

# 2,4-Toluene diisocyanate

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## Hazard Summary

2,4-Toluene diisocyanate is primarily used as a chemical intermediate in the production of polyurethane products. 2,4-Toluene diisocyanate is extremely toxic from acute (short-term) and chronic (long-term) exposures. Acute exposure to high levels of 2,4-toluene diisocyanate in humans, via inhalation, results in severe irritation of the skin and eyes and affects the respiratory, gastrointestinal, and central nervous systems (CNS). Chronic inhalation exposure to 2,4-toluene diisocyanate in humans has resulted in significant decreases in lung function in workers, an asthma-like reaction characterized by wheezing, dyspnea, and bronchial constriction. Animal studies have reported significantly increased incidences of tumors of the pancreas, liver, and mammary glands from exposure to 2,4-toluene diisocyanate via gavage (experimentally placing the chemical in the stomach). The International Agency for Research on Cancer (IARC) has classified 2,4-toluene diisocyanate as a Group 2B, possible human carcinogen.

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Please Note: The main sources of information for this fact sheet are the International Agency for Research on Cancer's (IARC's) Monograph on the Evaluation of the Carcinogenic Risk of Toluene 2,4-Diisocyanate to Humans (5), the Hazardous Substances Data Bank (HSDB) (2), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS) (4), a database of toxic effects that are not peer reviewed.

## Uses

- 2,4-Toluene diisocyanate is used as a chemical intermediate in the production of polyurethane products such as foams, coatings, and elastomers. (3)

## Sources and Potential Exposure

- Occupational exposure to 2,4-toluene diisocyanate can occur for those workers involved in its manufacture and use. (1)
- The general public may be exposed to 2,4-toluene diisocyanate through emissions from urethane foam production facilities. (1)
- Exposure usually occurs to a mixture of toluene 2,4- and 2,6-diisocyanate, and not to the individual compound. (12)

## Assessing Personal Exposure

- No information is available on the assessment of personal exposure to 2,4-toluene diisocyanate.

## Health Hazard Information

### Acute Effects:

- Acute exposure to high levels of 2,4-toluene diisocyanate in humans, via inhalation, results in severe irritation of the skin, eyes, and nose, and causes nausea and vomiting. (2,3)
- Acute animal tests in rats have shown 2,4-toluene diisocyanate to have moderate to extreme acute toxicity from inhalation exposure and low acute toxicity from oral exposure. (1,4)

#### Chronic Effects (Noncancer):

- Chronic inhalation exposure to 2,4-toluene diisocyanate in workers has caused significant decreases in lung function, an asthma-like reaction characterized by wheezing, dyspnea, and bronchial constriction. (2,3)
- Animal studies have reported irritation of respiratory tissues, bronchopneumonia, and weight loss from chronic exposure to 2,4-toluene diisocyanate. (1,2)
- EPA has not established a Reference Concentration ([RfC](#)) or a Reference Dose ([RfD](#)) for 2,4-toluene diisocyanate. However, EPA has established an [RfC](#) of 0.00007 milligrams per cubic meter ( $\text{mg}/\text{m}^3$ ) for the mixture of toluene 2,4- and 2,6-diisocyanate based on respiratory effects in humans. The [RfC](#) is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation 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 [RfC](#), the potential for adverse health effects increases. Lifetime exposure above the [RfC](#) does not imply that an adverse health effect would necessarily occur. (11)
- EPA has medium confidence in the study on which the [RfC](#) was based. Although the study was prospective and used appropriate endpoints and state-of-the-art methods in monitoring, the lack of exposure characterization in the first 2 years and the unknown relationship of peak exposures to lung function decline detract from clear identification of the no-observed-adverse-effect level ([NOAEL](#)) and lowest-observed-adverse-effect level ([LOAEL](#)); medium confidence in the database because of limitations in monitoring and analytical procedures in the majority of occupational studies cited and the uncertainties associated with peak vs. time-weighted-average ([TWA](#)) exposures as determinants of toxicity and, in addition, developmental toxicity data from a second species are lacking; and consequently medium confidence in the [RfC](#). (11)

#### Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of 2,4-toluene diisocyanate in humans.
- No reproductive or developmental effects were observed in rats exposed to a mixture of toluene 2,4- and 2,6-diisocyanate via inhalation (11).

#### Cancer Risk:

- Information is not adequate to determine the carcinogenic effects of 2,4-toluene diisocyanate in humans. Three epidemiology studies did not find an increased occurrence of cancer among exposed workers.
- Animal studies have reported significantly increased incidences of tumors of the pancreas, liver, and mammary glands from exposure to 2,4-toluene diisocyanate via gavage. Animal studies, via inhalation, did not report an increased incidence of tumors. (1,6)
- A study by the National Toxicology Program (NTP) on a mixture of toluene 2,4- and 2,6-diisocyanate administered by gavage showed an increase in tumors of subcutaneous tissues in male and female rats, the pancreas in male rats, mammary gland and liver in female rats, and liver and circulatory system in female mice. (12)
- EPA has not classified 2,4-toluene diisocyanate for carcinogenicity.
- IARC has classified 2,4-toluene diisocyanate as a Group 2B, possible human carcinogen. (5)
- The California Environmental Protection Agency (CalEPA) has calculated an oral cancer slope factor of  $3.9 \times 10^{-2}$  ( $\text{mg}/\text{kg}/\text{d}$ )<sup>-1</sup> and an inhalation unit risk factor of  $1.1 \times 10^{-5}$  ( $\mu\text{g}/\text{m}^3$ )<sup>-1</sup>. (3)

## Physical Properties

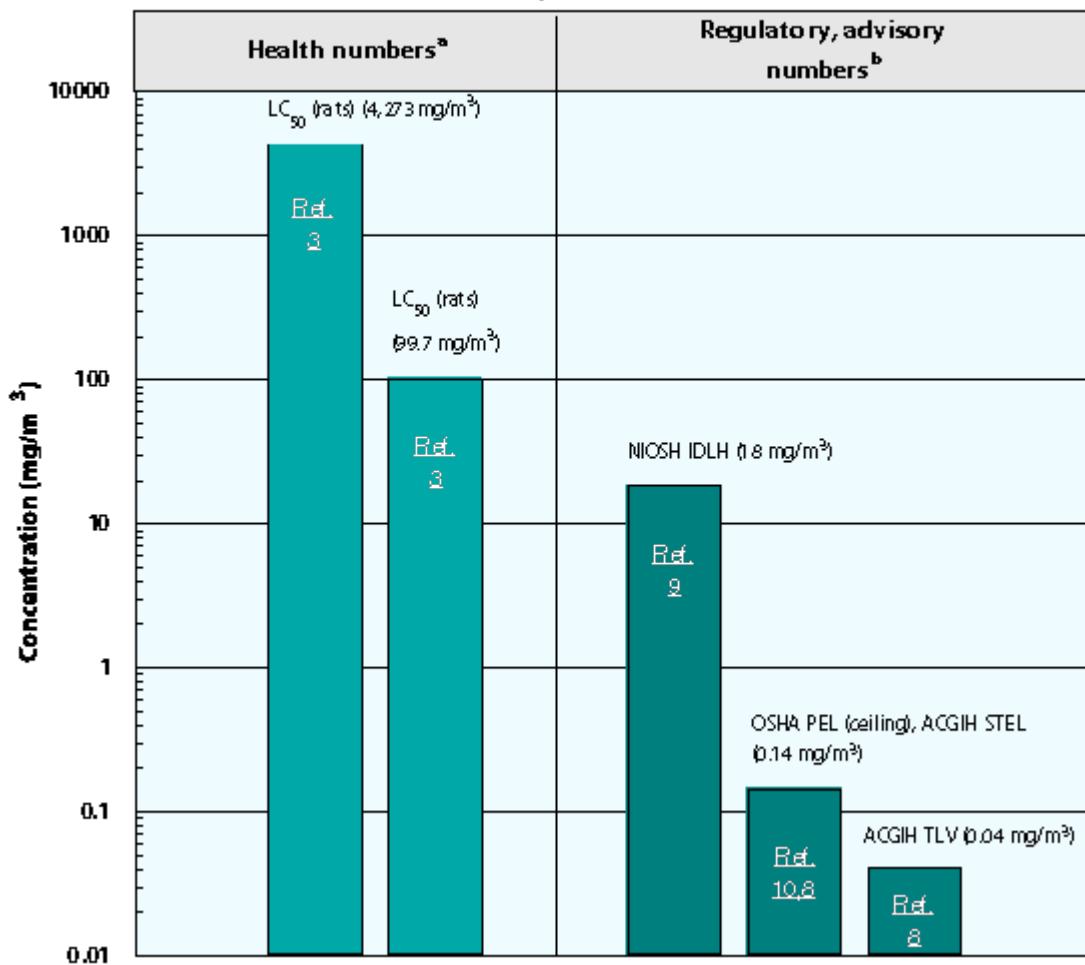
- 2,4-Toluene diisocyanate is a colorless, yellow, or dark liquid with a sharp, pungent odor. (7)
  - The odor threshold for 2,4-toluene diisocyanate is 0.17 parts per million (ppm). (8)
  - The chemical formula for 2,4-toluene diisocyanate is  $C_9H_{16}N_2O_2$ , and the molecular weight is 174.15 g/mol. (7)
  - The vapor pressure for 2,4-toluene diisocyanate is 0.01 mm Hg at 80 °C, and it has a log octanol/water partition coefficient ( $\log K_{ow}$ ) of 0 to 1 (estimated). (7)
  - Commercial toluene diisocyanate is comprised of approximately 80% 2,4-toluene diisocyanate and 20% toluene 2,6-diisocyanate. (2)
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Conversion Factors:

To convert concentrations in air (at 25 °C) from ppm to mg/m<sup>3</sup>:  $mg/m^3 = (ppm) \times (\text{molecular weight of the compound})/(24.45)$ . For 2,4-toluene diisocyanate: 1 ppm = 7.12 mg/m<sup>3</sup>.

### Health Data from Inhalation Exposure

## Toluene 2,4-Diisocyanate



ACGIH STEL--American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.

ACGIH TLV--ACGIH's 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.

**NIOSH IDLH**--National Institute of Occupational Safety and Health immediately dangerous to life and health; NIOSH concentration representing the maximum level of a pollutant from which an individual could escape within 30 minutes without escape-impairing symptoms or irreversible health effects.

**OSHA PEL ceiling**--Occupational Safety and Health Administration's permissible exposure limit ceiling value; the concentration of a substance that should not be exceeded at any time.

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. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.

Summary created in April 1992, updated January 2000

## References

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