,000

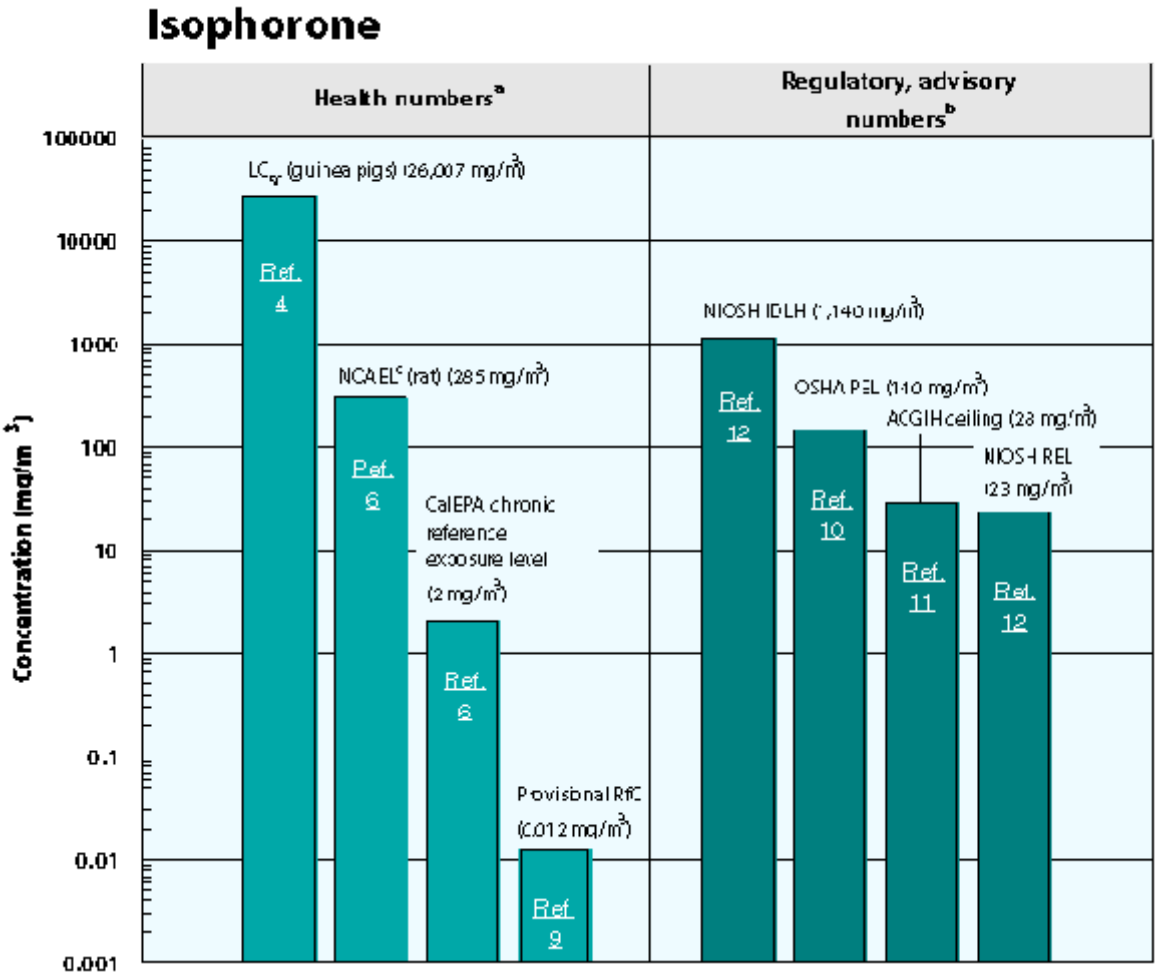
µg/L (4 mg/L) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (5)

Physical Properties

- Isophorone is a water-white colored liquid with a peppermint-like odor. (1,7)
- The chemical formula for isophorone is $C_9H_{14}O$ and the molecular weight is 138.21 g/mol. (1)
- The vapor pressure for isophorone is 0.3 mm Hg at 20 °C and it has an octanol/water partition coefficient (log K_{ow}) of 1.67. (1)
- Isophorone has an odor threshold of 0.20 parts per million (ppm). (8)
- Isophorone is slightly soluble in water. (1,7)

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 isophorone: 1 ppm = 5.7 mg/m^3.

Health Data from Inhalation Exposure



ACGIH TLV ceiling--American Conference of Governmental and Industrial Hygienists' threshold limit value ceiling; the concentration of a substance that should not be exceeded during any part of the working exposure.
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.
NIOSH IDLH -- NIOSH's immediately dangerous to life or health concentration; 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.
[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 This NOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

Summary created in April 1992, updated January 2000

References

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