

Safety Data Sheet

N-Nitroso- dimethylamine

Division of Safety
National Institutes
of Health



WARNING!

THIS COMPOUND IS TOXIC, CARCINOGENIC, AND MUTAGENIC. IT IS READILY ABSORBED BY VARIOUS BODY TISSUES. AVOID FORMATION AND BREATHING OF AEROSOLS OR VAPORS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND COLD WATER. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, INDUCE VOMITING. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. WASH DOWN AREA. SEE CASTEGNARO ET AL. (1982) FOR DETAILS. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY. MONITOR LABORATORY AIR AND CHECK FOR NITROSAMINE RESIDUES AFTER CLEANUP.

A. Background

N-Nitrosodimethylamine (DMN) is toxic, carcinogenic, and mutagenic in experimental test systems. Its primary use is for tumor induction in experimental animals and for related research. Use of this compound for other purposes, such as organic synthesis, should be avoided. The volatility of this compound requires use of special precautions and containment procedures to prevent its release into the laboratory and general environment.

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14. Flammable limits: No data.

Fire, Explosion, and Reactivity Hazard Data

1. Use dry chemical fire extinguisher, water, or soda-acid. Fire-fighting personnel should wear air-supplied respirators with full-face masks.
2. The explosive range of the vapors is unknown.
3. Decomposed by strong acids, liberating nitrous acid.
4. Absorbed by many elastomers. May cause deterioration of these materials.
5. Volatilization during combustion produces hazardous vapors. Combustion products contain nitrogen oxides.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving DMN.

DMN and solutions of DMN penetrate various glove materials (Walker et al., 1978). This factor should be taken into account when handling DMN.

1. Chemical inactivation: Validated methods have been reported (Castegnaro et al., 1982).
2. Decontamination: Turn off equipment that could be affected by DMN or the materials used for cleanup. If more than 10 ml has been spilled or if there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Consult Castegnaro et al. (1982) for details concerning decontamination of surfaces, glassware, and animal cages.
3. Disposal: It may be possible to decontaminate waste streams containing DMN before disposal. For details, see Castegnaro et al. (1982). No waste streams containing DMN shall be disposed of in sinks or general refuse. Surplus DMN or chemical waste streams contaminated with DMN shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing DMN shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing

DMN shall be packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with DMN shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing DMN shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store in sealed ampoules or in bottles with caps with polyethylene cone liners inside a sealed secondary container. This should be kept in a solvent storage cabinet, deep freeze, or explosion-safe refrigerator. Avoid exposure to light and moisture.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

1. Sampling: Air samples may be collected using cold traps, impingers (Fine et al., 1977), or solid adsorbents (Issenberg and Sornson, 1976; Pellizzari et al., 1976).
2. Separation and analysis: After extraction and concentration, volatile nitrosamines may be determined by GC using a thermal energy analyzer (TEA) detector or a nitrogen-specific detector, such as the thermionic nitrogen detector or Hall electrolytic conductivity detector, or by GC-MS. Electron capture detection of nitramine derivatives (Telling, 1972) or of heptafluorobutyrate derivatives of amines formed by cleavage of nitrosamines with hydrogen bromide in glacial acetic acid (Eisenbrand, 1972) may be appropriate for laboratories not equipped with more selective detectors. GC-TEA and GC-MS are the preferred methods. No acceptable direct field measurement methods are available.

Biological Effects (Animal and Human)

1. Absorption: DMN is rapidly absorbed by ingestion, inhalation, and parenteral injection. Data on skin absorption are not available; however, absorption by this route is likely in analogy with skin absorption of other volatile nitrosamines (e.g., diethylnitrosamine). No human data.
2. Distribution: DMN is rapidly distributed throughout the body water after administration by all routes.
3. Metabolism and excretion: DMN requires metabolic activation to exert its toxic and carcinogenic effects. Activation involves oxidative demethylation; the resulting monomethylnitrosamine spontaneously and rapidly decomposes to a reactive carbonium ion that alkylates proteins and nucleic acids. Expired air and urine of rats given DMN contain significant quantities of unchanged DMN, but most of the DMN administered is degraded to carbon dioxide.

water, and presumably nitrogen (Phillips et al., 1975).

4. Toxic effects: The acute LD50 of DMN is in the range of 15-40 mg/kg in rodents (mouse, rat, hamster) by the oral or parenteral route. Inhalation toxicity (LC50, 4-hour exposure) in the rat and mouse is 236 and 57 mg/m³, respectively, resulting in necrosis, with the liver as the main target organ. This is also shown in accidental DMN poisoning in man: liver cirrhosis, in some cases followed by death, has been reported (Barnes and Magee, 1954; Freund, 1937).
5. Carcinogenic effects: Oral and parenteral administration of DMN to rodents results in a variety of tumors, mainly in the liver, kidney, and lungs, with metastases; organ specificity varies with species and route of administration. Inhaled DMN in the rat produces almost exclusively carcinomas of the nasal cavity epithelium. DMN administered to pregnant rats in the later stages of gestation produces pulmonary adenomas and hepatomas in the offspring.
6. Mutagenic and teratogenic effects: DMN is mutagenic in Neurospora after activation by a hydroxylating system and in mammalian cell cultures. Teratogenic effects have been reported in the offspring of mice after treatment of pregnant dams with DMN.

G. Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes.
2. Ingestion: Drink plenty of water. Induce vomiting.
3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.
4. Refer to physician.

H. References

- Barnes, J.M., and P.N. Magee. 1954. Some toxic properties of dimethylnitrosamine. Br J Ind Med 11:167-174.
- Castegnaro, M., G. Eisenbrand, G. Ellen, L. Keefer, D. Klein, E.B. Sansone, D. Spincer, G. Telling, K. Webb, eds. 1982. Laboratory Decontamination and Destruction of Carcinogens in Laboratory Wastes: Some N-Nitrosamines, IARC Scientific Publications No. 43. World Health Organization, Geneva, Switzerland.
- Eisenbrand, G. 1972. Determination of volatile nitrosamines at low levels in food by acid catalyzed denitrosation and formation of derivatives from the resulting amines. Pages 64-70 in N-Nitroso

- Compounds Analysis and Formation, IARC Scientific Publications No. 3. World Health Organization, Geneva, Switzerland.
- Fine, D.H., D.P. Rounbehler, E. Sawicki, and K. Krost. 1977. Determination of dimethylnitrosamine in air and water by thermal energy analysis: Validation of analytical procedures. *Environ Sci Technol* 11:577-580.
- Freund, H.A. 1937. Clinical manifestation and studies in parenchymatous hepatitis. *Ann Intern Med* 10:1144-1155.
- Issenberg, P., and H. Sornson. 1976. A monitoring method for volatile nitrosamine levels in laboratory atmospheres. Pages 97-108 in *Environmental N-Nitroso Compounds Analysis and Formation*, IARC Scientific Publications No. 14. World Health Organization, Geneva Switzerland.
- Magee, P.N., R. Montesano, and R. Preussmann. 1976. N-Nitroso compounds and related carcinogens. Pages 491-625 in C. Searle, ed. *Chemical Carcinogens*, A.C.S. Monograph 173. American Chemical Society, Washington, DC.
- Mirvish, S.S., P. Issenberg, and H.C. Sornson. 1976. Air-water and ether-water distribution of N-nitroso compounds: Implications for laboratory safety, analytic methodology, and carcinogenicity for the rat esophagus, nose, and liver. *J Natl Cancer Inst* 56: 1125-1129.
- Pellizzari, E.D., J.E. Bunch, R.E. Berkley, and J. McRae. 1976. Collection and analysis of trace organic vapor pollutants in ambient atmospheres: The performance of a Tenax GC cartridge sampler for hazardous vapors. *Analyt Letters* 9:45-63.
- Pensabene, J.E., W. Fiddler, C.J. Dooley, R.C. Doerr, and A.E. Wasserman. 1972. Spectral and gas chromatographic characteristics of some N-nitrosamines. *J Agric Food Chem* 20:274.
- Phillips, J.C., B.G. Lake, C.E. Heading, S.D. Gangolli, and A.G. Lloyd. 1975. Studies on the metabolism of dimethylnitrosamine in the rat. I. Effect of dose, route of administration and sex. *Food Cosmet Toxicol* 13:203-209.
- Rainey, W.T., W.H. Christie, and W. Lijinsky. 1978. Mass spectrometry of N-nitrosamines. *Biomed Mass Spectrom* 5:395-408.
- Telling, G.M. 1972. A gas-liquid chromatographic procedure for the detection of volatile N-nitrosamines at the ten parts per billion level in foodstuffs after conversion to their corresponding nitramines. *J Chromatogr* 73:79-87.
- Walker, E.A., M. Castegnaro, L. Garren, and B. Pignatelli. 1978. Limitations to the protective effect of rubber gloves for handling nitrosamines. Pages 535-543 in *Environmental Aspects of N-Nitroso Compounds*, IARC Scientific Publications No. 19. World Health Organization, Geneva, Switzerland.