N-NITROSODIETHANOLAMINE CAS No. 1116-54-7

First Listed in the Second Annual Report on Carcinogens

$$\begin{array}{c|c} & & & & \\ & & & & \\ H_2 & & & & \\ C & & & \\ H_2 & & & \\ H_2 & & & \\ \end{array} \begin{array}{c} H_2 \\ C \\ C \\ H_2 \end{array} \begin{array}{c} OH \\ OH \\ OH \\ OH \\ \end{array}$$

CARCINOGENICITY

N-Nitrosodiethanolamine is reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity in experimental animals (IARC 1978, 1982). When administered in the drinking water, N-nitrosodiethanolamine induced hepatocellular carcinomas and renal adenomas in rats. When administered subcutaneously, the compound caused nasal cavity adenocarcinomas, papillary tumors of the trachea, hepatocellular adenomas, and injection site fibrosarcomas in hamsters of both sexes (IARC 1978, 1982).

No adequate human studies of the relationship between exposure to *N*-nitrosodiethanolamine and human cancer have been reported (IARC 1987, 2000).

PROPERTIES

N-Nitrosodiethanolamine is a yellow, viscous oil that is miscible with water in all proportions. It is soluble in polar solvents and insoluble in nonpolar organic solvents. N-Nitrosodiethanolamine is sensitive to light, especially ultraviolet light, and undergoes relatively rapid photolytic degradation (IARC 2000).

USE

The presence of *N*-nitrosodiethanolamine is widespread in the environment. There is presently no known commercial use for this compound. It is used primarily as a research chemical (IARC 2000).

PRODUCTION

N-Nitrosodiethanolamine is not currently commercially produced in the U.S. (HSDB 2001). The 1979 TSCA Inventory reported production of 5,000 lb of N-nitrosodiethanolamine by one U.S. manufacturer in 1977 (TSCA 1979). Chem Sources (2001) listed seven U.S. suppliers of this compound. No U.S. import or export data were available.

EXPOSURE

The primary routes of potential human exposure to *N*-nitrosodiethanolamine are dermal contact, ingestion, and inhalation. *N*-Nitrosodiethanolamine is a known contaminant of

cosmetics, lotions, shampoos, cutting fluids, certain pesticides, antifreeze, and tobacco at concentrations ranging from 1 to 130,000 ppb. As of 1980, FDA analyzed 335 cosmetic products and found that 42% were contaminated with N-nitrosodiethanolamine. This compound has been detected in facial cosmetics at concentrations ranging from 42 to 49,000 µg/kg, in lotions from <10 to 140 μg/kg, and in shampoos from <10 to 260 mg/kg (IARC 1978). N-Nitrosodiethanolamine is present in most cutting fluids containing triethanolamine and sodium nitrite at concentrations varying from 0.02% to 3% (IARC 1978). An atrazine pesticide formulation emulsified with triethanolamine was reported to contain 0.5 mg/kg Nnitrosodiethanolamine. N-Nitrosodiethanolamine is also present in tobacco and tobacco smoke. It has been detected in cigarette smoke at concentrations of 24 to 36 ng/cigarette and in smokeless tobacco products at 0.2 to 6.8 µg/g (Brunnemann and Hoffmann 1981, Brunnemann et al. 1982). The presence of N-nitrosodiethanolamine in tobacco is attributed to the use of a herbicide, maleic hydrazide-diethanolamine, commonly applied to tobacco. Occupational exposure to N-nitrosodiethanolamine could possibly occur during the use of synthetic cutting fluids to reduce the temperature of the metal-tool interface during metal cutting or grinding. Various synthetic cutting fluids are produced by over 1,000 companies in the United States, and NIOSH estimates that 780,000 persons are potentially exposed to cutting fluids during their manufacture and use (Sittig 1985). N-Nitrosodiethanolamine was not included in the National Occupational Hazard Survey or the National Occupational Exposure Survey conducted by NIOSH.

REGULATIONS

EPA regulates *N*-nitrosodiethanolamine under the Resource Conservation and Recovery Act (RCRA) and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). It is subjected to reporting and record-keeping requirements under the hazardous waste disposal rule of RCRA, and a reportable quantity (RQ) of 1 lb has been established for *N*-nitrosodiethanolamine under CERCLA.

FDA has alerted the cosmetic industry to the presence of *N*-nitrosodiethanolamine in a number of products and is conducting a survey for product contamination.

OSHA regulated *N*-nitrosodiethanolamine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 126.

REFERENCES

Brunnemann, K.D., J.C. Scott, and D. Hoffmann. *N*-Nitrosomorpholine and Other Volatile *N*-Nitrosamines in Snuff Tobacco. Carcinogenesis Vol. 3, No. 6, 1982, pp. 693-696.

Brunnemann, K.D. and D. Hoffmann. Assessment of the Carcinogenic *N*-Nitrosodiethanolamine in Tobacco Products and Tobacco Smoke. Carcinogenesis Vol. 2, 1981, pp. 1123-1127.

Chem Sources. Chemical Sources International, Inc. http://www.chemsources.com, 2001.

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. N-nitrosodiethanolamine. Profile last updated May 16, 2001. Last review date, January 31, 1998.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Some *N*-Nitroso Compounds. Vol. 17. 365 pp. Lyon, France: IARC, 1978.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. Supplement 4. 292 pp. Lyon, France: IARC, 1982.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Overall Evaluations of Carcinogenicity. Supplement 7. 440 pp. Lyon, France: IARC, 1987.

IARC. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. Some Industrial Chemicals. Vol. 77. 564 pp. Lyon, France: IARC, 2000.

Sittig, M. Handbook of Toxic and Hazardous Chemicals and Carcinogens, Second Edition. 950 pp. Park Ridge, NJ: Noyes Publications, 1985.

TSCA. Toxic Substances Control Act, Chemical Substance Inventory, 1979: public record.