United States Environmental Protection Agency

Technical Fact Sheet – N-Nitroso-dimethylamine (NDMA)

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At a Glance

- Yellow liquid with faint characteristic or no distinct odor.
- Formerly used in the production of rocket fuel, antioxidants and softeners for copolymers. Currently used only for research purposes.
- Unintended byproduct of chlorination of wastewater at wastewater treatment plants that use chloramines for disinfection, raising significant concern as a drinking water contaminant.
- Highly mobile in soil, with potential to leach into groundwater.
- Oral route is the primary human exposure pathway.
- Classified as a B2 (probable human) carcinogen.
- Listed as a priority pollutant by the EPA, but no federal standard has been established for drinking water.
- Detection methods include solid phase extraction, gas chromatography and liquid chromatography.
- Most common treatment method is via photolysis by ultraviolet radiation ranging in wavelength from 225 to 250 nanometers. Potential for aerobic and anaerobic biodegradation also exists.

Introduction

This fact sheet, developed by the U.S. Environmental Protection Agency (EPA) Federal Facilities Restoration and Reuse Office (FFRRO), provides a summary of the contaminant N-Nitrosodimethylamine (NDMA), including physical and chemical properties; environmental and health impacts; existing federal and state guidelines; detection and treatment methods; and additional sources of information. This fact sheet is intended for use by site managers and other field personnel who may address NDMA contamination at cleanup sites or in drinking water supplies.

NDMA is a drinking water contaminant of concern because of its miscibility with water, as well as its carcinogenicity and toxicity.

What is NDMA?

- NDMA is a semivolatile organic chemical that forms in both industrial and natural processes. It is member of N-ni- trosamines, a family of potent carcinogens (Cal/EPA 2006; Mitch and others 2003).
- Synonyms include dimethylnitrosamine (DMNA), nitrosodimethylamine, N-methyl-N-nitrosomethanamine and N,N-dimethylnitrosamine (EPA IRIS 1993).
- NDMA is not currently produced in pure form or commercially used in the United States, except for research purposes. It was formerly used in production of liquid rocket fuel, antioxidants, additives for lubricants and softeners for copolymers (ATSDR 1989; HSDB 2012).
- NDMA can be unintentionally produced in and released from industrial sources through chemical reactions, such as those that involve alkylamines with nitrogen oxides, nitrous acid or nitrite salts. Potential industrial sources include byproducts from tanneries, pesticide manufacturing plants, rubber and tire manufacturers, alkylamine manufacture and use sites, fish processing facilities, foundries and dye manufacturers (ATSDR 1989).
- NDMA is also an unintended byproduct of the chlorination of wastewater and drinking water at treatment plants that use chloramines for disinfection (Bradley and others 2005; Mitch and others 2003).

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Exhibit 1: Physical and Chemical Properties of NDMA
(ATSDR 1989; Cal/EPA 2006; HSDB 2012; NIOSH 2010)

Property	Value/Description
Chemical Abstract Systems (CAS) Number	62-75-9
Physical Description (physical state at room temperature)	Yellow liquid with no distinct odor (ATSDR 1989; Cal/EPA 2006) Yellow liquid with faint, characteristic odor (NIOSH 2010; HSDB 2012).
Molecular weight (g/mol)	74.08
Water solubility at 25°C	Miscible
Melting point (°C)	-25 (estimated)
Boiling point (°C)	152 (HSDB 2012) 154 (ATSDR 1989; Cal/EPA 2006)
Specific gravity/Density at 20/4 °C (g/mL)	1.0059 (ATSDR 2012; Cal/EPA 2006) 1.0048 (HSDB 2012)
Vapor pressure at 20°C (mm Hg)	2.7
Organic carbon partition coefficient (log K_{oc})	1.07 (estimated)
Octanol-water partition coefficient (log K_{ow})	-0.57
Henry's Law Constant at 20°C (atm - m^3/mol)	2.63×10^{-7} (ATSDR 1989) 1.08×10^{-6} (HSDB 2012)

Abbreviations: g/mol – grams per mole; °C – degrees Celsius; g/mL – grams per milliliter; mm Hg – millimeters of mercury; atm - m^3/mol – atmosphere-cubic meters per mole.

What are the environmental impacts of NDMA?

- NDMA contamination may be found in air, soil and water (ATSDR 1999).
- When released to the air, NDMA is expected to exist solely as vapor in the ambient atmosphere and is broken down quickly by direct photolysis in sunlight. The estimated half-life of NDMA vapor in the ambient atmosphere with direct photolysis is about 5 to 30 minutes (ATSDR 1989).
- When released to soil, NDMA can be highly mobile and has the potential to leach into groundwater (HSDB 2012; Swarm and others 1983).
- In water, NDMA is completely miscible and is not expected to sorb onto solid particles or sediment. As a result of exposure to sunlight or by natural biological processes, NDMA may break down in water. The estimated half-life for direct photolysis of NDMA in water is about 16 minutes. The rate of biodegradation in the natural environment has been observed to be highly variable (ATSDR 1999; HSDB 2012; Plumlee and Reinhard 2007).
- At rocket engine testing facilities in California, NDMA has been found at high concentrations in groundwater on site (up to 400,000 nanograms per liter [ng/L]) and also in downgradient drinking water wells (up to 20,000 ng/L) (Mitch and others 2003; EPA 2001b).
- In a 2002 survey conducted by the California Department of Health Services (CDHS), elevated concentrations of NDMA were detected in locations where wastewater treatment plant effluent was used for aquifer recharge and near facilities that use unsymmetrical dimethylhydrazine (UDMH)-based rocket fuel (CDHS 2002; Mitch and others 2003).
- As of March 2011, NDMA had been detected in 1,787 samples out of 17,900 samples obtained from public water systems, which were monitored as part of the unregulated contaminant monitoring rule (UCMR). The EPA uses the UCMR to monitor contaminants that are suspected to be present in drinking water but that do not currently have health-based standards under the Safe Drinking Water Act (EPA 2011a).

What are the routes of exposure and health effects of NDMA?

- NDMA exposure may occur through (1) ingesting food that contains nitrosamines, such as smoked or cured meats and fish; (2) ingesting food that contains alkylamines, which can cause NDMA to form in the stomach; (3) drinking contaminated water; (4) drinking malt beverages (such as beer and whiskey) that may contain low levels of nitrosamines formed during processing; (5) using toiletry and cosmetic products such as shampoos and cleansers that contain NDMA; and (6) breathing or inhaling cigarette smoke. Workplace exposure can occur at tanneries, pesticide manufacturing plants and rubber and tire plants (ATSDR 1989, 1999).
- The oral route, including consumption of contaminated food and water, is the primary human exposure pathway for NDMA (ATSDR 1989; Cal/EPA 2006).
- Exposure to high levels of NDMA may cause liver damage in humans (ATSDR 1999; HSDB 2012).
- Potential symptoms of overexposure include headache, fever, nausea, jaundice, vomiting, abdominal cramps, enlarged liver, reduced function of liver, kidneys and lungs and dizziness (HSDB 2012; O'Neil 2006).
- In animal studies of various species including rats and mice, exposure to NDMA has caused tumors primarily of the liver, respiratory tract, kidney and blood vessels (DHHS 2011; IARC 1998).
- NDMA is classified as a B2 (probable human) carcinogen based on the induction of tumors in both rodents and nonrodent mammals exposed to NDMA by various routes (EPA IRIS 1993).
- The U.S. Department of Health and Human Services states that NDMA is reasonably anticipated to be a human carcinogen (DHHS 2011).
- The American Conference of Governmental Industrial Hygienists (ACGIH) has classified NDMA as a Group A3 confirmed animal carcinogen with unknown relevance to humans (ACGIH 2012).

Are there any federal and state guidelines and health standards for NDMA?

- EPA and State Standards and Guidelines:
  - Although NDMA is listed as a priority toxic pollutant in the Code of Federal Regulations (CFR) (40 CFR 131.36), no federal maximum contaminant level (MCL) has been established for drinking water. An MCL is not necessary to establish cleanup levels (EPA 2011b, 2013).
  - The EPA has not derived a chronic oral reference dose (RfD) or a chronic inhalation reference concentration (RfC) for NDMA (EPA IRIS 1993).
  - EPA has assigned an oral slope factor for carcinogenic risk of 51 milligrams per kilogram per day (mg/kg/day) and a drinking water unit risk of 1.4×10^{-3} micrograms per liter (µg/L) (EPA IRIS 1993).
  - EPA risk assessments indicate that the drinking water concentration representing a 1×10^{-6} cancer risk level for NDMA is 0.7 ng/L (EPA IRIS 1993).
  - EPA included NDMA on the third Contaminant Candidate List (CCL3), which is a list of unregulated contaminants that are known to or anticipated to occur in public water systems and may require regulation under the Safe Drinking Water Act (EPA 2009; EPA 2011a).
  - In addition, EPA added NDMA to its UCMR 2, requiring many large water utilities to monitor for NDMA (EPA 2012a).
  - EPA established a preliminary remediation goal of 1.3 ng/L for NDMA in groundwater at the Aerojet General Corporation Superfund Site in Sacramento, California, based on a 1 in 10^{-6} lifetime excess cancer risk in drinking water (EPA 2001b).
  - For tap water, EPA calculated a screening level of 0.42 ng/L for NDMA, based on a 1 in 10^{-6} lifetime excess cancer risk (EPA 2013).[1],[2]

[1] Tap water screening levels differ from the Integrated Risk Information System (IRIS) drinking water concentrations because the tap water screening levels account for dermal, inhalation and ingestion exposure routes; age-adjust the intake rates for children and adults based on body weight; and time-adjust for exposure duration or days per year. The IRIS drinking water concentrations consider only the ingestion route, account only for adult-intake rates and do not time-adjust for exposure duration or days per year.

[2] Screening Levels are developed using risk assessment guidance from the EPA Superfund program. These risk-based concentrations are derived from standardized equations combining exposure information assumptions with EPA toxicity data. These calculated screening levels are generic and not enforceable cleanup standards but provide a useful gauge of relative toxicity.

Are there any federal and state guidelines and health standards for NDMA? (continued)

- EPA and State Standards and Guidelines(continued):
  - EPA has also calculated a residential soil screening level (SSL) of 2.3 x 10^{-3} milligrams per kilogram (mg/kg) and an industrial SSL of 3.4 x 10^{-2} mg/kg for NDMA. The soil-to-groundwater SSL is 1.0 x 10^{-7} mg/kg (EPA 2013).
  - EPA has calculated a residential air screening level of 6.9 x 10^{-5} micrograms per cubic meter (µg/m^3) and an industrial air screening level of 8.8 x 10^{-4} µg/m^3 (EPA 2013).
  - EPA requires that spills or accidental releases of 10 pounds or more of NDMA be reported to the EPA (EPA 2001a).
  - California has established a public health goal of 3 ng/L in drinking water, based on a 1 in 10^{-6} lifetime excess cancer risk. In addition, California has established a notification level of 0.01 µg/L, which is a health-based advisory level for chemicals in drinking water that lack a MCL (Cal/EPA 2006, CDPH 2010).
  - Massachusetts has established a regulatory limit of 1 x 10^{-5} milligrams per liter (mg/L) in drinking water (Mass DEP 2004).
- Workplace Exposure Limits:
  - Although no permissible exposure limits or other occupational exposure limits have been established by the Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH) or ACGIH, NDMA is regulated along with 13 other chemicals as a "potential occupational carcinogen" (NIOSH 2010; OSHA 2006).
  - OSHA regulations promulgated in 29 CFR)1910.1003, 29 CFR 1910.1016 and 29 CFR 1910.1116 require the use of engineering controls, works practices and personal protective equipment to control the exposure of workers to NDMA (OSHA 2006).
  - ACGIH states that exposure by all routes to NDMA should be reduced to the lowest possible levels (ACGIH 2012; DHHS 2011).

What detection and site characterization methods are available for NDMA?

- For drinking water, EPA Method 521 uses solid phase extraction (SPE) and capillary column gas chromatography (GC) with large-volume injection and chemical ionization tandem mass spectroscopy (MS) (EPA 2004).
- For wastewater, EPA Method 607 uses methylene chloride extraction, GC and a nitrogen-phosphorus detector (NPD) (EPA 2007a; EPA 2012b).
- For wastewater, EPA Method 1625 uses isotope dilution, GC and MS (EPA 2007a; EPA 2012b).
- For groundwater, wastewater, soil, sediment and sludges, EPA SW-846 Method 8070 uses methylene chloride extraction, GC and a NPD (EPA 1996).
- For solid waste matrices, soil, air sampling media and water samples, EPA SW-846 Method 8270 uses GC and MS (EPA 2007b).
- An analytical method has also been developed specifically to quantify NDMA precursors such as alkylamines in waste or wastewater (Mitch, Gerecke and Sedlak 2003).
- A method using liquid chromatography tandem MS (LC/MS/MS) detects both thermally stable and unstable nitrosamines in drinking water (Zhao and others 2006).
- A study developed a method that is a combination of SPE and LC/MS/MS for determination of NDMA in surface water, groundwater and wastewater samples. The quantification limit identified was 2 ng/L (Topuz and others 2012).
- Modifications to GC-MS and GC-NPD methods including sample evapoconcentration and low concentration instrument calibration can be used to detect NDMA in soil to levels below 1 microgram per kilogram (µg/kg) (USACE 2009).

What technologies are being used to treat NDMA?

- The most common method to treat NDMA in drinking water systems is photolysis by ultraviolet radiation in the wavelength range of 225 to 250 nanometers (nm). This treatment cleaves the N–N bond, yielding nitrite and small quantities of dimethylamine (Mitch and others 2003).
- Biological treatment, microfiltration and reverse osmosis treatment may be used to remove NDMA precursors from wastewater before chlorination (Mitch and others 2003).The Department of Defense's Strategic Environmental Research and Development Program (SERDP) is investigating abiotic, biotic and coupled abiotic/biotic processes to accelerate NDMA degradation in the subsurface (DoD SERDP 2008, 2009, 2012).
- Laboratory-scale studies have shown that aerobic and anaerobic biodegradation of NDMA to low ng/L concentrations in water and soil may be possible (Bradley and others 2005; DoD SERDP 2008).
- Recent laboratory-scale studies indicate that the use of a fluidized bed reactor may be an effective technology for treatment of NDMA-contaminated groundwater (Webster and others 2013).
- Laboratory-scale study results suggest that in situ coupled abiotic/biotic processes may efficiently degrade NDMA in groundwater (McKinley and others 2005; DoD SERDP 2009).
- An SERDP project was conducted to identify the organisms, enzymes and biochemical pathways involved in the aerobic biodegradation of NDMA. Laboratory-scale study results highlighted the importance of monooxygenases in the degradation of NDMA (DoD SERDP 2012).

Where can I find more information about NDMA?

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Where can I find more information about NDMA? (continued)

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- Occupational Safety and Health Administration (OSHA). 2006. Chemical Sampling Information – N-Nitrosodimethylamine. www.osha.gov/dts/chemicalsampling/data/CH_258000.html.
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Where can I find more information about NDMA? (continued)

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