

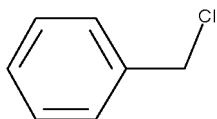
BENZYL CHLORIDE

CAS Number: 100-44-7

Synonym: α -Chlorotoluene

Molecular Formula: C₇H₇Cl

Structural Formula:



TLV-TWA, 1 ppm (5.2 mg/m³)

A3 — Confirmed Animal Carcinogen with Unknown Relevance to Humans

Summary

A TLV-TWA of 1 ppm (5.2 mg/m³) is recommended for occupational exposure to benzyl chloride. This value is intended to minimize the potential for acute ocular, nasal, and throat irritation and possible pulmonary edema from prolonged exposures. Based on the statistically significant increase of papillomas and carcinomas of the forestomach in mice administered benzyl chloride by gavage and positive genotoxicity data, an A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans, notation is assigned. Sufficient data were not available to recommend Skin or SEN notations or a TLV-STEL.

Chemical and Physical Properties

Benzyl chloride is a colorless, refractive liquid with an unpleasant, irritating odor. The stabilized form of benzyl chloride contains a fixed amount of a sodium carbonate solution or propylene oxide.

Chemical and physical properties include:⁽¹⁾

- Molecular weight: 126.58
- Specific gravity: 1.100 at 20°C
- Melting point: -43° to -48°C
- Boiling point: 179°C
- Vapor pressure: 1.23 torr at 25°C
- Flash points: 67°C, closed cup; 74°C, open cup
- Lower explosion limit: 1.1% by volume in air
- Autoignition temperature: 585°C
- Solubility: insoluble in water; miscible with most organic solvents
- Reactivity: very reactive; unless stabilized, it undergoes a Friedel-Crafts-type condensation when exposed to certain metals, liberating hydrogen chloride
- Conversion factors at 25°C and 760 torr:
1 ppm = 5.19 mg/m³; 1 mg/m³ = 0.193 ppm

Major Uses

Benzyl chloride is a chemical intermediate in the manufacture of dyes, plasticizers, lubricants, gasoline additives, pharmaceuticals, tanning agents, and quaternary ammonium compounds.

Animal Studies

Acute

Two-hour LC₅₀ values of 80 ppm and 150 ppm benzyl chloride were cited for the mouse and rat, respectively.⁽²⁾ Back et al.⁽³⁾ reported that all mice and rats survived a 1-hour exposure at 400 ppm. The difference in the results from these two studies cannot be explained. Rabbits and cats exposed 8 hours/day for 6 days at 95 ppm showed eye and respiratory tract irritation, while a dog died following 8 hours at 380 ppm.⁽⁴⁾ Skin sensitization in guinea pigs has been reported.⁽⁵⁾

Chronic/Carcinogenicity

Weekly, subcutaneous, high dose (80 mg/kg) administration of benzyl chloride for 51 weeks resulted in injection-site sarcomas, with lung metastases, in rats; the mean induction time was 500 days. At half this dosage, there were some local sarcomas but no metastases.^(4,6) The U.S. National Institute for Occupational Safety and Health (NIOSH) concluded that the presently available data were insufficient upon which to base a firm conclusion as to the carcinogenic potential of benzyl chloride.⁽⁴⁾

In a study by Lijinsky,⁽⁷⁾ benzyl chloride was administered by gavage in corn oil at a dose of 50 or 100 mg/kg body weight (mice) and 15 or 30 mg/kg (rats) 3 times/week for 2 years. A statistically significant increased incidence of papillomas and carcinomas of the forestomach was observed in mice of each sex. The only statistically significant increased incidence of neoplasms in the rats (female

only) was for thyroid C cell tumors. A few neoplasms of the forestomach were observed in male rats. Based on the subcutaneous and gavage studies, benzyl chloride was evaluated by the International Agency for Research on Cancer (IARC)⁽⁸⁾ to have limited evidence for carcinogenicity in animals.

Genotoxicity Studies

The IARC review of benzyl chloride⁽⁸⁾ reported that the substance did not induce micronuclei in mice treated *in vivo*. It induced DNA strand breaks, but not unscheduled DNA synthesis or chromosomal aberrations in cultured human cells. Conflicting results were obtained for the induction of sister-chromatid exchanges in human cells. In cultured rodent cells, benzyl chloride induced sister-chromatid exchanges, chromosomal aberrations, mutation, and DNA strand breaks. It induced somatic and sex-linked recessive lethal mutations in *Drosophila*; mitotic recombination, gene conversion, mutation and DNA damage in fungi; and mutation and DNA damage in bacteria.⁽⁸⁾

Human Studies

Smyth⁽⁹⁾ characterized benzyl chloride as a potent lacrimator, which was irritating to the eyes, nose, and throat and capable of causing lung edema. He inferred that the liquid could cause corneal injury. Smyth stated that a 1 ppm threshold limit could be derived from older human sensory data and that the 1 ppm was low enough to prevent lung injury.

From references cited in the NIOSH criteria document for benzyl chloride,⁽⁴⁾ exposure at 1.5 ppm for 5 minutes can result in slight conjunctivitis, and 8 ppm was the threshold for eye irritation in a 10-second exposure trial. A single breath of air containing 35 ppm of benzyl chloride reportedly caused nasal irritation. Flury and Zernik⁽¹⁰⁾ reported that a 1-minute exposure at 16 ppm was intolerable to humans.

TLV Recommendation

Based on the above data, a TLV-TWA of 1 ppm (5.2 mg/m³) is recommended for occupational exposure to benzyl chloride. This value should prevent lung injury and irritation of the eye, nose, and throat. In view of the reports on the carcinogenicity⁽⁷⁾ and genotoxicity⁽⁸⁾ of benzyl chloride, an A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans, notation is assigned for this chemical. Sufficient data were not available to recommend

Skin or SEN notations or a TLV-STEL. The reader is expected to be familiar with the section on *Excursion Limits* in the "Introduction to the Chemical Substance TLVs" of the current edition of the *Documentation of the TLVs and BEIs* for the guidance and control of excursions above the TLV-TWA, even when the 8-hour TWA is within the recommended limit.

Historical TLVs

1954: *Proposed*: TLV-TWA, 1 ppm
1956-present: TLV-TWA, 1 ppm
1995: *Proposed*: A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans
1996-present: TLV-TWA, 1 ppm; A3

References

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