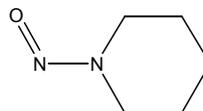


## **N-NITROSOPIPERIDINE**

**CAS No. 100-75-4**

First Listed in the *Second Annual Report on Carcinogens*



### **CARCINOGENICITY**

*N*-Nitrosopiperidine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1978, 1987). When administered in the diet, *N*-nitrosopiperidine induced squamous cell carcinomas of the forestomach, papillomas of the esophagus, hepatocellular adenomas and carcinomas, and liver hemangioendotheliomas in male mice. When administered in drinking water, *N*-nitrosopiperidine induced lung adenomas in mice of both sexes and esophageal carcinomas and hepatocellular carcinomas in rats. When administered orally, *N*-nitrosopiperidine induced hepatocellular carcinomas in monkeys. When administered by subcutaneous injection, the compound induced squamous cell carcinomas and other tumors of the nasal cavity and esophageal squamous cell carcinomas and papillomas in rats, and tumors of the nasal cavity, trachea, lung, tongue, palate, esophagus, forestomach, and liver in hamsters. When administered by intraperitoneal injection, *N*-nitrosopiperidine increased the incidence of adenomas of the lung in mice. When administered by intravenous injection, the compound induced carcinomas of the esophagus and pharynx in rats. When administered to pregnant hamsters, a low incidence of tumors of the upper respiratory tract was observed for the offspring and a high incidence of respiratory tract tumors was observed for the mothers (IARC 1978, 1987).

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

### **PROPERTIES**

*N*-Nitrosopiperidine is a yellow oil. It is soluble in water, organic solvents, lipids, and hydrochloric acid. It decomposes when exposed to light, and is especially sensitive to ultraviolet light. When heated to decomposition, it emits toxic fumes of nitrogen oxides. 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 hydrogen, but can be reduced by hydrogen bromide in acetic acid (IARC 1978, HSDB 2001, NTP 2001).

### **USE**

*N*-Nitrosopiperidine is used as a research chemical and in organic synthesis (HSDB 2001, NTP 2001).

## PRODUCTION

*N*-Nitrosopiperidine was first prepared in 1863 by the action of nitrogen dioxide on piperidine. Numerous patents have been issued for the production of *N*-nitrosopiperidine; however, there is no evidence that *N*-nitrosopiperidine has been manufactured on a commercial scale in the United States (IARC 1978). Synthetic production of nitrosamines is limited to small quantities, primarily as research chemicals (HEEP 1980). Chem Sources (2001) identified nine U.S. suppliers for *N*-nitrosopiperidine. No production, import, or export data were available.

## EXPOSURE

Due to the small quantities produced, potential exposure to *N*-nitrosopiperidine appears to be limited. According to the Toxic Chemical Release Inventory (TRI), environmental releases of *N*-nitrosopiperidine in 1999 were reported to be 14,756 lb. Three facilities reported releasing the chemical; however, approximately 99% of the total release were from one facility (TRI99 2001).

The general population may possibly be exposed to low concentrations of *N*-nitrosopiperidine from cigarette smoke and certain foods. Several researchers have reported trace amounts of *N*-nitrosopiperidine in cigarettes, but the chemical has not been found in all brands of cigarettes tested. Investigators have detected *N*-nitrosopiperidine concentrations as high as 64 µg/kg in meat and fish products such as bacon, bologna, wieners, and smoked cod; the presence of *N*-nitrosopiperidine in meat, cheese, and spices results from the use of sodium nitrite as a preservative (IARC 1978).

*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. The Consumer Product Safety Commission (CPSC) and the Food and Drug Administration (FDA) determined that the nitrosamines present in pacifiers and baby bottle nipples can migrate from the pacifier or nipple into saliva, which could result in ingestion of nitrosamines. 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*-nitrosopiperidine under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), and Superfund Amendments and Reauthorization Act (SARA). EPA has established a final RQ of 10 lb. *N*-Nitrosopiperidine is subject to reporting and record-keeping requirements under RCRA and SARA.

FDA regulates *N*-nitrosopiperidine under the Food, Drug, and Cosmetic Act (FD&CA), requiring separate packaging of spices and sodium nitrite in dry premixed cures. This action resulted in a dramatic decrease in the *N*-nitrosopiperidine content of dry mixes.

OSHA regulates *N*-nitrosopiperidine under the Hazard Communication Standard as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 136.

## REFERENCES

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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*-Nitrosopiperidine. 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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TRI99. Toxic Chemicals Release Inventory 1999. Data contained in the Toxic Chemical Release Inventory (TRI). Available from the U.S. Environmental Protection Agency Office of Environmental Information, <http://www.epa.gov/triexplorer/reports.htm>, 2001.