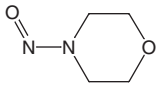
N-Nitrosomorpholine
CAS No. 59-89-2

Reasonably anticipated to be a human carcinogen
First Listed in the *Second Annual Report on Carcinogens* (1981)



Carcinogenicity

N-Nitrosomorpholine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1978, Lijinsky *et al.* 1988). When administered in the drinking water, *N*-nitrosomorpholine induced hepatocellular carcinomas, cystadenomas, cholangiofibromas, cholangiocarcinomas, and hemangiosarcomas of the liver, neoplasms of the tongue and esophagus, and epithelial kidney tumors in rats and benign hepatocellular neoplasms and lung adenomas in male mice. When administered by subcutaneous injection, *N*-nitrosomorpholine induced lung adenomas, neoplasms of the trachea, and nasal cavity squamous cell papillomas and carcinomas, anaplastic carcinomas, adenocarcinomas, olfactory neuroepitheliomas, and epidermoid carcinomas in hamsters of both sexes. When administered by intravenous injection, this chemical induced hepatocellular carcinomas and carcinomas of the ethmoturbinals in rats. When added to the water of tanks, *N*-nitrosomorpholine induced liver neoplasms in fish (IARC 1978).

No adequate human studies of the relationship between exposure to *N*-nitrosomorpholine and human cancer have been reported (IARC 1978).

Properties

N-Nitrosomorpholine occurs as yellow crystals. It is miscible in water and soluble in organic solvents and is sensitive to light. It is oxidized by strong oxidants to the corresponding nitramine, and it can be reduced to the corresponding hydrazine and/or amine. It is relatively resistant to hydrolysis but can be reduced by hydrogen bromide in acetic acid (IARC 1978, HSDB 2001).

Use

There is no evidence that *N*-nitrosomorpholine is used commercially in the United States, although patents have been issued for its use as a solvent for polyacrylonitrile and as an intermediate in the production of *N*-aminomorpholine. It was found to be effective as an antimicrobial agent, but there is no evidence that it is used in this manner (IARC 1978, HSDB 2001).

Production

Chem Sources identified 11 U.S. suppliers of *N*-nitrosomorpholine (Chem Sources 2001). Synthetic production of nitrosamines is limited to small quantities, produced primarily for research (HEEP 1980). No production, import, or export data were available.

Exposure

Workers in chemical research laboratories and in the rubber and tire manufacturing industry may possibly be exposed to *N*-nitrosomorpholine. In air samples from a tire factory, *N*-nitrosomorpholine levels ranged from 0.07 µg/m^3 to 5.1 µg/m^3, while levels in an aircraft tire factory ranged from 0.6 to 27 µg/m^3 (HSDB 2001). Investigators have detected *N*-nitrosomorpholine as a contaminant in analytical-grade dichloromethane at 10 to 32 µg/L and in chloroform at 2 to 376 µg/L (IARC 1978). *N*-Nitrosomorpholine has been detected in rubber nipples for baby bottles, at a concentration of 3.0 to 14.1 ppb (HSDB 2001). *N*-Nitroso compounds have been identified in a variety of vegetables, fruits, cheeses, meats, and alcoholic beverages (CHIP 1978, HSDB 2001). It was found to be present in tobacco snuff in the range of 24 to 690 ppb (Brunnemann *et al.* 1982).

Regulations

EPA

Clean Air Act
- NESHAP: Listed as a Hazardous Air Pollutant (HAP)

Clean Water Act
- Effluent Guidelines: Listed as a Toxic Pollutant (nitrosamines)
- Water Quality Criteria: Based on fish/shellfish and water consumption = 0.0008 µg/L (nitrosamines); based on fish/shellfish consumption only = 1.24 µg/L (nitrosamines)

Comprehensive Environmental Response, Compensation, and Liability Act
- Reportable Quantity (RQ) = 1 lb

Emergency Planning and Community Right-To-Know Act
- Toxics Release Inventory: Listed substance subject to reporting requirements

Resource Conservation and Recovery Act
- Listed as a Hazardous Constituent of Waste

FDA

Action level for *N*-nitrosamines in rubber baby bottle nipples is 10 ppb

REFERENCES

Brunnemann, K. D., J. C. Scott and D. Hoffmann. 1982. *N*-Nitrosomorpholine and other volatile *N*-nitrosamines in snuff tobacco. Carcinogenesis 3(6): 693-6.

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

CHIP. 1978. Chemical Hazard Information Profile. *N*-Nitroso Compounds. Washington, D.C.: U.S. Environmental Protection Agency, Office of Pesticide Programs and Toxic Substances.

HEEP. 1980. Health and Environmental Effects Profile. Nitrosamines, No. 137. Washington, D.C.: U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response.

HSDB. 2001. Hazardous Substances Data Base. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

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

Lijinsky, W., R. M. Kovatch, C. W. Riggs and P. T. Walters. 1988. Dose-response study with *N*-nitrosomorpholine in drinking water of F-344 rats. Cancer Res 48(8): 2089-95.