N-Nitrosodimethylamine

62-75-9

Hazard Summary

Individuals may be exposed to low levels of N-nitrosodimethylamine in occupational settings, through the ingestion of food that contains it (e.g., cured meat products and smoked fish), and from breathing cigarette smoke. Acute (short-term) exposure to N-nitrosodimethylamine may damage the liver in humans, with symptoms that include nausea, vomiting, headaches, and malaise. Chronic (long-term) exposure of humans toN-nitrosodimethylamine may cause liver damage and low platelet counts. Severe liver damage has been observed in animals. Limited human data are available on the carcinogenic effects of N-nitrosodimethylamine. Animal studies have suggested that chronic ingestion and inhalation of N-nitrosodimethylamine may cause an increase in liver tumors and other types of tumors. EPA has classified N-nitrosodimethylamine 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) (5), which contains information on the carcinogenic effects of N-nitrosodimethylamine including the unit cancer risk for inhalation exposure, the Hazardous Substances Data Bank (HSDB) (1), a database of summaries of peer-reviewed literature, the International Agency for Research on Cancer (IARC) monographs on chemicals carcinogenic to humans (3), and the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for N-Nitrosodimethylamine. (8)

Uses

- N-Nitrosodimethylamine is primarily used as a research chemical. (7,8)
- N-Nitrosodimethylamine has been used as an antioxidant, as an additive for lubricants, and as a softener of copolymers. (1,2,5,8)
- N-Nitrosodimethylamine was formerly used in the production of rocket fuels. (1,2,5)

Sources and Potential Exposure

- Individuals are most likely to be exposed to N-nitrosodimethylamine in occupational settings such as in the rubber, tannery, fish processing, dye, and surfactant industries. (1,8)
- Humans may be exposed to low levels of N-nitrosodimethylamine through the ingestion of food that contains it, such as cured meat products and smoked fish. Other exposures to the chemical may be from drinking contaminated water and from breathing cigarette smoke and contaminated ambient air. (1,2,8)

Assessing Personal Exposure

- N-Nitrosodimethylamine can be detected in blood and urine by a test. (8)

Health Hazard Information

Acute Effects:

- Acute exposure to N-nitrosodimethylamine may cause liver damage in humans, with symptoms that include nausea, vomiting, headaches, and malaise. (1,3-5,8)

- Hematological and severe liver effects (hemorrhagic necrosis) were reported in animals acutely exposed via inhalation and ingestion. (8)
- Tests involving acute exposure of rats, mice, and hamsters have demonstrated that N-nitrosodimethylamine has high to extreme acute toxicity from inhalation or oral exposure. (6)

Chronic Effects (Noncancer):
- Chronic exposure of humans to N-nitrosodimethylamine may cause liver damage (jaundice and swelling) and low platelet counts. (1,4,5,8)
- Chronic oral exposure has resulted in severe liver damage in animals. (8)
- EPA has not established a Reference Concentration (RfC) or a Reference Dose (RfD) for N-nitrosodimethylamine. (5)

Reproductive/Developmental Effects:
- No information is available on the reproductive or developmental effects of N-nitrosodimethylamine in humans.
- In a study of rats exposed to N-nitrosodimethylamine by injection, increased fetal mortality was observed but no birth defects were noted. (3)
- N-Nitrosodimethylamine, when administered to pregnant rats, mice, and hamsters by several routes, has been shown to cause cancer in the offspring. (1,5)

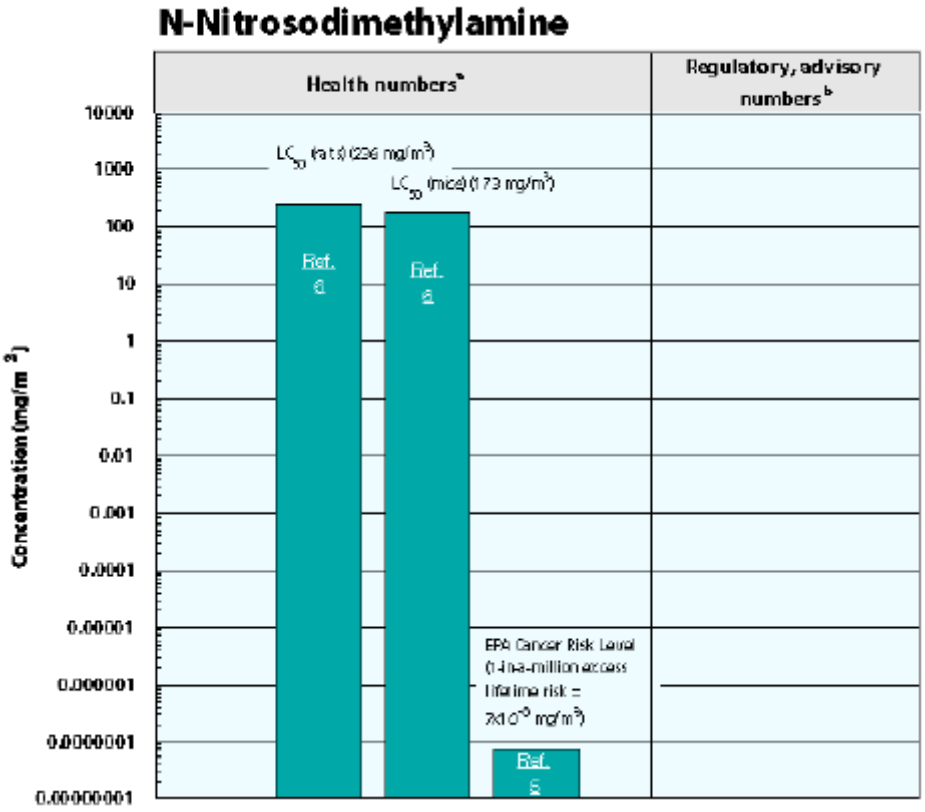
Cancer Risk:
- Data from human studies are of limited use because human exposure to nitrosamines generally results from contact with mixtures of these compounds. (5)
- N-Nitrosodimethylamine has been found to be carcinogenic in a number of animal species, inducing tumors in various organs and by various routes of exposure. Increased incidences of liver, kidney, and lung tumors have been observed in rats and mice that inhaled N-nitrosodimethylamine. Liver tumors have also been observed in orally exposed rats, mice, and hamsters. (1,3-5,7,8)
- EPA has classified N-nitrosodimethylamine as a Group B2, probable human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 1.4×10^{-2} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing N-nitrosodimethylamine at an average of 0.00007 micrograms per cubic meter ($\mu g/m^3$) (7×10^{-8} milligrams per cubic meter, mg/m^3) 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 breathing air containing this chemical. Similarly, EPA estimates that breathing air containing an average of 0.0007 $\mu g/m^3$ (7×10^{-7} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing an average of 0.007 $\mu g/m^3$ (7×10^{-6} mg/m^3) 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)
- EPA has calculated an oral cancer slope factor of 51 $(mg/kg/d)^{-1}$. (5)

Physical Properties

- The chemical formula for N-nitrosodimethylamine is $C_2H_6N_2O$, and its molecular weight is 74.08 g/mol. (2,8)
- N-Nitrosodimethylamine is a yellow, oily liquid that is very soluble in water. (1,2,7)
- N-Nitrosodimethylamine has a faint characteristic odor; the odor threshold has not been established. (5)
- The log octanol/water partition coefficient (log K_{ow}) is 0.57 and the vapor pressure is 2.7 mm Hg at 20° C. (1,8)

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 N-nitrosodimethylamine: 1 ppm = 3.03 mg/m^3. To convert concentrations in air from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) × (1 mg/1,000 µg).

Health Data from Inhalation 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.

The health 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.

References

Summary created in April 1992, updated in January 2000

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2. The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.
3. International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Some N-Nitroso Compounds. Volume 17. World Health Organization, Lyon. 1978.
4. M. Sittig. Handbook of Toxic and Hazardous Chemicals and Carcinogens. 2nd ed. Noyes Publications. Park Ridge, NJ. 1985.
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Development, Washington, DC. 1999.
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8. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for N-Nitrosodimethylamine. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1989.