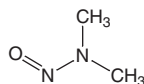


***N*-Nitrosodimethylamine**

CAS No. 62-75-9

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



Carcinogenicity

N-Nitrosodimethylamine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1978, 1982). When administered orally, *N*-nitrosodimethylamine induced liver hemangiosarcomas, hepatocellular carcinomas, and kidney and lung tumors in mice. When mice were exposed by inhalation, the compound induced tumors in the lung, liver, and kidney. When administered by intramuscular injection, the compound induced hemangiosarcomas of the liver and abdominal tissues and lung tumors in adult mice, and parenchymal cell and vascular tumors of the liver and lung adenomas in new born and suckling mice. When administered by intraperitoneal injection, the compound induced liver tumors in adult and newborn mice, and increased the incidence of lung and kidney tumors in mice. When administered orally, *N*-nitrosodimethylamine induced kidney and bile duct tumors in rats; when rats were exposed by inhalation, it induced tumors of the lung, liver, kidney, and nasal cavity. When administered by intramuscular injection, the compound induced kidney tumors in adult rats and kidney and liver tumors in newborn and suckling rats; it induced kidney and nasal cavity tumors in rats when administered by intraperitoneal injection. When administered orally, *N*-nitrosodimethylamine induced hepatocellular carcinomas and bile duct tumors in hamsters; when administered by intramuscular injection, it induced hemangiosarcomas in the liver and bile duct and nasal cavity tumors in hamsters. When administered orally, the compound induced hepatocellular carcinomas and bile duct tumors in rabbits and guinea pigs, liver hemangiosarcomas in ducks, and liver adenomas and adenocarcinomas in fish. When administered by intramuscular injection, the compound induced bile duct tumors in mastomys; when administered by intraperitoneal injection, it induced liver tumors in newts.

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

Properties

N-Nitrosodimethylamine is a volatile, yellow, oily liquid of low viscosity. It is soluble in water, alcohol, ether, other organic solvents, and lipids. The compound is sensitive to light, especially ultraviolet light, and undergoes relatively rapid photolytic degradation. *N*-Nitrosodimethylamine is combustible, and when heated to decomposition, it emits toxic fumes of nitrogen oxides. It is incompatible with strong oxidizers and strong bases (HSDB 2000).

Use

N-Nitrosodimethylamine is used primarily as a research chemical. Prior to April 1, 1976, the compound was used as an intermediate in the electrolytic production of 1,1-dimethylhydrazine, a storable liquid rocket fuel containing approximately 0.1% *N*-nitrosodimethylamine as an impurity. Other uses of *N*-nitrosodimethylamine include the control of nematodes, inhibition of nitrification in soil, plasticizer for rubber and acrylonitrile polymers, in active metal anode-electrolyte systems (high-energy batteries), in the preparation of thiocarbonyl

fluoride polymers, and as a solvent in the fiber and plastics industry, an antioxidant, a softener of copolymers, and an additive to lubricants (Sittig 1985, Merck 1983).

Production

Current production data were not available, and there was no evidence that *N*-nitrosodimethylamine is manufactured commercially in the United States (IARC 1978, HSDB 2000). Chem Sources (2001) reported that there were nine U.S. suppliers of *N*-nitrosodimethylamine in 2000. The 1979 TSCA Inventory reported four U.S. companies producing 1,000 lb in 1977 with some site limitations. No import or export data were reported (TSCA 1979). The last commercial producer of *N*-nitrosodimethylamine closed its plant in 1976. Commercial production began in the mid 1950s for use in the manufacture of 1,1-dimethylhydrazine (IARC 1978).

Exposure

The primary routes of potential human exposure to *N*-nitrosodimethylamine are ingestion, inhalation, and dermal contact. There is some potential for occupational exposure of laboratory, copolymer, lubricant, and pesticide workers. The National Occupational Exposure Survey (1981-1983) indicated that 747 workers, including 299 women, were potentially exposed to *N*-nitrosodimethylamine (NIOSH 1984). OSHA regulations concerning *N*-nitrosodimethylamine designate strict procedures to avoid worker contact. Mixtures containing $\geq 1.0\%$ *N*-nitrosodimethylamine must be maintained in isolated or closed systems, workers must observe special hygiene rules, and certain procedures must be followed for movement of the material and in case of accidental spills and emergencies. The general population may possibly be exposed to unknown quantities of *N*-nitrosodimethylamine present in foods and beverages, tobacco smoke, herbicides, pesticides, drinking water, and industrial pollution. Estimates indicate that air, diet, and smoking contribute to potential human exposure at levels of a few micrograms per day. *N*-Nitrosodimethylamine is present in a variety of foods including cheeses, soybean oil, canned fruit, various meat products, bacon, various cured meats, frankfurters, ham (cooked), fish and fish products, spices used for meat curing, apple brandy, other alcoholic beverages, and beer. Concentrations in these foodstuffs have been measured to be between 0 and 85 $\mu\text{g}/\text{kg}$. FDA and CPSC have determined that *N*-nitrosamines, such as *N*-nitrosodimethylamine, are frequently produced during rubber processing and may be present as contaminants in the final rubber product. Potential exposure depends on the ability of the nitrosamine to migrate from the product into the body. *N*-Nitrosodimethylamine has been detected in numerous drugs formulated with aminopyrine, including tablets, suppositories, injections, drops, and syrups, at concentrations ranging from <10 to 371 $\mu\text{g}/\text{kg}$. *N*-Nitrosodimethylamine has been detected in tobacco smoke at concentrations of 0 to 140 ng/cigarette. Mainstream smoke of nonfiltered cigarettes contained 13 to 65 ng/cigarette, and 5.7 to 43 ng/cigarette for filtered cigarettes. Sidestream smoke of nonfiltered cigarettes contained 680 to 823 ng/cigarette, and 1,040 to 1,770 ng/cigarette for filtered cigarettes. An analysis of smoke-filled rooms, such as bars, indicated concentrations of 90 to 240 ng/m^3 *N*-nitrosodimethylamine, and residences contained <5 ng/m^3 . Indoor air polluted with tobacco smoke has been shown to contain up to 0.24 ng/L *N*-nitrosodimethylamine (HEEP 1980).

N-Nitrosodimethylamine is widespread in the environment, but it is rapidly decomposed by sunlight, and thus does not usually persist in ambient air or water illuminated by sunlight (HEEP 1980). *N*-Nitrosodimethylamine was detected as an air pollutant in Baltimore, MD, and in Belle, WV. In Baltimore, the prime source was found to be a chemical plant that manufactured 1,1-dimethylhydrazine. The concentration of *N*-nitrosodimethylamine at the factory ranged from

6,000 to 36,000 ng/m³, 1,000 ng/m³ in adjacent residential neighborhoods, and approximately 100 ng/m³ two miles away in downtown Baltimore. This plant was closed in April 1976. In Belle, the source of the *N*-nitrosodimethylamine was found to be a chemical factory manufacturing and using dimethylamine; the *N*-nitrosodimethylamine was being produced as an unwanted by-product. Concentrations in downtown Belle and Charleston, WV ranged from 1 to 40 ng/m³. Similar concentrations of *N*-nitrosodimethylamine have been detected at chemical factories making and/or using dimethylamine, including plants in New York City, Boston, and New Jersey. *N*-Nitrosodimethylamine has been detected in sea water adjacent to the Baltimore factory at concentrations of 0.08 to 0.25 µg/L and in an adjacent sewage treatment facility at 3 µg/L. Industrial wastewater from chemical factories was found to contain 0.2 to 5 µg/L (IARC 1978). *N*-Nitrosodimethylamine has been detected in deionized water at concentrations of 0.012 to 0.34 µg/L, in high-nitrate well water at <0.01 µg/L, and in chlorinated drinking water at 0.02 to 0.82 µg/L. Soil samples taken from locations near industrial plants contained 0 to 15.1 ng/g *N*-nitrosodimethylamine. Dimethylamine-formulated pesticides and herbicides were found to contain 190 to 640 mg/L (IARC 1978). Additional exposure information may be found in the ATSDR Toxicological Profile for *N*-Nitrosodimethylamine (ATSDR 1989).

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 = 0.00069 µg/L; based on fish/shellfish consumption only = 3.0 µg/L

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable Quantity (RQ) = 10 lb

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements

Reportable Quantity (RQ) = 10 lb

Threshold Planning Quantity (TPQ) = 1,000 lb

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - P082

Listed as a Hazardous Constituent of Waste

FDA

Action levels for *N*-nitrosodimethylamine in barley malt and malt beverages range from 5-10 ppb

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

OSHA

Potential occupational carcinogen: Engineering controls, work practices, and personal protective equipment required

Guidelines

ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = as low as possible

NIOSH

Listed as a potential occupational carcinogen

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