

4,4'-Methylenediphenyl Diisocyanate (MDI)

101-68-8

Hazard Summary

The commercial form of 4,4'-methylenediphenyl diisocyanate (MDI) is used to produce polyurethane foams. Acute (short-term) inhalation of high concentrations of MDI may cause sensitization and asthma in humans. Acute dermal contact with MDI has induced dermatitis and eczema in workers. MDI has been observed to irritate the skin and eyes of rabbits. Chronic (long-term) inhalation exposure to MDI has been shown to cause asthma, dyspnea, and other respiratory impairments in workers. Respiratory effects have also been observed in animals. No adequate information is available on the reproductive, developmental, or carcinogenic effects of MDI in humans. EPA has classified MDI as a Group D, not classifiable as to human carcinogenicity.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS) (5), which contains information on inhalation chronic toxicity of MDI and the [RfC](#), EPA's Toxicological Review of Methylenediphenyl Diisocyanate (MDI) (6), and EPA's Health and Environmental Effects Profile for 4,4'-Methylenediphenyl Isocyanate. (3)

Uses

- The commercial form of MDI is primarily used to produce polyurethane foams. (6)

Sources and Potential Exposure

- Occupational exposure to MDI occurs predominantly through inhalation and dermal contact. (1,6)

Assessing Personal Exposure

- No information was located regarding the measurement of personal exposure to MDI.

Health Hazard Information

Acute Effects:

- Acute inhalation of high concentrations of MDI may cause sensitization and asthma in humans. (6)
- Dermal contact with MDI has induced dermatitis and eczema in workers. MDI has been observed to irritate the skin and eyes of rabbits. (2,3)
- Tests involving acute exposure of rats and mice have demonstrated MDI to have **high** to **extreme** acute toxicity by inhalation and **moderate** acute toxicity by oral exposure. (4)

Chronic Effects (Noncancer):

- Exposure to isocyanates is a leading cause of occupational asthma. (6)
- Chronic inhalation exposure to MDI has been shown to cause asthma, dyspnea, and other respiratory impairments in workers. Some of the effects of MDI may be due to immune system reactions in individuals who have been sensitized to high levels of MDI, above the occupational exposure limit of 20 ppb. Such sensitized individuals may experience effects when exposed to low levels of MDI. (3,6)

- Respiratory effects such as nasal and lung lesions, consistent with exposure to an irritant, have been reported in chronically exposed animals. (6)
- The Reference Concentration (RfC) for MDI is 0.0006 milligrams per cubic meter (mg/m^3) based on irritation of the nasal membranes in rats. 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. (5,6)
- EPA has medium confidence in the RfC based on: high confidence in the principal study because it was well designed, used an adequate number of animals, and indicated a concentration–response relationship; and medium confidence in the database due to the lack of data on reproductive and developmental endpoints and exposure–response data for asthma in humans. (5,6)
- EPA has not established a Reference Dose (RfD) for MDI. (5,6) However, it is unlikely that humans would be exposed to MDI by the oral route.

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of MDI in humans.
- Decreased placental and fetal weights and an increased number of fetuses per litter with skeletal variations were reported in one inhalation study in rats. (6) These effects were observed only at the highest dose, and may have been related to maternal toxicity.

Cancer Risk:

- Information is not adequate to determine the carcinogenic effects of MDI in humans.
- Pulmonary adenomas were reported in one strain of rats exposed to polymeric MDI. (6)
- EPA has classified MDI as a Group D, not classifiable as to human carcinogenicity. (5,6)

Physical Properties

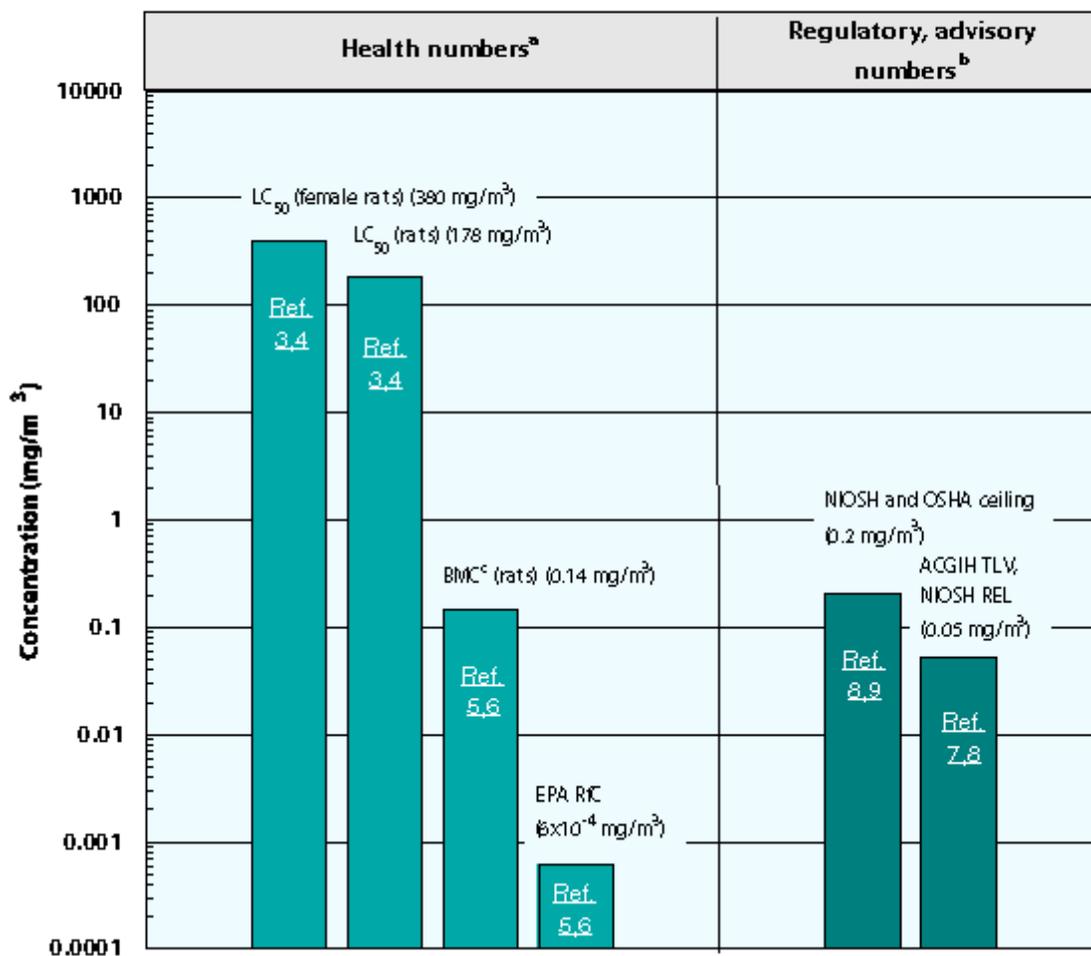
- The chemical formula for MDI is $\text{C}_{15}\text{H}_{10}\text{N}_2\text{O}_2$, and its molecular weight is 250.3 g/mol. (3)
- MDI occurs as a light–yellow fused solid or crystals. (1)
- The odor threshold for MDI is 0.4 ppm.
- The vapor pressure for MDI is 5×10^{-6} mm Hg at 25 °C. (3)

Conversion Factors:

To convert concentrations in air (at 25 °C) from ppm to mg/m^3 : $\text{mg}/\text{m}^3 = (\text{ppm}) \times (\text{molecular weight of the compound}) / (24.45)$. For MDI: $1 \text{ ppm} = 10.2 \text{ mg}/\text{m}^3$.

Health Data from Inhalation Exposure

MDI



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.

BMC--Benchmark concentration.

LC₅₀ (Lethal Concentration₅₀)--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 recommended exposure limit; NIOSH--recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH ceiling--NIOSH's recommended exposure limit ceiling; the concentration that should not be exceeded at any time.

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 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.

^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 The BMC is from the critical study used as the basis for the RfC.

Summary created in April 1992, updated January 2000

References

1. 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.
2. International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Some Monomers, Plastics and Synthetic Elastomers, and Acrolein. Volume 19. World Health Organization. Lyon. 1979.
3. U.S. Environmental Protection Agency. Health and Environmental Effects Profile for 4,4'-Methylenediphenyl Isocyanate. EPA/600/x-85/111. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1985.
4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
5. U.S. Environmental Protection Agency. Integrated Risk Information System (IRIS) on 4,4'-Methylenediphenyl Isocyanate. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.
6. U.S. Environmental Protection Agency. Toxicological Review of Methylene Diphenyl Diisocyanate (MDI) (CAS No. 101-68-8 and 9016-87-9) in Support of Summary Information on the Integrated Risk Information System (IRIS). National Center for Environmental Assessment, Office of Research and Development, Research Triangle Park, NC. 1998.
7. American Conference of Governmental Industrial Hygienists (ACGIH). 1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices. Cincinnati, OH. 1999.
8. National Institute for Occupational Safety and Health (NIOSH). Pocket Guide to Chemical Hazards. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.
9. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. Code of Federal Regulations 29 CFR 1910.1000. 1998.