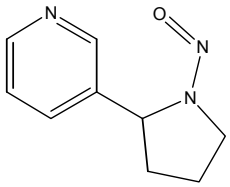
## *N*-NITROSONORNICOTINE
**CAS No. 16543-55-8**
First Listed in the *Second Annual Report on Carcinogens*




## CARCINOGENICITY

*N*-Nitrosonornicotine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1978, 1985, 1987). When administered in the drinking water, *N*-nitrosonornicotine induced esophageal carcinomas and papillomas and carcinomas of the nasal cavity in rats of both sexes, nasal cavity adenocarcinomas in female rats, and papillomas of the nasal cavity and trachea in hamsters of both sexes. When administered in the diet, *N*-nitrosonornicotine induced esthesioneuroepitheliomas and squamous cell carcinomas of the nasal cavity, and squamous cell carcinomas of the esophagus in male rats. When administered by subcutaneous injection, *N*-nitrosonornicotine induced olfactory neuroblastomas, rhabdomyosarcomas, esthesioneuroepitheliomas, squamous cell and anaplastic carcinomas, spindle cell sarcomas, and lung adenomas in rats of both sexes and tracheal papillomas in hamsters of both sexes. Intraperitoneal injection of *N*-nitrosonornicotine induced multiple pulmonary adenomas in mice of both sexes, lung adenomas in female mice, and nasal cavity tumors and tracheal papillomas in male hamsters (IARC 1985).

No adequate human studies of the relationship between exposure to *N*-nitrosonornicotine and human cancer have been reported (IARC 1978, 1985, 1987).

## PROPERTIES

*N*-Nitrosonornicotine is a yellow oily liquid that solidifies at cold temperatures. It is insoluble in water and soluble in ethanol and methylene chloride. *N*-Nitroso compounds are readily degraded in the presence of ultraviolet or visible light. When heated to decomposition, it emits toxic fumes of nitrogen oxides. *N*-Nitrosonornicotine can be reduced to the corresponding hydrazine with lithium aluminum hydride (HSDB 2001, NTP 2001).

## USE

The only use identified for *N*-nitrosonornicotine is as a research chemical (IARC 1985).

## PRODUCTION

*N*-Nitrosonornicotine is not produced commercially in the U.S. Chem Sources (2001) identified one U.S. supplier of *N*-nitrosonornicotine. *N*-Nitrosonornicotine may be synthesized

in small quantities primarily for use in research (HEEP 1980). No import or export data were available.

## EXPOSURE

*N*-Nitrosonornicotine has been found in a variety of tobacco products (chewing tobacco, snuff, cigarettes, and cigars), in mainstream and sidestream smoke from cigars and cigarettes, in saliva of chewers of betel quid with tobacco, and in saliva of oral-snuff users. Some of the *N*-nitrosonornicotine in saliva appears to be formed endogenously from nitrite in saliva and tobacco alkaloids. Thus, there is widespread exposure to *N*-nitrosonornicotine among users of tobacco products and those exposed to sidestream smoke. *N*-Nitrosonornicotine is reported to be produced by nitrosation of nicotine during the curing, ageing, processing, and smoking of tobacco. About half of the *N*-nitrosonornicotine originates in the unburnt tobacco, whereas the remainder is formed during burning. *N*-Nitrosonornicotine has been found in cigarettes at concentrations of 0.3 to 9 mg/kg, in snuff products at 12 to 29 mg/kg, in chewing tobacco at 3.5 to 90.6 mg/kg, and in cigarette smoke at 0.14 μg/cigarette (IARC 1978, 1985).

*N*-Nitrosamines are frequently produced during rubber processing and may be present as contaminants in the final rubber products. Potential exposure depends on the ability of the nitrosamines to migrate from the product and enter the body. Significant levels of *N*-nitroso compounds have been identified in a number of materials including pesticides, cosmetics, cutting fluids, and fire resistant hydraulic fluids. The *N*-nitroso compounds found in these products were apparently formed *in situ* during storage or handling as the result of a reaction between amines present in the mixture and inorganic nitrite, which may have been added as a corrosion inhibitor (CHIP 1978).

## REGULATIONS

EPA regulates *N*-nitrosonornicotine under the Resource Conservation and Recovery Act (RCRA) and Superfund Amendments and Reauthorization Act (SARA). *N*-Nitrosonornicotine is subject to reporting and record-keeping requirements under RCRA and SARA. EPA solicited comments on the designation of a reportable quantity (RQ) for *N*-nitrosonornicotine under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA).

OSHA regulates *N*-nitrosonornicotine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 135.

## REFERENCES

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

CHIP. Chemical Hazard Information Profile. *N*-Nitroso Compounds. Office of Pesticide Programs and Toxic Substances, U.S. EPA, Washington, DC, 1978.

HEEP. Health and Environmental Effects Profile. Nitrosamines, No. 137. Washington, DC: Office of Solid Waste and Emergency Response, U.S. EPA, 1980.

HSDB. Hazardous Substances Data Bank. Online database produced by the National Library of Medicine. *N*-Nitrosonornicotine. Profile last updated August 9, 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.

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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.

NTP. National Toxicology Program. NTP Chemical Repository. *N*-Nitrosonornicotine. Last updated August 13, 2001. (http://ntp-server.niehs.nih.gov and search 6543-55-8).