

Sources of Exposure

Toxicokinetics and Biomonitoring

Biomarkers/Environmental Levels

General Populations

- For most people, the largest source of exposure to NDMA is from it being made naturally in your body from precursors that normally exist in the body and in foods.
- The general population may also be exposed to trace amounts of NDMA through ingesting foods containing nitrosamines such as cured or smoked meats and fish; ingesting foods containing alkylamines, which can form NDMA in the stomach; ingesting drinking water or malt beverages containing NDMA; and inhaling tobacco smoke.
- NDMA has been detected in some prescription and over-the-counter pharmaceutical products (many of these drugs have been recalled).
- Exposure to small amounts of NDMA in water can arise from drinking or through inhalation and dermal contact when showering, bathing, or swimming in water treated with chlorine or chloramines for disinfection.

Occupational Populations

- Occupational exposure to NDMA may occur in people who work in leather tanneries, rubber and tire industries, dye manufacturers, soap, detergent and surfactant industries, foundries, fish-processing industries, pesticide manufacturers, and warehouse and sales rooms (especially for rubber products), and research laboratories where NDMA is synthesized or studied.

Toxicokinetics

- Available data on toxicokinetics of NDMA come mostly from animal studies.
- NDMA is absorbed rapidly following oral exposure, primarily in the small intestine. Oral bioavailability varies widely across species (10% in rats to 90% in beagles).
- Absorption of inhaled NDMA is inferred from human fatalities after inhalation and limited animal data.
- Unmetabolized NDMA passes freely between blood and tissues, with little to no accumulation in any given tissue. NDMA can also cross the placenta.
- Clearance of NDMA from blood is primarily via metabolism. NDMA is metabolized by microsomal membrane-bound CYP2E1 to hydroxymethyl-nitrosamine.
- Very little unchanged NDMA is excreted in urine after oral exposure. Methylamine is the primary urinary metabolite in rats exposed to NDMA orally.

NHANES Biomonitoring

- There are no data regarding levels of NDMA in the general population.

Biomarkers

- Urinary NDMA can be measured and used as a biomarker of exposure. Urinary metabolites of NDMA may not be specific for NDMA.

Environmental Levels

Air

- There are no recent monitoring data for air levels of NDMA in the United States.

Water

- In U.S. public water systems, the median and mean NDMA concentrations were 0.0041 and 0.008 µg/L, respectively. Samples of water from 23 indoor pools in the United States showed NDMA concentrations from 0.002 to 0.083 µg/L. NDMA has been detected in effluents from wastewater plants.

Sediment and Soil

- There are no monitoring data for levels of NDMA in the sediment or soil in the United States.

Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2021. Toxicological Profile for N-Nitroso-dimethylamine (NDMA) (Draft for Public Comment). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Services.

ToxGuide™ for N-Nitroso- dimethylamine (NDMA)



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U.S. Department of Health and
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www.atsdr.cdc.gov



Chemical and Physical Information

Routes of Exposure

Relevance to Public Health (Health Effects)

NDMA

- N-Nitrosodimethylamine (NDMA) is a volatile nitrosamine that occurs widely in the environment due to its ready formation from commonly found precursors.
- At room temperature, NDMA is a yellow liquid with no distinct odor.
- NDMA was used to make rocket fuel, but this use was stopped after unusually high levels of this chemical were found in the environment near a rocket fuel manufacturing plant.
- NDMA is no longer used in the United States except for research purposes; however, it is readily formed when alkylamines come in contact and react with nitrogen oxides, nitrous acid, or nitrite salts, or when trans-nitrosation via nitro or nitroso compounds occurs. Thus, potential exists for release into the environment from industries.
- NDMA commonly occurs at low levels as a byproduct of disinfection in water treatment plants during the chlorination or chlorination of drinking water and wastewater.
- NDMA and other nitrosamines also occur unintentionally in certain foods, beverages, herbicides, and pharmaceutical products.

- Inhalation – Likely route of exposure for the general and occupational populations.
- Oral – Likely route of exposure for the general population through ingestion of certain foods and contaminated water.
- Dermal – Likely route of exposure for occupational population and general population via bathing or swimming in contaminated water.

NDMA in the Environment

- In the air, NDMA is expected to exist in the vapor phase and not partition to particulates in the atmosphere.
- NDMA degrades rapidly by direct photolysis (half-life of about 5–30 minutes). In the absence of sunlight, NDMA will likely undergo biodegradation.
- In water, NDMA is not expected to volatilize, and adsorption to solids and sediments is thought to be low.
- NDMA is expected to have high mobility in soil and has the potential to leach into groundwater supplies.
- NDMA is not likely to bioconcentrate in aquatic organisms

Health effects are determined by the dose (how much), the duration (how long), and the route of exposure.

Minimal Risk Levels (MRLs)

Inhalation

- No acute-(≤ 14 days), intermediate-(15–364 days), or chronic-(≥ 365 days) duration inhalation MRLs were derived for NDMA.

Oral

- A provisional acute-duration (≤ 14 days) oral MRL of 0.00001 mg/kg/day was derived for NDMA.
- No intermediate- (15–364 days) or chronic- (≥ 365 days) duration oral MRLs were derived for NDMA.

Health Effects

- Liver effects of NDMA have been seen in humans after poisoning incidents.
- Animals exposed orally to NDMA (both acutely and chronically) developed severe liver injury (hemorrhagic necrosis, fibrosis, and/or cirrhosis).
- Oral exposure may lead to increased fetal or neonatal mortality in animals (limited data).
- Oral exposure to NDMA primarily induces liver and lung tumors in animals but has also induced kidney tumors (rats and mice) and testicular tumors (rats).
- Occupational exposure by inhalation was associated with higher risks of gastric, liver, bladder, and prostate cancers, and also with increased risks of leukemia and multiple myeloma. Epidemiological studies have reported associations between NDMA exposure in the diet and gastric and colorectal cancers.
- The U.S. Department of Health and Human Services (HHS) has classified NDMA as reasonably anticipated to be a human carcinogen. The U.S. Environmental Protection Agency (EPA) has categorized NDMA a probable human carcinogen (Group 2B) and the International Agency for Research on Cancer (IARC) has classified NDMA as probably carcinogenic to humans (Group 2A).

Children's Health

- It is not known if children are more sensitive to NDMA exposure than adults.