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Environmental Protection
Agency

Six-Year Review 3 Technical Support Document for Nitrosamines

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Abbreviations

ADAF	Age Dependent Adjustment Factors
AOP	Advanced Oxidation Process
BD	Berlin-Druckrey
CAS	Chemical Abstracts Service
CCL 3	Third Contaminant Candidate List
CI-MS/MS	Chemical ionization tandem mass spectrometry
CSF	Cancer Slope Factor
CT	Concentration × Time
CWS	Community Water System
CWSS	Community Water Systems Survey
CYP	Cytochrome P450
DBA	Dibutylamine
DBP	Disinfection By-Products
D/DBPR	Disinfectants and Disinfection By-Products Rule
DEA	Diethylamine
DL	Detection Limit
DMA	Dimethylamine
DMAP	4-dimethylaminoantipyrine
DMBzA	Dimethylbenzylamine
DMiPA	Dimethylisopropylamine
DNA	Deoxyribonucleic Acid
DO	Dissolved Oxygen
DOC	Dissolved Organic Carbon
DOM	Dissolved Organic Matter
DON	Dissolved Organic Nitrogen
DPA	Dipropylamine
EP	Entry Point (to the distribution system)
EPA	U.S. Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
FP	Formation Potential
GAC	Granular Activated Carbon
GC	Gas Chromatography
GWR	Ground Water Rule
GWUDI	Ground Water Under the Direct Influence of Surface Water
HAA	Haloacetic Acid
HPLC	High Performance Liquid Chromatography
HRL	Health Reference Level
HSDB	Hazardous Substances Data Bank
IARC	International Agency for Research on Cancer
LAA	Locational Annual Average
LCMRL	Lowest Concentration Minimum Reporting Level
MDBP	Microbial and Disinfection Byproduct
MDL	Method Detection Limit
MEA	Methylethylamine
MF	Microfiltration

MIEX	Magnetic Ion Exchange Resin
MOA	Mode of Action
MR	Maximum Residence (location in the distribution system)
MRL	Minimum Reporting Limit
MSR	Method Sensitivity Ratio
NDBA	*N*-Nitroso-di-n-butylamine
NDEA	*N*-Nitrosodiethylamine
NDMA	*N*-Nitrosodimethylamine
NDPA	*N*-Nitrosodipropylamine
NDPhA	*N*-Nitrosodiphenylamine
NF	Nanofiltration
NMEA	*N*-Nitrosomethylethylamine
NMOR	*N*-Nitrosomorpholine
NO	Nitric Oxide
NOM	Natural Organic Matter
NPA	n-Propylamine
NPDWR	National Primary Drinking Water Regulation
NPIP	*N*-Nitrosopiperidine
NPYR	*N*-Nitrosopyrrolidine
NTNCWS	Non-Transient Non-Community Water System
PAC	Powdered Activated Carbon
PBT	Persistence, Bioaccumulation and Toxicity
PWS	Public Water System
PYR	Pyrrolidine
RO	Reverse Osmosis
RSD	Relative Standard Deviation
SDWIS	Safe Drinking Water Information System
SM	Standard Methods
SPE	Solid Phase Extraction
SUVA	Specific Ultraviolet Absorbance
SYR	Six-Year Review
SYR3	Third Six-Year Review
THM	Trihalomethane
TMA	Trimethylamine
TOC	Total Organic Carbon
TONO	Total N-nitrosamines
TRI	Toxics Release Inventory
UCMR 2	Second Unregulated Contaminant Monitoring Regulation
UDMH	Unsymmetrical Dimethylhydrazine
UF	Ultrafiltration
USEPA	U.S. Environmental Protection Agency
UV	Ultraviolet
UVA	Ultraviolet Absorbance

1 Introduction

The Safe Drinking Water Act requires the United States Environmental Protection Agency (EPA) to conduct a periodic review of existing National Primary Drinking Water Regulations (NPDWRs) and determine which, if any, are candidates for revision. The purpose of the review, called the Six-Year Review (SYR), is to evaluate current information for each NPDWR to determine if there is new information on: health effects, treatment technology, analytical methods, occurrence and exposure, implementation, and/or other factors that provide a health or technical basis to support a regulatory revision that will improve or strengthen public health protection.

Under the Third Six-Year Review (SYR3), EPA is reviewing the regulated chemical, radiological and microbiological contaminants included in previous reviews, as well as the Microbial and Disinfection By-Products (MDBP) regulations that were promulgated under the following actions: the Disinfectants and Disinfection By-Products Rules (D/DBPRs), the Surface Water Treatment Rules, the Ground Water Rule (GWR) and the Filter Backwash Recycling Rule. The Surface Water Treatment Rules consist of the Surface Water Treatment Rule, the Interim Enhanced Surface Water Treatment Rule, the Long Term 1 Enhanced Surface Water Treatment Rule (LT1) and the Long Term 2 Enhanced Surface Water Treatment Rule (LT2). This is the first time that EPA is reviewing the MDBP rules. For more information about the SYR of the D/DBPRs, the reader is referred to EPA's *Six-Year Review 3 Technical Support Document for the Disinfectants/Disinfection Byproducts Rules* (USEPA, 2016a). Under the SYR3, EPA also is evaluating unregulated disinfection by-products (DBPs): for example, nitrosamines and chlorate.

In the Federal Register notice for Preliminary Regulatory Determination 3 (USEPA, 2014a), the Agency stated that "because chlorate and nitrosamines are DBPs that can be introduced or formed in PWSs partly because of disinfection practices, the Agency believes it is important to evaluate these unregulated DBPs in the context of the review of the existing DBP regulations. DBPs need to be evaluated collectively, because the potential exists that the chemical disinfection used to control a specific DBP could affect the concentrations of other DBPs. Therefore, the Agency is not making a regulatory determination for chlorate and nitrosamines at this time."

Due to the limitations of available analytical methods, only six nitrosamines were included in EPA's Second Unregulated Contaminant Monitoring Rule (UCMR 2) (monitored using EPA Method 521) and evaluated together as candidates for regulation under the Third Regulatory Determinations program in 2014. They are: *N*-nitrosodi-n-butylamine (NDBA), *N*-nitrosodiethylamine (NDEA), N-nitrosodimethylamine (NDMA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosomethylethylamine (NMEA) and *N*-nitrosopyrrolidine (NPYR). Four of these nitrosamines (NDEA, NDMA, NDPA, and NPYR) were included on EPA's Third Contaminant Candidate List (CCL 3).[1]

[1] An additional nitrosamine, *N*-nitrosodiphenylamine (NDPhA), was also on the CCL 3, but was not included in UCMR 2 because of the lack of an adequate analytical method.

Nitrosamines are a class of nitrogen-containing organic compounds that share a common nitrosamino functional group. Since nitrosamines have increasingly attracted attention in both field and laboratory studies, a considerable amount of information on the formation, fate, occurrence and health effects of this group of compounds in water has become available. Of the six nitrosamines covered in this document, NDMA is the focus of discussion in many chapters. This is because NDMA is the nitrosamine contaminant with the most information available and with the highest occurrence in drinking water. However, it should be noted that NDMA may account for only approximately five percent of total nitrosamines in chloraminated drinking waters, where it tends to occur most (see Section 5.1).

The remainder of this document provides a summary of available information and data relevant to EPA's understanding of the: contaminant background, health effects, analytical methods, occurrence and exposure, formation and treatment/control strategies for nitrosamines. The information cutoff date for the SYR3 was December 2015. That is, information published after December 2015 was not considered for this document. The Agency recognizes that scientists and other stakeholders are continuing to investigate and publish information relevant information subsequent to the cutoff date. While not considered as part of the SYR3, the Agency anticipates providing consideration for that additional information in subsequent activities.

2 Contaminant Background

This chapter presents background information on six unregulated nitrosamine compounds that EPA is evaluating under the SYR3 program: *N*-nitrosodi-n-butylamine (NDBA), *N*-nitrosodiethylamine (NDEA), *N*-nitrosodimethylamine (NDMA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosomethylethylamine (NMEA) and *N*-nitrosopyrrolidine (NPYR). The following topics are covered in the chapter: physical and chemical properties; production, use and release; formation in environmental media; environmental fate and transport; and regulatory and non-regulatory actions.

2.1 Physical and Chemical Properties

Nitrosamines share a common structure, illustrated in Exhibit 2.1. In the case of the nitrosamines discussed in this report, the R_1 and R_2 substituents/side chains are normal alkyl groups or cyclic moieties. NDBA, NDEA, NDMA, and NDPA are symmetrical dialkylnitrosamines, NMEA is an asymmetrical dialkylnitrosamine, and NPYR is a cyclic nitrosamine.

Exhibit 2.1: Chemical Structure for Nitrosamines

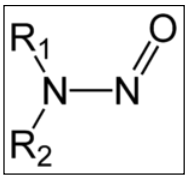
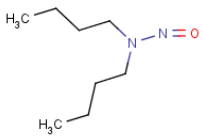
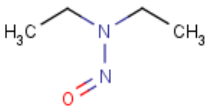
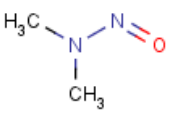
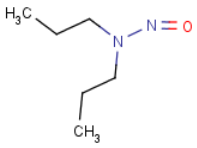
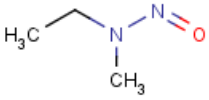
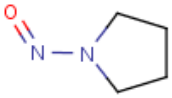


Exhibit 2.2 presents the chemical structures of NDBA, NDEA, NDMA, NDPA, NMEA and NPYR. Physical and chemical properties and other reference information for these nitrosamines are listed in Exhibit 2.3. NDMA is the smallest molecule among nitrosamines.

Exhibit 2.2: Chemical Structures of NDBA, NDEA, NDMA, NDPA, NMEA, and NPYR

NDBA	NDEA	NDMA	NDPA	NMEA	NPYR
					

Source: ChemIDPlus, 2010

Exhibit 2.3: Physical and Chemical Properties of NDBA, NDEA, NDMA, NDPA, NMEA, and NPYR

Property	NDBA	NDEA	NDMA	NDPA	NMEA	NPYR
Chemical Abstracts Service (CAS) Registry Number	924-16-3	55-18-5	62-75-9	621-64-7	10595-95-6	930-55-2
Chemical Formula	$C_8H_{18}N_2O$	$C_4H_{10}N_2O$	$C_2H_6N_2O$	$C_6H_{14}N_2O$	$C_3H_8N_2O$	$C_4H_8N_2O$
Molecular Weight	158.24 g/mol (HSDB, 2010; ChemIDPlus, 2010)	102.14 g/mol (HSDB, 2010; ChemIDPlus, 2010)	74.0822 g/mol (Lide, 1995-96)	130 g/mol (RAIS, 2009; HSDB, 2010; ChemIDPlus, 2010)	88.1 g/mol (HSDB, 2010; ChemIDPlus, 2010)	100.12 g/mol (HSDB, 2010; ChemIDPlus, 2010)
Color/Physical State	Yellow oil (HSDB, 2010)	Slightly yellow liquid (HSDB, 2010)	Yellow liquid at 25 deg C (O'Neil et al., 2001; Lewis, 1981)	Yellow liquid (HSDB, 2010)	Yellow liquid (HSDB, 2010)	Yellow liquid (HSDB, 2010)
Boiling Point	116 deg C at 14 mm Hg (HSDB, 2010)	175-177 deg C (HSDB, 2010)	151-153 deg C (O'Neil et al., 2001)	206 deg C (RAIS, 2009)	163 deg C at 747 mm Hg (HSDB, 2010)	214 deg C at 760 mm Hg (HSDB, 2010)
Melting Point	< 25 deg C (ChemIDPlus, 2010)	< 25 deg C (ChemIDPlus, 2010)	-50 deg C (WHO, 2008)	-12 – 6.6 deg C (estimated) (ATSDR, 1989a)	--	--
Vapor Density	0.9009 g/mL at 20 deg C/4 deg C (HSDB, 2010)	0.9422 g/mL at 20 deg C/4 deg C (HSDB, 2010)	1.0059 g/mL (Bednar et al., 2009)	0.916 g/mL (HSDB, 2010)	0.9448 g/mL at 18 deg C/4 deg C (HSDB, 2010)	1.1 g/mL (HSDB, 2010)
Freundlich Adsorption Coefficient	--	--	6.9E-05 $(mg/g)/(mg/L)^{1/n}$ (Faust and Aly, 1998)	--	--	--
Vapor Pressure (Pv)	4.69E-2 mm Hg at 25 deg C (Extrapolated) (HSDB, 2010)	0.86 mm Hg at 20 deg C (ChemIDPlus, 2010)	360 Pa at 20 deg C (International Occupational Safety and Health Centre, 2001)	0.086 mm Hg (HSDB, 2010)	1.100 mm Hg at 25 deg C (ChemIDPlus, 2010)	0.06 mm Hg at 20 deg C (HSDB, 2010; ChemIDPlus, 2010)
Henry's Law Constant	1.32E-5 atm-m^3/mol at 37 deg C (HSDB, 2010; ChemIDPlus, 2010)	3.63E-06 atm-m^3/mol (HSDB, 2010; ChemIDPlus, 2010)	1.82E-06 atm-m^3/mol at 37 deg C (HSDB, 2010; ChemIDPlus, 2010)	5.38E-06 atm-m^3/mol at 37 deg C (ChemIDPlus, 2010; HSDB, 2010)	1.44E-06 atm-m^3/mol at 25 deg C (ChemIDPlus, 2010)	4.89E-08 atm-m^3/mol at 37 deg C (HSDB, 2010; ChemIDPlus, 2010)

Property	NDBA	NDEA	NDMA	NDPA	NMEA	NPYR
Log K_{ow}	2.63 (dimensionless) (HSDB, 2010; ChemIDPlus, 2010)	0.48 (dimensionless) (HSDB, 2010; ChemIDPlus, 2010)	-0.57 (dimensionless) (International Occupational Safety and Health Centre, 2001; HSDB, 2010; ChemIDPlus, 2010)	1.36 (dimensionless) (HSDB, 2010; ChemIDPlus, 2010)	0.04 (dimensionless) (HSDB, 2010; ChemIDPlus, 2010)	-0.19 (dimensionless) (HSDB, 2010; ChemIDPlus, 2010)
K_{oc}	642 L/kg, estimated (HSDB, 2010)	43 L/kg, estimated (HSDB, 2010)	12 L/kg (HSDB, 2010)	130 L/kg, estimated (HSDB, 2010)	25 L/kg, estimated (HSDB, 2010)	19 L/kg, estimated (HSDB, 2010)
Water Solubility (C_{sat})	1,270 mg/L at 24 deg C (HSDB, 2010; ChemIDPlus, 2010)	106,000 mg/L at 24 deg C (ChemIDPlus, 2010)	1,000,000 mg/L at 24 deg C (ChemIDPlus, 2010)	13,000 mg/L (RAIS, 2009; ChemIDPlus, 2010)	300,000 mg/L at 20 deg C (ChemIDPlus, 2010)	1,000,000 mg/L at 24 deg C (ChemIDPlus, 2010)
Solubility in Other Solvents	Organic solvents & vegetable oils (HSDB, 2010)	Alcohol, ether, organic solvents, & lipids (HSDB, 2010)	Alcohols, ether, organic solvents, and lipids (ACGIH, 1991; O'Neil et al., 2001)	Alcohol, ether, and other organic solvents (ATSDR, 1989a)	Organic solvents & lipids (HSDB, 2010)	Organic solvents & lipids (HSDB, 2010)
Conversion Factors (at 20 deg C, 1 atm)	1 ppm = 6.58 mg/m^3 1 mg/m^3 = 0.152 ppm (calculated at 20 deg C)	1 ppm = 4.25 mg/m^3 1 mg/m^3 = 0.235 ppm (calculated at 20 deg C)	1 ppm = 3.08 mg/m^3; 1 mg/m^3 = 0.325 ppm (Verscheuren, 1996)	1 ppm (v/v) = 5.41 mg/m^3; 1 mg/m^3 = 0.185 ppm (v/v) (ATSDR, 1989a)	1 ppm = 3.66 mg/m^3 1 mg/m^3 = 0.273 ppm (calculated at 20 deg C)	1 ppm = 4.16 mg/m^3; 1 mg/m^3 = 0.240 ppm (calculated at 20 deg C)

2.2 Production, Use and Release

This section presents information about the production, use and release of members of the nitrosamine group.

2.2.1 Production and Use

Each of the six nitrosamines can be produced as an unintended byproduct of manufacturing processes that involve the use of nitrite or nitrate and amines. For example, nitrosamines may form at tanneries; fish processing plants; foundries; and pesticide, dye, rubber, and tire manufacturing plants. Nitrosamines have been found in tobacco products, cured meat, ham, bacon, beer, whiskey, fish, cheese, canned fruit, soybean oil, toiletries, household cleaners, pesticides, rubber baby bottle nipples and pacifiers, and drugs formulated with aminopyrine (ATSDR 1989b; NTP, 2005b; Fine et al. 1977; Yurchenko and Mölder, 2007; Drabik-Markiewicz et al. 2009; Pérez et al. 2008). NDMA is currently used only in research but was once used in the production of rocket fuel, as a solvent and as a rubber accelerator (an aid to vulcanization in the manufacturing process). It was also used or proposed for use as an antioxidant, an additive for lubricants, and a softener for copolymers (ATSDR, 1989b). NDMA is no longer produced commercially in the United States (HSDB, 2010).

NDEA is produced commercially. It is used as an additive in gasoline and in lubricants, as an antioxidant and as a stabilizer in plastics, although no data are available on quantities produced for commerce (HSDB, 2010).

NDBA, NDPA, NMEA and NPYR are not produced commercially but may be produced in small quantities for research purposes (HSDB, 2010).

No production data on any of the six compounds are available from EPA's Inventory Update Reporting or Chemical Data Reporting program.

2.2.2 Environmental Release

EPA's Toxics Release Inventory (TRI) and other sources provide information about industrial, commercial and consumer releases of NDBA, NDEA, NDMA, NDPA, NMEA and NPYR. That information is summarized in this section. In addition, this section discusses releases from municipal wastewater.

2.2.2.1 Industrial and Commercial Releases

Toxics Release Inventory (TRI)

EPA established TRI in 1987 in response to Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA). EPCRA Section 313 requires the reporting of annual information on toxic chemical releases from facilities that meet specific criteria. This reported information is maintained in a database accessible through TRI Explorer (USEPA, 2012).

Although TRI can provide a general idea of release trends, it has limitations. Not all facilities are required to report all releases. Facilities are required to report releases, both on-site and off-site, if they manufacture or process more than 25,000 pounds of a chemical or use more than 10,000

pounds. On-site releases are subdivided by environmental media. Reporting requirements have changed over time (e.g., reporting thresholds have decreased); this creates the potential for misleading data trends over time (USEPA, 1996a). TRI data are meant to reflect releases and should not be used to estimate general public exposure to a chemical (USEPA, 2004a). For the purposes of TRI, "State" counts include the District of Columbia and U.S. territories in addition to the 50 states.

TRI contains release data for NDBA, NDEA, NDMA and NDPA. No data on NMEA and NPYR releases are available from TRI. Neither of these nitrosamines has ever been included in the TRI list of chemicals for which reporting is required.

TRI data for NDMA are reported for the years 1998 through 2000 and 2005 through 2007. The only non-zero reported releases of NDMA during those years were air emissions reported from South Carolina in 1998 and California in 1999, in the amounts of 129 pounds and 5 pounds, respectively (USEPA, 2012). More recently, amine-based carbon dioxide capture systems used for post-combustion carbon sequestration could have released some nitrosamines into the environment (Dai et al., 2012; Dai and Mitch, 2015).

Exhibit 2.4 through Exhibit 2.6 summarize TRI data for NDBA, NDEA and NDPA, respectively, from the years 1998 to 2010. Though there were significant (up to almost 10,000 pounds annually) on-site releases of NDEA to land in 1999 and 2001, off-site releases dominated the total releases of NDEA. Off-site releases also dominate reported releases of NDPA and NDBA. TRI reports on-site air emissions of NDPA in the range of hundreds of pounds annually, and smaller on-site releases of NDBA in the form of air emissions and surface water discharges.

Exhibit 2.4: Environmental Releases (in pounds) of NDBA in the United States, 1998–2010

Year	On-Site Air Emissions	On-Site Surface Water Discharges	On-Site Underground Injection	On-Site Releases to Land	Off-Site Releases	Total On- & Off-Site Releases
1998	--	--	--	--	--	0
1999	2	1	0	0	4	7
2000	5	0	0	0	10	15
2001	5	0	0	0	4,505	4,510
2002	0	0	0	0	500	500
2003	0	0	0	0	255	255
2004	0	0	0	0	5	5
2005	1	0	0	0	500	501
2006	0	0	0	0	500	500
2007	0	0	0	0	500	500
2008	0	0	0	0	185	185
2009	0	0	0	0	398	398
2010	0	0	0	0	383	383

Note: "--" represents releases that fell below minimum reporting thresholds, or non-responses from facilities, or information that was not required to be reported in a particular year (as reporting forms changed over time).

Exhibit 2.5: Environmental Releases (in pounds) of NDEA in the United States, 1998-2010

Year	On-Site Air Emissions	On-Site Surface Water Discharges	On-Site Underground Injection	On-Site Releases to Land	Off-Site Releases	Total On- & Off-Site Releases
1998	2	--	0	0	0	2
1999	30	1	0	7,640	4,124	11,795
2000	5	0	0	0	10	15
2001	234	0	0	9,959	7,597	17,790
2002	0	0	0	0	500	500
2003	0	0	0	0	255	255
2004	0	0	0	0	1,000	1,000
2005	0	0	0	0	500	500
2006	0	0	0	0	500	500
2007	0	0	0	0	500	500
2008	0	0	0	0	650	650
2009	0	0	0	0	651	651
2010	0	0	0	0	633	633

Note: "--" represents releases that fell below minimum reporting thresholds, or non-responses from facilities, or information that was not required to be reported in a particular year (as reporting forms changed over time).

Exhibit 2.6: Environmental Releases (in pounds) of NDPA in the United States, 1998-2010

Year	On-Site Air Emissions	On-Site Surface Water Discharges	On-Site Underground Injection	On-Site Releases to Land	Off-Site Releases	Total On- & Off-Site Releases
1998	879	--	0	0	1,500	2,379
1999	5	--	0	0	--	5
2000	2	--	0	0	0	2
2001	6	0	0	0	505	511
2002	2	0	0	0	255	257
2003	1	0	0	0	257	258
2004	251	0	0	0	255	506
2005	252	0	0	0	503	755
2006	251	0	0	0	500	751
2007	251	0	0	0	500	751
2008	93	0	0	0	330	423
2009	100	0	0	0	328	428
2010	67	0	0	0	315	382

Note: "-- " represents releases that fell below minimum reporting thresholds, or non-responses from facilities, or information that was not required to be reported in a particular year (as reporting forms changed over time).

Exhibit 2.7 through Exhibit 2.9 present the TRI total releases and total surface water discharges of NDBA, NDEA and NDPA, respectively, for the years 2002, 2004, 2006, 2008 and 2010. No surface water discharges were reported for any of these three contaminants. Reported total

releases of these compounds during the years listed came consistently from Ohio (all three compounds in all years) and Indiana (NDPA in all years).

Exhibit 2.7: Summary of Total Releases and Total Surface Water Discharges (in pounds) of NDBA in 2002, 2004, 2006, 2008 and 2010

Year	Total Releases	Count of States with Releases	Total Surface Water Discharges	Count of States with Surface Water Discharges
2002	500	1	0	0
2004	5	1	0	0
2006	500	1	0	0
2008	185	1	0	0
2010	383	1	0	0

Exhibit 2.8: Summary of Total Releases and Total Surface Water Discharges (in pounds) of NDEA in 2002, 2004, 2006, 2008 and 2010

Year	Total Releases	Count of States with Releases	Total Surface Water Discharges	Count of States with Surface Water Discharges
2002	500	1	0	0
2004	1,000	1	0	0
2006	500	1	0	0
2008	650	1	0	0
2010	633	1	0	0

Exhibit 2.9: Summary of Total Releases and Total Surface Water Discharges (in pounds) of NDPA in 2002, 2004, 2006, 2008 and 2010

Year	Total Releases	Count of States with Releases	Total Surface Water Discharges	Count of States with Surface Water Discharges
2002	257	2	0	0
2004	506	2	0	0
2006	751	2	0	0
2008	423	2	0	0
2010	382	2	0	0

Additional Information on Industrial Releases

NDMA may be present in waste streams from manufacturing facilities where the compound was inadvertently generated as a byproduct. Such facilities may include amine manufacturing plants, tanneries, food processing industries, foundries, and manufacturers of rubber and tires, rocket fuel, pesticides, dyes, soaps, detergents, surfactants, lubricants and copolymers (ATSDR, 1989b; HSDB, 2010; WHO, 2008). Such releases are typically to surface water, although atmospheric releases are also a concern (ATSDR, 1989b; WHO, 2008) and ground water contamination was observed at a rocket fuel manufacturing facility (Fleming et al., 1996). NDMA has been

identified as both an impurity and a breakdown product of hydrazine-based rocket fuels (Rajat, 2008).

Industrial releases of NDBA, NDEA and NPYR have been detected in waste streams from rubber manufacturers and chemical plants. For example, 132 ng/L of NDEA was found in receiving river waters from a chemical plant (HSDB, 2010). NDBA can be formed as a waste product and has been detected in ambient air in rubber manufacturing plants and in factories using metal-working fluids (HSDB, 2010). Concentrations of NDEA ranging from 0.04 to 0.39 $\mu g/m^3$ were also found in the air in the passenger compartment of new 1979 cars (HSDB, 2010). NPYR has been detected in air samples from rubber tire plants and in effluent water from chemical factories. The average concentration of NPYR in the air of seven rubber manufacturers was 0.26 $\mu g/m^3$. NPYR concentrations detected in effluent water from multiple chemical plants are reported to have ranged from 0.02 to 0.09 µg/L (20–90 ng/L) (HSDB, 2010).

Commercial and Consumer Releases

Nitrosamine compounds have been found in tobacco products, cured meats, ham, bacon, beer, whiskey, fish, cheese, soybean oil, toiletries, household cleaners, pesticides, and rubber baby bottle nipples and pacifiers (ATSDR, 1989b; NTP, 2011; Fine et al*.,* 1977; Yurchenko and Mölder, 2007; Drabik-Markiewicz et al*.,* 2009; Pérez et al*.*, 2008). NPYR can be found in processed meats and spice premixes (HSDB, 2010). Consumption and disposal of food items, cigarettes and other products contaminated with NDMA and other nitrosamines may lead to environmental releases.

NDBA, NDEA, NMEA and NPYR have all been found in tobacco smoke. Higher concentrations were found in tobacco grown in high-nitrogen soil (HSDB, 2010). NDMA has been detected in the exhaust of diesel vehicles (Health Canada, 2011). Studies have found that rubber gaskets may leach NDMA into drinking water distribution systems (Morran et al., 2011; Teefy et al., 2011).

NDPA has been found as a contaminant in substituted dinitrotrifluralin herbicides (HSDB, 2010). NDMA can be present as a contaminant in dimethylamine (DMA)-based pesticides such as bromacil, benzolin, 2,4-D, dicamba, 2-methyl-4-chlorophenoxyacetic acid, and mecoprop. Use of such pesticides in agricultural settings, hospitals and homes can lead to environmental release of NDMA (WHO, 2008). Testing of over 100 samples of DMA-formulated phenoxy acid herbicides in Canada since 1990 revealed that NDMA was present in 49 samples, with an average concentration of 0.44 µg/g and maximum concentration of 2.32 µg/g. Six samples contained concentrations above 1.0 µg/g (Health Canada, 2011). On the whole, concentrations of NDMA in pesticides appears to be decreasing over time (WHO, 2008).

2.2.2.2 Releases from Wastewater Treatment Facilities

NDMA is commonly present in municipal sewage sludge, and has been measured at concentrations ranging from 0.6 to 45 parts per billion (ppb) (ATSDR, 1989b; HSDB, 2010). To a lesser extent, NPYR has also been observed in sewage sludge (HSDB, 2010). Investigators attribute nitrosamine formation in sewage sludge to interaction between alkylamines and nitrite (ATSDR, 1989b).

2.3 Formation in Environmental Media

Nitrosamines may form in air, soil, water, sewage, food, and animal and microbial systems where precursors (e.g., amines and nitrite) are present. Formation in those media is discussed in this section. Formation of the nitrosamines as disinfection by-products (DBPs) in drinking water is discussed in Chapter 6.

2.3.1 NDMA

NDMA can form in small quantities in air, water and soil as a result of biological, chemical and photochemical processes. The precursor DMA and other precursors occur naturally in the environment (e.g., in plants, fish, algae, urine and feces), and may be introduced by human activity as well (e.g., via pesticides) (ATSDR, 1989b).

Biological formation involves the reaction of secondary or tertiary amines with nitrite. The nitrite can be produced by microbial action from ammonia or nitrate, or it may be of anthropogenic origin (ATSDR, 1989b). NDMA can also be produced endogenously in humans from the interaction of nitrates and nitrites with amines in the stomach (Mirvish 1974, 1992; Tricker et al., 1994). Fristachi and Rice (2007) estimated that the mean endogenous formation for adults was about 20 µg/day.

Chemical formation occurs when primary, secondary or tertiary amines react with nitrite. Acidic conditions are most favorable. DMA has been found to react at night in the atmosphere with oxides of nitrogen to form NDMA (ATSDR, 1989b).

Photochemical formation of NDMA from DMA and nitrite, unlike chemical formation, occurs most readily under alkaline conditions (ATSDR, 1989b).

2.3.2 Other Nitrosamines

Limited data are available on the formation of other nitrosamines in environmental media.

NDEA may be formed by nitrate-reducing bacteria. In addition, a study concluded that formation of NDEA in river water samples at concentrations ranging from 0.13 to 7.02 µg/L (130–7,020 ng/L) was due to the reaction of nitrite with two different tracer dyes (Rhodamine B and Rhodamine WT) (HSDB, 2010).

NMEA may form in the atmosphere at night (i.e., while not subject to photodegradation) when atmospheric amines react with nitrous acid. NMEA can form from methylethyl amine or from any tertiary amine containing one each of methyl and ethyl functional groups (HSDB, 2010).

Wastewater effluent from industries using amines has led to the formation of nitrosamines in ocean water and river water (HSDB, 2010).

2.4 Environmental Fate and Transport

This section presents information on the environmental fate and transport of the six nitrosamines. Information was gathered from EPA's Persistence, Bioaccumulation and Toxicity (PBT) Profiler and other sources.

The nitrosamines are subject to a variety of natural processes when present in soil and water, including volatilization, photodegradation and microbial degradation. Under some circumstances, nitrosamines may persist in ambient waters that are used as drinking water sources, especially ground waters, at levels that could result in contamination of finished drinking water. However, as indicated by the occurrence monitoring data in Chapter 5 and the literature review of formation in Chapter 6, the formation of nitrosamines (particularly NDMA) during certain disinfection processes is understood to be the major source of nitrosamines found in finished drinking water.

2.4.1 Persistence, Bioaccumulation and Toxicity (PBT) Profiler

EPA developed the PBT Profiler to serve as a screening tool for estimating the percentage of a contaminant that is predicted to partition to water, air, soil, and sediment in a four-compartment system as well as the half-life of the contaminant in each medium (biodegradation half-life in the case of water, soil, and sediment, and half-life based on photochemical reactions with hydroxyl radicals and ozone in the case of air). Exhibit 2.10 presents the results of PBT Profiler modeling for NDBA, NDEA, NDMA, NDPA, NMEA and NPYR (PBT Profiler, 2010).

Exhibit 2.10: PBT Profiler Data for Six Nitrosamines

PBT Profiler Data	NDBA	NDEA	NDMA	NDPA	NMEA	NPYR
% partition to water	26%	53%	52%	44%	52%	48%
% partition to soil	72%	46%	44%	55%	46%	51%
% partition to air	1%	2%	4%	1%	2%	1%
% partition to sediment	0%	0%	0%	0%	0%	0%
Half-life in water	15 days	38 days	38 days	38 days	38 days	38 days
Half-life in soil	30 days	75 days	75 days	75 days	75 days	75 days
Half-life in air	0.58 days	0.92 days	6.2 days	0.67 days	1.6 days	1 day
Half-life in sediment	140 days	340 days	340 days	340 days	340 days	340 days

Source: PBT Profiler, 2010

2.4.1.1 Additional Information on Environmental Fate and Transport

NDBA

Based on partitioning coefficients, the Hazardous Substances Data Bank (HSDB) reports that NDBA will have “low mobility” in soil. The Henry’s Law constant for NDBA suggests that volatilization from moist soil will be an important fate process. The vapor pressure value indicates that NDBA is not expected to volatilize from dry soils (HSDB, 2010).

Partitioning coefficients suggest that NDBA may adsorb to suspended solids and sediment in water. The Henry's Law constant for NDBA suggests that it is expected to volatilize from water surfaces. A modeling study suggests NDBA volatilization half-lives of 2.4 days from rivers and 30 days from lakes. Bioconcentration is expected to be moderate for NDBA (HSDB, 2010).

In water, nitrosamines exposed to sunlight photolyze rapidly to amino radicals and nitric oxide. However, at neutral pH and in the absence of radical scavengers, the amino radicals and nitric oxide (NO) may recombine. HSDB reports that one study measured NDBA photolysis half-lives ranging from 16 minutes to 3.6 hours at various pH values. Hydrolysis is not expected to be an important fate process for NDBA. Reports on the likelihood of nitrosamine biodegradation in water are mixed (HSDB, 2010).

In the atmosphere, NDBA is expected to exist solely in the vapor phase and to be subject to degradation by photochemically produced hydroxyl radicals. The estimated atmospheric NDBA half-life for degradation by photochemically produced hydroxyl radicals is 1.4 hours (HSDB, 2010).

NDEA

Based on partitioning coefficients, HSDB reports that NDEA will have "very high mobility" in soil. The Henry's Law constant for NDEA suggests that volatilization from moist soil will be an important fate process. Comparison of vapor pressure values given by HSDB for NDEA and NMEA suggest that NDEA, like NMEA, may volatilize from dry soils. HSDB reports that 30–80 percent of NDEA applied to a soil surface volatilized within a few hours, while less than 25 percent of NDEA incorporated 7.5 cm below a soil surface volatilized in two days (HSDB, 2010). The half-life for mineralization of NDEA in soil has been measured as slightly longer than one week (HSDB, 2010).

Partitioning coefficients suggest that NDEA will not adsorb to suspended solids and sediment in water. The Henry's Law constant for NDEA suggests that it is expected to volatilize from water surfaces. A model estimates NDEA volatilization half-lives of 10 days from rivers and 78 days from lakes. Bioconcentration is expected to be low for NDEA (HSDB, 2010).

In water, NDEA exposed to sunlight photolyzes rapidly to amino radicals and nitric oxide. However, at neutral pH and in the absence of radical scavengers, the amino radicals and NO may recombine. HSDB reports that one study measured 88.7 percent photolysis of NDEA in solution after seven hours. NDEA was stable in lake water for 108 days in the absence of light. Hydrolysis is not expected to be an important fate process for NDEA. One set of authors identifies three microbes as capable of metabolizing NDEA, but several other studies found no convincing evidence of NDEA biodegradation (HSDB, 2010).

In the atmosphere, NDEA is expected to exist solely in the vapor phase and to be subject to degradation by photochemically produced hydroxyl radicals. The estimated atmospheric half-life for degradation by photochemically produced hydroxyl radicals is 22 hours for NDEA (HSDB, 2010).

NDMA

With a vapor pressure of approximately 2.7 mm Hg, significantly higher than the threshold for partition to the atmospheric particulate phase (10^{-4} mm Hg), NDMA is expected to be present in the atmosphere only in the vapor phase (ATSDR, 1989b). NDMA is not expected to persist long in the atmosphere, being subject to rapid photolysis to DMA in direct sunlight. The half-life for photolysis has been estimated as 5–30 minutes (ATSDR, 1989b) and 30–60 minutes (WHO, 2008). NDMA is also subject to degradation by hydroxyl radicals, with a half-life of approximately 6.3 days (HSDB, 2010) or between 25.4 and 254 hours (WHO, 2008). ATSDR (1989b) concludes that degradation by hydroxyl radicals or ozone would be too slow to be environmentally significant.

The high water solubility and low soil organic carbon-water partitioning coefficient (K_{oc}) of NDMA suggest that it is mobile in soils and can enter ground water. High vapor pressure suggests that NDMA on a dry soil surface will be subject to volatilization (HSDB, 2010; Health Canada, 2011); the half-life for volatilization has been estimated as 1–2 hours (ATSDR, 1989b). Photolysis should also be significant at the soil surface. In the subsurface, microbial degradation may be significant (ATSDR, 1989b). Aerobic conditions may be more favorable to biodegradation than anaerobic conditions (WHO, 2002). The half-life for NDMA in aerobic soil was found to be about three weeks under laboratory conditions, with volatilization and biodegradation dominating (HSDB, 2010). The rate and extent of NDMA removal/degradation appears to correlate strongly with the amount of organic matter present in sandy loam soils (HSDB, 2010).

NDMA readily dissolves in water and is unlikely to adsorb to particulates (WHO, 2008). In surface water, photodegradation and volatilization are the most important fate processes. In the laboratory, a photodegradation half-life of 79 hours was measured for NDMA in distilled water (HSDB, 2010). Under environmental conditions, photodegradation may be slowed or inhibited by suspended solids, organic material, or ice cover (WHO, 2008). Based on the measured Henry's Law constant of 1.82×10^{-6} atm-m^3/mol, modeling indicates an estimated volatilization half-life of 17 days from a river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) and 130 days from a lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) (HSDB, 2010). Oxidation, hydrolysis, biotransformation and biodegradation are not expected to be significant fate processes in surface water (WHO, 2008; Health Canada, 2011). When lake water samples were stored in the dark for 3.5 months at 30 degrees C, no change in NDMA concentration was observed (HSDB, 2010).

In ground water, where photolysis and volatilization do not occur, microbial transformation may be the most important fate process (ATSDR, 1989b). Biodegradation has been observed in the laboratory (HSDB, 2010). Assuming aerobic conditions for biodegradation, Howard et al. (1991) estimated that the half-life of NDMA in ground water would range from 42 to 360 days.

NDMA may be taken up by organisms in the environment. In an experimental setting, lettuce and spinach plants were found to be capable of absorbing NDMA from sand, soil and water (ATSDR, 1989b). Once taken up, NDMA may be subject to biotransformation.

NDPA

Some wastewater studies have shown biodegradation of NDPA, although other studies on soil and sewage have not shown any microbial biodegradation. In one wastewater study, the extent of biodegradation after seven days of incubation was 27 percent, with subcultures yielding biodegradation of 37, 47 and 50 percent, respectively. Other sludge studies and lake die-away studies have yielded zero percent degradation. In a static culture flask biodegradability test based on the biochemical oxygen demand, slow degradation of NDPA (40–50 percent after 28 days) was observed under the test conditions established (5 mg yeast/L, 5 mg/L test compound) (HSDB, 2010).

When applied to the soil surface, NDPA will rapidly volatilize; one study demonstrated a 50 percent loss after six hours (HSDB, 2010). However, when incorporated into the soil, NDPA volatilization is slower. One experiment showed only six percent volatilization after eight days (HSDB, 2010). Under anaerobic conditions, NDPA degraded slowly in sandy and silty loam with over half of the applied NDPA remaining after 60 days. Under aerobic conditions, NDPA dissipated in these two soils to less than 10 percent and 1 percent, respectively, of the initially applied amount after 69 days. However, much of the dissipation in the aerobic experiment was attributed to volatilization (Sacher et al., 2008). The dissipation half-life was 21–40 days in a field study with sandy and silty clay loam soils (HSDB, 2010). NDPA's K_{oc} value is suggestive of high mobility in soil (HSDB, 2010), and thus NDPA has the potential to leach into ground water (ATSDR, 1989a). Under aerobic conditions, the half-life for NDPA in subsurface soil is 14–40 days (ATSDR, 1989a). Under anaerobic conditions, the half-life for degradation is 47–80 days (ATSDR, 1989a). Three strains of nonpathogenic microorganisms (*Rhizopus oryzae, Streptococcus cremoris*, and *Saccaromyces rouxii*) were found to degrade 80, 70, and 50 percent of NDPA, respectively. NDPA was therefore degraded more rapidly than the other nitrosamines tested (NDEA and NDMA). In cells pre-cultured with NDPA, the degradation of NDPA was slightly improved (ca. 10 percent higher yield), suggesting that the degradation might rely on an inducible enzyme (Sacher et al., 2008).

NDPA will photolyze in surface waters; this appears to be the most significant degradation pathway (HSDB, 2010). Photolytic degradation in lake water shows a half-life of about 2.5 hours and 90 percent degradation after 8 hours (HSDB, 2010; ATSDR, 1989a). Otherwise, ATSDR (1989a) reports that NDPA is not expected to undergo abiotic degradation in natural waters. With a low Henry's Law constant, NDPA is expected to volatilize slowly from surface waters (HSDB, 2010). In one study, NDPA did not disappear from samples of lake water incubated at 30 deg C over a period of nearly four months (Sacher et al., 2008). NDPA is not expected to adsorb to sediment in water (ATSDR, 1989a).

Based on the octanol-water partition coefficient (log K_{ow}), a bioconcentration factor of 6 has been assigned to NDPA, indicating that accumulation in aquatic species will be low (HSDB, 2010).

In the atmosphere, NDPA is expected to exist solely in vapor form (HSDB, 2010). In the vapor phase, the half-life of NDPA is estimated to be 16 hours, with degradation occurring by reaction with photochemically produced hydroxyl radicals (HSDB, 2010).

NMEA

Based on partitioning coefficients, HSDB reports that NMEA will have "very high mobility" in soil. Henry's Law constant for NMEA suggests that volatilization from moist soil will be an important fate process. The vapor pressure value for NMEA indicates that NMEA may volatilize from dry soils (HSDB, 2010).

Partitioning coefficients suggest that NMEA will not adsorb to suspended solids and sediment in water. The Henry's Law constant for NMEA suggests that it is expected to volatilize slowly from water surfaces. A modeling study suggests NMEA volatilization half-lives of 24 days from rivers and 180 days from lakes. Bioconcentration is expected to be low for NMEA (HSDB, 2010).

In water, nitrosamines exposed to sunlight photolyze rapidly to amino radicals and nitric oxide. However, at neutral pH and in the absence of radical scavengers, the amino radicals and NO may recombine. The photolysis half-life for NMEA in aqueous solution exposed to sunlight is estimated to be 5.8 minutes. Hydrolysis is not expected to be an important fate process for NMEA. Reports on the likelihood of nitrosamine biodegradation in water are mixed (HSDB, 2010).

In the atmosphere, NMEA is expected to exist solely in the vapor phase and to be subject to degradation by photochemically produced hydroxyl radicals. The estimated atmospheric half-life for degradation by photochemically produced hydroxyl radicals is 1.6 days for NMEA. The photolysis half-life of NMEA exposed to sunlight in the vapor phase is estimated to be 5.8 minutes (HSDB, 2010).

NPYR

Based on partitioning coefficients, HSDB reports that NPYR will have "high mobility" in soil. The Henry's Law constant for NPYR suggests that volatilization from moist soil will not be an important fate process. The vapor pressure value indicates that NPYR will not volatilize from dry soils (HSDB, 2010).

Partitioning coefficients suggest that NPYR will not adsorb to suspended solids and sediment in water. The Henry's Law constant for NPYR suggests that NPYR will not volatilize from water surfaces. Bioconcentration is expected to be low for NPYR (HSDB, 2010).

In water, nitrosamines exposed to sunlight photolyze rapidly to amino radicals and nitric oxide. However, at neutral pH and in the absence of radical scavengers, the amino radicals and NO may recombine. In the absence of light, NPYR was found to be stable in neutral or alkaline water at room temperature for more than 14 days. Hydrolysis is not expected to be an important fate process for NPYR. Reports on the likelihood of nitrosamine biodegradation in water are mixed (HSDB, 2010).

In the atmosphere, NPYR is expected to exist solely in the vapor phase and to be subject to degradation by photochemically produced hydroxyl radicals. The estimated atmospheric half-life for NPYR degradation by photochemically produced hydroxyl radicals is 20 hours (HSDB, 2010)

2.5 Regulatory and Non-Regulatory Actions for Nitrosamines

Several U.S. states and foreign agencies have established regulations or advisories to address nitrosamine contamination of drinking water.

The World Health Organization issued a guideline value (non-enforceable standard) of 100 ng/L (0.1 μg/L) for NDMA in drinking water, based on the organization's estimated 10^{-5} cancer risk level (WHO, 2008). In 2011, Health Canada adopted a maximum acceptable concentration (an enforceable standard) of 40 ng/L for NDMA in drinking water, based on the agency's estimated 10^{-5} cancer risk level (Health Canada, 2011). The Australian Drinking Water Guidelines (Australia NHMRC, 2013) list a health-based guideline value of 100 ng/L for NDMA.

California has created regulatory and advisory levels for NDEA, NDMA, and NDPA in drinking water (CalEPA, 2006; CDPH, 2013). For NDMA, California has established a public health goal (a non-enforceable standard) of 3 ng/L, a notification level (an enforceable standard) of 10 ng/L and a response level (an enforceable standard) of 300 ng/L. At the response level, the California Department of Public Health recommends removing a contaminated source from service. For NDEA, the State has issued a notification level of 10 ng/L and a response level of 100 ng/L. For NDPA, the State has issued a notification level of 10 ng/L and a response level of 500 ng/L. California has not established public health goals for NDEA and NDPA.

New Jersey has issued ground water quality criteria of 0.7 ng/L for NDMA and 5 ng/L for NDPA (NJDEP, 2014). These ground water criteria are considered enforceable, but they may be limited by the State's practical quantitation levels.

Massachusetts has established a regulatory limit of 10 ng/L for NDMA in drinking water (Massachusetts DEP, 2004). This limit is based on the practical quantitation limit identified by California as the concentration of NDMA that most analytical laboratories can detect in drinking water.

3 Health Effects

This chapter presents information on the health effects of six nitrosamine compounds that the U.S. Environmental Protection Agency (EPA) is evaluating under the third Six-Year Review (SYR3) program: *N*-nitrosodi-n-butylamine (NDBA), *N*-nitrosodiethylamine (NDEA), *N*-nitrosodimethylamine (NDMA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosomethylethylamine (NMEA) and *N*-nitrosopyrrolidine (NPYR).

Section 3.1 presents a summary of health effects for each nitrosamine. Those data are used to derive health reference levels (HRLs), which are presented in Section 3.2. The HRL is a risk-derived concentration against which occurrence data from public water systems (PWSs) can be compared to determine if a nitrosamine occurs with a frequency and at levels of public health concern.

3.1 Health Effects Assessments for Individual Nitrosamine Compounds

The health endpoints that have been most thoroughly investigated for the nitrosamines are carcinogenicity and genotoxicity. There are very few studies published regarding the systemic, reproductive, developmental, neurological, or immunological impacts of nitrosamine exposures. The majority of the epidemiology studies examined the association of total nitrosamine exposure, mostly dietary, with the increased risk for a variety of tumor types. Several studies are specific to the relationship between dietary NDMA exposure and cancer (Knekt et al., 1999; Larsson et al., 2006; Loh et al., 2011; Jakszyn et al., 2011), and others apply to nitrosamines as a group (e.g., Jakszyn and González, 2006; Larsson et al., 2006). The NDMA-specific studies identify an increased risk for gastrointestinal and bladder tumors.

In accordance with the most recent *Guidelines for Carcinogen Risk Assessment* (USEPA, 2005a), EPA (USEPA, 2014a) categorized the six nitrosamine compounds as *likely to be carcinogenic to humans by a mutagenic mode of action* based on sufficient evidence of carcinogenicity in animal studies (Clapp et al., 1968, 1971; Druckrey et al., 1967; Lijinsky, 1987a, 1987b; Peto et al., 1991a, 1991b). These studies found tumors in multiple organs (predominately liver, esophageal and lung) in both sexes and in multiple animal species (e.g., rats, mice and hamsters). All of the six nitrosamines have been determined to cause cancer through a mutagenic MOA because of DNA adduct formation leading to errors in DNA replication, altered cell proliferation and, ultimately, tumors (Diaz Gomez et al., 1986; Goto et al., 1999; Jarabek et al., 2009; Souliotis et al., 1998). The mutagenic MOA is supported by positive findings from mutagenicity and genotoxicity *in vitro* and *in vivo* studies (Gollapudi et al., 1998; Kushida et al., 2000; Martelli et al., 1988; Robbiano et al., 1996; Tinwell et al., 1994). The EPA classifications of carcinogenicity are in agreement with those of other institutions like the International Agency for Research on Cancer (IARC) and the National Toxicology Program.

Fetuses, newborns and infants may be potentially sensitive to the carcinogenic effects of nitrosamines due to nitrosamines' mutagenic MOA and evidence of transplacental mutagenicity (Donovan and Smith, 2008; Althoff et al., 1977). Fetuses, infants and children appear to be at increased risk for mutagenic changes to deoxyribonucleic acid (DNA) from nitrosamine exposure, based on animal studies that found younger animals more susceptible to the development of liver tumors than older animals (Peto et al., 1984; Vesselinovitch et al., 1984; Gray et al., 1991). In addition, habitual consumers of alcohol may be a sensitive population

because alcohol increases the metabolism of nitrosamines via a metabolic pathway that leads to the formation of mutagenic DNA adducts. Co-exposure to ethanol can exacerbate the cancer effects of nitrosamines in animal studies (McCoy et al., 1986; Anderson et al., 1993; Kamataki et al., 2002). There are approximately 5 million people in the U.S. who suffer from alcoholism (O'Day et al., 1998), and these individuals may be at increased risk if co-exposed to nitrosamines (Verna et al. 1996; Amelizad et al. 1989). Individuals with genetic defects in DNA repair enzymes (Hannson, 1992) may also be at increased risk.

3.1.1 NDBA

No short-term human case reports or epidemiologic studies were identified for NDBA. However, some epidemiology studies tentatively associate ingestion of foods containing high levels of total nitrosamines, including foods containing NDBA, with gastric and esophageal cancer (Jakszyn and González, 2006; Larsson et al., 2006).

No studies on the subchronic, chronic (non-cancer), reproductive, or developmental effects of NDBA in animals were identified. Hematuria in mice was observed in one study; however, the study authors noted that the hematuria was related to the developing bladder tumors in the affected animals (Bertram and Craig, 1970).

Several chronic animal studies demonstrate the carcinogenic effects of NDBA and its metabolites. Oral administration of NDBA predominantly resulted in liver, esophageal and bladder tumors in rats, mice and guinea pigs (Druckrey et al., 1967; Bertram and Craig, 1970; Lijinsky and Reuber, 1983; Tsuda et al., 1987; Nishikawa et al., 2003). NDBA was tested and found positive for mutagenicity and genotoxicity in a number of *in vitro* and *in vivo* assays (Prival et al., 1979; Negishi and Hayatsu, 1980; Andrews and Lijinsky, 1980; Brambilla et al., 1981, 1987; Parodi et al., 1983; Araki et al., 1984; Mochizuki et al., 1986; Langenbach, 1986; Martelli et al., 1988; Janzowski et al., 1989; Negishi et al., 1991; Shu and Hollenberg, 1996; Kushida et al., 2000; Fujita and Kamataki, 2001).

EPA classified NDBA as *likely to be carcinogenic to humans by a mutagenic mode of action* under the EPA (2005a) *Guidelines for Carcinogen Risk Assessment*, based on evidence of carcinogenicity in animal studies (USEPA, 2014a). The cancer slope factor (CSF) for NDBA is 0.4 $(mg/kg/day)^{-1}$, as derived by linear low-dose extrapolation from the point of departure for the incidence of liver and esophageal and/or pharyngeal tumors in a lifetime diet study in Berlin-Druckrey (BD) rats (Druckrey et al., 1967). NDBA was determined to cause cancer through a mutagenic mode of action (MOA) for all but the bladder tumors. The bladder tumors are linked to metabolites that lack direct DNA alkylating ability and have an undetermined MOA. Mutagenicity results for the metabolites linked to the bladder tumors are equivocal (Nagao et al., 1977; Olajos et al., 1978; Pool et al., 1988; Brendler et al., 1992; Janzowski et al., 1994). No NDBA-specific data quantifying the increased cancer risk due to early-life exposure were available. Therefore, based on recommendations of the EPA's *Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens* (USEPA, 2005b), Age Dependent Adjustment Factors (ADAFs) and age-specific exposure factors (USEPA, 2011) were applied in the evaluation of risk from early-life exposures.

The fetus, newborns and infants may be particularly sensitive to the carcinogenic effects of NDBA as a consequence of early-life exposures, because NDBA has a mutagenic MOA.

Tracheal, nasal, larynx and bronchial tumors were exhibited in offspring of hamsters treated during pregnancy (Althoff et al., 1977). Löfberg and Tjälve (1986) found that NDBA is distributed across the placenta, and becomes activated in the fetus during the late stage of gestation. Fujii et al. (1977) injected infant mice subcutaneously with NDBA or its metabolites, and a large proportion of the animals were found to develop lung or liver tumors. A study in mice suggests that males are potentially more sensitive than females to bladder tumors from NDBA exposure (Bertram and Craig, 1970). However, other studies in different strains of mice did not identify an increased sensitivity of males (Irving et al., 1984; He et al., 2012). Among the six nitrosamines monitored under EPA's Second Unregulated Contaminant Monitoring Regulation (UCMR 2), NDBA has the strongest link to bladder cancer. Habitual consumers of alcoholic beverages may also be a sensitive population, based on animal study findings that demonstrated enhanced effects of the other nitrosamines following co-exposures to ethanol (Griciute et al., 1982; McCoy et al., 1986; Anderson et al., 1993). No data specific to NDBA were identified in these studies.

3.1.2 NDEA

No short-term human case reports or epidemiologic studies were identified for NDEA. However, some epidemiology studies tentatively associate ingestion of foods containing high levels of total nitrosamines, including foods containing NDEA, with gastric or esophageal cancer (Jakszyn and González, 2006; Larsson et al., 2006).

Limited animal studies of short-term, subchronic, or chronic (non-cancer) effects of NDEA were identified. The few available studies reported adverse effects on liver and kidney enzymes (Bansal et al., 2000) and increased levels of cholesterol in the liver (Tang et al., 1992). No studies on the developmental or reproductive effects of NDEA were identified.

Many chronic animal studies demonstrate the carcinogenic effects of NDEA. Oral administration of NDEA resulted in liver, esophageal, nasal cavity and kidney tumors in rats; liver, esophageal, lung and forestomach tumors in mice; tracheal, lung, liver, nasal cavity and bronchial tumors in Syrian golden hamsters; forestomach, esophageal and liver tumors in Chinese hamsters; liver tumors in guinea pigs and rabbits; liver and nasal cavity tumors in dogs; and liver tumors in monkeys (IARC, 1978; NTP, 2011). NDEA was tested and found positive for mutagenicity and genotoxicity in a numerous *in vitro* and *in vivo* assays (McCann et al., 1975; Montesano and Bartsch, 1976; Dean and Senner, 1977; Kuroki et al., 1977; Yahagi et al., 1977; Amacher and Paillet, 1983; Quillardet and Hofnung, 1985; Mochizuki et al., 1986; Zeiger et al., 1987; Liu and Guttenplan, 1992; Yamazaki et al., 1992a,b; Vogel and Nivard, 1993; Goto et al., 1999; Aiub et al., 2003, 2006; Donovan and Smith, 2008).

EPA classified NDEA as *likely to be carcinogenic to humans by a mutagenic mode for action* under the USEPA (2005a) *Guidelines for Carcinogen Risk Assessment,* based on evidence of carcinogenicity in animal studies (USEPA, 2014a). The CSF for NDEA is 30 $(mg/kg/day)^{-1}$, as derived by linear low-dose extrapolation from the point of departure for the incidence of combined total liver tumors and esophageal tumors in a study in rats (Peto et al., 1991a, b). NDEA causes cancer through a mutagenic MOA, but there are no NDEA-specific data quantifying the increased cancer risk due to early-life exposure (Peto et al., 1984; Gray et al., 1991). Therefore, based on recommendations of the EPA's *Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens* (USEPA, 2005b), ADAFs and age-

specific exposure factors (USEPA, 2011) were applied in the evaluation of risk from early-life exposures.

The fetus, newborns and infants may be particularly sensitive to the carcinogenic effects of NDEA. In mice and hamsters, NDEA exposure of pregnant animals resulted in an increased incidence of liver and lung tumors in their offspring (Mohr and Althoff, 1965; Mohr et al., 1966; Anderson et al., 1989). Another study on NDEA found that younger rats were more susceptible to the development of liver tumors, with a six-fold increase in tumor onset rates compared to rats exposed as adults (Peto et al., 1984; Gray et al., 1991). Habitual consumers of alcoholic beverages may also be considered a sensitive population based on animal studies that have shown an increase in esophageal tumors (Gibel, 1967; Aze et al., 1993) and liver tumors (Takada et al., 1986) in rats after administration of NDEA and ethanol, compared to animals administered NDEA alone.

3.1.3 NDMA

Limited human data are available from NDMA poisoning incidents wherein the following clinical symptoms have been reported: irritation of eyes, skin irritation, irritation of the respiratory tract, nausea, vomiting, diarrhea, abdominal cramps, headache, sore throat, cough, weakness, fever, enlarged liver, jaundice and low platelet count (OSHA, 2006). Reports from cases of human intentional (poisoning) or accidental ingestion identify the liver as the organ of greatest toxicological concern (Cooper and Kinbrough, 1980; Pedal et al., 1982).

Epidemiological studies reported mixed results on the association between NDMA and several types of cancer (gastric, lung and brain cancer). Several studies reported a positive association between NDMA exposure and gastric cancer (González et al., 1994; La Vecchia, 1995; Pobel et al., 1995), while other studies did not report an association (Risch et al., 1985; Knekt et al., 1999; Straif et al., 2000; Jakszyn et al., 2006). A positive association was noted between NDMA and upper digestive tract cancers (Rogers et al., 1995), lung cancer (Goodman et al., 1992; De Stefani et al., 1996), brain cancer in men (Giles et al., 1994) and childhood brain cancer from gestational exposure through the maternal diet (Preston-Martin, 1989); no association was reported between NDMA and brain cancer in women (Giles et al., 1994).

NDMA is acutely toxic to rodents when exposure occurs orally and by inhalation at high concentrations (ATSDR, 1989b; RTECS, 2002). In studies conducted in rats, the liver was the primary target organ after short-term exposures, with effects observed after 1- and 30-day exposures at levels as low as 0.7 and 1 mg/kg/day, respectively (Korsrud et al., 1973; Maduagwu and Bassir, 1980). According to subchronic and chronic studies, the liver appears to be the primary target organ in rats, mice and hamsters. Observed hepatotoxic effects include centrilobular congestion, hepatocyte vacuolization and increased serum levels of liver enzymes (Takayama and Oota, 1965; Otsuka and Kuwahara, 1971; Anderson et al., 1986; Desjardins et al., 1992). Limited data from reproductive/developmental studies in rats and mice indicate reduced fetal body weights and increased fetal mortality (Bhattacharyya, 1965; Napalkov and Aleksandrov, 1968; Nishie, 1983; Anderson et al., 1989; ATSDR, 1989b). However, there are many limitations to these publications, including lack of controls and insufficient information on study design and outcomes.

Many chronic animal studies demonstrate the carcinogenic effects of NDMA. Oral administration of NDMA resulted in liver, lung, nasal cavity, bile duct and kidney tumors in rats; liver, lung and kidney tumors in mice; liver, nasal cavity and bile duct tumors in hamsters; and liver and bile duct tumors in rabbits and guinea pigs (Tomatis et al., 1964; IARC, 1978; Lijinsky, 1983; Preussmann and Stewart, 1984; ATSDR, 1989b; Peto et al., 1991a,b; IPCS, 2002; Terracini et al., 1966, 1967). An increased incidence of tumors was reported in the offspring of rats and mice administered NDMA during pregnancy (Aleksandrov, 1968; Tomatis, 1973; Althoff et al., 1977; Anderson et al., 1979). NDMA was tested and found positive for mutagenicity and genotoxicity in a number of *in vitro* and *in vivo* assays (ATSDR, 1989b; IPCS, 2002; CalEPA, 2006; Health Canada, 2010).

EPA classified NDMA as *likely to be carcinogenic to humans by a mutagenic mode of action* under the USEPA (2005a) *Guidelines for Carcinogen Risk Assessment,* based on evidence for human carcinogenicity in epidemiologic studies and substantial animal data demonstrating carcinogenicity (USEPA, 2014a). The CSF for NDMA is 21 $(mg/kg/day)^{-1}$, as derived by linear low-dose extrapolation from the point of departure for the incidence of liver tumors in a study in rats (Peto et al., 1991a, b). NDMA causes cancer through a mutagenic MOA but there are no NDMA-specific data quantifying the increased cancer risk due to early-life exposure (Peto et al., 1984; Gray et al., 1991). Therefore, based on recommendations of the EPA's *Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens* (USEPA, 2005b), ADAFs and age-specific exposure factors (USEPA, 2011) were applied in the evaluation of risk from early-life exposures.

The fetus, newborns and infants can be particularly sensitive to the carcinogenic effects of NDMA. Several studies have demonstrated an increase in tumors in the offspring of pregnant animals exposed to NDMA by oral exposure (Aleksandrov, 1968; Anderson et al., 1979; Tomatis, 1973; Althoff et al., 1977). Habitual consumers of alcoholic beverages may also be a sensitive population, based on animal studies showing an increased incidence of lung tumors or tumors of the nasal cavity in mice exposed to NDMA and ethanol, compared to NDMA alone (IARC, 2010).

3.1.4 NDPA

No short-term human case reports or epidemiologic studies were identified for NDPA. Some epidemiology studies that examined ingestion of foods containing high levels of total nitrosamines report an association between ingestion of foods known to contain nitrosamines and gastric or esophageal cancer (Jakszyn and González, 2006; Larsson et al., 2006); those studies, however, were not specific to NDPA.

Very limited animal data are available on the short-term, subchronic, or chronic (non-cancer) effects of NDPA. No reproductive studies are available. One developmental study reported increased mortality in hamster offspring born to dams administered NDPA by subcutaneous injection (Althoff et al., 1977).

Many chronic animal studies demonstrate the carcinogenic effects of NDPA. Oral administration of NDPA to rats and mice resulted in liver, nasal cavity, esophageal, tongue, forestomach and lung tumors and lymphomas (Druckrey et al., 1967; Lijinsky and Taylor, 1978, 1979; Lijinsky and Reuber, 1981, 1983; Griciute et al., 1982, Griciute and Barauskaĭte, 1989). NDPA was tested

and found positive for mutagenicity and genotoxicity in a number of *in vitro* and *in vivo* assays (e.g., Montesano and Bartsch, 1976; Brambilla et al., 1981; Shu and Hollenberg, 1997).

EPA classified NDPA as *likely to be carcinogenic to humans by a mutagenic mode of action* under the USEPA (2005a) *Guidelines for Carcinogen Risk Assessment*, based on evidence of carcinogenicity in animal studies (USEPA, 2014a). The CSF for NDPA is 2 $(mg/kg/day)^{-1}$, as derived by linear low-dose extrapolation from the point of departure for the incidence of liver tumors in a study in rats (Druckrey et al., 1967). As a result of the findings on NDPA mutagenicity and the MOA information available for the other dialkylnitrosamines, the cancer recommendations of the EPA's *Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens* (USEPA, 2005b) were applied in the evaluation of risk from early-life exposures.

The fetus, newborns and infants may be particularly sensitive to the carcinogenic effects of NDPA, since NDPA has a mutagenic MOA. In hamsters, single subcutaneous injections of NDPA during gestation resulted in respiratory and digestive tract tumors in both the dams and their offspring (Althoff et al., 1977; Althoff and Grandjean, 1979). Habitual consumers of alcoholic beverages may also be considered a sensitive population based on animal studies that have shown an increase in spinocellular, esophageal and forestomach tumors in mice after administration of NDPA and ethanol, compared to animals administered NDPA in water (Griciute et al., 1982).

3.1.5 NMEA

No short-term human case reports or epidemiologic studies are available for NMEA. However, some epidemiology studies tentatively associate ingestion of foods containing high levels of total nitrosamines, including foods containing NMEA, with gastric or esophageal cancer (Jakszyn and González, 2006; Larsson et al., 2006). An LD_{50} value of 90 mg/kg in rats suggests that NMEA has a moderate potential for acute toxicity when administered orally as a single dose (Druckrey et al., 1967). No studies on the short-term, subchronic, reproductive, or developmental effects of NMEA are available. Lung inflammation was noted in one chronic oral study in rats (Lijinsky and Reuber, 1981). These data were from a single-dose study without a control group and are not suitable for derivation of a reference value.

Multiple chronic animal studies demonstrate the carcinogenic effects of NMEA. Oral administration of NMEA resulted in liver, esophageal, renal, lung and nasal tumors in rats (Druckrey et al., 1967; Lijinsky and Reuber, 1980, 1981; Michejda et al., 1986; Lijinsky et al., 1987) and liver and nasal mucosa tumors in hamsters (Lijinsky et al., 1987). NMEA was tested and found positive for mutagenicity and genotoxicity in a number of *in vitro* and *in vivo* assays (Phillipson and Ioannides, 1985; Kerklaan et al., 1986; Brambilla et al., 1987; Vogel and Nivard, 1993; Morita et al., 1997; Fujita and Kamataki, 2001).

EPA classified NMEA as *likely to be carcinogenic to humans by a mutagenic mode of action* the USEPA (2005a) *Guidelines for Carcinogenic Risk Assessment,* based on evidence of carcinogenicity in animal studies (USEPA, 2014a). The CSF for NMEA is 4 $(mg/kg/day)^{-1}$, as derived by linear low-dose extrapolation from the point of departure for the incidence of liver tumors in a study in rats (Druckrey et al., 1967). NMEA has been determined to cause cancer through a mutagenic MOA, but no chemical-specific data quantifying the increased cancer risk

due to early-life exposure were available. Therefore, based on the recommendations of the EPA's *Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens* (USEPA, 2005b), ADAFs and age-specific exposure factors (USEPA, 2011) were applied in the evaluation of risk from early-life exposures.

The fetus, newborns and infants may be particularly sensitive to the effects of NMEA due to early-life exposure because NMEA has a mutagenic MOA, however data demonstrating sensitivity from early life studies are lacking. Habitual consumers of alcoholic beverages may also be a sensitive population, based on studies that have shown that exposure of animals to NMEA and ethanol result in increased tumor incidence compared to animals exposed to NMEA alone (Anderson et al., 1993; McCoy et al., 1986).

3.1.6 NPYR

No short-term human case reports or epidemiologic studies are available for NPYR. However, some epidemiology studies tentatively associate ingestion of foods containing high levels of total nitrosamines with gastric and esophageal cancers (Jakszyn and González, 2006; Larsson et al., 2006).

Limited animal data are available on the short-term, subchronic or chronic (non-cancer) effects of NPYR. Studies in rats and hamsters suggest that NPYR has low potential for acute toxicity when administered orally as a single dose (Druckrey et al., 1967; Ketkar et al., 1982). In chronic toxicity studies in animals, oral administration of NPYR is associated with decreased body weights and survival rates (Greenblatt and Lijinsky, 1972a,b; Chung et al., 1986). No studies on the reproductive or developmental effects of NPYR were identified.

Many chronic animal studies for NPYR demonstrate the carcinogenic effects of NPYR (Greenblatt and Lijinsky 1972a,b; Preussmann et al., 1977; Lijinsky and Reuber, 1981; Ketkar et al., 1982; Peto et al., 1984; Chung et al., 1986; Berger et al., 1987; Gray et al., 1991). Oral administration of NPYR in rats and hamsters consistently resulted in liver tumors. NPYR was tested and found positive for mutagenicity and genotoxicity in a number of *in vitro* and *in vivo* assays (Gilbert et al., 1984; Martelli et al., 1988; Zielenska et al., 1990; Vogel and Nivard, 1993; Kanki et al., 2005; Wang et al., 2007).

EPA classified NPYR as *likely to be carcinogenic to humans by a mutagenic mode of action* under the EPA (2005a) *Guidelines for Carcinogen Risk Assessment*, based on evidence of carcinogenicity in animal studies (USEPA, 2014a). The CSF for NPYR is 7.0 $(mg/kg/day)^{-1}$, as derived by linear low-dose extrapolation from the point of departure for the incidence of liver tumors in a well-conducted and well-reported lifetime drinking water study in rats (Peto et al. 1984; Gray et al., 1991). NPYR has been determined to cause cancer through a mutagenic MOA, but no chemical-specific data quantifying the increased cancer risk due to early-life exposure are available. In the absence of life-stage specific data the cancer recommendations of the EPA's *Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens* (USEPA, 2005b) were applied in the evaluation of risk from early-life exposures based on the mutagenicity information and the identification of modified DNA bases in studies of exposed animals.

No data examining the impact of early life exposure to NPYR were identified. However, NPYR-DNA adducts were detected in liver and kidney DNA of rat pups nursed by mothers exposed to

NPYR, indicating exposure via breast milk with subsequent modification of DNA in early life (Diaz Gomez et al., 1986). Habitual consumers of alcoholic beverages may also be a sensitive population, based on studies that have shown that exposure of animals to NPYR and ethanol result in increased tumor incidence compared to animals exposed to NPYR alone (Anderson et al., 1993; McCoy et al., 1986).

3.1.7 Sensitive Populations

Fetuses, infants and children can be more susceptible than adults to the mutagenic effects of the six nitrosamines. Although studies are available that indicate an increased risk to fetuses, infants and children, the data may be inadequate to support developing an alternative to the agency's default ADAFs. ADAFs are values recommended by EPA (USEPA, 2005b) to adjust CSFs for chemicals when chemical-specific data that quantify the increased risk are lacking.

Exposure to alcohol along with nitrosamines has been proposed to lead to enhanced carcinogenic effects (Chhabra et al., 1995). The International Agency for Research on Cancer (IARC) (2010) reviewed available studies on the impact of NDEA, NDMA or NDPA combined with ethanol, and found an increased incidence of esophageal, liver, lung, nasal cavity, or forestomach tumors in the animals given the mixture, compared to the animals administered nitrosamine without ethanol. Anderson et al. (1993) found a doubling of lung tumor incidence and a 5.5 fold increase in tumor multiplicity in mice given a mixture of 10 percent ethanol and 40 ppm NPYR (6.6 mg/kg/day) for four weeks in their drinking water, compared to mice given NPYR alone. IARC (2010) concluded that alcohol ingestion enhanced the carcinogenic potency of nitrosamine mixtures via induction of CYP2E1, an enzyme that converts nitrosamines to carcinogenic intermediates. Although it is clear that chronic alcohol exposure can induce the metabolism of the nitrosamines and the formation of mutagenic metabolites, adequate information may not be available to justify any toxicity adjustment factor for this effect in human populations, either for the individual nitrosamines or the group as a whole. Based on the information presented in the section above for individual compounds, the availability of data on which nitrosamines may affect sensitive populations is summarized in Exhibit 3.1.

Exhibit 3.1: Sensitive Populations, as Suggested by Data from Animal Studies

Population	NDBA	NDEA	NDMA	NDPA	NMEA	NPYR
Fetus, infants, children	Fetus, Infants, Children	Fetus, Infants, Children	Fetus, Infants, Children	Fetus, Infants, Children	No data	Infants, Children
Chronic alcohol consumers	No data	Increased tumors with mixture	Increased tumors with mixture	Increased tumors with mixture	No data	Increased tumors with mixture

Other potential sensitive subpopulations include individuals with enhanced expression of the activating cytochrome P450 (CYP) enzymes, individuals with compromised DNA repair capacity, individuals undergoing cancer therapy, and individuals with enhanced exposure to

chemical genotoxins or radiation by medical or industrial exposure routes. However, EPA did not identify any epidemiology studies regarding increased risk for these groups.

3.2 Calculation of Health Reference Levels (HRLs) for Nitrosamine Compounds

To evaluate the number of PWSs and PWS-served individuals exposed to nitrosamines in drinking water, as described in more detail in Chapter 5, EPA screened the UCMR 2 monitoring data for each chemical against several thresholds. These included a health-based threshold called the HRL. The HRL is a risk-derived concentration in drinking water against which occurrence data from PWSs can be compared to determine if a nitrosamine occurs with a frequency and at levels of public health concern. In the case of chemicals that are *known* or *likely* to cause cancer, the HRL is the concentration in drinking water associated with an increased risk of one excess cancer case above background among a million exposed persons over a lifetime exposure (i.e., estimated lifetime excess cancer risk of one-in-a-million, $1x\ 10^{-6}$) (USEPA, 2014a). The HRL is a benchmark that is set to compare the risks of different chemicals based on drinking water being the sole route of exposure. It does not integrate added risks associated with other exposure media (e.g., food, air). It does not consider whether or not analytical methods are able to accurately measure the concentration at the stated level or the feasibility to treat water in a way that reduces the concentration to that level.

There are two general approaches to the derivation of an HRL for carcinogens. One approach is used for chemicals that cause cancer and exhibit a linear response to dose and the other applies to carcinogens evaluated using a non-linear approach. For those contaminants that are considered to be likely or probable human carcinogens by a mutagenic or unknown MOA, the agency calculates a toxicity value that defines the relationship between dose and response (i.e., the CSF). There are two approaches for the derivation of the HRL for cancer effects depending on whether or not there is information to support a mutagenic MOA. In the absence of data, the dose response is assumed to be linear but there is no requirement for application of the *Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens* (USEPA, 2005b). Application of the supplemental guidance is required only for chemicals with a demonstrated mutagenic MOA

(1) *MOA: Unknown*

In cases where the data on the MOA are lacking, EPA typically uses a default low dose linear extrapolation to calculate a CSF. The unit risk is the estimated upper-bound excess lifetime cancer risk from a continuous exposure to a chemical at a concentration of 0.001 mg/L in drinking water and expressed in units of $(\mu g/L)^{-1}$. The exposure estimate assumes an adult body weight of 70 kg and the 90th percentile adult drinking water intake of 2 L/day.

$$\text{Unit Risk } (\mu g/L)^{-1} = CSF \times [(DWI \times UA)/BW]$$

where:

CSF = Cancer Slope Factor $(mg/kg/day)^{-1}$

DWI = Drinking Water Intake for an adult, assumed to be 2 L/day (90th percentile)

UA = Unit adjustment, from mg to µg

BW = Body Weight for an adult, assumed to be 70 kilograms (kg)

The cancer HRL is the concentration of a contaminant in drinking water corresponding to an excess estimated lifetime cancer risk of one-in-a-million ($1x\ 10^{-6}$), calculated as follows:

$$\text{HRL } (\mu g/L) = \text{Risk Level of } 10^{-6} \div \text{Unit Risk } (\mu g/L)^{-1}$$

As noted above, HRLs are not final determinations about the level of a contaminant in drinking water that must not be exceeded to protect any particular population. Rather, HRLs are risk derived concentrations against which to evaluate the occurrence data during the regulatory determination process to determine if contaminants occur at levels of *potential* public health concern.

(2) *MOA: Mutagenic*

If the chemical has a mutagenic MOA, low dose linear extrapolation is used to calculate the CSF as described in the preceding paragraph. The U.S. EPA's 2005 *Guidelines for Carcinogen Risk Assessment* (USEPA, 2005a) requires that the potential increased cancer risk due to early-life exposure be taken into account for chemicals with a mutagenic MOA. When chemical-specific data to quantify the increased risk are lacking, ADAFs are applied to estimate age-adjusted unit risks. The age-adjusted unit risk is determined by using the sum of the unit risks for each of the three ADAF developmental groups (birth to < 2 yrs; 2 yrs to < 16 yrs; 16 yrs to 70 yrs). The age-adjusted unit risks include a ten-fold adjustment for early life (birth to < 2 yrs) exposures, a three-fold adjustment for childhood/adolescent (2 yrs to < 16 yrs) exposures, and no additional adjustment for exposures later in life (16 yrs to 70 yrs), in conjunction with age-specific drinking water intake values derived from the U.S. EPA's 2011 Exposure Factors Handbook (USEPA, 2011), and the fraction of a 70 year lifetime applicable to each age period. The increase in risk during early life results from active tissue growth resulting in limited time for repair of DNA replication errors. The age-adjusted unit risk is the upper-bound excess lifetime cancer risk estimated to result from continuous postnatal exposure to a chemical at a concentration of 0.001 mg/L in drinking water.

$$\text{Age-Adjusted Unit Risk } (\mu g/L)^{-1} = \sum(\text{CSF x ADAF x DWI/BWR x UA x F})$$

where:

CSF = Cancer Slope Factor $(mg/kg/day)^{-1}$

ADAF = The Age Dependent Adjustment Factor for the age group birth to two-years (ADAF=10), two years to sixteen years (ADAF=3), and sixteen to seventy years (ADAF=1)

DWI/BWR	=	Drinking Water Intake Body Weight Ratio (DWI/BWR) expressed as liters per day per kg body weight for the age-specific group (90th percentile, consumers only)[2]
UA	=	Unit adjustment, from mg to µg
F	=	The fraction of a 70 year lifetime applicable to the age period: 2/70 for birth to two years, 14/70 for two years to sixteen years and 54/70 for sixteen years to seventy years

The cancer HRL is the concentration of a contaminant in drinking water corresponding to an excess estimated lifetime cancer risk of one-in-a-million ($1x\ 10^{-6}$), calculated as follows:

HRL (µg/L) = Risk Level of 10^{-6} ÷ Age-Adjusted Unit Risk $(\mu g/L)^{-1}$

The six nitrosamines had data available to classify them as known or likely human carcinogens with a mutagenic MOA. Low-dose linear extrapolations and ADAFs were applied to all four of the CCL 3 nitrosamines: NDMA, NDPA, NDEA and NPYR, as well as the two non-CCL 3 nitrosamines, NMEA and NDBA.

The HRL for each nitrosamine was derived from the CSF using the age-adjusted unit risk. Since the nitrosamines were determined to cause cancer by way of a mutagenic MOA, the unit risk is adjusted for the increased risk associated with early life exposures through the application of ADAFs and age-specific exposure factors. The HRL concentration for each nitrosamine is presented in Exhibit 3.2. In some cases, the MRLs of the analytical methods used for UCMR 2 are above the HRL. The available data indicate that each of the six nitrosamines presents a cancer risk with unit risks that span a range of values. Moreover, when multiple nitrosamines from this group are present in finished water together their individual cancer risks are additive (Berger et al., 1987). Therefore, EPA finds that the nitrosamines individually or as a group may have an adverse effect on the health of persons.

Exhibit 3.2: EPA-Derived Cancer Risk Values and HRLs for Six Nitrosamines

Nitrosamines	Studies Used to Establish a Slope Factor	Cancer Slope Factor $(mg/kg\text{-}day)^{-1}$	Age-Adjusted Unit Risk $(\mu g/L)^{-1}$	HRL[1] (µg/L)	HRL[2] (ng/L)
NDBA	Liver and esophageal tumors in rats (Druckrey et al., 1967)	0.4	3.0×10^{-5}	3.0×10^{-2}	30
NDEA	Liver and esophageal tumors in rats (Peto et al., 1991a,b)	30	2.3×10^{-3}	4.0×10^{-4}	0.4
NDMA	Liver tumors in rats (Peto et al., 1991a,b)	21	1.6×10^{-3}	6.0×10^{-4}	0.6

[2] The drinking water intake values were derived from the data in the U.S. EPA's Exposure Factors Handbook (USEPA, 2011).

Nitrosamines	Studies Used to Establish a Slope Factor	Cancer Slope Factor $(mg/kg\text{-}day)^{-1}$	Age-Adjusted Unit Risk $(\mu g/L)^{-1}$	HRL[1] (µg/L)	HRL[2] (ng/L)
NDPA	Liver and esophageal tumors in rats (Druckrey et al., 1967)	2	1.5×10^{-4}	7.0×10^{-3}	7
NMEA	Liver tumors in rats (Druckrey et al., 1967)	4	3.0×10^{-4}	3.0×10^{-3}	3
NPYR	Liver tumors in rats (Peto et al., 1984; Gray et al., 1991)	7	5.3×10^{-4}	2.0×10^{-3}	2

Note: Source: USEPA, 2014a.

1) The cancer HRL is determined by dividing the population risk level of one in a million (1×10^{-6}) by the age-adjusted unit risk.
2) The nitrosamine HRL values were converted to ng/L by multiplying the µg/L values by 1000

4 Analytical Methods

4.1 Introduction

This chapter presents information on analytical methods for detection and quantitation of nitrosamines in drinking water and other aqueous media. The focus is on the six nitrosamines that EPA is evaluating under the third Six-Year Review (SYR3) program: i.e., *N*-nitrosodi-n-butylamine (NDBA), *N*-nitrosodiethylamine (NDEA), *N*-nitrosodimethylamine (NDMA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosomethylethylamine (NMEA), and *N*-nitrosopyrrolidine (NPYR).

Methods capable of detecting nitrosamines in drinking water include one EPA-developed method and two Standard Methods (SM): EPA Method 521, SM 6450B and SM 6450C. All three methods include all six nitrosamines of interest on their list of analytes. Section 4.2 describes EPA Method 521, Version 1.0, *Determination of Nitrosamines in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionization Tandem Mass Spectrometry* (CI-MS/MS) (USEPA, 2004b) and discusses the sensitivity of the method relative to the six nitrosamines' health reference levels (HRLs). EPA Method 521 is the method that was approved for use under the second cycle of the Unregulated Contaminant Monitoring Rule (UCMR 2) to monitor the six nitrosamines. A brief description of SM 6450B and SM 6450C (SM, 2012a, b) is provided in Section 4.3.

Section 4.4 provides a brief overview of other published analytical methods that may be used to quantitate various nitrosamines in aqueous matrices (but not specifically drinking water). Section 4.5 discusses several methods recently used in research, including a method for the analysis of total nitrosamines in disinfected water (Kulshrestha et al., 2010), and methods using various types of liquid chromatography followed by either photolysis and colorimetric determination (Lee et al., 2013) or tandem mass spectrometry (Kadmi et al., 2014).

Exhibit 4.1 shows the analytical methods that can potentially be used for quantitation of each nitrosamine in water.

Exhibit 4.1: Analytical Methods for SYR3 Nitrosamines

Analyte	Included in EPA 521?	Included in SM 6450B and SM 6450C?	Other Analytical Methods for Water Analysis
NDBA	Yes	Yes	EPA 8015C, EPA 8260B w/5031 prep., EPA 8270D
NDEA	Yes	Yes	EPA 8270D
NDMA	Yes	Yes	EPA 1625, EPA 607, EPA 625, EPA 8270D, SM 6410B, USGS O-3118-83
NDPA	Yes	Yes	EPA 1625, EPA 607, EPA 625, EPA 8270D, DOE OM100R, SM 6410B, USGS O-3118-83
NMEA	Yes	Yes	EPA 8270D
NPYR	Yes	Yes	EPA 8270D

Method Citations:
DOE Method OM100R (USDOE, 1997)
EPA Method 8260B (USEPA, 1996b)
EPA Method 5031 (USEPA, 1996c)
EPA Method 1625 (USEPA, 2001a)
EPA Method 607 (USEPA, 2001b)
EPA Method 625 (USEPA, 2001c)
EPA Method 521 (USEPA, 2004b)
EPA Method 8015C (USEPA, 2007a)
EPA Method 8270D (USEPA, 2007b)
SM 6450B/C (SM, 2012a, b)
SM 6410B (SM, 2012c)
USGS Method O-3118-83 (USGS, 1983)

4.2 EPA Method 521

EPA Method 521 relies on solid phase extraction (SPE) followed by capillary column gas chromatography (GC) with large volume injection coupled with chemical ionization tandem mass spectrometry (CI-MS/MS). In EPA Method 521, Version 1.0 (USEPA, 2004b), a 0.5-L water sample containing a known concentration of a surrogate analyte is extracted by passing through a SPE cartridge containing 80-120 mesh coconut charcoal. Contaminants and the surrogate are eluted from the cartridge with methylene chloride. Following drying, concentration and the addition of an internal standard, the components are separated, identified and measured by injection of an aliquot of the extract onto a fused silica capillary column in a GC/MS/MS system equipped with a large-volume injector and operated in chemical ionization mode.

Contaminants are identified by comparing their product ion mass spectra and retention times to reference spectra and retention times obtained through analysis of calibration standards measured under the same conditions as the samples. Analytes and surrogates are quantified by measuring their product ion responses relative to those of the internal standard. The surrogate analyte is added to each water sample to evaluate extraction efficiency, while the internal standard is added to each concentrated extract to evaluate run-to-run and/or day-to-day changes in sensitivity of the GC/MS/MS instrumentation.

To describe how well the method performs, EPA Method 521 reports EPA-determined values for the detection limit (DL) and lowest concentration minimum reporting level (LCMRL). The DL appears in place of the method detection limit (MDL) in the more recent EPA-developed methods. Over time, drinking water compliance methods have migrated away from requiring MDL determinations in favor of confirming minimum reporting levels (MRLs). Various regulatory bodies often still require determination of DLs. As a result, most of the newer

drinking water analytical methods incorporate a DL determination that is defined and conducted exactly like the MDL as described in 40 CFR Part 136, Appendix B.

EPA Method 521 also includes values for the LCMRL for each analyte in the method. The LCMRL is a single-laboratory reporting level and represents a change from how analytical methods have typically presented performance data in the past (in the past, the DL was the focus; in EPA Method 521, the MRL is the focus). The LCMRL is defined as the lowest spiking concentration such that the probability of spike recovery in the 50 percent to 150 percent range is at least 99 percent.

The LCMRL serves as a laboratory- and analyte-specific reporting level. Different analysts using different equipment in different laboratories will not necessarily be able to achieve the LCMRLs that are published in EPA analytical methods; however, EPA's published LCMRLs are an indication that low analyte concentrations can be reliably reported.

In conjunction with the LCMRL, EPA has developed a statistically derived MRL that is determined using raw LCMRL study data and represents an estimate of the lowest concentration of a contaminant that can be reliably measured by members of a group of experienced drinking water laboratories. Note that MRLs are not established in a published analytical method; rather, they are derived from the LCMRLs obtained by laboratories using a specific analytical method in an LCMRL study. Hence, the nitrosamine MRLs defined for laboratories that participated in the analysis of drinking water samples under UCMR 2 are not published as part of EPA Method 521, but they are method-specific (see Section 7.2.1).

Exhibit 4.2 summarizes the DLs, LCMRLs, MRLs, average percent recoveries and percent relative standard deviation (RSD) results for six nitrosamines in EPA Method 521.

Exhibit 4.2: Performance Metrics for Six Nitrosamines in EPA Method 521

Analyte	DL (ng/L)	LCMRL (ng/L)	MRL (ng/L)	Recovery Range[1]	Relative Standard Deviation (RSD) Range[1]
NDBA	0.36	1.4	4	79.7%-104%	2.9%-16%
NDEA	0.26	2.1	5	84.6%-95.6%	6.5%-14%
NDMA	0.28	1.6	2	83.7%-94.7%	3.8%-12%
NDPA	0.32	1.2	7	77.1%-97.0%	3.7%-10.2%
NMEA	0.28	1.5	3	81.4%-91.0%	4.5%-9.6%
NPYR	0.35	1.4	2	85.2%-102%	4.0%-12%

Source: USEPA, 2004b (DL, LCMRL, Recovery Range and RSD Range); USEPA, 2005c (MRL)
Note:
1) Recoveries and RSDs measured in reagent water, and in chlorinated drinking water from three sources: ground water, surface water, and surface water with high total organic carbon levels.

4.2.1 Calculation of EPA Method 521 Nitrosamine MRLs

The procedure EPA used to determine the LCMRLs and MRLs for the nitrosamines in EPA Method 521 was developed during the years 2003-2005 for eventual use in UCMR 2. The procedure was described in EPA's Proposed Rule for UCMR 2 (USEPA, 2005c):

"To determine the MRLs listed in today's action, each laboratory that conducted the primary analytical method development, or second or third laboratory studies, determined LCMRLs as

detailed in the statistical protocol. The mean of these LCMRL values was calculated for each analyte. In cases where data from three or more laboratories were available, three times the standard deviation of the LCMRLs was added to the mean of the LCMRLs, to establish the MRL. In cases where data from two laboratories were available, three times the difference of the LCMRLs was added to the mean of the LCMRLs. In statistical theory (Chebyshev's Inequality), three standard deviations around the mean incorporates the vast majority (at least 88.9 percent) of the data points. In the case where there are only two laboratories, the difference serves as a surrogate for the standard deviation due to the uncertainty in the estimate of the standard deviation with only two data points."

Since the implementation of UCMR 2, the LCMRL and MRL determination procedures have been substantially upgraded by incorporating more rigorous statistics. These new procedures were implemented for UCMR 3. While it may be possible to process the nitrosamine LCMRL data from UCMR 2 development through the revised procedures for LCMRL and MRL determination, it is unlikely that lower values for the LCMRLs or MRLs would be obtained. The low ng/L range may be the practical limit of quantitation for nitrosamines using any analytical method given difficulties differentiating true analyte signals from the instrument baseline and background levels of nitrosamines.

4.2.2 Comparison of EPA Method 521 Performance to HRLs

A key factor in evaluating the performance of an analytical method is the comparison of anticipated reporting levels to concentrations of concern to human health (e.g., HRLs). Reporting levels can be estimated as approximately 5-10 times the MDL or DL, but in the case of EPA Method 521, EPA's single-laboratory reporting level (the LCMRL) and a national reporting level (the MRL) are available. Since the MRL served as a national reporting level for laboratories that analyzed samples for UCMR 2 (USEPA, 2007c), it is the ideal metric for comparison to HRLs.

For each of the six nitrosamines, a method sensitivity ratio (MSR) was calculated to determine whether the available analytical method is capable of reliable quantitation at or below the HRL (see Exhibit 4.3). The MSR is calculated from the following equation:

MSR = HRL (ng/L) / MRL (ng/L)

A favorable MSR is one that is greater than 10. That is, it is preferable that the HRL be at least 10 times greater than the concentration at which data can be reliably reported. This provides a margin of safety for uncertainty in the HRL and/or method performance (see USEPA, 2009). For information on the calculation of HRLs, see Chapter 3.

Exhibit 4.3: Method Sensitivity Ratios (MSRs) for Nitrosamines

Analyte	MRL (ng/L)	HRL (ng/L)	MSR
NDBA	4	30	7.5
NDEA	5	0.4	0.08
NDMA	2	0.6	0.3
NDPA	7	7	1
NMEA	3	3	1
NPYR	2	2	1

The MSRs based on the HRLs are all less than 10. Hence, EPA Method 521 is not capable of quantitation at levels at least 10 times below the HRLs. With an MSR of 7.5, NDBA has the most favorable MSR. For NDPA, NMEA, and NPYR, the MRL is equal to the HRL, leaving no margin for uncertainty in discerning concentrations at the threshold of health concern. For NDEA and NDMA, the MSR is less than one, indicating that reliable quantitation is not possible at the level of the HRL.

4.3 Other Drinking Water Methods

Two additional drinking water methods, SM 6450B and SM 6450C, were identified as applicable to the nitrosamines. Method 6450B is a solid-phase extraction method that uses a granular carbonaceous adsorbent resin. With a 500- to 1000-fold concentration factor, it can achieve MDLs in the range of 0.5 to 2.0 ng/L. Method 6450C is a micro-liquid-liquid extraction method. This method achieves a 200-fold concentration factor, with MDLs in the 2- to 4-ng/L range (SM, 2012a, b).

While contaminant-specific reporting levels are not available for SM 6450B and SM 6450C, comparison of MDLs suggests that they may be comparable to, or slightly higher than, reporting levels for EPA Method 521.

4.4 Other Published Methods for Measurement of Nitrosamines in Aqueous Media

Exhibit 4.4 presents a list of analytical methods that are available for the analysis of nitrosamines in aqueous matrices but are not specifically intended for drinking water. The exhibit also lists performance metrics, when available, including DLs, MDLs, Minimum Levels, Lower Limits of Quantitation and Reporting Levels. For comparison, the DLs and LCMRLs for EPA Method 521 and MDLs for SM 6450B and SM 6450C are also included.

The methods listed in Exhibit 4.4 demonstrate variable coverage of the six nitrosamines. The aqueous methods that are not specified for drinking water analyses are less sensitive than EPA Method 521, SM 6450B and SM 6450C, sometimes by several orders of magnitude.

Exhibit 4.4: Method Performance Metrics for Nitrosamines Using Various Methods Applicable to Aqueous Matrices[1]

Method[2]	Metric[3]	NDBA (ng/L)	NDEA (ng/L)	NDMA (ng/L)	NDPA (ng/L)	NMEA (ng/L)	NPYR (ng/L)
EPA Method 521	DL	0.36	0.26	0.28	0.32	0.28	0.35
EPA Method 521	LCMRL	1.4	2.1	1.6	1.2	1.5	1.4
SM 6450B	MDL	0.71	0.81	0.84	1.08	0.45	0.71
SM 6450C	MDL	2.2	2.5	1.7	2.1	1.7	4.4
EPA 1625	ML	N/A	N/A	50,000	20,000	N/A	N/A
EPA 607	MDL	N/A	N/A	150	460	N/A	N/A
EPA 625	none	N/A	N/A	listed only	listed only	N/A	N/A
EPA 8015C	none	listed only	N/A	N/A	N/A	N/A	N/A
EPA 8260B/5031	MDL	14,000	N/A	N/A	N/A	N/A	N/A
EPA 8270D	LLQ	10,000	20,000	listed only	10,000	listed only	40,000
DOE OM100R	LLQ	N/A	N/A	N/A	5,000	N/A	N/A
SM 6410B	none	N/A	N/A	listed only	listed only	N/A	N/A
USGS O-3118-83	RL	N/A	N/A	5,000	10,000	N/A	N/A

Note:

1) Some published methods do not provide detection or quantitation values for some or all listed analytes. Analytes that are listed in a published method without performance metrics are designated in the exhibit as "listed only"; analytical difficulties may be encountered if using the indicated methods for these analytes. "N/A" = not applicable (the contaminant is not listed in the published method).
2) Method Citations:
   DOE Method OM100R (USDOE, 1997)
   EPA Method 8260B (USEPA, 1996b)
   EPA Method 5031 (USEPA, 1996c)
   EPA Method 1625 (USEPA, 2001a)
   EPA Method 607 (USEPA, 2001b)
   EPA Method 625 (USEPA, 2001c)
   EPA Method 521 (USEPA, 2004b)
   EPA Method 8015C (USEPA, 2007a)
   EPA Method 8270D (USEPA, 2007b)
   SM 6450B/C (SM, 2012a, b)
   SM 6410B (SM, 2012c)
   USGS Method O-3118-83 (USGS, 1983)
3) Detection-based metrics include:
   Detection Limit (DL) Method Detection Limit (MDL)
   Quantitation-based metrics include:
   Minimum Level (ML) Lowest Concentration Minimum Reporting Level (LCMRL)
   Reporting Level (RL) Lower Limit of Quantitation (LLQ)

4.5 Other Methods Used in Research

A method for the determination of total *N*-nitrosamines (TONO) in disinfected water used for swimming pools, as well as the source water used to fill the pools, was described in Kulshrestha et al. (2010). This TONO method is an adaptation and optimization of an assay used for the determination of nitrite, *S*-nitrosothiols and *N*-nitrosamines in biological samples. The goal of the study was to gather data on whether NDMA and other nitrosamines of interest are dominant or minor constituents of the TONO measured. The method is summarized here, and its possible usefulness is discussed.

In this analytical method, disinfected water samples are analyzed for nitrosamines via reduction by aqueous tri-iodide in glacial (i.e., concentrated, anhydrous) acetic acid. The acidic solution reduces nitrosamines to nitric oxide (NO) which is measured by chemiluminescence. Major interferences (i.e., other compounds also reduced to NO) in the reaction may include S-

nitrosothiols and nitrite; these two interferences are eliminated by the sequential addition of mercuric chloride and sulfanilamide, respectively.

Using NDMA as a model nitrosamine, the authors report an MDL of 0.11 µM (8,200 ng/L) and a method reporting limit of 0.3 µM (22,000 ng/L) (Kulshrestha et al., 2010). To improve method sensitivity to approach the ng/L–scale concentrations of NDMA and other nitrosamines anticipated to be found in the subject water samples, a continuous liquid-liquid extraction procedure was employed using ethyl acetate. This allowed for improved extraction of polar nitrosamines (which extract more poorly relative to NDMA and other less polar nitrosamines when using a less polar extraction solvent) and a decreased MDL. The MDL was further decreased by the implementation of a multi-step extraction procedure in which 400 mL of ethyl acetate was used over three extractions and then evaporated and blown down to 1 mL. The resultant MDL for total nitrosamines was 5 ng/L (as NDMA). The results were cross-evaluated by performing duplicate analysis of the samples using EPA Method 521 to identify NDMA concentrations and to establish the predominance of NDMA in the TONO analyses. The authors reported that NDMA represents a range of approximately 3 to 46 percent of the TONO results.

This TONO assay may require further testing and adaptation for establishing the occurrence of nitrosamines in drinking water. It may have applications as a screening tool in the analysis of *N*-nitrosamines.

Other techniques have been proposed recently in the published literature as described below. These techniques may need further testing and adaptation before they could be employed for analysis of nitrosamines in finished drinking water samples.

Lee et al. (2013) photolytically converted nitrosamines to nitrite at UV-254 nm. Nitrite was subsequently converted to a highly colored azo dye via the Griess reaction and detected spectrophotometrically. SPE was used to pre-concentrate nitrosamines in the samples. The SPE was conducted using carbon columns, and extraction efficiencies were 45 to 96 percent. The extracted nitrosamines were then separated by high performance liquid chromatography (HPLC. In a post-column reactor, the nitrosamines were photolyzed to nitrite, which was detected and quantitated using the Griess colorimetric determination. The MDLs with SPE ranged from 5.9 ng/L for NDMA to 27.6 ng/L for NDBA. Note that these MDLs are approximately one order of magnitude greater than MDLs obtained using EPA Method 521.

Kadmi et al., (2014) proposed a method for NMEA that uses SPE followed by HPLC coupled with tandem mass spectrometry (MS/MS). They reported a linear calibration curve from 0.1 to 100 µg/L. The extraction efficiency was 86 percent and the level of quantitation was reported as 0.8 ng/L. Although this single-laboratory value is less than EPA's LCMRL for NMEA of 1.5 ng/L, it is not clear how comparable the level of quantitation is to EPA's LCMRL.

5 Occurrence and Exposure in Drinking Water

5.1 Introduction

Data are available for nitrosamine occurrence in finished drinking water in public water systems (PWSs) from the nationally representative monitoring completed under the Second Unregulated Contaminant Monitoring Rule (UCMR 2). UCMR 2 monitoring included monitoring for all six nitrosamines discussed in this document: *N*-nitrosodi-n-butylamine (NDBA), *N*-nitrosodiethylamine (NDEA), *N*-nitrosodimethylamine (NDMA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosomethylethylamine (NMEA) and *N*-nitrosopyrrolidine (NPYR). EPA consulted other sources as well to gather additional data on the occurrence of the nitrosamines in ambient water and drinking water. These data are presented in Appendix A. On the whole, data from these additional sources support the conclusions reached from the UCMR 2 analyses.

Of the six nitrosamines, NDMA is the only one that had a sufficient number of samples with detections under UCMR 2 to allow for modeled estimates of occurrence and population exposure below the detection limit (DL). Nitrosamines detectable with EPA Method 521 (which include these six nitrosamines, plus *N*-nitrosopiperidine) may constitute only 5-10 percent (as molar percentage) of total nitrosamines in drinking water (Kulshrestha et al., 2010; Dai and Mitch, 2013; Krasner et al., 2013). Krasner et al. (2013) found that NDMA alone may account for about five percent of total nitrosamines in chloraminated waters, where it tends to occur most. As mentioned in Chapter 4 of this document, while some studies have been conducted to quantify total *N*-nitrosamines (TONO) in disinfected water, the analytical methods reported in the literature may require further adaptation before they can be used to establish the occurrence of TONO in drinking water. While occurrence and exposure data for all six nitrosamines are discussed in this chapter, and some indications of national occurrence and co-occurrence are provided for all six, EPA has focused primarily on using the NDMA UCMR 2 data to characterize national occurrence and exposure in detail.

Exhibit 5.1 recaps the health reference levels (HRLs) for each of the six nitrosamines discussed in Chapter 3 and also shows the corresponding UCMR 2 minimum reporting levels (MRLs). (See Section 4.2.1 for background on the derivation of MRLs). As discussed in Chapter 3, HRLs are risk-derived concentrations against which contaminant occurrence data from PWSs can be compared to determine if the contaminant occurs with a frequency and at levels of public health concern. It is important to note that because the HRLs for nitrosamines are based on carcinogenic effects, long-term average concentrations are more relevant than intermittent or short-term peak concentrations for making those comparisons. For four of the six nitrosamines (NDBA, NDPA, NMEA and NPYR), the MRL values in UCMR 2 are equal to or below their corresponding HRLs. For two of the nitrosamines (NDMA and NDEA), however, the MRLs are greater than the corresponding HRL values. Specifically, NDMA has an MRL of 2 ng/L, which is greater than its HRL of 0.6 ng/L, and NDEA has an MRL of 5 ng/L, which is greater than its HRL of 0.4 ng/L. The significance of this is that one cannot directly observe the number of NDMA and NDEA samples with concentrations at or above their respective HRLs.

While it is possible to develop estimates of a contaminant's occurrence below its MRL value using modeling techniques, there must be a substantial number of positive sample results (that is, at or above the MRL value) to support such modeling efforts. Only NDMA had sufficient positive samples in the UCMR 2 occurrence dataset to support this type of modeling.

Exhibit 5.1: HRLs and MRLs for the Six Nitrosamine Compounds

Contaminant	Health Reference Level (HRL), in ng/L	Minimum Reporting Level (MRL), in ng/L
NDBA	30	4
NDEA	0.4	5
NDMA	0.6	2
NDPA	7	7
NMEA	3	3
NPYR	2	2

The remainder of this chapter presents a detailed analysis of information from UCMR 2 on the occurrence of the nitrosamines in drinking water. The following topics are covered:

- Description of the UCMR 2 monitoring program and dataset;
- Occurrence of the nitrosamines, in aggregate and individually, on the basis of simple detections and HRL exceedances (at the level of individual samples and at the level of PWSs);
- Co-occurrence analysis for six nitrosamines in the UCMR 2; and
- Parametric modeling of NDMA mean concentrations, including occurrence below the MRL.

5.2 UCMR 2 Monitoring Program and Dataset

The purpose of EPA's Unregulated Contaminant Monitoring Rules is to collect occurrence data on contaminants that do not have established health-based national standards under the Safe Drinking Water Act but are suspected to be present in drinking water. UCMR 2 monitoring, conducted between January 2008 and December 2010, provided the data for the nitrosamine occurrence analysis presented in this section. This dataset is available from the agency's website (https://www.epa.gov/dwucmr/occurrence-data-unregulated-contaminant-monitoring-rule#2). A more comprehensive discussion of UCMR 2, and results for all contaminants included in the survey, are provided in *Occurrence Data from the Second Unregulated Contaminant Monitoring Regulation (UCMR 2)* (USEPA, 2014b).

The occurrence analyses that are described in this chapter were based on data collected through June 2011 and released in July 2011. A relatively small amount of additional data was received and added to the UCMR 2 dataset after June 2011. The UCMR 2 dataset was not considered "final" until December 2011. The "final" numbers are presented and analyzed in the UCMR 2 Occurrence Document (USEPA, 2014b).

Section 5.2.1 provides a description of data collected for UCMR 2. Section 5.2.2 presents the stratification of UCMR 2 data for the purposes of nitrosamines occurrence analysis, and Section 5.2.3 summarizes the dataset of nitrosamine results.

5.2.1 Description of Data Collected Under UCMR 2

The UCMR 2 involved two types of occurrence monitoring. Selected community water systems (CWSs) and non-transient non-community water systems (NTNCWSs) were required to conduct Assessment Monitoring of 10 chemicals using common laboratory analytical techniques and a Screening Survey of 15 chemicals by means of analytical techniques that are not commonly used in drinking water analysis. The six nitrosamines included in UCMR 2 were part of the Screening Survey and underwent monitoring using EPA Method 521 (described in more detail in Chapter 4). Although other nitrosamines (e.g., *N*-nitrosomorpholine, *N*-nitrosopiperidine) have been identified in finished water (Mitch et al., 2009), they were not included in the UCMR 2 due to limitations of this analytical method. Under the UCMR 2, PWSs were required to collect a sample at each entry point to the distribution system, as well as at the maximum residence time locations within the distribution system associated with each entry point, and to report the disinfectant type in use at these locations while the samples were being taken.

For the Screening Survey component, all CWSs and NTNCWSs serving more than 100,000 people ("very large" systems) and a representative sample of 800 CWSs and NTNCWSs serving 100,000 or fewer people (320 "large" systems serving 10,001 to 100,000 people and 480 "small" systems serving 10,000 or fewer people) were required to participate. Transient non-community water systems (TNCWSs) and any PWSs that purchase all of their water from other PWSs were not required to conduct sampling under UCMR 2. (Note: The population served by these purchasing PWSs is considered in the national occurrence analyses, as discussed below.)

To obtain a nationally representative sample of CWSs and NTNCWSs serving 100,000 or fewer people, EPA statistically categorized (stratified) the PWSs by their source water type (ground or surface water) and by the size of the population served, using data from EPA's Safe Drinking Water Information System (SDWIS). (The SDWIS system source water and population served data used for the analyses is from July 2005, so that these system inventory data are consistent with the approximate timeframe of the UCMR 2 sampling.) The initial stratification by source water type was consistent with SDWIS classification protocol, meaning that PWSs using ground water under the direct influence of surface water (GWUDI) and those using a mix of ground water and surface/GWUDI sources were classified as surface water PWSs. EPA used a different source water type stratification for the nitrosamines analysis, as is explained in Section 5.2.2.

To stratify PWSs by population served, EPA used data representing the total population served by a PWS. Adjustments were made to populations served by systems to include the populations served by PWSs that purchase water (since these systems were not required to conduct UCMR 2 monitoring) and to avoid double counting of populations served by some systems. In cases where one PWS sells water to another PWS (or multiple PWSs), EPA added the population served by each PWS that purchases water to the population served by the PWS that sells water to calculate the total population served as represented by UCMR 2 sampling systems. (The PWS that purchases water was not required to conduct UMCR 2 sampling and the systems that sells water did conduct UCMR 2 sampling.) For example, if PWS A serving 10,000 people also sells water to PWS B serving 20,000 people, the total population served by PWS A, the system that conducted sampling, would be considered 30,000 people. Prior to analyzing UCMR 2 results, EPA also made another adjustment to the population served data to address potential double counting in cases where a PWS purchases water from more than one seller (which was the case for 386 PWSs). If a system purchased water from two or more systems, the population associated

with the purchasing system was equally divided across (added to) the population-served values of the selling systems. This proportionate distribution of purchasing system populations to selling systems was done because data on the relative quantities of water purchased from each seller were not available.

Exhibit 5.2 shows PWS stratification for two source water and six population categories, information on total population served by PWSs in each category based on SDWIS system inventory data and adjusted population served by each category following the correction for double counting. (The SDWIS inventory data are from July 2005 so that systems information is consistent with the dates of UCMR 2 sampling. Some system source water classifications and other systems properties had changed after the systems were selected for UCMR 2 monitoring.) See Exhibit 5.5 for the breakdown of system size, source water classifications, etc., for nitrosamines in the final dataset.

Exhibit 5.2: PWS and Population Stratification for UCMR 2 Screening Survey Monitoring

Source Water Type	Size Category (Population Served)	Number of PWSs[2]	Total Population Served[3]	Adjusted Population Served Corrected for Double Counting[4]
Ground Water	Small (25-500)	80	11,774	11,774
Ground Water	Small (501-3,300)	80	95,960	95,960
Ground Water	Small (3,301-10,000)	80	440,630	440,630
Ground Water	Large (10,001-50,000)	75	1,680,865	1,679,711
Ground Water	Large (50,001-100,000)	76	5,011,923	4,904,473
Ground Water	Very Large (>100,000)	63	17,363,412	17,269,919
Surface Water[1]	Small (25-500)	80	18,507	18,507
Surface Water[1]	Small (501-3,300)	80	149,657	149,494
Surface Water[1]	Small (3,301-10,000)	80	502,109	492,556
Surface Water[1]	Large (10,001-50,000)	85	1,888,542	1,804,026
Surface Water[1]	Large (50,001-100,000)	84	5,922,105	5,640,805
Surface Water[1]	Very Large (>100,000)	335	129,475,277	124,711,765
Totals		**1,198**	**162,560,761**	**157,219,620**

Note:

1) Includes PWSs using GWUDI and PWSs that use a mix of ground water and surface or GWUDI sources.
2) Includes CWSs and NTNCWSs. A minimum of two PWSs are located in each state.
3) Total population used for PWS stratification for UCMR 2. Based on combined retail and wholesale population as reported in SDWIS (July 2005).
4) Total population served after adjustments made for those PWSs that purchase water from more than one seller (386 PWSs).

In coordination with the states, EPA assigned a monitoring schedule to each participating PWS. Surface water PWSs (including GWUDI and mixed PWSs) were required to monitor quarterly (i.e., every three months) over a 12-month period. Ground water PWSs were required to monitor twice (at a five- to seven-month interval) over a 12-month period. As noted previously, monitoring was primarily conducted between January 2008 and December 2010.

Two aspects of the UCMR 2 sampling were unique to the nitrosamines. First, while all UCMR 2 PWSs were required to collect samples at all entry points (EPs) to their distribution systems, the PWSs sampling for nitrosamines were also required to collect samples at maximum residence

(MR) time locations. UCMR 2 also required that the PWSs indicate which MR location(s) was or were associated with each EP location.

The other aspect unique to nitrosamine monitoring under UCMR 2 was the requirement that the PWSs also report the type of disinfection in use at each relevant EP when those samples were collected. (Note that disinfection type at the MR locations was not explicitly reported in UCMR 2, but was inferred from the dataset, as described further in the next section.)

EPA conducted several quality assurance reviews including completeness of the entire UCMR 2 dataset. For more information on quality assurance steps, see the UCMR 2 Occurrence Document (USEPA, 2014b).

5.2.2 Stratification of UCMR 2 Data for Nitrosamine Group Analysis

As described in the previous section, the UCMR 2 included all very large PWSs (serving more than 100,000 people) in the Screening Survey and used a stratification approach for selecting a nationally representative sample of 800 PWSs serving 100,000 or fewer people. The sample of smaller systems was stratified by source water type (ground or surface water) and PWS size (based on five population-served categories), with some additional consideration given to geographic location to ensure minimum representation from each state. To enhance the representativeness of the UCMR 2 for developing national occurrence and exposure estimates, EPA further stratified the results to reflect more specific aspects of source water and disinfection type at the PWS and at EP and MR locations. The approach to those additional stratification aspects is described in this section.

5.2.2.1 Source Water Type

The UCMR 2 required PWSs to report the source water type (surface water, GWUDI or ground water) for each EP location for each sampling event. Also, for each EP location and sampling event, PWSs were required to identify the associated MR locations. EPA used this information to develop a source water classification scheme for PWSs, EP locations and MR locations as shown in Exhibit 5.3. Note that in this further stratification, EPA included a source water category of "mixed" to capture those PWSs, EP locations and MR locations that reported using both ground water and surface water (or GWUDI) sources during the UCMR 2 monitoring period.

Exhibit 5.3: Source Water Type Classification Scheme

Source Water Type Designation	Rules for Assigning the Source Water Type to PWSs	Rules for Assigning the Source Water Type to EP Sites	Rules for Assigning the Source Water Type to MR Sites[1]	Rules for Assigning the Source Water Type to MR Sites (If No Associated EP)[1]
Ground Water	All entry points at the PWS are GW only	The entry point uses GW only	All associated entry points are GW only	Entry points at the PWS are GW only
Surface Water	All entry points at the PWS are SW or GWUDI only	The entry point uses SW and/or GWUDI only	All associated entry points are SW or GWUDI only	Entry points at the PWS are SW or GWUDI only
Mixed	Entry points at the PWS are a mix of GW and SW and/or GWUDI	The entry point uses a mix of GW and SW and/or GWUDI	Associated entry points are a mix of GW and SW and/or GWUDI	Entry points at the PWS are a mix of GW and SW and/or GWUDI

Abbreviations: EP = entry point; GWUDI = ground water under the direct influence of surface water; GW = ground water; MR = maximum residence time location; SW = surface water

Note:

1) For EP sites, PWSs reported associated MR sites. In some cases, MR sites did not have associated EP sites.

5.2.2.2 Disinfection Type

The UCMR 2 required PWSs to report the type of disinfectant in use at the time of sampling for each EP location and associated MR location and for each sampling event. If the PWS did not report a disinfectant type with the sample results, EPA reviewed other data submitted by the PWS and, as appropriate, contacted the PWS to determine the disinfectant in use for all sample results.

For the analysis of the nitrosamine results, EPA developed a stratification scheme involving six categories of disinfectant type, as shown in Exhibit 5.4. The disinfectant of primary interest with respect to nitrosamine formation is chloramine, used either alone or in conjunction with free chlorine or some other disinfectant. The six disinfectant types used for this analysis are: (1) chloramines only, (2) chloramines in combination with another disinfectant, (3) chlorine only, (4) chlorine in combination with another disinfectant other than chloramines, (5) a disinfectant other than chlorine or chloramines and (6) no disinfection. Disinfection is required at systems using surface water. Four small surface water PWSs are listed in the dataset as “ND” (no disinfection); this is presumably due to incorrect self-reporting.

Exhibit 5.4: Disinfectant Classification Scheme

Disinfectant Designation	Rules for Assigning Disinfectant Designation to PWSs	Rules for Assigning Disinfectant Designation to EP Sites	Rules for Assigning Disinfectant Designation to MR Sites[1]	Rules for Assigning Disinfectant Designation to MR Sites (If No Associated EP)[1]
CA Only	All entry points with disinfection use chloramine (some may be ND)	The entry point uses only CA when disinfecting (but may be ND at some times)	At least one associated entry point has CA, none have CL or OT (some may be ND)	All entry points from the PWS have CA, none have CL or OT (some may be ND)
CA with CL/OT	At least one entry point uses CA, one or more others use chlorine or other disinfectants	The entry point uses CA for at least one sampling period, but also uses CL or OT for at least one other sampling period	At least one associated entry point has CA, one or more have CL or OT (and some may be ND)	At least one entry point from the PWS has CA, one or more have CL or OT (and some may be ND)
CL Only	All entry points with disinfection use chlorine (some may be ND)	The entry point uses only CL when disinfecting (but may be ND in some sampling periods)	At least one associated entry point has CL, none have CA or OT (some may be ND)	All entry points from the PWS have CL, none have CA or OT (some may be ND)
CL with OT	At least one entry uses CL and one or more entry points use OT (and some others may be ND)	The entry point uses CL for at least one sampling period, but also uses OT for at least one other sampling period	At least one associated entry point has CL, one or more have OT (and some may be ND)	At least one entry point from the PWS has CL, one or more have OT (and some may be ND)
OT Only	All entry points with disinfection use OT (some may be ND)	The entry point uses OT for at least one sampling period, but never CA or CL (some periods may be ND)	At least one associated entry point has OT, none have CA or CL (some may be ND)	At least one entry point from the PWS has OT, none have CA or CL (some may be ND)
No Disinfection (ND)[2]	All entry points are ND	There is no disinfection at the entry point for any sampling periods	No disinfection at any of the associated entry points for any sampling periods	All entry points from the PWS are ND only

Abbreviations: CL = chlorine; CA = chloramine; OT = all other types of disinfectant (e.g., chlorine dioxide or ozone); EP = entry point; MR = maximum residence time location; ND = no disinfectant

Note:

1) For EP sites, PWSs reported associated MR sites. In some cases, MR sites did not have associated EP sites.
2) Disinfection is required for surface water. Four small surface water PWSs are listed in the dataset as "ND." This is presumably due to incorrect self-reporting.

5.2.3 Summary of UCMR 2 Dataset for Nitrosamines

Exhibit 5.5 presents the total number of PWSs, EP sample locations and MR sample locations in the UCMR 2 dataset for nitrosamines, reflecting the addition of mixed sources to the source water stratification. In summary, the dataset includes monitoring results for 1,198 PWSs, 4,666 EP locations and 2,397 MR locations. Exhibit 5.5 also presents the population served by the UCMR 2 PWSs in the nitrosamine dataset. Note that the PWSs in the UCMR 2 Screening Survey included both CWSs and NTNCWSs. CWSs predominate. Most analyses presented in this chapter use data from both CWSs and NTNCWSs. Modeled national extrapolations on NDMA occurrence, however (presented and described in Section 5.5), apply to CWSs only.

Exhibit 5.5: Summary of UCMR 2 Dataset for Nitrosamines

PWS Size[1]	Source Water Type	Total Number of PWSs	Total Population Served	Total Number of EPs	Total Number of MRs
Small	**All PWSs**	**480**	**1,208,921**	**677**	**503**
Small	Surface Water	222	573,691	232	226
Small	Ground Water	240	548,364	399	238
Small	Mixed Water	18	86,866	46	39
Large	**All PWSs**	**320**	**14,029,015**	**1,124**	**544**
Large	Surface Water	120	5,187,934	153	145
Large	Ground Water	163	7,021,968	770	311
Large	Mixed Water	37	1,819,112	201	88
Very Large	**All PWSs**	**398**	**141,981,684**	**2,865**	**1,350**
Very Large	Surface Water	218	89,237,751	400	367
Very Large	Ground Water	72	18,472,835	1,042	490
Very Large	Mixed Water	108	34,271,098	1,423	493
Totals		**1,198**	**157,219,620**	**4,666**	**2,397**

Note: Dataset includes CWSs and NTNCWSs. Population served based on 2005 SDWIS data.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.6 through Exhibit 5.8 show the number of PWSs, EP locations and MR locations, respectively, in the UCMR 2 nitrosamines dataset, broken out by PWS size, source water type and disinfection type. Most PWSs and sampling locations are classified as using free chlorine only, with the proportion of PWSs using only free chlorine higher in small PWSs compared to large and very large PWSs. Exhibit 5.6 shows that 283 PWSs (approximately 24 percent) in the dataset use chloramines alone or with another disinfectant.

Exhibit 5.6: Number of PWSs in the UCMR 2 Dataset for Nitrosamines by Disinfectant Type

PWS Size[1]	Source Water Type	CA Only: Number of PWSs	CA with CL/OT: Number of PWSs	CL Only: Number of PWSs	CL with OT: Number of PWSs	OT Only: Number of PWSs	ND Only: Number of PWSs
Small	**All PWSs**	**20**	**25**	**378**	**1**	**1**	**55**
Small	Surface Water	14	14	188	1	1	4
Small	Ground Water	3	3	183	0	0	51
Small	Mixed Water	3	8	7	0	0	0
Large	**All PWSs**	**55**	**9**	**240**	**8**	**5**	**3**
Large	Surface Water	30	2	85	1	2	0
Large	Ground Water	21	1	130	5	3	3
Large	Mixed Water	4	6	25	2	0	0
Very Large	**All PWSs**	**129**	**45**	**207**	**13**	**3**	**1**
Very Large	Surface Water	84	17	110	6	1	0
Very Large	Ground Water	17	4	45	4	1	1
Very Large	Mixed Water	28	24	52	3	1	0

PWS Size[1]	Source Water Type	CA Only: Number of PWSs	CA with CL/OT: Number of PWSs	CL Only: Number of PWSs	CL with OT: Number of PWSs	OT Only: Number of PWSs	ND Only: Number of PWSs
Totals		**204**	**79**	**825**	**22**	**9**	**59**

Abbreviations: CA = chloramine; CL = chlorine; OT = all other types of disinfectant (e.g., chlorine dioxide); ND = no disinfectant.
Note: See Section 5.2.2 for assumptions used to classify PWSs by source water and disinfectant type.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.7: Number of Entry Points in the UCMR 2 Nitrosamines Dataset by Disinfectant Type

PWS Size[1]	Source Water Type	CA Only: Number of EPs	CA with CL/OT: Number of EPs	CL Only: Number of EPs	CL with OT: Number of EPs	OT Only: Number of EPs	ND Only: Number of EPs
Small	**All PWSs**	**31**	**27**	**537**	**1**	**1**	**80**
Small	Surface Water	15	14	197	1	1	4
Small	Ground Water	4	5	314	0	0	76
Small	Mixed Water	12	8	26	0	0	0
Large	**All PWSs**	**91**	**12**	**950**	**12**	**8**	**51**
Large	Surface Water	44	2	104	1	2	0
Large	Ground Water	31	1	679	7	6	46
Large	Mixed Water	16	9	167	4	0	5
Very Large	**All PWSs**	**450**	**56**	**2,243**	**25**	**9**	**82**
Very Large	Surface Water	142	25	225	5	3	0
Very Large	Ground Water	68	8	942	12	3	9
Very Large	Mixed Water	240	23	1,076	8	3	73
Totals		**572**	**95**	**3,730**	**38**	**18**	**213**

Abbreviations: CA = chloramine; CL = chlorine; OT = all other types of disinfectant (e.g., chlorine dioxide); ND = no disinfectant.
Note: See Section 5.2.2 for assumptions used to classify PWSs by source water and disinfectant type.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.8: Number of Maximum Residence Time Locations in the UCMR 2 Nitrosamines Dataset by Disinfectant Type

PWS Size[1]	Source Water Type	CA Only: Number of MRs	CA with CL/OT: Number of MRs	CL Only: Number of MRs	CL with OT: Number of MRs	OT Only: Number of MRs	ND Only: Number of MRs
Small	**All PWSs**	**31**	**25**	**428**	**1**	**1**	**17**
Small	Surface Water	15	14	191	1	1	4
Small	Ground Water	4	3	218	0	0	13
Small	Mixed Water	12	8	19	0	0	0
Large	**All PWSs**	**75**	**12**	**438**	**11**	**7**	**1**
Large	Surface Water	39	2	101	1	2	0
Large	Ground Water	28	1	268	8	5	1
Large	Mixed Water	8	9	69	2	0	0
Very Large	**All PWSs**	**288**	**52**	**987**	**14**	**6**	**3**
Very Large	Surface Water	131	19	210	4	3	0
Very Large	Ground Water	32	5	448	3	2	0
Very Large	Mixed Water	125	28	329	7	1	3
Totals		**394**	**89**	**1,853**	**26**	**14**	**21**

Abbreviations: CA = chloramine; CL = chlorine; OT = all other types of disinfectant (e.g., chlorine dioxide); ND = no disinfectant.
Note: See Section 5.2.2 for assumptions used to classify PWSs by source water and disinfectant type.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.9 through Exhibit 5.11 show the number of samples, EP location samples and MR location samples, respectively, for NDMA (as a representative Screening Survey analyte) in the UCMR 2 nitrosamines dataset, broken out by PWS size, source water type and disinfection type. The numbers for other Screening Survey contaminants (including the other nitrosamines) vary only slightly from the NDMA numbers. Most samples are from sampling locations associated with the use of chlorine only.

Exhibit 5.9: Number of Samples in the UCMR 2 Dataset for NDMA by Disinfectant Type

PWS Size[1]	Source Water Type	CA Only: Number of Samples	CA with CL/OT: Number of Samples	CL Only: Number of Samples	CL with OT: Number of Samples	OT Only: Number of Samples	ND Only: Number of Samples
Small	**All PWSs**	**169**	**2,650**	**203**	**8**	**195**	**8**
Small	Surface Water	106	1,503	116	8	28	8
Small	Ground Water	16	1,038	16	0	167	0
Small	Mixed Water	47	109	71	0	0	0
Large	**All PWSs**	**80**	**3,220**	**524**	**60**	**95**	**36**
Large	Surface Water	16	784	322	8	0	16
Large	Ground Water	4	1,826	116	30	86	20

PWS Size[1]	Source Water Type	CA Only: Number of Samples	CA with CL/OT: Number of Samples	CL Only: Number of Samples	CL with OT: Number of Samples	OT Only: Number of Samples	ND Only: Number of Samples
Large	Mixed Water	60	610	86	22	9	0
Very Large	**All PWSs**	**387**	**7,679**	**2,401**	**116**	**164**	**45**
Very Large	Surface Water	175	1,617	1,068	36	0	24
Very Large	Ground Water	28	2,750	204	30	18	9
Very Large	Mixed Water	184	3,312	1,129	50	146	12
Totals		**636**	**13,549**	**3,128**	**184**	**454**	**89**

Abbreviations: CA = chloramine; CL = chlorine; OT = all other types of disinfectant (e.g., chlorine dioxide); ND = no disinfectant.
Note: See Section 5.2.2 for assumptions used to classify sampling locations by source water and disinfectant type. The number and distribution of samples in the dataset vary slightly from contaminant to contaminant. The numbers shown here represent NDMA.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.10: Number of Samples at Entry Points in the UCMR 2 Dataset for NDMA by Disinfectant Type

PWS Size[1]	Source Water Type	CA Only: Number of EP Samples	CA with CL/OT: Number of EP Samples	CL Only: Number of EP Samples	CL with OT: Number of EP Samples	OT Only: Number of EP Samples	ND Only: Number of EP Samples
Small	**All PWSs**	**88**	**1,451**	**102**	**4**	**158**	**4**
Small	Surface Water	54	769	59	4	15	4
Small	Ground Water	10	618	8	0	143	0
Small	Mixed Water	24	64	35	0	0	0
Large	**All PWSs**	**34**	**2,090**	**285**	**32**	**94**	**19**
Large	Surface Water	8	401	170	4	0	8
Large	Ground Water	2	1,300	60	14	85	11
Large	Mixed Water	24	389	55	14	9	0
Very Large	**All PWSs**	**192**	**4,919**	**1,397**	**70**	**158**	**25**
Very Large	Surface Water	99	846	552	20	0	12
Very Large	Ground Water	16	1,863	136	24	18	5
Very Large	Mixed Water	77	2,210	709	26	140	8
Totals		**314**	**8,460**	**1,784**	**106**	**410**	**48**

Abbreviations: CA = chloramine; CL = chlorine; OT = all other types of disinfectant (e.g., chlorine dioxide); ND = no disinfectant.
Note: See Section 5.2.2 for assumptions used to classify sampling locations by source water and disinfectant type.
The number and distribution of samples in the dataset vary slightly from contaminant to contaminant. The numbers shown here represent NDMA.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.11: Number of Samples at Maximum Residence Time Locations in the UCMR 2 Dataset for NDMA by Disinfectant Type

PWS Size[1]	Source Water Type	CA Only: Number of MR Samples	CA with CL/OT: Number of MR Samples	CL Only: Number of MR Samples	CL with OT: Number of MR Samples	OT Only: Number of MR Samples	ND Only: Number of MR Samples
Small	**All PWSs**	**81**	**1,199**	**101**	**4**	**37**	**4**
Small	Surface Water	52	734	57	4	13	4
Small	Ground Water	6	420	8	0	24	0
Small	Mixed Water	23	45	36	0	0	0
Large	**All PWSs**	**46**	**1,130**	**239**	**28**	**1**	**17**
Large	Surface Water	8	383	152	4	0	8
Large	Ground Water	2	526	56	16	1	9
Large	Mixed Water	36	221	31	8	0	0
Very Large	**All PWSs**	**195**	**2,760**	**1,004**	**46**	**6**	**20**
Very Large	Surface Water	76	771	516	16	0	12
Very Large	Ground Water	12	887	68	6	0	4
Very Large	Mixed Water	107	1,102	420	24	6	4
Totals		**322**	**5,089**	**1,344**	**78**	**44**	**41**

Abbreviations: CA = chloramine; CL = chlorine; OT = all other types of disinfectant (e.g., chlorine dioxide); ND = no disinfectant.
Note: See Section 5.2.2 for assumptions used to classify sampling locations by source water and disinfectant type.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

The number and distribution of samples in the dataset vary slightly from contaminant to contaminant. The numbers shown here represent NDMA.

5.3 Summary of UCMR 2 Occurrence Findings for Nitrosamines

A total of 18,040 samples were collected and analyzed for all six nitrosamines at the 1,198 PWSs included in UCMR 2. Of these, 10,792 samples (59.8 percent) were collected from 398 very large PWSs serving more than 100,000 people, 4,015 samples (22.3 percent) from 320 large PWSs serving between 10,001 and 100,000 people, and 3,233 samples (17.9 percent) from 480 small PWSs serving 10,000 people or fewer.

Section 5.3.1, below, provides an overview of detection rates for contaminants in the nitrosamine group. Section 5.3.2 discusses the range of observed concentrations. Section 5.3.3 breaks down the data at the level of the PWS and the sampling location (EP versus MR point in the distribution system). Section 5.3.4 provides an analysis of the estimated populations exposed to contamination at PWSs participating in the UCMR 2 survey.

5.3.1 Rates of Detection

Exhibit 5.12 and Exhibit 5.13 show the detection rates (i.e., the percentage of samples in which a nitrosamine was measured at or above its MRL) for each of these six compounds and for the group as a whole. Results are broken down by PWS size and source water type in Exhibit 5.12 and by disinfectant type in Exhibit 5.13.

Exhibit 5.12: Nitrosamine Detection Rates for UCMR 2 Data by PWS Size and Source Water Type

PWS Size[1]	Source Water Type	All Six Nitrosamines: % Sample Detections	NDBA: % Sample Detections	NDEA: % Sample Detections	NDMA: % Sample Detections	NDPA: % Sample Detections	NMEA: % Sample Detections	NPYR: % Sample Detections
Small	Surface Water	13.8% (245 of 1,769)	0% (0 of 1,769)	0% (0 of 1,769)	13.8% (245 of 1,769)	0% (0 of 1,769)	0.2% (3 of 1,769)	0.6% (11 of 1,769)
Small	Ground Water	1.5% (18 of 1,237)	0.2% (3 of 1,237)	0.1% (1 of 1,237)	1.1% (14 of 1,237)	0% (0 of 1,237)	0% (0 of 1,237)	0% (0 of 1,237)
Small	Mixed Water	35.7% (81 of 227)	0% (0 of 227)	0% (0 of 227)	35.7% (81 of 227)	0% (0 of 227)	0% (0 of 227)	0% (0 of 227)
Large	Surface Water	16.3% (187 of 1,146)	0% (0 of 1,146)	0.1% (1 of 1,146)	16% (183 of 1,146)	0% (0 of 1,146)	0% (0 of 1,146)	0.5% (6 of 1,146)
Large	Ground Water	2.4% (51 of 2,084)	0% (0 of 2,082)	0.1% (3 of 2,070)	2.3% (48 of 2,082)	0% (0 of 2,082)	0% (0 of 2,082)	0% (0 of 2,082)
Large	Mixed Water	16.3% (128 of 787)	0% (0 of 787)	0.6% (5 of 787)	15.5% (122 of 787)	0% (0 of 787)	0% (0 of 787)	0.1% (1 of 787)
Very Large	Surface Water	18.3% (536 of 2,924)	0% (0 of 2,921)	0.4% (11 of 2,923)	17.7% (518 of 2,920)	0% (0 of 2,922)	0% (0 of 2,921)	0.5% (15 of 2,921)
Very Large	Ground Water	2.2% (67 of 3,041)	0.1% (3 of 3,039)	0.2% (7 of 3,041)	1.9% (57 of 3,039)	0% (0 of 3,041)	0% (0 of 3,039)	0.03% (1 of 3,039)
Very Large	Mixed Water	12.3% (594 of 4,838)	0.06% (3 of 4,835)	0.4% (18 of 4,838)	11.9% (573 of 4,833)	0% (0 of 4,838)	0% (0 of 4,835)	0.1% (7 of 4,835)
All	**Surface Water**	**16.6% (968 of 5,839)**	**0% (0 of 5,836)**	**0.2% (12 of 5,838)**	**16.2% (946 of 5,835)**	**0% (0 of 5,837)**	**0.1% (3 of 5,836)**	**0.5% (32 of 5,836)**
All	**Ground Water**	**2.1% (136 of 6,362)**	**0.09% (6 of 6,358)**	**0.2% (11 of 6,348)**	**1.9% (119 of 6,358)**	**0% (0 of 6,360)**	**0% (0 of 6,358)**	**0.02% (1 of 6,358)**
All	**Mixed Water**	**13.7% (803 of 5,852)**	**0.05% (3 of 5,849)**	**0.4% (23 of 5,852)**	**13.3% (776 of 5,847)**	**0% (0 of 5,852)**	**0% (0 of 5,849)**	**0.1% (8 of 5,849)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.13: Nitrosamine Detection Rates for UCMR 2 Data by Disinfectant

Disinfectant	All Six Nitrosamines: % Sample Detections	NDBA: % Sample Detections	NDEA: % Sample Detections	NDMA: % Sample Detections	NDPA: % Sample Detections	NMEA: % Sample Detections	NPYR: % Sample Detections
Any chloramine	34.5% (1,301 of 3,768)	0% (0 of 3,765)	0.3% (11 of 3,767)	34.1% (1,284 of 3,764)	0% (0 of 3,767)	0% (0 of 3,765)	0.7% (25 of 3,765)
Chlorine or other	4.3% (593 of 13,831)	0.07% (9 of 13,824)	0.2% (29 of 13,817)	4.0% (549 of 13,822)	0% (0 of 13,828)	0.02% (3 of 13,824)	0.1% (16 of 13,824)
No disinfection	2.9% (13 of 454)	0% (0 of 454)	1.3% (6 of 454)	1.8% (8 of 454)	0% (0 of 454)	0% (0 of 454)	0% (0 of 454)
All Disinfectant Categories	**10.6% (1,907 of 18,053)**	**0.05% (9 of 18,043)**	**0.3% (46 of 18,038)**	**10.2% (1,841 of 18,040)**	**0% (0 of 49)**	**0.02% (3 of 18,043)**	**0.2% (41 of 18,043)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

Among the six nitrosamines, NDMA was by far the most frequently detected. Across all PWS types, NDMA was detected in 10.2 percent (1,841 of 18,040) of the samples. By comparison, the detection rates for the other five nitrosamines were between 0 percent and 0.3 percent (46 of 18,038). NDMA accounted for most of the 10.6 percent (1,907 of 18,053) of samples reported to have one or more nitrosamine detection.

Exhibit 5.12 shows that the NDMA detection rate was significantly higher in samples from PWSs using surface water (16.2 percent; 946 of 5,835) or mixed water sources (13.3 percent; 776 of 5,847) than in samples from PWSs using ground water only (1.9 percent; 119 of 6,358). This pattern for NDMA of higher frequency of detections in surface water and mixed water PWS samples was similar for all three PWS size categories. (Note that the markedly higher frequency of 35.7 percent [81 of 227] in samples from the small mixed water PWSs may be due to the relatively small number of PWSs, and thus samples, in that category.)

The NDMA data in Exhibit 5.13 show a clear pattern of occurrence associated with the PWS's residual disinfection type. As expected (see Chapter 6), NDMA detection rates are much higher in samples from PWSs using chloramines (34.1 percent; 1,284 of 3,764) than those from PWSs using free chlorine or other disinfectants (4.0 percent; 549 of 13,822) or samples from non-disinfecting PWSs (1.8 percent; 8 of 454). Significantly lower detection rates of NDMA in non-disinfected samples than in disinfected samples indicate that NDMA is formed as a result of disinfection practices, rather than occurring in source water.

Because of the extremely low sample detection rates for the other five nitrosamines, it is not possible to discern patterns as clearly as those seen for NDMA. Caution should be exercised in drawing any conclusions regarding patterns of occurrence in different types of PWSs without additional information, possibly including (though not limited to) information about source water quality, treatment processes and disinfection operations.

5.3.2 Detected Concentrations

Exhibit 5.14 shows for each of the six nitrosamines the minimum, 5th percentile, median, 95th percentile and maximum concentration for the subset of samples with detections at or above the MRL. Exhibit 5.15 and Exhibit 5.16 break these results down by sample location (EP and MR, respectively). The median concentrations of NDEA and NDBA for all samples are higher than the median concentrations of NDMA, NMEA and NPYR; this reflects at least in part the higher MRLs of NDEA and NDBA. Among the nitrosamines, NDEA's 95th percentile concentration is highest (followed by NDMA), and NDMA's maximum concentration is by far the highest (followed by NDEA). Across disinfection types there is not much variation in median concentration values, but the highest concentrations were generally found in chloraminating PWSs.

Exhibit 5.14: Summary of Nitrosamine Concentrations in Samples with Detections at All Sampling Locations, by Disinfectant Type

Disinfectant Type	Summary Statistic	NDBA	NDEA	NDMA	NDPA	NMEA	NPYR
All	***# Detects***	***9***	***46***	***1,841***	***0***	***3***	***41***
All	Min (ng/L)	4	5	2	N/A	3.6	2.1
All	5%tile (ng/L)	4.2	5.2	2.1	N/A	3.7	2.1
All	Median (ng/L)	6.7	7.1	4.1	N/A	4.5	3.9
All	95%tile (ng/L)	16.4	46.8	26.2	N/A	4.9	14.4
All	Max (ng/L)	20.6	100.0	630.0	N/A	4.9	23.8
Any chloramine	***# Detects***	***0***	***11***	***1,284***	***0***	***0***	***25***
Any chloramine	Min (ng/L)	N/A	5.7	2	N/A	N/A	2.1
Any chloramine	5%tile (ng/L)	N/A	5.9	2.1	N/A	N/A	2.1
Any chloramine	Median (ng/L)	N/A	13.0	4.2	N/A	N/A	3.7
Any chloramine	95%tile (ng/L)	N/A	92.5	26.6	N/A	N/A	12.7
Any chloramine	Max (ng/L)	N/A	100.0	630.0	N/A	N/A	17.2
Chlorine or other	***# Detects***	***9***	***29***	***549***	***0***	***3***	***16***
Chlorine or other	Min (ng/L)	4	5	2	N/A	3.6	2.1
Chlorine or other	5%tile (ng/L)	4.2	5.1	2.1	N/A	3.7	2.2
Chlorine or other	Median (ng/L)	6.7	7.0	4.0	N/A	4.5	5.1
Chlorine or other	95%tile (ng/L)	16.4	32.6	26.1	N/A	4.9	13.2
Chlorine or other	Max (ng/L)	20.6	50.0	84.6	N/A	4.9	23.8
No disinfection	***# Detects***	***0***	***6***	***8***	***0***	***0***	***0***
No disinfection	Min (ng/L)	N/A	6	2	N/A	N/A	N/A
No disinfection	5%tile (ng/L)	N/A	6.2	2.1	N/A	N/A	N/A
No disinfection	Median (ng/L)	N/A	6.9	3.4	N/A	N/A	N/A
No disinfection	95%tile (ng/L)	N/A	8.3	7.4	N/A	N/A	N/A
No disinfection	Max (ng/L)	N/A	8.4	8.0	N/A	N/A	N/A

Note: This table shows statistics for samples in the UCMR 2 dataset for nitrosamines with concentrations at or above the MRL only. See Exhibit 5.1 for the MRLs for each nitrosamine.

Exhibit 5.15: Summary of Nitrosamine Concentrations in Samples from EP Locations, with Detections by Disinfectant Type

Disinfectant Type	Summary Statistic	NDBA	NDEA	NDMA	NDPA	NMEA	NPYR
All	***# Detects***	***8***	***28***	***736***	***0***	***0***	***17***
All	Min (ng/L)	4	5	2	N/A	N/A	2.1
All	5%tile (ng/L)	4.1	5.3	2.1	N/A	N/A	2.1
All	Median (ng/L)	6.5	7.0	4.2	N/A	N/A	3.0
All	95%tile (ng/L)	16.9	26.6	27.7	N/A	N/A	7.0
All	Max (ng/L)	20.6	50.0	470.0	N/A	N/A	7.6
Any chloramine	***# Detects***	***0***	***5***	***503***	***0***	***0***	***9***
Any chloramine	Min (ng/L)	N/A	5.7	2	N/A	N/A	2.1
Any chloramine	5%tile (ng/L)	N/A	5.8	2.1	N/A	N/A	2.1
Any chloramine	Median (ng/L)	N/A	6.6	4.6	N/A	N/A	3.0
Any chloramine	95%tile (ng/L)	N/A	27.2	27.9	N/A	N/A	5.8
Any chloramine	Max (ng/L)	N/A	28.0	470.0	N/A	N/A	6.1
Chlorine or other	***# Detects***	***8***	***18***	***227***	***0***	***0***	***8***
Chlorine or other	Min (ng/L)	4	5	2	N/A	N/A	2.2
Chlorine or other	5%tile (ng/L)	4.1	5.3	2.1	N/A	N/A	2.2
Chlorine or other	Median (ng/L)	6.5	7.5	3.6	N/A	N/A	4.5
Chlorine or other	95%tile (ng/L)	16.9	26.2	26.4	N/A	N/A	7.3
Chlorine or other	Max (ng/L)	20.6	50.0	61.7	N/A	N/A	7.6
No disinfection	***# Detects***	***0***	***5***	***6***	***0***	***0***	***0***
No disinfection	Min (ng/L)	N/A	6	2	N/A	N/A	N/A
No disinfection	5%tile (ng/L)	N/A	6.1	2.3	N/A	N/A	N/A
No disinfection	Median (ng/L)	N/A	7.1	3.4	N/A	N/A	N/A
No disinfection	95%tile (ng/L)	N/A	8.3	7.6	N/A	N/A	N/A
No disinfection	Max (ng/L)	N/A	8.4	8.0	N/A	N/A	N/A

Note: This table shows statistics for samples in the UCMR 2 dataset for nitrosamines with concentrations at or above the MRL only. See Exhibit 5.1 for the MRLs for each nitrosamine.

Exhibit 5.16: Summary of Nitrosamine Concentrations in Samples from MR Locations, by Disinfectant Type

Disinfectant Type	Summary Statistic	NDBA	NDEA	NDMA	NDPA	NMEA	NPYR
All	***# Detects***	***1***	***18***	***1,105***	***0***	***3***	***24***
All	Min (ng/L)	9	5	2	N/A	3.6	2.1
All	5%tile (ng/L)	9.3	5.2	2.1	N/A	3.7	2.2
All	Median (ng/L)	9.3	7.6	4.1	N/A	4.5	4.6
All	95%tile (ng/L)	9.3	87.3	25.0	N/A	4.9	16.8
All	Max (ng/L)	9.3	100.0	630.0	N/A	4.9	23.8
Any chloramine	***# Detects***	***0***	***6***	***781***	***0***	***0***	***16***
Any chloramine	Min (ng/L)	N/A	6.0	2	N/A	N/A	2.1
Any chloramine	5%tile (ng/L)	N/A	6.2	2.1	N/A	N/A	2.4
Any chloramine	Median (ng/L)	N/A	23.5	4.1	N/A	N/A	4.3
Any chloramine	95%tile (ng/L)	N/A	96.3	24.0	N/A	N/A	15.1
Any chloramine	Max (ng/L)	N/A	100.0	630.0	N/A	N/A	17.2
Chlorine or other	***# Detects***	***1***	***11***	***322***	***0***	***3***	***8***
Chlorine or other	Min (ng/L)	9	5	2	N/A	3.6	2.1
Chlorine or other	5%tile (ng/L)	9.3	5.1	2.1	N/A	3.7	2.2
Chlorine or other	Median (ng/L)	9.3	7.0	4.2	N/A	4.5	5.2
Chlorine or other	95%tile (ng/L)	9.3	31.5	25.4	N/A	4.9	18.9
Chlorine or other	Max (ng/L)	9.3	37.0	84.6	N/A	4.9	23.8
No disinfection	***# Detects***	***0***	***1***	***2***	***0***	***0***	***0***
No disinfection	Min (ng/L)	N/A	6.6	2	N/A	N/A	N/A
No disinfection	5%tile (ng/L)	N/A	6.6	2.1	N/A	N/A	N/A
No disinfection	Median (ng/L)	N/A	6.6	2.9	N/A	N/A	N/A
No disinfection	95%tile (ng/L)	N/A	6.6	3.7	N/A	N/A	N/A
No disinfection	Max (ng/L)	N/A	6.6	3.8	N/A	N/A	N/A

Note: This table shows statistics for samples in the UCMR 2 dataset for nitrosamines with concentrations at or above the MRL only. See Exhibit 5.1 for the MRLs for each nitrosamine.

Exhibit 5.17 shows the mean concentrations among detections for each nitrosamine. The mean concentrations vary and have a wider range of values than the median concentrations shown in Exhibit 5.14. For example, while the median concentrations of NDEA and NDBA are approximately 7 ng/L (see Exhibit 5.14), the mean concentration of NDEA is significantly higher at 15.3 ng/L, almost twice that of the mean concentration of NDBA, 8.4 ng/L. For NDEA and (to a lesser extent) NDMA, mean concentrations vary considerably across the three disinfection categories presented. Exhibit 5.14 and Exhibit 5.17 together show that NDMA concentrations are significantly higher in samples from disinfecting PWSs than in samples from non-disinfecting PWSs. This observation, along with the higher frequency of detection at disinfecting PWSs (Exhibit 5.13), provides further evidence that NDMA occurs significantly as a byproduct of disinfection. NDEA too has higher mean and maximum concentrations at disinfecting PWSs, though Exhibit 5.13 shows a higher frequency of detection in samples from non-disinfecting

PWSs. NMEA, NDBA and NPYR were not detected at all in samples from non-disinfecting PWSs.

Exhibit 5.17: Mean Nitrosamine Concentrations (in ng/L) in Samples with Detections by Disinfectant Type

Sampling Points	Disinfectant Type	Mean of NDBA	Mean of NDEA	Mean of NDMA	Mean of NDPA	Mean of NMEA	Mean of NPYR
All	**All samples**	**8.4**	**15.3**	**8.8**	**N/A**	**4.3**	**5.2**
All	Any chloramine	N/A	28.7	9.2	N/A	N/A	4.8
All	Chlorine or other	8.4	11.9	8.0	N/A	4.3	5.9
All	No disinfection	N/A	7.2	4.0	N/A	N/A	N/A
EP locations	**All samples**	**8.2**	**11.0**	**8.5**	**N/A**	**N/A**	**3.9**
EP locations	Any chloramine	N/A	14.1	9.2	N/A	N/A	3.3
EP locations	Chlorine or other	8.2	11.1	7.3	N/A	N/A	4.6
EP locations	No disinfection	N/A	7.3	4.3	N/A	N/A	N/A
MR locations	**All samples**	**9.3**	**22.0**	**9.0**	**N/A**	**4.3**	**6.1**
MR locations	Any chloramine	N/A	40.8	9.2	N/A	N/A	5.6
MR locations	Chlorine or other	9.3	13.2	8.6	N/A	4.3	7.2
MR locations	No disinfection	N/A	6.6	2.9	N/A	N/A	N/A

Note: This table shows statistics for samples in the UCMR 2 dataset for nitrosamines with concentrations at or above the MRL only. See Exhibit 5.1 for the MRLs for each nitrosamine.

5.3.3 Sample Location Analysis

The preceding sections presented a sample-level analysis of UCMR 2 results. This section describes the frequency of detection of nitrosamines expressed as a percentage of PWSs, EP locations and MR locations.

Exhibit 5.18 through Exhibit 5.23 show the percentage of PWSs, EP locations and MR locations with detections of nitrosamines at least once during the UCMR 2 sampling period. Results are organized by PWS size, source water type and disinfectant type. It is important to note that the UCMR 2 survey represents a combination of samples and census, and therefore summary statistics from the survey should not be interpreted as a simple surrogate for national occurrence. Modeled national occurrence and exposure estimates based on the UCMR 2 data for NDMA, taking into account appropriate weighting of these results with respect to the national distribution of PWSs with various source water types, sizes and disinfection practice characteristics, are presented in Section 5.5.

All three analyses (for PWSs, EP locations and MR locations) show similar trends, with higher detection rates at surface water and mixed water systems than at ground water systems, and higher detection rates at PWSs using chloramine disinfection than at PWSs with other disinfection practices. For example, Exhibit 5.19 shows that 73.5 percent (208 of 283) of PWSs using chloramines detected NDMA at least once, with only 13.3 percent (114 of 856) of PWSs using other disinfectants detecting NDMA.

Exhibit 5.20, Exhibit 5.21, Exhibit 5.22 and Exhibit 5.23 show that, compared to EPs, MR locations have higher NDMA detection rates for all PWS sizes, source water types and disinfectant types. This observation is especially significant for chloraminating PWSs: 31.2 percent (208 of 667) of chloraminating PWSs detected NDMA at EPs, but 61.9 percent (299 of 483) detected NDMA at MR locations, indicating that formation of NDMA continues in the distribution system. This conclusion is consistent with findings from the literature presented in Chapter 6. In all three analyses, NDBA, NDPA and NMEA are detected at very low levels.

Exhibit 5.18: Percentage of PWSs in the UCMR 2 Dataset Detecting Nitrosamines At Least Once by PWS Size and Source Water Type

PWS Size[1]	Source Water Type	Nitrosamine Group: % PWSs with Detects	NDBA: % PWSs with Detects	NDEA: % PWSs with Detects	NDMA: % PWSs with Detects	NDPA: % PWSs with Detects	NMEA: % PWSs with Detects	NPYR: % PWSs with Detects
Small	Surface Water	27.5% (61 of 222)	0% (0 of 222)	0% (0 of 222)	27.5% (61 of 222)	0% (0 of 222)	1.4% (3 of 222)	1.4% (3 of 222)
Small	Ground Water	5.4% (13 of 240)	0.8% (2 of 240)	0.4% (1 of 240)	4.2% (10 of 240)	0% (0 of 240)	0% (0 of 240)	0% (0 of 240)
Small	Mixed Water	72.2% (13 of 18)	0% (0 of 18)	0% (0 of 18)	72.2% (13 of 18)	0% (0 of 18)	0% (0 of 18)	0% (0 of 18)
Large	Surface Water	36.7% (44 of 120)	0% (0 of 120)	0.8% (1 of 120)	35% (42 of 120)	0% (0 of 120)	0% (0 of 120)	4.2% (5 of 120)
Large	Ground Water	9.2% (15 of 163)	0% (0 of 163)	0.6% (1 of 163)	9.2% (15 of 163)	0% (0 of 163)	0% (0 of 163)	0% (0 of 163)
Large	Mixed Water	43.2% (16 of 37)	0% (0 of 37)	5.4% (2 of 37)	37.8% (14 of 37)	0% (0 of 37)	0% (0 of 37)	2.7% (1 of 37)
Very Large	Surface Water	44.5% (97 of 218)	0% (0 of 218)	2.3% (5 of 218)	42.7% (93 of 218)	0% (0 of 218)	0% (0 of 218)	3.2% (7 of 218)
Very Large	Ground Water	30.6% (22 of 72)	1.4% (1 of 72)	7% (5 of 72)	25% (18 of 72)	0% (0 of 72)	0% (0 of 72)	1.4% (1 of 72)
Very Large	Mixed Water	57.4% (62 of 108)	1.9% (2 of 108)	10.2% (11 of 108)	53.7% (58 of 108)	0% (0 of 108)	0% (0 of 108)	3.7% (4 of 108)
All	**Surface Water**	**36.1% (202 of 560)**	**0% (0 of 560)**	**1.1% (6 of 560)**	**35% (196 of 560)**	**0% (0 of 560)**	**0.5% (3 of 560)**	**2.7% (15 of 560)**
All	**Ground Water**	**10.5% (50 of 475)**	**0.6% (3 of 475)**	**1.5% (7 of 475)**	**9.1% (43 of 475)**	**0% (0 of 475)**	**0% (0 of 475)**	**0.2% (1 of 475)**
All	**Mixed Water**	**55.8% (91 of 163)**	**1.2% (2 of 163)**	**8% (13 of 163)**	**52.2% (85 of 163)**	**0% (0 of 163)**	**0% (0 of 163)**	**3.1% (5 of 163)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.19: Percentage of PWSs in the UCMR 2 Dataset Detecting Nitrosamines At Least Once by Disinfectant Type

Disinfectant	Nitrosamine Group: % PWSs with Detects	NDBA: % PWSs with Detects	NDEA: % PWSs with Detects	NDMA: % PWSs with Detects	NDPA: % PWSs with Detects	NMEA: % PWSs with Detects	NPYR: % PWSs with Detects
Any chloramine	75.3% (213 of 283)	0% (0 of 283)	3.5% (10 of 283)	73.5% (208 of 283)	0% (0 of 283)	0% (0 of 283)	3.5% (10 of 283)
Chlorine or other	15% (128 of 856)	0.6% (5 of 856)	1.9% (16 of 856)	13.3% (114 of 856)	0% (0 of 856)	0.4% (3 of 856)	1.3% (11 of 856)
No disinfection	3.4% (2 of 59)	0% (0 of 59)	0% (0 of 59)	3.4% (2 of 59)	0% (0 of 59)	0% (0 of 59)	0% (0 of 59)
All Disinfectant Categories	**28.6% (343 of 1,198)**	**0.4% (5 of 1,198)**	**2.2% (26 of 1,198)**	**27.0% (324 of 1,198)**	**0% (0 of 1,198)**	**0.3% (3 of 1,198)**	**1.8% (21 of 1,198)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

Exhibit 5.20: Percent of Entry Points in the UCMR 2 Dataset Detecting Nitrosamines At Least Once by PWS Size and Source Water Type

PWS Size[1]	Source Water Type	Nitrosamine Group: % EPs with Detects	NDBA: % EPs with Detects	NDEA: % EPs with Detects	NDMA: % EPs with Detects	NDPA: % EPs with Detects	NMEA: % EPs with Detects	NPYR: % EPs with Detects
Small	Surface Water	19.4% (45 of 232)	0% (0 of 232)	0% (0 of 232)	19.4% (45 of 232)	0% (0 of 232)	0% (0 of 232)	0.9% (2 of 232)
Small	Ground Water	2.3% (9 of 399)	0.8% (3 of 399)	0.3% (1 of 399)	1.3% (5 of 399)	0% (0 of 399)	0% (0 of 399)	0% (0 of 399)
Small	Mixed Water	39.1% (18 of 46)	0% (0 of 46)	0% (0 of 46)	39.1% (18 of 46)	0% (0 of 46)	0% (0 of 46)	0% (0 of 46)
Large	Surface Water	22.2% (34 of 153)	0% (0 of 153)	0% (0 of 153)	20.9% (32 of 153)	0% (0 of 153)	0% (0 of 153)	2.61% (4 of 153)
Large	Ground Water	2.7% (21 of 770)	0% (0 of 770)	0.3% (2 of 770)	2.5% (19 of 770)	0% (0 of 770)	0% (0 of 770)	0% (0 of 770)
Large	Mixed Water	19.4% (39 of 201)	0% (0 of 201)	2% (4 of 201)	17.4% (35 of 201)	0% (0 of 201)	0% (0 of 201)	0% (0 of 201)
Very Large	Surface Water	19.8% (79 of 400)	0% (0 of 400)	1% (4 of 400)	18.3% (73 of 400)	0% (0 of 400)	0% (0 of 400)	1.5% (6 of 400)
Very Large	Ground Water	2.6% (27 of 1,042)	0.2% (2 of 1,042)	0.3% (3 of 1,042)	2.2% (23 of 1,042)	0% (0 of 1,042)	0% (0 of 1,042)	0% (0 of 1,042)
Very Large	Mixed Water	8.9% (126 of 1,424)	0.2% (3 of 1,423)	0.8% (11 of 1,424)	8% (114 of 1,423)	0% (0 of 1,424)	0% (0 of 1,423)	0.2% (3 of 1,423)
All	**Surface Water**	**20.1% (158 of 785)**	**0% (0 of 785)**	**0.5% (4 of 785)**	**19.1% (150 of 785)**	**0% (0 of 785)**	**0% (0 of 785)**	**1.5% (12 of 785)**
All	**Ground Water**	**2.6% (57 of 2,211)**	**0.2% (5 of 2,211)**	**0.3% (6 of 2,211)**	**2.1% (47 of 2,211)**	**0% (0 of 2,211)**	**0% (0 of 2,211)**	**0% (0 of 2,211)**
All	**Mixed Water**	**11% (183 of 1,671)**	**0.2% (3 of 1,670)**	**0.9% (15 of 1,671)**	**10% (167 of 1,670)**	**0% (0 of 1,671)**	**0% (0 of 1,670)**	**0.2% (3 of 1,670)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.21: Percent of Entry Points in the UCMR 2 Dataset Detecting Nitrosamines At Least Once by Disinfectant Type

Disinfectant	Nitrosamine Group: % EPs with Detects	NDBA: % EPs with Detects	NDEA: % EPs with Detects	NDMA: % EPs with Detects	NDPA: % EPs with Detects	NMEA: % EPs with Detects	NPYR: % EPs with Detects
Any chloramine	32.2% (215 of 667)	0% (0 of 667)	0.8% (5 of 667)	31.2% (208 of 667)	0% (0 of 667)	0% (0 of 667)	1.1% (7 of 667)
Chlorine or other	4.5% (172 of 3,787)	0.2% (8 of 3,786)	0.4% (15 of 3,787)	4% (150 of 3,786)	0% (0 of 3,787)	0% (0 of 3,786)	0.2% (8 of 3,786)
No disinfection	5.2% (11 of 213)	0% (0 of 213)	2.4% (5 of 213)	2.8% (6 of 213)	0% (0 of 213)	0% (0 of 213)	0% (0 of 213)
All Disinfectant Categories	**8.5% (398 of 4,667)**	**0.2% (8 of 4,666)**	**0.5% (25 of 4,667)**	**7.8% (364 of 4,666)**	**0% (0 of 4,667)**	**0% (0 of 4,666)**	**0.3% (15 of 4,666)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

Exhibit 5.22: Percent of Maximum Residence Time Locations in the UCMR 2 Dataset Detecting Nitrosamines At Least Once by Size and Source Water Type

PWS Size[1]	Source Water Type	Nitrosamine Group: % MRs with Detects	NDBA: % MRs with Detects	NDEA: % MRs with Detects	NDMA: % MRs with Detects	NDPA: % MRs with Detects	NMEA: % MRs with Detects	NPYR: % MRs with Detects
Small	Surface Water	24.8% (56 of 226)	0% (0 of 226)	0% (0 of 226)	24.8% (56 of 226)	0% (0 of 226)	1.3% (3 of 226)	1.3% (3 of 226)
Small	Ground Water	2.9% (7 of 238)	0% (0 of 238)	0% (0 of 238)	2.9% (7 of 238)	0% (0 of 238)	0% (0 of 238)	0% (0 of 238)
Small	Mixed Water	48.7% (19 of 39)	0% (0 of 39)	0% (0 of 39)	48.7% (19 of 39)	0% (0 of 39)	0% (0 of 39)	0% (0 of 39)
Large	Surface Water	31.7% (46 of 145)	0% (0 of 145)	0.7% (1 of 145)	31% (45 of 145)	0% (0 of 145)	0% (0 of 145)	1.4% (2 of 145)
Large	Ground Water	4.8% (15 of 311)	0% (0 of 311)	0.3% (1 of 311)	4.5% (14 of 311)	0% (0 of 311)	0% (0 of 311)	0% (0 of 311)
Large	Mixed Water	34.1% (30 of 88)	0% (0 of 88)	0% (0 of 88)	33% (29 of 88)	0% (0 of 88)	0% (0 of 88)	1.1% (1 of 88)
Very Large	Surface Water	35.7% (131 of 367)	0% (0 of 367)	1.4% (5 of 367)	34.1% (125 of 367)	0% (0 of 367)	0% (0 of 367)	2.2% (8 of 367)
Very Large	Ground Water	5.7% (28 of 490)	0.2% (1 of 493)	0.8% (4 of 493)	4.5% (22 of 493)	0% (0 of 493)	0% (0 of 493)	0.2% (1 of 493)
Very Large	Mixed Water	30.6% (151 of 493)	0% (0 of 493)	1.2% (6 of 493)	29.2% (144 of 493)	0% (0 of 493)	0% (0 of 493)	0.8% (4 of 493)
All	**Surface Water**	**31.6% (233 of 738)**	**0% (0 of 738)**	**0.8% (6 of 738)**	**30.6% (226 of 738)**	**0% (0 of 738)**	**0.4% (3 of 738)**	**1.8% (13 of 738)**
All	**Ground Water**	**4.8% (50 of 1,039)**	**0.1% (1 of 1,039)**	**0.5% (5 of 1,039)**	**4.1% (43 of 1,039)**	**0% (0 of 1,039)**	**0% (0 of 1,039)**	**0.1% (1 of 1,039)**
All	**Mixed Water**	**32.3% (200 of 620)**	**0% (0 of 620)**	**1% (6 of 620)**	**31% (192 of 620)**	**0% (0 of 620)**	**0% (0 of 620)**	**0.8% (5 of 620)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.23: Percent of Maximum Residence Time Locations in the UCMR 2 Dataset Detecting Nitrosamines At Least Once by Disinfectant

Disinfectant	Nitrosamine Group: % MRs with Detects	NDBA: % MRs with Detects	NDEA: % MRs with Detects	NDMA: % MRs with Detects	NDPA: % MRs with Detects	NMEA: % MRs with Detects	NPYR: % MRs with Detects
Any chloramine	63.4% (306 of 483)	0% (0 of 483)	1.2% (6 of 483)	61.9% (299 of 483)	0% (0 of 483)	0% (0 of 483)	2.3% (11 of 483)
Chlorine or other	9.2% (175 of 1,893)	0.1% (1 of 1,893)	0.5% (10 of 1,893)	8.5% (160 of 1,893)	0% (0 of 1,893)	0.2% (3 of 1,893)	0.4% (8 of 1,893)
No disinfection	9.5% (2 of 21)	0% (0 of 21)	4.8% (1 of 21)	9.52% (2 of 21)	0% (0 of 21)	0% (0 of 21)	0% (0 of 21)
All Disinfectant Categories	**20.2% (483 of 2,397)**	**0.04% (1 of 2,397)**	**0.7% (17 of 2,397)**	**19.2% (461 of 2,397)**	**0% (0 of 2,397)**	**0.1% (3 of 2,397)**	**0.8% (19 of 2,397)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

5.3.4 Population Affected

Exhibit 5.24 through Exhibit 5.29 show the percentage of the population served by PWSs, EP locations and MR locations, respectively, for which at least one detection was reported during the UCMR 2 sampling period. Results are organized by PWS size, source water type and disinfectant type. It is important to note that the UCMR 2 monitoring results represent a combination of sample (statistically representative samples of small and large systems) and census (a census of very large systems), and therefore summary statistics from the survey should not be interpreted as a simple surrogate for national occurrence. Modeled national occurrence and exposure estimates based on the UCMR 2 data for NDMA, taking into account appropriate weighting of these results with respect to the national distribution of PWSs with various source water types, sizes and disinfection practice characteristics, are presented in Section 5.5.

All three analyses (for PWSs, EP locations and MR locations) show similar trends: Rates of nitrosamine exposure are higher for populations served by surface water and mixed water systems than for populations served by ground water systems; rates of exposure are also higher for populations served by systems employing chloramine disinfection than for populations served by systems in other disinfection categories. For example, Exhibit 5.25 shows that 79.1 percent (52 million of 65 million) of the population served by PWSs using chloramines was served by PWS where NDMA was detected at least once, while only 15.0 percent (14 million of 92 million) of the population served by PWSs using other disinfectants was served by PWSs detecting NDMA. Exhibit 5.26 through Exhibit 5.29 show that more people are served by water from MR locations with NDMA detections than are served by water from EP locations with NDMA detections, and that this is true across all PWS sizes, source water types and disinfectant types. This observation is especially significant for populations served by chloraminating PWSs, where 27.4 percent (8.7 million of 32 million) of the population was served by PWSs detecting NDMA at EPs, but 64.4 percent (17 million of 26 million) of the population was served by PWSs that detected NDMA at the MR locations, indicating that formation of NDMA continues in the distribution system. This conclusion is consistent with the literature findings presented in Chapter 6. In all three analyses, the percentage of the population served by PWSs detecting NDBA, NDPA and NMEA was very low.

Exhibit 5.24: Percentage of Population Served by PWSs in the UCMR 2 Dataset Detecting Nitrosamines At Least Once, by PWS Size and Source Water Type

PWS Size[1]	Source Water Type	Nitrosamine Group: % Pop. Served by PWSs with Detects	NDBA: % Pop. Served by PWSs with Detects	NDEA: % Pop. Served by PWSs with Detects	NDMA: % Pop. Served by PWSs with Detects	NDPA: % Pop. Served by PWSs with Detects	NMEA: % Pop. Served by PWSs with Detects	NPYR: % Pop. Served by PWSs with Detects
Small	Surface Water	33.6% (193K of 574K)	0% (0 of 574K)	0% (0 of 574K)	33.6% (193K of 574K)	0% (0 of 574K)	0.8% (4.5K, of 574K)	2.5% (15K of 574K)
Small	Ground Water	8.6% (47K of 548K)	2.6% (14K of 548K)	1.2% (6.6K of 548K)	4.8% (26K of 548K)	0% (0 of 548K)	0% (0 of 548K))	0% (0 of 548K)
Small	Mixed Water	76.8% (68K of 87K)	0% (0 of 87K)	0% (0 of 87K)	76.8% (67K of 87K)	0% (0 of 87K)	0% (0 of 87K)	0% (0 of 87K)
Large	Surface Water	38.1% (2.0M of 5.2M)	0% (0 of 5.2M)	0.3% (14K of 5.2M)	37.1% (2.0M of 5.2M)	0% (0 of 5.2M)	0% (0 of 5.2M)	3.3% (169K of 5.2M)
Large	Ground Water	11.9% (837K of 7M)	0% (0 of 7M)	1.3% (94K of 7M)	11.9% (837K of 7M)	0% (0 of 7M)	0% (0 of 7M)	0% (0 of 7M)
Large	Mixed Water	47.2% (859K of 1.8M)	0% (0 of 1.8M)	7.4% (135K of 1.8M)	42.3% (770K of 1.8M)	0% (0 of 1.8M)	0% (0 of 1.8M)	1.1% (20K of 1.8M)
Very Large	Surface Water	46.6% (42M of 89M)	0% (0 of 89M)	4.6% (4.1M of 89M)	44.3% (40M of 89M)	0% (0 of 89M	0% (0 of 89M	2.6% (2.3 M of 89M)
Very Large	Ground Water	36.02% (6.7M of 19M)	5.7% (1.1M of 19M)	3.6% (669K of 19M)	32.7% (6.1M of 19M)	0% (0 of 18M)	0% (0 of 18M)	0.8% (148K of 19M)
Very Large	Mixed Water	60.6% (21M of 34M)	1.8% (626K of 34M)	18.2% (6.2M of 34M)	46.5% (16M of 34M)	0% (0 of 34M)	0% (0 of 34M)	14% (0 of 34M)
All	**Surface Water**	**46.1% (44M of 95M)**	**0% (0 of 95M)**	**4.3% (4.1M of 95M)**	**43.8% (42M of 95M)**	**0% (0 of 95M)**	**0.005% (4.5K of 95M)**	**2.6% (2.5M of 95M)**
All	**Ground Water**	**29% (7.5M of 26M)**	**4.07% (1.1M of 26M)**	**3% (769K of 26M)**	**26.5% (6.9M of 26M)**	**0% (0 of 26M)**	**0% (0 of 26M)**	**0.6% (148K of 26M)**
All	**Mixed Water**	**59.9% (22M of 36M)**	**1.7% (626K of 36M)**	**17.6% (6.4M of 36M)**	**46.4% (17M of 36M)**	**0% (0 of 36M)**	**0% (0 of 36M)**	**13.3% (4.8M of 36M)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.25: Percentage of Population Served by PWSs in the UCMR 2 Dataset Detecting Nitrosamines At Least Once, by Disinfectant Type

Disinfectant	Nitrosamine Group: % Pop. Served by PWSs with Detects	NDBA: % Pop. Served by PWSs with Detects	NDEA: % Pop. Served by PWSs with Detects	NDMA: % Pop. Served by PWSs with Detects	NDPA: % Pop. Served by PWSs with Detects	NMEA: % Pop. Served by PWSs with Detects	NPYR: % Pop. Served by PWSs with Detects
Any chloramine	80.9% (53M of 65M)	0% (0 of 65M)	6.3% (4.1M of 65M)	79.1% (52M of 65M)	0% (0 of 65M)	0% (0 of 65M)	4% (2.6M of 65M)
Chlorine or other	22.7% (20M of 92M)	1.8% (1.7M of 92M)	7.8% (7.2 M of 92M)	15.0% (14M of 92M)	0% (0 of 92M)	0.005% (4.5K of 92M)	5.3% (4.9M of 92M)
No disinfection	2.7% (8.7K of 318K)	0% (0 of 317K)	0% (0 of 317K)	2.7% (8.7K of 317K)	0% (0 of 317K)	0% (0 of 317K)	0% (0 of 317K)
All Disinfectant Categories	**46.4% (73M of 157M)**	**1.1% (1.7M of 157M)**	**7.1% (11M of 157M)**	**41.5% (65M of 157M)**	**0% (0 of 157M)**	**0.003% (4.5K of 157M)**	**4.7% (7.4M of 157M)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

Exhibit 5.26: Percentage of Population at Entry Points in the UCMR 2 Dataset Detecting Nitrosamines At Least Once, by PWS Size and Source Water Type

PWS Size[1]	Source Water Type	Nitrosamine Group: % Pop. Served at EPs with Detects	NDBA: % Pop. Served at EPs with Detects	NDEA: % Pop. Served at EPs with Detects	NDMA: % Pop. Served at EPs with Detects	NDPA: % Pop. Served at EPs with Detects	NMEA: % Pop. Served at EPs with Detects	NPYR: % Pop. Served at EPs with Detects
Small	Surface Water	25.7% (74K of 289K)	0% (0 of 289K)	0% (0 of 289K)	25.7% (74K of 289K)	0% (0 of 289K)	0% (0 of 289K)	1.4% (3.9K of 289K)
Small	Ground Water	2.7% (9.3K of 340K)	0.7% (2.5K of 340K)	0.2% (822 of 340K)	1.6% (5.9K of 340K)	0% (0 of 340K)	0% (0 of 340K)	0% (0 of 340K)
Small	Mixed Water	41.8% (20K of 49K)	0% (0 of 49K)	0% (0 of 49K)	41.4% (20K of 49K)	0% (0 of 49K)	0% (0 of 49K)	0% (0 of 49K)
Large	Surface Water	25.6% (676K of 2.6M)	0% (0 of 2.6M)	0% (0 of 2.6M)	24.7% (650K of 2.6M)	0% (0 of 2.6M)	0% (0 of 2.6M)	2.9% (77K of 2.6M)
Large	Ground Water	3.6% (168K of 4.7M)	0% (0 of 4.7M)	0.1% (4.5K of 4.7M)	3.5% (163K of 4.7M)	0% (0 of 4.7M)	0% (0 of 4.7M)	0% (0 of 4.7M)
Large	Mixed Water	17.4% (209K of 1.2M)	0% (0 of 1.2M)	1.3% (16K of 1.2M)	16.03% (193K of 1.2M)	0% (0 of 1.2M)	0% (0 of 1.2M)	0% (0 of 1.2M)

PWS Size[1]	Source Water Type	Nitrosamine Group: % Pop. Served at EPs with Detects	NDBA: % Pop. Served at EPs with Detects	NDEA: % Pop. Served at EPs with Detects	NDMA: % Pop. Served at EPs with Detects	NDPA: % Pop. Served at EPs with Detects	NMEA: % Pop. Served at EPs with Detects	NPYR: % Pop. Served at EPs with Detects
Very Large	Surface Water	18.9% (8.8M of 47M)	0% (0 of 47M)	2.1% (957K of 47M)	16.5% (7.7M of 47M)	0% (0 of 47M)	0% (0 of 47M)	0.9% (422K of 47M)
Very Large	Ground Water	3.4% (401K of 12M)	0.04% (4.4K of 12M)	0.7% (78K of 12M)	2.6% (320K of 12M)	0% (0 of 12M)	0% (0 of 12M)	0% (0 of 12M)
Very Large	Mixed Water	12.6% (2.7M of 22M)	0.03% (5.6K of 22M)	1.8% (388K of 22M)	10.6% (2.3M of 22M)	0% (0 of 22M)	0% (0 of 22M)	1.5% (324K of 22M)
All	**Surface Water**	**19.3% (9.6M of 50M)**	**0% (0 of 50M)**	**1.9% (957K of 50M)**	**17% (8.4M of 50M)**	**0% (0 of 50M)**	**0% (0 of 50M)**	**1.01% (503K of 50M)**
All	**Ground Water**	**3.5% (578K of 17M)**	**0.04% (6.9K of 17M)**	**0.5% (83K of 17M)**	**3% (490K of 17M)**	**0% (0 of 17M)**	**0% (0 of 17M)**	**0% (0 of 17M)**
All	**Mixed Water**	**12.9% (2.9M of 23M)**	**0.02% (5.6K of 23M)**	**1.8% (404K of 23M)**	**11% (2.5M of 23M)**	**0% (0 of 23M)**	**0% (0 of 23M)**	**1.4% (324K of 23M)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.27: Percentage of Population at Entry Points in the UCMR 2 Dataset Detecting Nitrosamines At Least Once, by Disinfectant Type

Disinfectant	Nitrosamine Group: % Pop. Served at EPs with Detects	NDBA: % Pop. Served at EPs with Detects	NDEA: % Pop. Served at EPs with Detects	NDMA: % Pop. Served at EPs with Detects	NDPA: % Pop. Served at EPs with Detects	NMEA: % Pop. Served at EPs with Detects	NPYR: % Pop. Served at EPs with Detects
Any chloramine	28.6% (9.1M of 32M)	0% (0 of 32M)	0.5% (146K of 32M)	27.4% (8.7M of 32M)	0% (0 of 32M)	0% (0 of 32M)	0.8% (268K of 32M)
Chlorine or other	7.04% (4M of 56M)	0.02% (13K of 56M)	2.3% (1.3M of 56M)	4.7% (2.7M of 56M)	0% (0 of 56M)	0% (0 of 56M)	1% (560K of 56M)
No disinfection	2.9% (28K of 966K)	0% (0 of 966K)	1.4% (14K of 966K)	1.5% (14K of 966K)	0% (0 of 966K)	0% (0 of 966K)	0% (0 of 966K)
All Disinfectant Categories	**14.7% (13M of 89M)**	**0.01% (13K of 89M)**	**1.6% (1.4M of 89M)**	**12.8% (11M of 89M)**	**0% (0 of 89M)**	**0% (0 of 89M)**	**0.9% (827K of 89M)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

Exhibit 5.28: Percentage of Population at Maximum Residence Time Locations in the UCMR 2 Dataset Detecting Nitrosamines At Least Once, by Size and Source Water Type

PWS Size[1]	Source Water Type	Nitrosamine Group: % Pop. Served at MRs with Detects	NDBA: % Pop. Served at MRs with Detects	NDEA: % Pop. Served at MRs with Detects	NDMA: % Pop. Served at MRs with Detects	NDPA: % Pop. Served at MRs with Detects	NMEA: % Pop. Served at MRs with Detects	NPYR: % Pop. Served at MRs with Detects
Small	Surface Water	29.9% (85K of 285K)	0% (0 of 285K)	0% (0 of 285K)	30% (85K of 285K)	0% (0 of 285K)	0.8% (2.2K of 285K)	2.6% (7.3K of 285K)
Small	Ground Water	2.4% (5K of 209K)	0% (0 of 209K)	0% (0 of 209K)	2.4% (5K of 209K)	0% (0 of 209K)	0% (0 of 209K)	0% (0 of 209K)
Small	Mixed Water	43.9% (17K of 38K)	0% (0 of 38K)	0% (0 of 38K)	43.9% (17K of 38K)	0% (0 of 38K)	0% (0 of 38K)	0% (0 of 38K)
Large	Surface Water	33.9% (864K of 2.6M)	0% (0 of 2.6M)	0.3% (7K of 2.6M)	33.2% (845K of 2.6M)	0% (0 of 2.6M)	0% (0 of 2.6M)	1.02% (26K of 2.6M)
Large	Ground Water	7.5% (178K of 2.4M)	0% (0 of 2.4M)	0.09% (2.2K of 2.4M)	7.4% (176K of 2.4M)	0% (0 of 2.4M)	0% (0 of 2.4M)	0% (0 of 2.4M)
Large	Mixed Water	35.5% (219K of 617K)	0% (0 of 617K)	0% (0 of 617K)	34.6% (214K of 617K)	0% (0 of 617K)	0% (0 of 617K)	0.8% (5K of 617K)
Very Large	Surface Water	37.5% (16M of 43M)	0% (0 of 43M)	3.3% (1.4M of 43M)	34.6% (15M of 43M)	0% (0 of 43M)	0% (0 of 43M)	1.4% (605K of 43M)
Very Large	Ground Water	19% (1.3M of 6.8M)	0.03% (2.2K of 6.8M)	1.06% (72K of 6.8M)	17.2% (1.2M of 6.8M)	0% (0 of 6.8M)	0% (0 of 6.8M)	0.7% (49K of 6.8M)
Very Large	Mixed Water	28.8% (3.7M of 13M)	0% (0 of 13M)	0.5% (59K of 13M)	27.8% (3.6M of 13M)	0% (0 of 13M)	0% (0 of 13M)	0.7% (90Kof 13M)
All	**Surface Water**	**37.2% (17M of 45M)**	**0% (0 of 45M)**	**3.2% (1.4M of 45M)**	**34.5% (16M of 45M)**	**0% (0 of 45M)**	**0% (0 of 45M)**	**1.4% (638K of 45M)**
All	**Ground Water**	**15.7% (1.5M of 9.4M)**	**0.02% (2.2K of 9.4M)**	**0.8% (75K of 9.4M)**	**14.4% (1.4M of 9.4M)**	**0% (0 of 9.4M)**	**0% (0 of 9.4M)**	**0.5% (49K of 9.4M)**
All	**Mixed Water**	**29.2% (3.9M of 14M)**	**0% (0 of 14M)**	**0.4% (59K of 14M)**	**28.2% (3.8M of 14M)**	**0% (0 of 14M)**	**0% (0 of 14M)**	**0.7% (95K of 14M)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.29: Percentage of Population at Maximum Residence Time Locations in the UCMR 2 Dataset Detecting Nitrosamines At Least Once, by Disinfectant Type

Disinfectant	Nitrosamine Group: % Pop. Served at MRs with Detects	NDBA: % Pop. Served at MRs with Detects	NDEA: % Pop. Served at MRs with Detects	NDMA: % Pop. Served at MRs with Detects	NDPA: % Pop. Served at MRs with Detects	NMEA: % Pop. Served at MRs with Detects	NPYR: % Pop. Served at MRs with Detects
Any chloramine	66.2% (17M of 26M)	0% (0 of 26M)	2.4% (634K of 26M)	64.4% (17M of 26M)	0% (0 of 26M)	0% (0 of 26M)	2.2% (569K of 26M)
Chlorine or other	11.7% (5M of 42M)	0.01% (2.2K of 42M)	2.2% (926K of 42M)	9.3% (4M of 42M)	0% (0 of 42M)	0.01% (2.2K of 42M)	0.5% (214K of 42M)
No disinfection	36.03% (5.5K of 15K)	0% (0 of 15K)	18.02% (2.8K of 15K)	36.03% (5.5K of 15K)	0% (0 of 15K)	0% (0 of 15K)	0% (0 of 15K)
All Disinfectant Categories	**32.7% (22M of 68M)**	**0.003% (2.2K of 68M)**	**2.29% (1.6M of 68M)**	**30.5% (21M of 68M)**	**0% (0 of 68M)**	**0.003% (2.2K of 68M)**	**1.15% (780K of 68M)**

Note: See Exhibit 5.1 for the MRLs for each nitrosamine.

5.4 Nitrosamine Co-Occurrence and Aggregate Occurrence in UCMR 2 Sampling

Although NDMA occurs most frequently in finished water among six nitrosamines, the UCMR 2 data also indicate that other nitrosamines can co-occur with NDMA and with each other in PWSs. This section provides an analysis of nitrosamine co-occurrence as well as aggregate occurrence in UCMR 2 monitoring. In this analysis, "co-occurrence" means the detection of two or more analytes (of the six in UCMR 2) at a single PWS during the course of monitoring, not necessarily detection in the same sample. Co-occurrence results should be interpreted with caution since MRLs vary from contaminant to contaminant. "Aggregate occurrence" is the occurrence of any one or more members of the nitrosamine group.

Exhibit 5.30 is a Venn diagram that provides a visual overview of nitrosamine co-occurrence within the UCMR 2 dataset. The diagram shows which nitrosamines co-occur and the number of PWSs at which they occur and co-occur. Of the 343 PWSs with nitrosamine detections, 34 have two or more co-occurring nitrosamines. NDMA co-occurred with every other nitrosamine (except NDPA, which was not detected at all). Two PWSs detected three nitrosamines; in each case, NDMA and NPYR were two of the three. There is only one instance of co-occurrence not involving NDMA: one PWS detected NDEA and NPYR but not NDMA. Overall, the UCMR 2 data show that the nitrosamines have significant co-occurrence, mostly involving NDMA.

Exhibit 5.30: Co-Occurrence Venn Diagram

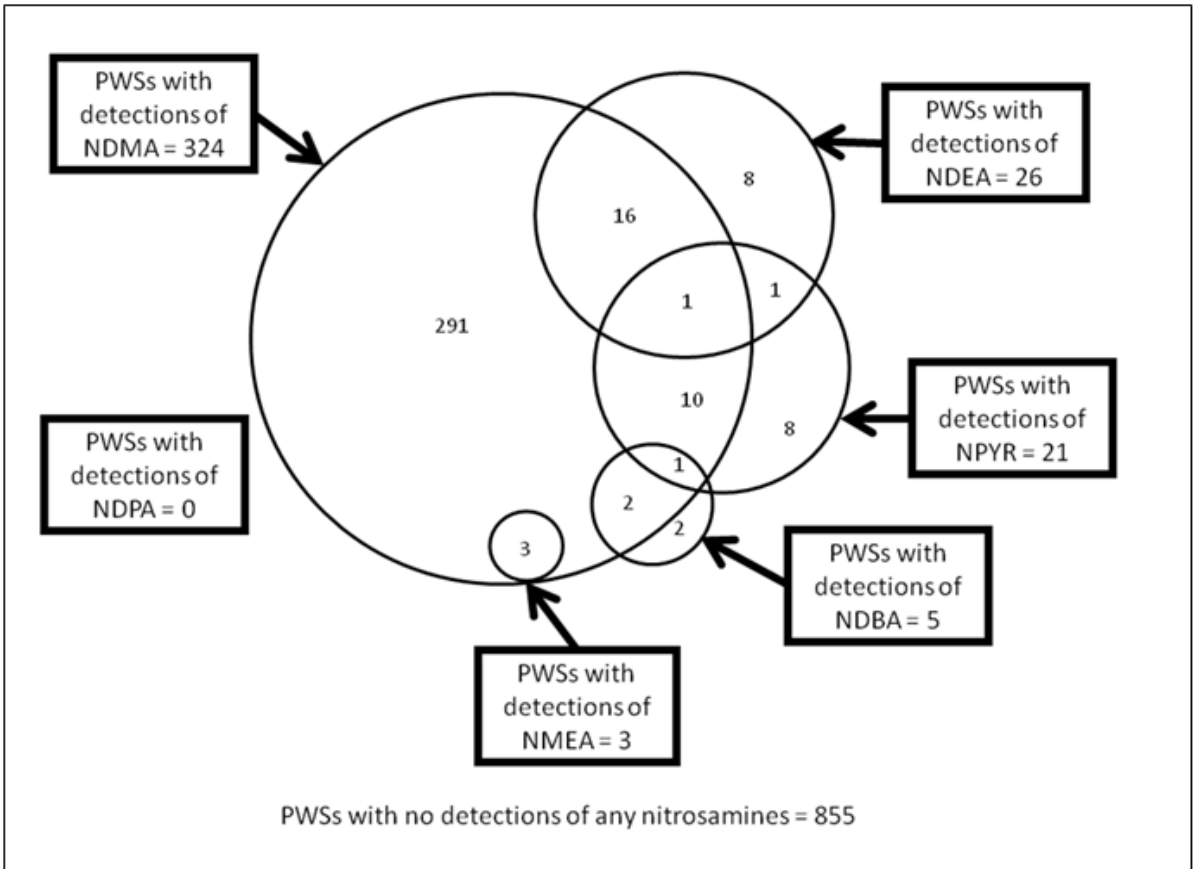


Exhibit 5.31 provides an overview of aggregate occurrence of the nitrosamines. A total of 28.6 percent of PWSs participating in the UCMR 2 Screening Survey, serving 46.4 percent of the customers of participating PWSs, had detections of one or more nitrosamine. The higher percentage for population than for PWSs reflects the generally higher rates of detection at larger PWSs. Ground water PWSs generally had lower rates of detection than surface water and mixed water PWSs. It is important to note that because the UCMR 2 survey represents a combination of samples and census, summary statistics from the survey should not be interpreted as a simple surrogate for national occurrence. Modeled national occurrence and exposure estimates based on the UCMR 2 data for NDMA, taking into account appropriate weighting of these results with respect to the national distribution of PWSs with various source water types, sizes and disinfection practice characteristics, are presented in Section 5.5.

Exhibit 5.31: Aggregate Occurrence of Nitrosamines (UCMR 2 PWSs and Population Exposed)

PWS Size[1]	Source Water Type	UCMR 2 PWSs with At Least One Detection of Any Nitrosamine (Percent)	Population Served by UCMR 2 PWSs with At Least One Detection of Any Nitrosamine (Percent)
Small	**All Types**	**87 (18.1%)**	**306,211 (25.3%)**
Small	Surface Water	61 (27.5%)	192,568 (33.6%)
Small	Ground Water	13 (5.4%)	46,926 (8.6%)
Small	Mixed Water	13 (72.2%)	66,717 (76.8%)
Large	**All Types**	**75 (23.4%)**	**3,673,223 (26.2%)**
Large	Surface Water	44 (36.7%)	1,978,092 (38.1%)
Large	Ground Water	15 (9.2%)	836,633 (11.9%)
Large	Mixed Water	16 (43.2%)	858,499 (47.2%)
Very Large	**All Types**	**181 (45.5%)**	**69,024,919 (48.6%)**
Very Large	Surface Water	97 (44.5%)	41,614,960 (46.6%)
Very Large	Ground Water	22 (30.6%)	6,654,815 (36.0%)
Very Large	Mixed Water	62 (57.4%)	20,755,144 (60.6%)
Total		**343 (28.6%)**	**73,004,353 (46.4%)**

Note: This table presents detection-based analysis of results from participating UCMR 2 systems. Nitrosamines detected under the UCMR 2 are NDBA, NDEA, NDMA, NMEA and NPYR. NDPA was not detected by any PWS. See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.32 shows the significance of NDMA in nitrosamine co-occurrence in the UCMR 2 dataset and presents co-occurrence results by PWS size and source water type. The first two columns show PWSs with detections of NDMA only (count and percentage). These PWSs are the 291 depicted in the non-overlapping portion of the NDMA circle in the Venn diagram above. The second set of columns shows PWSs with detections of other nitrosamines but not NDMA. These are the PWSs that lie in the portions of the NDEA, NPYR and NDBA circles that are outside the NDMA circle in the Venn diagram. The third set of columns shows PWSs that detected NDMA and one or more other nitrosamine. These are the PWSs in the areas of overlap between the NDMA circle and the other four circles in the Venn diagram. The final set of columns shows the aggregate results. The table shows that occurrence rates are higher in surface water and mixed water PWSs than in PWSs served only by ground water within each of the size

categories, and that for both surface water and ground water PWSs, occurrence rates increase with increasing PWS size category.

Exhibit 5.32: Co-Occurrence of NDMA with Other Nitrosamines: UCMR 2 PWSs Affected

PWS Size[1]	Source Water Type	UCMR 2 PWSs with At Least One Detection of NDMA Only (Percent)	UCMR 2 PWSs with At Least One Detection of Other Nitrosamines Only (Percent)	UCMR 2 PWSs with At Least One Detection of NDMA *and* Another Nitrosamine (Percent)	UCMR 2 PWSs with At Least One Detection of Any Nitrosamine (Percent)
Small	**All PWSs**	**78 (16.3%)**	**3 (0.6%)**	**6 (1.3%)**	**87 (18.1%)**
Small	Surface Water	55 (24.8%)	0 (0.0%)	6 (2.7%)	61 (27.5%)
Small	Ground Water	10 (4.2%)	3 (1.3%)	0 (0.0%)	13 (5.4%)
Small	Mixed Water	13 (72.2%)	0 (0.0%)	0 (0.0%)	13 (72.2%)
Large	**All PWSs**	**66 (20.6%)**	**4 (1.3%)**	**5 (1.6%)**	**75 (23.4%)**
Large	Surface Water	39 (32.5%)	2 (1.7%)	3 (2.5%)	44 (36.7%)
Large	Ground Water	14 (8.6%)	0 (0.0%)	1 (0.6%)	15 (9.2%)
Large	Mixed Water	13 (35.1%)	2 (5.4%)	1 (2.7%)	16 (43.2%)
Very Large	**All PWSs**	**147 (36.9%)**	**12 (3.0%)**	**22 (5.5%)**	**181 (45.5%)**
Very Large	Surface Water	85 (39.0%)	4 (1.8%)	8 (3.7%)	97 (44.5%)
Very Large	Ground Water	15 (20.8%)	4 (5.6%)	3 (4.2%)	22 (30.6%)
Very Large	Mixed Water	47 (43.5%)	4 (3.7%)	11 (10.2%)	62 (57.4%)
Total		**291 (24.3%)**	**19 (1.6%)**	**33 (2.8%)**	**343 (28.6%)**

Note: Represents detection-based analysis of results from participating UCMR 2 systems. "Other nitrosamines" detected under the UCMR 2 are NDBA, NDEA, NMEA and NPYR. NDPA was not detected by any PWS. See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.33 presents corresponding information about the population exposed to NDMA only, nitrosamines other than NDMA, and both NDMA and other nitrosamines, at PWSs participating in the UCMR 2 Screening Survey. The information presented in this exhibit is consistent with the trends observed in Exhibit 5.32. The proportion of the population served by PWSs with detections is often higher than the proportion of PWSs with detections because the larger PWSs (those serving larger populations) have more detections.

Exhibit 5.33: Co-Occurrence of NDMA with Other Nitrosamines: UCMR 2 Population Exposed

PWS Size[1]	Source Water Type	Population Served by UCMR 2 PWSs with At Least One Detection of NDMA Only (Percent)	Population Served by UCMR 2 PWSs with At Least One Detection of Other Nitrosamines Only (Percent)	Population Served by UCMR 2 PWSs with At Least One Detection of NDMA *and* Another Nitrosamine (Percent)	Population Served by UCMR 2 PWSs with At Least One Detection of Any Nitrosamine (Percent)
Small	**All PWSs**	**266,292 (22.0%)**	**20,867 (1.7%)**	**19,052 (1.6%)**	**306,211 (25.3%)**
Small	Surface Water	173,516 (30.2%)	0 (0.0%)	19,052 (3.3%)	192,568 (33.6%)

PWS Size[1]	Source Water Type	Population Served by UCMR 2 PWSs with At Least One Detection of NDMA Only (Percent)	Population Served by UCMR 2 PWSs with At Least One Detection of Other Nitrosamines Only (Percent)	Population Served by UCMR 2 PWSs with At Least One Detection of NDMA *and* Another Nitrosamine (Percent)	Population Served by UCMR 2 PWSs with At Least One Detection of Any Nitrosamine (Percent)
Small	Ground Water	26,059 (4.8%)	20,867 (3.8%)	0 (0.0%)	46,926 (8.6%)
Small	Mixed Water	66,717 (76.8%)	0 (0.0%)	0 (0.0%)	66,717 (76.8%)
Large	**All PWSs**	**3,256,392 (23.2%)**	**141,093 (1.0%)**	**275,738 (2.0%)**	**3,673,223 (26.2%)**
Large	Surface Water	1,809,584 (34.9%)	52,137 (1.0%)	116,371 (2.2%)	1,978,092 (38.1%)
Large	Ground Water	742,973 (10.6%)	0 (0.0%)	93,660 (1.3%)	836,633 (11.9%)
Large	Mixed Water	703,836 (38.7%)	88,956 (4.9%)	65,707 (3.6%)	858,499 (47.2%)
Very Large	**All PWSs**	**53,138,701 (37.4%)**	**7,530,629 (5.3%)**	**8,355,589 (5.9%)**	**69,024,919 (48.6%)**
Very Large	Surface Water	35,243,460 (39.5%)	2,109,340 (2.4%)	4,262,160 (4.8%)	41,614,960 (46.6%)
Very Large	Ground Water	4,792,295 (25.9%)	609,237 (3.3%)	1,253,283 (6.8%)	6,654,815 (36.0%)
Very Large	Mixed Water	13,102,946 (38.2%)	4,812,052 (14.0%)	2,840,146 (8.3%)	20,755,144 (60.6%)
Total		**56,661,385 (36.0%)**	**7,692,589 (4.9%)**	**8,650,379 (5.5%)**	**73,004,353 (46.4%)**

Note: Represents detection-based analysis of results from participating UCMR 2 systems. "Other nitrosamines" detected under the UCMR 2 are NDBA, NDEA, NMEA and NPYR. NDPA was not detected by any PWS. See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

As shown in Exhibit 5.30 above, only two PWSs detected more than two nitrosamines during the UCMR 2 Screening Survey. One was a large surface water PWS and the other was a very large mixed water PWS. Together these two PWSs serve 182,540 customers.

EPA also evaluated the UCMR 2 dataset to determine the occurrence of multiple nitrosamines in the same sample. Results show that 18 PWSs (1.5 percent) had at least one sample with exactly 2 nitrosamines present, and 1 PWS (0.1 percent) had at least one sample with exactly 3 nitrosamines present. No PWSs had any samples with more than three nitrosamines present.

Exhibit 5.34 provides some additional summary statistics about nitrosamine co-occurrence in the UCMR 2 dataset. The average frequency of detections of any nitrosamine monitored under UCMR 2 is 5.7 detections per PWS (among those PWSs with detections). NDMA represents the majority (95 percent; 1,841 of 1,940) of detections. There is significant co-occurrence between the nitrosamines. In most cases of co-occurrence at PWSs, NDMA is one of the co-occurring nitrosamines. The third column in Exhibit 5.34 shows that 63.5 percent (33 of 52) of the PWSs that detected any non-NDMA nitrosamine also detected NDMA. The last column shows that 9.9 percent (34 of 343) of PWSs that detected any nitrosamine had co-occurrence of two or more nitrosamines.

Exhibit 5.34: UCMR 2 Co-Occurrence Summary Statistics

Chemical	Average Number of Detections per PWS[1]	Co-Occurrence with NDMA at the PWS Level[2]	Co-Occurrence with Any Other Nitrosamine at the PWS Level[3]
NDBA	1.8 (9/5)	3/5 (60%)	3/5 (60%)
NDEA	1.8 (46/26)	17/26 (65.4%)	18/26 (69.2%)
NDMA	5.7 (1,841/324)	NA	33/324 (10.2%)
NDPA	0	0	0
NMEA	1 (3/3)	3/3 (100%)	3/3 (100%)
NPYR	2 (41/21)	12/21 (57.1%)	13/21 (61.9%)
Any nitrosamine	5.7 (1,940/343)	33/52 (63.5%)	34/343 (9.9%)

Note:
1) The average number of detections per PWS at PWSs with at least one detection. (The number of detections and the number of PWSs are shown in parenthesis.)
2) The number and percent of PWSs with detections that also had NDMA present at any time during the monitoring period.
3) The number and percent of PWSs with detections that had another nitrosamine present at any time during the monitoring period.

5.5 Modeling of NDMA Occurrence

As noted earlier, of the six nitrosamines NDMA is the only one with a sufficient number of positive samples from the UCMR 2 data to support detailed extrapolations of occurrence to the national level. Since the MRL of NDMA (2 ng/L) is substantially lower than the HRL (0.6 ng/L), EPA used modeling methodologies, described below, to develop a more fully rounded picture of NDMA occurrence and estimate national NDMA occurrence and exposure at the HRL along with other thresholds.

Section 5.5.1 summarizes the modeling approach used to develop national occurrence and exposure estimates for NDMA. Sections 5.5.2, 5.5.3 and 5.5.3.3 present the modeled national occurrence and exposure estimates for NDMA, on the basis of detection at a PWS or sampling point, mean concentration at a PWS or sampling point, and locational annual average (LAA) at a sampling point, respectively. Since NDMA is a carcinogen, the mean concentration at a PWS is an appropriate benchmark for evaluating health outcomes based on chronic exposure. EPA modeled the LAA as well as the mean to see how well a hypothetical monitoring regime, similar to that used under the Stage 2 D/DBPRs, would change the estimated number of systems and population with exceedance of a threshold.

5.5.1 Overview of the Modeling Approach for Generating National Occurrence

The modeling approach developed to estimate national occurrence for NDMA was designed to accomplish a number of objectives. The key objectives and how the modeling approach addresses them are as follows:

- *Estimation of occurrence and exposure for NDMA above any specified concentration (threshold) of interest.* The MRL of 2 ng/L for NDMA means that evaluations of occurrence based on the UCMR 2 dataset are limited to observable occurrence at or above that concentration. Describing occurrence and exposure above thresholds of health interest—most notably, the HRL of 0.6 ng/L—requires modeling that uses probability

distributions to characterize estimated occurrence along a continuum of below-MRL concentrations.

- *Estimation of occurrence and exposure for NDMA both on the basis of individual detections exceeding thresholds of interest (based on maximum concentrations, approximating acute exposure) and on the basis of long-term average concentrations exceeding thresholds of interest (based on mean concentrations, approximating chronic exposure).* Detection at concentrations above a given threshold indicates occurrence and exposure, while a long-term average above a given threshold provides a more meaningful indication of the public health risk at PWSs in the case of nitrosamines, because the health end-point, the basis of the HRL, is carcinogenicity. Modeling based on continuous occurrence probability distributions can produce estimates of both of those occurrence measures. To produce these estimates, the expected contaminant concentration is first computed for each sample given what is known about the sampling point where the sample was collected, including the treatment used (if any) at the sampling point at that time. The results of these sample level computations are then appropriately aggregated to the sampling point level and then to the PWS level. In the presentation of results below, the two approaches are labeled as "detection-based modeling" and "mean-based modeling."

- *Estimation of occurrence and exposure for NDMA in a manner that properly reflects the expected influences of source water type, PWS size, PWS type, sample location (i.e., EP or MR) and disinfection practices.* The UCMR 2 dataset indicates that NDMA occurrence at PWSs is influenced by source, size, PWS type, sample location, and disinfection type. To capture these influences in the modeling, EPA estimated occurrence probability distributions separately for EP locations and MR locations and parameterized the distributions using data that were stratified to reflect PWS source and size characteristics. EPA incorporated "fixed effects" into the model to reflect the influence of different PWS types, types of source water (separating strictly ground water from strictly surface water and strictly surface water from mixtures of ground and surface water) and disinfection practices.

- *Characterization of the uncertainty in the estimation of occurrence and exposure for NDMA.* Recognizing that the UCMR 2 dataset has inherent limitations with respect to the proportion of PWSs sampled in the "small" and "large" size categories, the short length of the sampling period (one year), the limited number of samples taken during that year (generally two at each sampling location for ground water systems and four for surface water systems) and others, any national occurrence and exposure estimates derived from those data will necessarily have some uncertainty associated with them. The Bayesian modeling approach, used to obtain the parameters for the occurrence probability distributions, is intended to explicitly reflect the uncertainty in those parameter estimates, and that uncertainty is carried forward in applying those occurrence distributions to making the national estimates. Specifically, estimates produced by the Bayesian modeling approach are presented as a range, the 90 percent credible interval, defined as the range into which there is a 90 percent chance that the actual value falls. There is a 5 percent chance that the actual value is above the highest value in the range, and a 5 percent chance that the actual value is below the lowest value in the range.

The following two subsections present a summary of the key methods and assumptions and describe how these results were used to generate the national estimates reflecting the various source water types, sizes, and disinfection practices at PWSs, EPs and MRs.

5.5.1.1 Generating the Parametric Occurrence Probability Distributions

EPA used a Bayesian methodology to obtain NDMA occurrence parameter estimates. This approach for estimating occurrence parameters has been used previously to support drinking water contaminant occurrence and exposure efforts, including *Cryptosporidium* occurrence analysis for the Long-Term 2 Enhanced Surface Water Treatment Rule, occurrence analyses in support of the first Six-Year Review (SYR) of National Primary Drinking Water Regulations (NPDWRs) (USEPA, 2003) and an analysis of perchlorate occurrence using data from UCMR 1 (USEPA, 2010). The Bayesian modeling conducted for NDMA was based largely on the approach used in the peer-reviewed analysis of perchlorate; however, a number of modifications to the specifics of that approach were necessary to accommodate features of the UCMR 2 dataset specific to NDMA.

The occurrence distributions for NDMA were estimated at the EP and MR sampling point levels. An assumption was made that the log of NDMA concentration is normally distributed at each EP or MR sampling point; that is, observations for multiple samples taken at a given sample point over time would reflect a lognormal distribution of values. A lognormal probability distribution is specified by a parameter *mu* reflecting the central tendency (i.e., mean of log concentration, also known as logmean) and a parameter *sigma* reflecting dispersion (i.e., standard deviation of log concentration) around that central tendency.

The central tendency parameters were estimated to reflect the following observable differences among sampling points:

- Sample point type (EP or MR),
- Size of the PWS in which the sample point is located (i.e., small, large or very large),
- Source water type at that sample point when the sample was collected,
- Disinfectant used at that sample point when the sample was collected, and
- PWS type (i.e., CWS or NTNCWS)

Four types of variance parameters were built into the model (and because EPs were estimated separately from MRs, those four types of variance parameters were estimated separately for EPs and for MRs). The first variance parameter reflects the temporal variability among sample concentrations within a sample point. The other three variance parameters reflect heterogeneity at the sampling point, PWS and strata levels. Specifically, these address the variability between sampling point logmeans within a particular PWS, the variability between PWS logmeans within a stratum and the variability between strata logmeans within the nation.

Each PWS was assigned to one of nine strata. These included the three major PWS size categories (very large, large and small) that were used in the UCMR 2 sampling scheme for

nitrosamines as discussed in Section 5.2.1 and the three PWS source water categories of surface, ground and mixed water as described in Section 5.2.2.

Fixed effects were incorporated into the model to adjust the central tendency results for the sampling locations in the nine strata to account for the following influences:

- Two PWS types (CWS and NTNCWS);
- Six disinfection categories at the sample point (CA only, CA with CL/OT, CL Only, CL with OT, OT Only or ND Only); and
- For the stratum of PWSs designated as mixed source water locations, a fixed effect was incorporated at the sampling point level to reflect whether that specific location was a ground water, surface water or mixed water location.

Note that for NDMA occurrence modeling results presented in this document, the PWS type was set to CWS only. EPA decided to focus exclusively on CWSs because there were too few NTNCWSs in the UCMR 2 dataset for an NTNCWS-focused analysis. In addition, because NTNCWSs do not have distribution systems like CWSs do, it was determined that NTNCWS results could not simply be extrapolated from CWS data.

The Bayesian estimation process begins with a description of the uncertainty on each parameter's value, prior to observing the UCMR 2 data, with a statistical distribution. In this case, the prior distributions used are "flat" (i.e., uninformative, capturing the complete uncertainty that is implicitly assumed in classical statistical methods). The estimation process then updates those priors with the information learned about the parameters from the UCMR 2 data to produce posterior distributions of uncertainty over the parameters' values. The technical implementation of this estimation process uses Markov Chain Monte Carlo, which generates a sequence of random draws that converge to the joint posterior distribution. Each drawn set of parameters, or "realization," represents a consistent estimate, with the central clustering of those realizations representing the best estimate and dispersion around that central cluster representing the uncertainty in that best estimate.

5.5.1.2 Generating the National Occurrence Estimates from the Probability Distributions

For generating the NDMA national occurrence and exposure estimates, the Bayesian process generated over 500 realizations (exactly 534 realizations) of occurrence probability distributions for each of the 4,666 EP and 2,397 MR locations. Each of those 534 distributions at a given location reflects central tendency and temporal variability among samples taken at those locations that is consistent with the observations in UCMR 2. The differences among those 534 realizations for each location reflect the uncertainty in the estimate of the central tendency and temporal variability parameter estimates.

To address concerns that 534 realizations of the occurrence probability distribution might not be enough, the model was later run again with 1,000 realizations, as discussed below in the subsection on "Model Validation." The results (central tendencies and 90 percent credible intervals) from the second effort were substantially the same as the initial results presented in this report.

Although the UCMR 2 dataset includes all of the very large PWSs serving more than 100,000 people, it included only a sample of the PWSs serving 100,000 or fewer people. It was, therefore, necessary to "scale up" the UCMR 2 results from that sample to the national level to obtain the overall national occurrence and exposure estimates.

To accomplish this, the following basic assumptions were used:

- To maintain consistency with the UCMR 2 census of very large PWSs, EPA used the 2005 SDWIS inventory as the basis for the total number of PWSs and population served by those PWSs for the small and large PWSs using surface water or ground water. (The 2005 SDWIS data served as the basis for identifying and selecting PWSs for UCMR 2).

- Because SDWIS classifies mixed PWSs as surface water PWSs, EPA used information from the 2006 Community Water Systems Survey (CWSS) to estimate the number of PWSs nationally in the small and large size groups that are purely surface water and the number that are mixed water PWSs.

- Although UCMR 2 required PWSs to report information on the type of disinfection used at the sampling locations when the NDMA samples were taken, the selection of the sample of 800 PWSs for the small and large size PWSs was not specifically designed to be nationally representative of those disinfection practices among these PWSs. In the absence of information to the contrary, EPA assumed that the proportion of UCMR 2 PWSs and sampling locations reporting the various types of disinfection was a reasonable approximation of the proportion using those disinfection methods nationally. A comparison with data from the 2006 CWSS for the two major types of practices—chlorination and chloramination—showed similar proportions.

- EPA also assumed that the numbers of EPs and MRs per PWS for the small and large PWSs in the UCMR 2 dataset were representative of those fractions nationally, and again a comparison with the 2006 CWSS data indicated that assumption to be reasonable.

- Lastly, because no data are available on the proximity of sampling locations to customers' taps, it was assumed, for this analysis, that each sampling location was equally representative of water delivered to customers. Customers were assigned in equal measure to each sampling location. For example, if a PWS had two EPs and one MR, one-third of its population was assigned to each EP and one-third to the MR.

Using the occurrence distributions at EP and MR locations from the modeling described above, EPA obtained occurrence and exposure estimates for the census of very large PWSs in UCMR 2 and combined these with the estimates for the small and large UCMR 2 PWSs that were "scaled up" to the national level using the above assumptions. The estimates for the various categories of PWSs in the various strata were combined to obtain the overall estimates of national occurrence and exposure.

Three forms of national occurrence and exposure estimates were generated and are presented in the sections that follow:

- One or more detections at PWSs, EPs and MRs exceeding various thresholds;

- PWS, EP and MR mean concentrations exceeding various thresholds; and
- PWS LAAs exceeding various thresholds

The national estimates of occurrence and exposure for the above measures are presented as the percentage of PWSs and associated populations exceeding each of three "threshold" concentrations of interest:

- 0.6 ng/L (the HRL and 10^{-6} cancer risk value),
- 2 ng/L (the MRL), and
- 6 ng/L (the 10^{-5} cancer risk value)

In the tables presenting the results, the column labeled "mean" reflects the central estimate within the full range of uncertainty reflected by the 534 realizations of occurrence distributions as described above, and these are accompanied by the lower and upper 90 percent credible intervals for those estimates, capturing the uncertainty around the mean or central estimates.

Note that the percentages exceeding the 2 ng/L MRL in the national estimates shown below will differ from those shown previously for the UCMR 2 dataset alone. For example, Exhibit 5.19 indicates that 27 percent of PWSs in the UCMR 2 Screening Survey detected NDMA in one or more samples. However, in Exhibit 5.39, based on the modeling and the "scaling up" of UCMR 2 results to the national level, only 10.3 percent of all PWSs nationally are expected to have NDMA present in one or more samples above the MRL value of 2 ng/L (assuming that the number of samples taken per system is similar to that taken in UCMR 2). This divergence is not unexpected. It reflects the fact that UCMR 2 included a census of larger systems, which had higher occurrence rates, and only a statistical sample of smaller systems, which had lower occurrence rates. Because there are many more small systems nationally than were included in the sample, the extrapolated national occurrence of NDMA would be expected to be much lower than the simple aggregate of UCMR 2 observations.

5.5.1.3 Model Validation

Model validation efforts included the following:

- Using the model to reproduce results from the analysis of UCMR 2 PWSs with one or more detections presented above (Section 5.3.3). A comparison of the output of the model with UCMR 2 observed findings is presented in Appendix B. The comparison of the modeled results and the observed results for one or more detections above various thresholds showed a high degree of concordance in the aggregate and for specific subsets of systems, based on size, source and disinfection practice.
- Running the model again, with 1,000 iterations rather than 534. The output values (mean and 90 percent credible interval values for national occurrence and exposure) for the larger number of iterations did not differ significantly from those obtained with fewer iterations.

5.5.2 National Occurrence and Exposure Estimates: One or More Detections

As described in the previous section, EPA used modeling to estimate the percentage of sampling locations and PWSs with one or more detections of NDMA exceeding a given threshold value, along with the associated population served by those locations and PWSs. Results are presented first for EP and MR locations, then for PWSs as a whole.

5.5.2.1 Entry Points and Maximum Residence Locations

Exhibit 5.35 and Exhibit 5.36 summarize results of the detection-based modeling analysis for EP and MR locations, respectively. They show the mean expected values and the 90 percent credible intervals for 3 size categories and for 3 threshold values for NDMA: 0.6 ng/L (the HRL), 2 ng/L (the MRL) and 6 ng/L. See Appendix C for results for other thresholds and for predictions of the total population exposed (extrapolated from the UCMR 2 population). The analysis based on EPs gives lower bound estimates of exposure based on NDMA concentrations in drinking water leaving the treatment plant. The analysis based on MRs gives estimates of higher exposure, as the highest concentrations of NDMA would be expected at the MR time location, since NDMA forms over time.

Exhibit 5.35: Percentage of Entry Points Predicted To Have One or More Detections Exceeding the Threshold and the Associated Population Exposed

PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	Percentage of EPs Predicted To Have Any Detections Exceeding Threshold: Expected Value (90% CI)	Percentage of Population Served by EPs Predicted To Have Any Detections Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	11.0% (7.0% - 16.1%)	16.5% (10.8% - 23.4%)
Small	41,962	41,154,840	2	4.0% (2.7% - 5.6%)	6.8% (4.5% - 9.9%)
Small	41,962	41,154,840	6	1.5% (1.1% - 2.1%)	2.5% (1.7% - 3.8%)
Large	2,812	84,318,927	0.6	20.6% (16.2% - 25.9%)	25.0% (19.3% - 31.9%)
Large	2,812	84,318,927	2	9.0% (7.3% - 11.0%)	11.5% (9.2% - 14.6%)
Large	2,812	84,318,927	6	3.1% (2.3% - 4.0%)	4.6% (3.5% - 5.8%)
Very Large	394	141,407,211	0.6	21.0% (17.6% - 24.9%)	31.4% (25.0% - 39.5%)
Very Large	394	141,407,211	2	7.7% (6.7% - 8.9%)	13.5% (11.2% - 16.5%)
Very Large	394	141,407,211	6	2.6% (2.2% - 3.0%)	4.9% (4.1% - 5.9%)
All	45,168	266,880,978	0.6	12.7% (8.6% - 17.7%)	26.8% (20.8% - 34.3%)
All	45,168	266,880,978	2	4.8% (3.5% - 6.5%)	11.7% (9.5% - 14.8%)
All	45,168	266,880,978	6	1.8% (1.3% - 2.4%)	4.4% (3.5% - 5.5%)

Source: Appendix C.
Abbreviation: CI = credible interval; EP = entry point
Note: Result of detection-based modeling of NDMA occurrence. Assumes that the number of samples taken per PWS is comparable to the number taken for UCMR 2 sampling.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.36: Percentage of Maximum Residence Time Locations Predicted To Have One or More Detections Exceeding the Threshold and the Associated Population Exposed

PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	Percentage of MRs Predicted To Have Any Detections Exceeding Threshold: Expected Value (90% CI)	Percentage of Population Served by MRs Predicted To Have Any Detections Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	20.7% (13.8% - 28.5%)	27.9% (19.7% - 36.8%)
Small	41,962	41,154,840	2	6.4% (4.5% - 9.0%)	11.0% (8.1% - 15.1%)
Small	41,962	41,154,840	6	2.1% (1.5% - 2.9%)	4.3% (3.2% - 5.8%)
Large	2,812	84,318,927	0.6	40.9% (33.4% - 49.0%)	45.3% (36.7% - 54.8%)
Large	2,812	84,318,927	2	18.9% (15.7% - 22.8%)	22.8% (19.2% - 27.5%)
Large	2,812	84,318,927	6	7.3% (5.8% - 8.9%)	10.3% (8.3% - 12.6%)
Very Large	394	141,407,211	0.6	42.9% (37.6% - 48.8%)	55.6% (47.6% - 64.4%)
Very Large	394	141,407,211	2	21.8% (19.9% - 24.2%)	31.9% (28.3% - 36.7%)
Very Large	394	141,407,211	6	9.2% (8.2% - 10.2%)	13.0% (11.1% - 15.2%)
All	45,168	266,880,978	0.6	23.4% (16.5% - 31.2%)	48.7% (40.6% - 57.8%)
All	45,168	266,880,978	2	8.1% (6.1% - 10.8%)	26.3% (22.9% - 31.0 %)
All	45,168	266,880,978	6	2.9% (2.1% - 3.7%)	11.0% (9.2% - 13.1%)

Source: Appendix C.
Abbreviation: CI = credible interval; MR = maximum residence time location
Note: This exhibit shows the results of detection-based modeling of NDMA occurrence. It is assumed that the number of samples taken per PWS is comparable to the number taken for UCMR 2 sampling.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

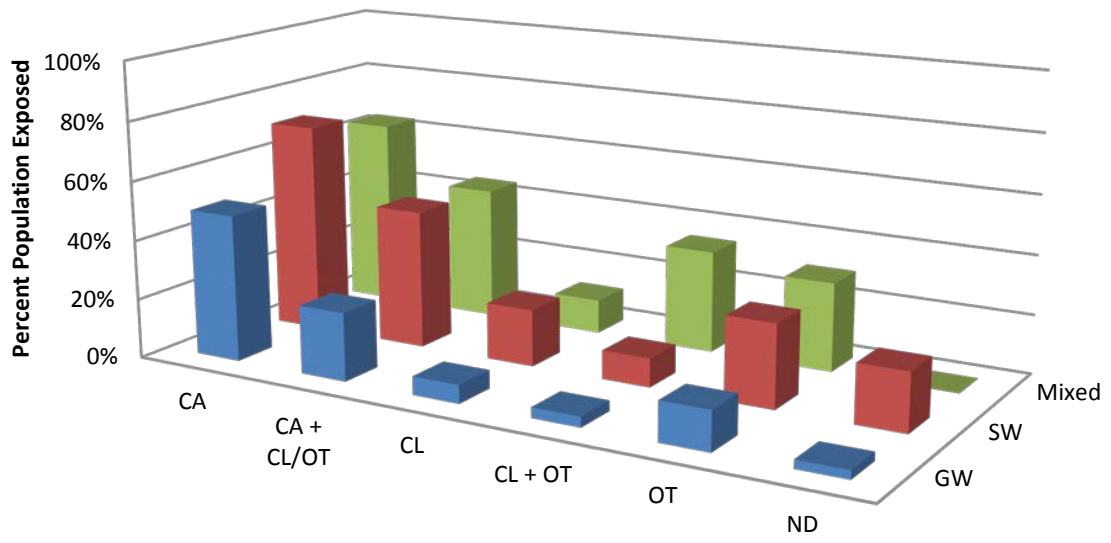
Exhibit 5.35 shows that between 8.6 and 17.7 percent of EPs are predicted to exceed the HRL (0.6 ng/L) at least once. Results are slightly higher for very large PWSs compared to large and small PWSs, although the difference is small compared to the confidence bounds. The associated percentage of the population served by EP locations predicted to exceed the HRL at least once is between 21.8 and 34.3 percent. The percentage of population served is higher than the percentage of EPs because UCMR 2 detections are somewhat higher in the larger PWSs (with more customers served) within each size category.

As expected for a disinfection byproduct, the percentage of locations with one or more detections is greater for MR than for EP locations. As shown in Exhibit 5.36, between 16.5 and 31.2 percent of MR locations are expected to exceed the HRL (0.6 ng/L) at least once. Very large PWSs exhibit higher predicted detection rates than the large or small PWSs, which is expected due to their larger distribution systems and thus, potentially higher MR times.

Exhibit 5.37 and Exhibit 5.38 compare the predicted percentage of population exposed to at least one sample with an NDMA concentration greater than the HRL at EPs and MRs, respectively, for each combination of source water and disinfectant type. As is consistent with the literature

and proposed formation mechanisms discussed in Chapter 6, predictions are greater for chloramines than for other disinfectant types. For EP sites, the percentage of the population exposed is approximately three times greater for PWSs using chloramines than other disinfectants. The percentage of population exposed is also generally greater for surface water and mixed water PWSs than for ground water PWSs.

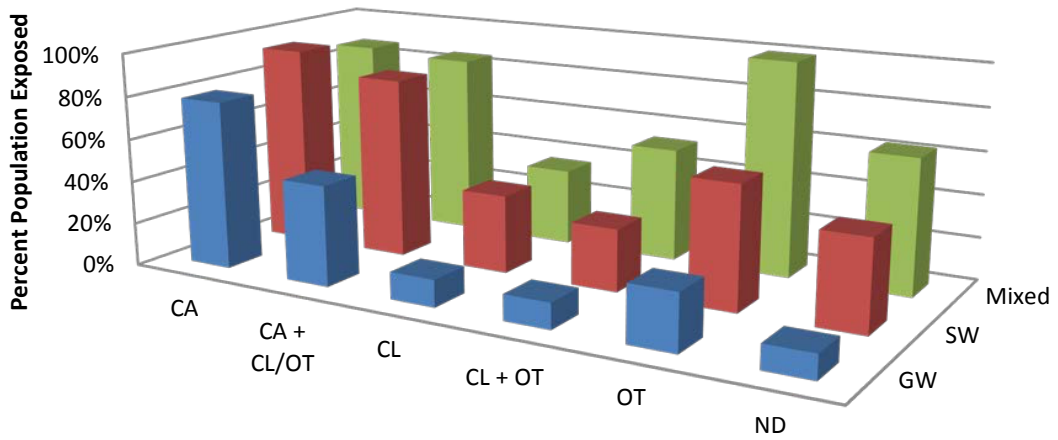
Exhibit 5.37: Percentage of the Population Predicted To Be Exposed to One or More Detections at Levels Above the HRL (0.6 ng/L) at Entry Points



	CA	CA + CL/OT	CL	CL + OT	OT	ND
GW	49.4%	22.9%	6.2%	3.5%	13.3%	2.9%
SW	70.9%	46.6%	19.1%	9.6%	28.0%	19.7%
Mixed	63.9%	45.0%	11.5%	34.4%	29.9%	0.0%

Source: Appendix C.
Abbreviations: HRL = health reference level; CA = chloramines; CL = chlorine; ND = no disinfectant; OT = other.
Note: This exhibit shows the results of detection-based modeling of NDMA occurrence.

Exhibit 5.38: Percentage of the Population Predicted To Be Exposed to One or More Detections at Levels Above the HRL (0.6 ng/L) at Maximum Residence Time Locations



	CA	CA + CL/OT	CL	CL + OT	OT	ND
GW	78.4%	46.6%	12.5%	11.9%	26.2%	11.1%
SW	93.4%	84.3%	36.4%	28.9%	57.0%	42.2%
Mixed	87.1%	85.0%	35.8%	52.9%	99.7%	63.0%

Source: Appendix C.
Abbreviations: HRL = health reference level; CA = chloramines; CL = chlorine; ND = no disinfectant; OT = other.
Note: This exhibit shows the results of detection-based modeling of NDMA occurrence.

5.5.2.2 PWSs

EPA also used modeling to predict the percentage of PWSs with at least one NDMA detection at levels above various thresholds. The analysis aggregates results from all sampling locations within the PWS—in other words, if one sampling location has a detection but the rest do not, the PWS is still counted as having one or more NDMA detections. To determine the associated population exposed, however, EPA used only the population served by sampling locations within the PWS with one or more detections. As noted earlier in this chapter, specific information on population served per sampling location was not available from the UCMR 2 dataset; thus, EPA assumed that each sampling location serves an equal proportion of the population within the PWS.

Exhibit 5.39 displays the results by size category for this analysis. It shows the mean expected values and the 90 percent credible interval for three size categories and for three threshold values: 0.6 ng/L (the HRL), 2 ng/L (the MRL) and 6 ng/L. Exhibit 5.40 shows predicted total population exposed at those thresholds. See Appendix D for results at other thresholds.

Exhibit 5.39: PWSs Predicted To Have One or More Detections Exceeding Various Thresholds

PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	PWSs Predicted To Have Any Detections Exceeding Threshold: Expected Value (90% CI)	Percentage of PWSs Predicted To Have Any Detections Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	11,309 (8,426 - 14,366)	27.0% (20.1% - 34.2%)
Small	41,962	41,154,840	2	3,673 (2,687 - 4,811)	8.8% (6.4% - 11.5%)
Small	41,962	41,154,840	6	1,276 (959 - 1,696)	3.0% (2.3% - 4.0%)
Large	2,812	84,318,927	0.6	1,616 (1,347 - 1,876)	57.5% (47.9% - 66.7%)
Large	2,812	84,318,927	2	790 (662 – 950)	28.1% (23.5% - 33.8%)
Large	2,812	84,318,927	6	353 (295 – 419)	12.6% (10.5% - 14.9%)
Very Large	394	141,407,211	0.6	296 (268 – 324)	74.5% (67.4% - 81.3%)
Very Large	394	141,407,211	2	182 (164 – 203)	45.7% (41.3% - 50.9%)
Very Large	394	141,407,211	6	89 (80 – 99)	22.4% (20.1% - 24.9%)
All	45,168	266,880,978	0.6	13,221 (10,041 - 16,565)	29.3% (22.2% - 36.7%)
All	45,168	266,880,978	2	4,644 (3,513 - 5,963)	10.3% (7.8% - 13.2%)
All	45,168	266,880,978	6	1,719 (1,334 - 2,214)	3.8% (3.0% - 4.9%)

Source: Appendix D.
Abbreviation: CI = credible interval
Note: This exhibit shows the results of detection-based modeling of NDMA occurrence. It is assumed that the number of samples taken per PWS is comparable to the number taken for UCMR 2 sampling.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.40: Populations Served by PWSs Predicted To Have One or More Detections Exceeding Various Thresholds

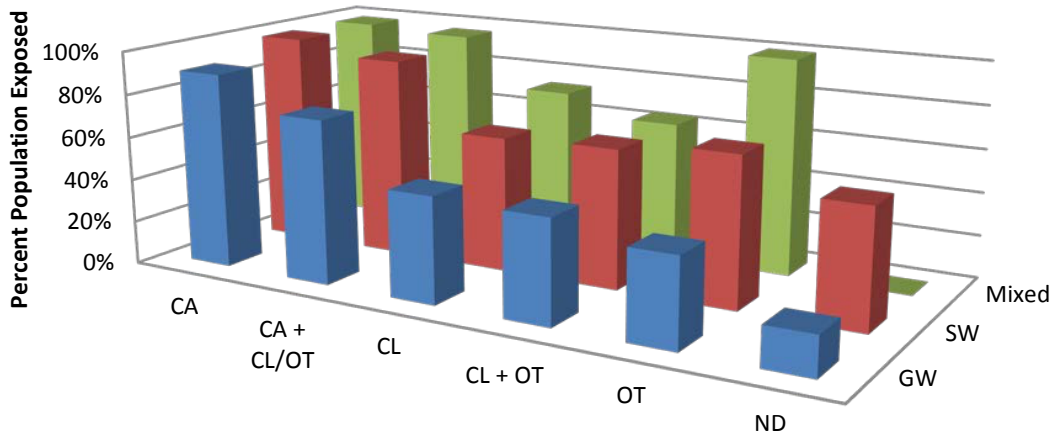
PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	Population Served by PWSs Predicted To Have Any Detections Exceeding Threshold: Expected Value (90% CI)	Percentage of Population Served by PWSs Predicted To Have Any Detections Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	15,690,723 (12,017,905 - 19,464,953)	38.1% (29.2% - 47.3%)
Small	41,962	41,154,840	2	6,728,174 (4,731,066 - 8,860,238)	16.4% (11.5% - 21.5%)
Small	41,962	41,154,840	6	2,808,022 (2,121,357 - 3,881,905)	6.8% (5.2% - 9.4%)
Large	2,812	84,318,927	0.6	51,521,139 (42,815,800 - 59,615,539)	61.1% (50.8% - 70.7%)
Large	2,812	84,318,927	2	26,391,618 (22,285,126 - 31,541,136)	31.3% (26.4% - 37.4%)
Large	2,812	84,318,927	6	12,399,960 (10,343,152 - 14,790,641)	14.7% (12.3% - 17.5%)
Very Large	394	141,407,211	0.6	110,803,964 (95,110,205 - 123,563,993)	78.0% (67.0% - 87.0%)
Very Large	394	141,407,211	2	68,223,812 (60,037,674 - 80,915,126)	48.1% (42.3% - 57.0%)
Very Large	394	141,407,211	6	33,492,275 (28,213,900 - 39,584,290)	23.6% (19.9% - 27.9%)
All	45,168	266,880,978	0.6	178,015,826 (149,943,910 - 202,644,485)	66.6% (56.1% - 75.8%)
All	45,168	266,880,978	2	101,343,604 (87,053,866 - 121,316,500)	37.9% (32.6% - 45.4%)
All	45,168	266,880,978	6	48,700,256 (40,678,409 - 58,256,836)	18.2% (15.2% - 21.8%)

Source: Appendix D.
Abbreviation: CI = credible interval
Note: This exhibit shows the results of detection-based modeling of NDMA occurrence. It is assumed that the number of samples taken per PWS is comparable to the number taken for UCMR 2 sampling.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

As shown in Exhibit 5.39, the predicted percentage of PWSs having one or more NDMA detections above the HRL (0.6 ng/L) is between 22.2 and 36.7 percent. Results are significantly higher for very large PWSs (74.5 percent) than for large and small PWSs (57.5 and 27.0 percent, respectively). This outcome reflects the fact that very large PWSs have more sample locations and thus have more opportunities to observe an NDMA concentration above the HRL. It also reflects the longer residence time in very large PWSs' distribution systems.

Exhibit 5.41 compares the predicted population exposed to at least one sample with levels greater than the HRL (0.6 ng/L) for different source water and disinfectant types. Results for PWSs follow a similar pattern to results for EP and MR location analysis: exposure is highest in PWSs with surface water or mixed sources and those using chloramines. Note that in Exhibit 5.41 there is no predicted exposure in the "mixed water ND" category, while the same is not true in Exhibit 5.38. This is a consequence of the way PWSs, EPs, and MRs are classified, as described in Section 5.2.2. No PWSs in the data set are classified as "mixed water ND."

Exhibit 5.41: Percentage of the Population Predicted To Be Exposed to One or More Detections at Levels Above the HRL (0.6 ng/L), Based on PWSs



	CA	CA + CL/OT	CL	CL + OT	OT	ND
GW	90.2%	75.4%	48.7%	47.5%	40.3%	18.0%
SW	98.3%	92.4%	62.3%	64.0%	68.7%	54.5%
Mixed	98.3%	96.3%	73.4%	64.2%	99.8%	0.0%

Source: Appendix D.
Abbreviations: HRL = health reference level; CA = chloramines; CL = chlorine; ND = no disinfectant; OT = other.
Note: This exhibit shows the results of detection-based modeling of NDMA occurrence.

5.5.3 National Occurrence and Exposure Estimates: Mean Concentrations

In addition to predicting the percentage of sampling locations and PWSs with one or more detections over given thresholds, EPA used modeling to predict the percentage of sampling locations and PWSs with a mean NDMA concentration over the same thresholds. The mean NDMA concentration is the annual average value calculated by the model. For the EP and MR analyses, it is the average annual value at each location based on four quarterly samples for surface water and mixed PWSs and two semiannual samples for ground water PWSs (i.e., the LAA). For the PWS analysis, it is the average of all annual average values at all EP and MR sample locations within the PWS (i.e., PWS annual average). Results are presented first for EP and MR locations, then for PWSs as a whole.

5.5.3.1 Entry Points and Maximum Residence Locations

Exhibit 5.42 and Exhibit 5.43 summarize results of the mean-based modeling analysis for EP and MR locations, respectively. They show the mean expected value concentrations and the 90 percent credible intervals for three size categories and for three threshold values. See Appendix E for results for other thresholds and for predictions of the total population exposed (extrapolated from the UCMR 2 population). Similar to the modeled analysis of detections, the analysis of mean concentrations at EPs gives a lower bound estimate of exposure based on NDMA concentrations in finished water entering the distribution system. The analysis based on MRs

gives an upper bound estimate of exposure at locations that are expected to represent higher NDMA concentrations.

Exhibit 5.42: Percentage of Entry Points with the Predicted Mean Concentration Exceeding the Threshold and the Associated Population Exposed

PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	Percentage of EPs with Mean Exceeding Threshold: Expected Value (90% CI)	Percentage of Population Served by EPs with Mean Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	17.3% (12.9% - 22.9%)	22.7% (16.5% - 30.2%)
Small	41,962	41,154,840	2	7.1% (5.0% - 9.1%)	10.8% (7.6% -14.3%)
Small	41,962	41,154,840	6	3.0% (2.1% - 4.3%)	4.6% (3.0% - 7.2%)
Large	2,812	84,318,927	0.6	14.1% (10.3% - 18.9%)	19.7% (14.4% - 26.6%)
Large	2,812	84,318,927	2	5.1% (3.6% - 6.9%)	7.7% (5.4% - 10.6%)
Large	2,812	84,318,927	6	1.4% (0.7% - 2.2%)	2.5% (1.3% - 4.0%)
Very Large	394	141,407,211	0.6	15.7% (12.6% - 19.3%)	23.6% (18.1% - 31.3%)
Very Large	394	141,407,211	2	4.7% (3.8% - 5.9%)	8.4% (6.4% - 10.6%)
Very Large	394	141,407,211	6	1.2% (0.8% - 1.6%)	2.5% (1.7% - 3.5%)
All	45,168	266,880,978	0.6	15.5% (12.1% - 19.7%)	23.2% (17.8% - 30.9%)
All	45,168	266,880,978	2	5.2% (3.9% - 6.6%)	8.3% (6.3% - 10.6%)
All	45,168	266,880,978	6	1.5% (0.9% - 2.1%)	2.5% (1.7% - 3.6%)

Source: Appendix E.
Abbreviation: CI = credible interval; EP = entry point
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.43: Percentage of Maximum Residence Time Locations with the Predicted Mean Concentration Exceeding the Threshold and the Associated Population Exposed

PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	Percentage of MRs with Mean Exceeding Threshold: Expected Value (90% CI)	Percentage of Population Served by MRs with Mean Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	29.5% (23.3% - 37.0%)	34.5% (26.5% - 43.9%)
Small	41,962	41,154,840	2	11.8% (9.3% - 14.7%)	15.9% (12.1% - 20.0%)
Small	41,962	41,154,840	6	5.1% (3.8% - 6.8%)	7.7% (5.6% - 10.8%)
Large	2,812	84,318,927	0.6	28.6% (22.1% - 36.2%)	36.5% (28.2% - 46.4%)
Large	2,812	84,318,927	2	11.0% (8.3% - 14.2%)	16.2% (12.4% - 20.9%)

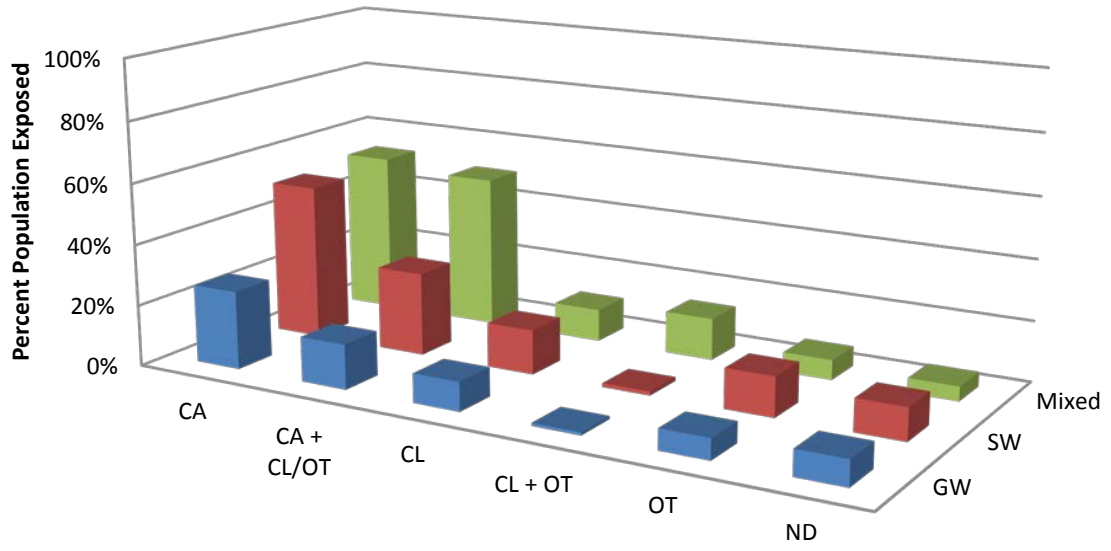
PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	Percentage of MRs with Mean Exceeding Threshold: Expected Value (90% CI)	Percentage of Population Served by MRs with Mean Exceeding Threshold: Expected Value (90% CI)
Large	2,812	84,318,927	6	3.6% (2.2% - 5.5%)	6.1% (3.5% - 8.9%)
Very Large	394	141,407,211	0.6	34.9% (29.7% - 41.0%)	46.6% (38.4% - 56.6%)
Very Large	394	141,407,211	2	16.5% (14.4% - 18.9%)	23.8% (19.9% - 28.8%)
Very Large	394	141,407,211	6	4.7% (3.7% - 5.9%)	6.0% (4.4% - 9.1%)
All	45,168	266,880,978	0.6	32.3% (26.6% - 39.1%)	45.7% (37.5% - 55.7%)
All	45,168	266,880,978	2	14.2% (11.9% - 16.9%)	23.1% (19.3% - 28.1%)
All	45,168	266,880,978	6	4.5% (3.4% - 6.0%)	6.0% (4.4% - 9.1%)

Source: Appendix E.
Abbreviation: CI = credible interval; MR = maximum residence time location
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.42 and Exhibit 5.43 show that between 12.1 and 19.7 percent of EP locations and between 26.6 and 39.1 percent of MR locations are predicted to have mean NDMA concentrations greater than the HRL (0.6 ng/L). These results are lower than the detection-based modeled predictions shown in Section 5.5.2 (i.e., Exhibit 5.35 and Exhibit 5.36), which is expected because individual samples greater than the HRL may be averaged with lower values to result in a mean below the HRL for the present modeled analysis, whereas they would be counted as above the HRL for the detection-based modeled analysis.

Exhibit 5.44 and Exhibit 5.45 show the results of mean-based modeling by disinfectant type and source water type for EP and MR locations, respectively. Similar to the results of detection-based modeling, results of mean-based modeling are highest in PWSs using chloramines alone and are also significantly higher in PWSs using chloramines in combination with chlorine. Other disinfectants, including chlorine alone, chlorine with other disinfectants, other disinfectants alone and no disinfection show lower exposures to mean concentrations above the MRL, especially at EP locations. It is interesting to note that for the MR analysis, a high percentage of the population is predicted to be exposed to mean NDMA concentrations over the HRL for mixed source waters using other or no disinfectants. This result may be influenced by the small number of PWSs in this category.

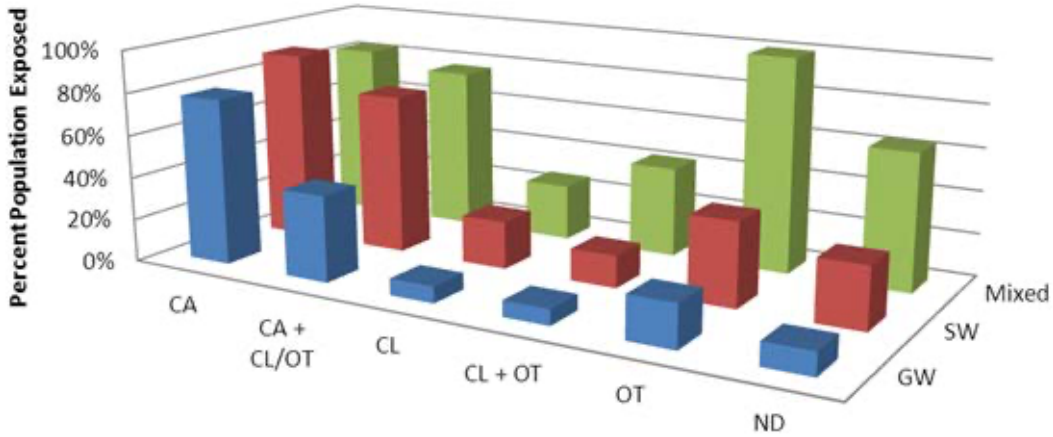
Exhibit 5.44: Percentage of the Population Predicted To Be Exposed to Mean Concentrations Greater Than the HRL (0.6 ng/L) at Entry Points



	CA	CA + CL/OT	CL	CL + OT	OT	ND
GW	25.6%	14.6%	9.5%	1.0%	6.8%	8.3%
SW	50.9%	27.2%	14.5%	1.3%	13.1%	10.6%
Mixed	52.7%	50.0%	10.6%	13.8%	6.6%	4.8%

Source: Appendix E.
Abbreviations: HRL = health reference level; CA = chloramines; CL = chlorine; ND = no disinfectant; OT = other.
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.

Exhibit 5.45: Percentage of the Population Predicted To Be Exposed to Mean Concentrations Greater Than the HRL (0.6 ng/L) at Maximum Residence Time Locations



	CA	CA + CL/OT	CL	CL + OT	OT	ND
GW	77.9%	40.3%	7.7%	7.4%	19.9%	10.5%
SW	89.5%	74.7%	22.3%	15.1%	38.9%	28.7%
Mixed	83.4%	76.9%	26.3%	42.2%	100.0%	63.8%

Source: Appendix E.
Abbreviations: HRL = health reference level; CA = chloramines; CL = chlorine; ND = no disinfectant; OT = other.
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.

5.5.3.2 PWSs

EPA also used modeling to predict the number and percentage of PWSs with a PWS-wide average NDMA concentration greater than each of the three thresholds. Exhibit 5.46 shows the expected mean values and the 90 percent credible interval for three size categories and for three threshold values. Exhibit 5.47 shows predicted total population exposed at those thresholds. See Appendix F for results at other thresholds.

Results show that between 4.8 and 11.2 percent of PWSs are predicted to have average NDMA concentrations greater than the HRL (0.6 ng/L).

Exhibit 5.46: PWSs with Predicted Mean Concentration Exceeding Various Thresholds

PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	PWSs with Predicted Mean Exceeding Threshold: Expected Value (90% CI)	Percentage of PWSs with Predicted Mean Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	2,705 (1,669 - 4,207)	6.5% (4.0% - 10.0%)
Small	41,962	41,154,840	2	1,056 (546 -1,591)	2.5% (1.3% - 3.8%)
Small	41,962	41,154,840	6	415 (340 – 483)	1.0% (0.8% - 1.2%)
Large	2,812	84,318,927	0.6	541 (408 – 695)	19.2% (14.5% - 24.7%)
Large	2,812	84,318,927	2	222 (150 – 296)	7.9% (5.3% - 10.5%)
Large	2,812	84,318,927	6	76 (58 – 120)	2.7% (2.1% - 4.3%)
Very Large	394	141,407,211	0.6	121 (101 – 145)	30.5% (25.4% - 36.4%)
Very Large	394	141,407,211	2	46 (37 – 55)	11.7% (9.3% - 13.8%)
Very Large	394	141,407,211	6	14 (10 – 17)	3.5% (2.5% - 4.3%)
All	45,168	266,880,978	0.6	3,367 (2,178 - 5,048)	7.5% (4.8% - 11.2%)
All	45,168	266,880,978	2	1,324 (733 - 1,942)	2.9% (1.6% - 4.3%)
All	45,168	266,880,978	6	505 (408 – 620)	1.1% (0.9% - 1.4%)

Source: Appendix F.
Abbreviation: CI = credible interval
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

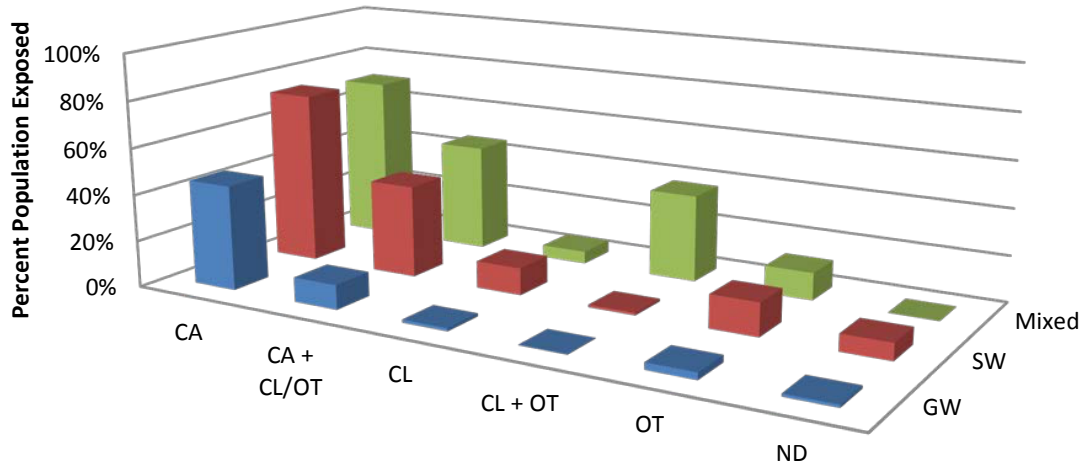
Exhibit 5.47: Population Served by PWSs with Predicted Mean Concentration Exceeding Various Thresholds

PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	Population Served by PWSs with Predicted Mean Exceeding Threshold: Expected Value (90% CI)	Percentage of Population Served by PWSs with Predicted Mean Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	4,885,569 (3,172,960 - 7,631,299)	11.9% (7.7% - 18.5%)
Small	41,962	41,154,840	2	1,995,203 (1,092,084 - 2,846,984)	4.9% (2.7% - 6.9%)
Small	41,962	41,154,840	6	752,480 (481,741 - 1,045,792)	1.8% (1.2% - 2.5%)
Large	2,812	84,318,927	0.6	17,731,575 (14,201,885 - 22,622,389)	21.0% (16.8% - 26.8%)
Large	2,812	84,318,927	2	7,866,335 (5,235,856 - 10,817,716)	9.3% (6.2% - 12.8%)
Large	2,812	84,318,927	6	2,252,768 (1,757,426 - 4,420,072)	2.7% (2.1% - 5.2%)
Very Large	394	141,407,211	0.6	42,734,267 (32,742,467 - 54,906,687)	30.1% (23.1% - 38.7%)
Very Large	394	141,407,211	2	14,892,932 (12,187,487 - 18,796,017)	10.5% (8.6% - 13.2%)
Very Large	394	141,407,211	6	3,168,706 (2,231,047 - 3,966,754)	2.2% (1.6% - 2.8%)
All	45,168	266,880,978	0.6	65,351,410 (50,117,312 - 85,160,375)	24.4% (18.7% - 31.8%)
All	45,168	266,880,978	2	24,754,470 (18,515,427 - 32,460,717)	9.3% (6.9% - 12.1%)
All	45,168	266,880,978	6	6,173,954 (4,470,214 - 9,432,618)	2.3% (1.7% - 3.5%)

Source: Appendix F.
Abbreviation: CI = credible interval
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.48 shows trends with respect to source water and disinfection type based on mean-based modeling for PWSs. With limited exceptions (namely, mixed water PWSs using chlorine in combination with other disinfectants), PWSs using non-chloramine disinfectants are predicted to have less than 15 percent of their served population exposed to mean concentrations greater than the HRL. Nearly 74 percent of customers served by surface water PWSs using chloramines are predicted to be exposed to average NDMA concentrations above the HRL. The percentage of the population exposed for ground water PWSs is significantly lower than that for surface water and mixed water PWSs in all disinfectant categories.

Exhibit 5.48: Percentage of the Population Predicted To Be Exposed to Mean Concentrations Greater Than the HRL (0.6 ng/L) in PWSs



	CA	CA + CL/OT	CL	CL + OT	OT	ND
GW	45.0%	10.5%	1.3%	0.2%	2.9%	1.2%
SW	73.9%	39.7%	11.6%	1.1%	14.2%	7.2%
Mixed	70.6%	46.2%	5.3%	37.5%	11.8%	0.0%

Source: Appendix F.
Abbreviations: HRL = health reference level; CA = chloramines; CL = chlorine; ND = no disinfectant; OT = other.
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.

5.5.3.3 National Occurrence and Exposure Estimates: Locational Annual Average

EPA modeled the LAA of NDMA at each UCMR 2 monitoring location. (Note that these LAAs are not necessarily the same as the LRAAs identified for the Stage 2 D/DBPR.) EPA conducted the LAA analysis at the PWS level, meaning that if one location in a PWS exceeded the threshold based on the LAA, the entire PWS was counted. The associated population exposed to LAAs above the threshold, however, was based on the population served by individual sampling locations. As discussed earlier in this chapter, specific information on population served per sampling location was not available from the UCMR 2 dataset; thus, EPA assumed that an equal proportion of the population served could be assigned to each sampling location within the PWS. It is important to note that because the UCMR 2 dataset contains only one year of data, the LAA is equivalent to the annual average value at each location.

Exhibit 5.49 shows the expected mean percentages and the 90 percent credible interval for 3 size categories and for 3 threshold values for the LAA analysis. See Appendix G for results for other thresholds and for associated predicted total population exposed (extrapolated from the UCMR 2 population). Results show that between 15.1 and 29.8 percent of PWSs are predicted to exceed the HRL (0.6 ng/L) at one or more sampling locations, based on the LAA. Predicted percentages are significantly higher for very large PWSs compared to large PWSs and for large PWSs compared to small PWSs. This may be due to the higher number of sampling locations in larger PWSs and thus the greater chance for an LAA to have an occasional high concentration. Note

that the percentage of PWSs predicted to have an LAA above the HRL and the associated population served are roughly equivalent to the sum of the predicted values for EP and MR locations based on the annual mean (see Section 5.5.3).

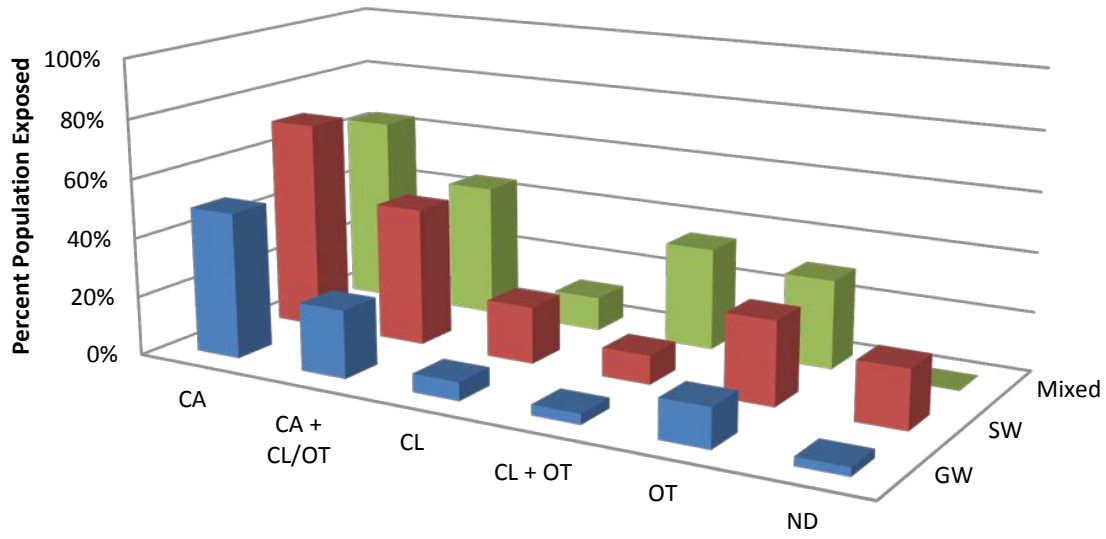
Exhibit 5.49: Percentage of PWSs Predicted To Have an LAA Greater Than the Threshold and the Associated Population Exposed

PWS Size[1]	Total National Inventory: PWS Count	Total National Inventory: Population Served	Threshold (ng/L)	Percentage of PWSs Predicted To Have LAA Exceeding Threshold: Expected Value (90% CI)	Percentage of Population Served by PWSs Predicted To Have LAA Exceeding Threshold: Expected Value (90% CI)
Small	41,962	41,154,840	0.6	20.2% (13.4% - 27.7%)	16.5% (11.4% - 22.9%)
Small	41,962	41,154,840	2	5.4% (3.3% - 8.3%)	6.0% (3.9% - 9.0%)
Small	41,962	41,154,840	6	1.8% (1.3% - 3.0%)	2.1% 1.5% - 3.3%)
Large	2,812	84,318,927	0.6	45.2% (34.8% - 56.5%)	26.3% (21.2% - 32.5%)
Large	2,812	84,318,927	2	18.6% (14.0% - 23.9%)	11.1% (9.0% - 13.8%)
Large	2,812	84,318,927	6	7.0% (4.8% - 11.4%)	3.9% (2.4% - 5.6%)
Very Large	394	141,407,211	0.6	62.2% (53.3% - 70.9%)	33.7% (28.5% - 40.6%)
Very Large	394	141,407,211	2	33.1% (28.4% - 38.4%)	15.1% (12.7% - 17.8%)
Very Large	394	141,407,211	6	10.5% (7.3% - 14.1%)	4.0% (3.1% - 5.7%)
All	45,168	266,880,978	0.6	22.1% (15.1% - 29.8%)	28.7% (23.5% - 35.3%)
All	45,168	266,880,978	2	6.5% (4.2% - 9.5%)	12.5% (10.2% - 15.2%)
All	45,168	266,880,978	6	2.2% (1.5% - 3.6%)	3.7% (2.6% - 5.3%)

Source: Appendix G.
Abbreviation: CI = credible interval; LAA = locational annual average.
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.
1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

Exhibit 5.50 compares population exposed for different source water and disinfection types. As with previous analyses, results are higher in surface water and mixed water PWSs compared to ground water PWSs, as well as for PWSs using chloramines compared to other disinfectants. The predicted percentage of the population exposed to LAAs greater than the HRL ranges from nearly 71 percent for surface water PWSs using chloramines to 3 percent for ground water PWSs using other disinfectants with chlorine or not disinfecting.

Exhibit 5.50: Percentage of the Population Predicted To Be Exposed to LAAs Greater Than the HRL (0.6 ng/L) in PWSs



	CA	CA + CL/OT	CL	CL + OT	OT	ND
GW	49.4%	22.9%	6.2%	3.5%	13.3%	2.9%
SW	70.9%	46.6%	19.1%	9.6%	28.0%	19.7%
Mixed	63.9%	45.0%	11.5%	34.4%	29.9%	0.0%

Source: Appendix G.
Abbreviations: HRL = health reference level; CA = chloramines; CL = chlorine; LAA = locational annual average; ND = no disinfectant; OT = other.
Note: This exhibit shows the results of mean-based modeling of NDMA occurrence.

5.5.4 National Co-Occurrence of Nitrosamines

Exhibit 5.51 shows co-occurrence results within the nitrosamine group, based on exposure at or above the MRLs (see Section 5.4, in particular Exhibit 5.32 and Exhibit 5.33), extrapolated from the UCMR 2 study population to the national population. These national extrapolations are produced by multiplying occurrence rates from the study by national baseline inventory numbers for PWSs in various size and source water categories. Since UCMR 2 monitoring included a census of very large systems, no extrapolation was necessary in that size category. Note that the simple extrapolation methodology used here produces different results for NDMA than the modeling process described in Section 5.5. As noted in earlier discussions of co-occurrence, these results should be interpreted with caution since MRLs vary from contaminant to contaminant.

In summary, an estimated 4,591 PWSs serving a population of just over 101 million people are potentially exposed to detectable levels of nitrosamines (NDMA or other) in finished water. An estimated 123 PWSs serving a population of approximately 10.5 million people are potentially exposed to more than one nitrosamine.

Exhibit 5.51: Co-Occurrence of Nitrosamines (National Extrapolation from UCMR 2)

PWS Size[1]	Source Water Type	National Estimate of PWSs with At Least One Detection of NDMA Only	National Estimate of Population Served by PWSs with At Least One Detection of NDMA Only	National Estimate of PWSs with At Least One Detection of Other Nitrosamines (No NDMA)	National Estimate of Population Served by PWSs with At Least One Detection of Other Nitrosamines (No NDMA)	National Estimate of PWSs with Detection of NDMA *and* Another Nitrosamine	National Estimate of Population Served by PWSs with Detection of NDMA *and* Another Nitrosamine	National Estimate of PWSs with At Least One Detection of Any Nitrosamine	National Estimate of Population Served by PWSs with At Least One Detection of Any Nitrosamine
Small	All PWSs	3,145	6,330,127	482	1,058,317	54	126,180	3,680	7,514,624
Small	Surface Water	492	1,242,334	0	0	54	126,180	546	1,368,514
Small	Ground Water	1,605	2,268,705	482	1,058,317	0	0	2,087	3,327,022
Small	Mixed Water	1,048	2,819,088	0	0	0	0	1,048	2,819,088
Large	All PWSs	627	21,073,473	55	1,584,277	48	2,014,691	729	24,672,442
Large	Surface Water	238	7,823,545	12	266,072	18	576,193	268	8,665,811
Large	Ground Water	111	3,435,597	0	0	8	464,811	119	3,900,408
Large	Mixed Water	278	9,814,331	43	1,318,205	21	973,687	342	12,106,223
Very Large	All PWSs	147	53,138,701	12	7,530,629	22	8,355,589	181	69,024,919
Very Large	Surface Water	85	35,243,460	4	2,109,340	8	4,262,160	97	41,614,960
Very Large	Ground Water	15	4,792,295	4	609,237	3	1,253,283	22	6,654,815
Very Large	Mixed Water	47	13,102,946	4	4,812,052	11	2,840,146	62	20,755,144
Total		3,919	80,542,301	549	10,173,223	123	10,496,460	4,591	101,211,984

Note: Based on UCMR 2 survey results, extrapolated to the national level using information from SDWIS on the population served by PWSs in various size and source water categories. "Other nitrosamines" detected under the UCMR 2 are NDBA, NDEA, NMEA and NPYR. NDPA was not detected by any PWS. See Exhibit 5.1 for the MRLs for each nitrosamine.

1) Small = serving ≤ 10,000; Large = serving 10,001 – 100,000; Very Large = serving > 100,000.

5.6 Summary and Discussion

EPA used data from the UCMR 2 (2008-2010) Screening Survey to evaluate occurrence of the contaminants in six specific nitrosamines in U.S. drinking water. Under the UCMR 2 Screening Survey, all very large PWSs and a sample of small and large PWSs were required to collect samples at each EP to the distribution system and at the MR time locations within the distribution system associated with each EP with disinfection, for a period of one year. Monitoring was conducted quarterly at surface water PWSs and semi-annually at ground water PWSs. PWSs were required to report the type of disinfection in use at the time of sample collection.

Detections of one or more nitrosamines occurred in 10.6 percent (1,907 of 18,053) of samples and at 28.6 percent (343 of 1,198) of UCMR 2 PWSs. All nitrosamines except NDPA were detected during the course of the survey. NDMA predominated, with detections in 10.2 percent (1,841 of 18,040) of samples and 27.0 percent (324 of 1,198) of PWSs. There was substantial co-occurrence (i.e., detection of two or more nitrosamines at the same PWS during the year of monitoring). In all but one instance, NDMA was one of the co-occurring nitrosamines. Detection rates appear to be lower at ground water PWSs than at surface and mixed water PWSs. Three points of caution should be borne in mind when interpreting nitrosamine results from UCMR 2. First, reporting thresholds (MRLs) were not uniform, making contaminant-to-contaminant comparisons uncertain. Second, MRLs were not always low enough to capture occurrence at levels of health concern (i.e., the MRLs were above the contaminants' respective HRLs). In the case of NDMA and NDEA, HRLs were lower than MRLs, and therefore the summary statistics based on MRLs probably underestimate exposure to those contaminants at levels of health concern. Third, the UCMR 2 survey of PWSs represents a combination of sample and census, and therefore summary statistics from the survey should not be interpreted as a simple surrogate for national occurrence.

Detection rates for NDMA were high enough to support modeling that allowed for characterization of occurrence at concentrations below the MRL, to overcome the limitation that its HRL was below its MRL. Modeling suggests that monitoring at the national level (under the same schedule as UCMR 2), with sufficiently sensitive analytical methods, would show NDMA occurring at levels of health concern (>HRL) in 22.1 percent to 36.7 percent (90 percent credible interval range) of the nation's PWSs, affecting approximately 149.9 million to 202.6 million people. Modeling also predicts that approximately 4.9 percent to 11.1 percent PWSs nationally (again, a 90 percent credible interval range), serving approximately 50.1 million to 85.2 million people, would be found to have *average* NDMA concentrations in excess of the HRL. For NDMA, which is a carcinogen, the average concentration at a PWS is an appropriate benchmark for evaluating health outcomes based on chronic exposure.

Since nitrosamines are disinfection by-products (DBPs), one would expect to see variations in occurrence depending on the disinfectant in use. In particular, higher concentrations and higher frequencies of detection would be expected at PWSs and at monitoring locations where chloramines are in use, alone or in combination with other disinfectants. The UCMR 2 data bear out these correlations. The formation of nitrosamines (including NDMA) is discussed in more detail in Chapter 6.

UCMR 2 data are subject to limitations including some that are particular to the nitrosamines. For example, UCMR 2 monitoring occurred between 2008 and 2010, and thus does not capture

treatment adjustments that were made by utilities between 2011 and 2015 in response to LT2SWTR and Stage 2 D/DBPR. The treatment changes under Stage 2 D/DBPR are anticipated to increase the use of chloramines to reduce the formation of certain other chlorination DBPs (trihalomethanes [THMs] and haloacetic acids) (USEPA, 2005d), and a possible consequence will be additional utilities having the increased formation of nitrosamines. A comparison of disinfectant uses between the period of 2008-2010 (based on UCMR 2 data) and 2013-2015 (based on UCMR 3 data) is presented and discussed in *Six Year Review 3 Technical Support Document for Chlorate* (USEPA, 2016b). Such a comparison confirms an increasing trend of chloramines usage in the nation. Thus, current national occurrence and exposure baselines of nitrosamines (including NDMA) could be higher than the UCMR 2 data indicate.

Another limitation is that UCMR 2 did not involve monitoring at consecutive systems (PWSs that purchase 100 percent of their water from other systems and are "downstream" of the system selling and providing the water). Although the population-served values of participating UCMR 2 wholesale systems (systems selling water to other systems) were adjusted to account for populations served by purchasing systems, the nitrosamine levels observed in wholesale systems might not be representative of levels present in the consecutive purchasing systems. A study by Krasner et al. (2012a) found that NDMA levels increased in distribution systems of consecutive systems (primarily because of increased residence time). Both of these limitations suggest the UCMR 2 results may underestimate current, and possibly future, public exposure to nitrosamines in drinking water.

It is worth bearing in mind that the six nitrosamines discussed in this document are only a subset of the nitrosamines that may occur in drinking water, many of which have not yet been identified. Dai and Mitch (2013) developed a TONO assay and applied it to 36 finished water samples from 11 drinking water treatment plants (including 9 plants using chloramines for secondary disinfection) and found that NDMA accounted for only around 5 percent of the total nitrosamines present, and other nitrosamines detectable with EPA Method 521 (including the other five discussed in this document) accounted for less. Application of the assay to influent waters indicates that while source waters impaired by algal blooms are not an important source of NDMA and other nitrosamines detectable with EPA Method 521, they are an important source of total *N*-nitrosamines.

6 Formation

6.1 Introduction

Although nitrosamines have been found in drinking water sources due to contamination from chemical manufacturing and the degradation of hydrazine rocket fuel, as discussed in Chapter 2, their occurrence in source water appears infrequent and at low concentrations when they are present. However, as described in Chapter 5, data from Second Unregulated Contaminant Monitoring Regulation (UCMR 2) show that *N*-nitrosodimethylamine (NDMA) occurs frequently in treated drinking water, especially at utilities that use chloramines for disinfection. (Other nitrosamines have also been detected to a much lesser extent.) These observations are supported by other studies showing that NDMA formation is elevated when chloramination is used in surface water where nitrogen-containing organic precursors are present.

This chapter presents information on the mechanisms of formation, sources and types of precursors, factors impacting formation, formation kinetics, and predictive models. The main focus of this chapter is NDMA, which is most frequently detected in the UCMR 2, though information about the other nitrosamines is also included.

Data from the literature on a range of chloraminated natural and wastewater-impacted waters indicates that the formation potential (FP) for the nitrosamines *N*-nitrosodi-n-butylamine (NDBA), *N*-nitrosodiethylamine (NDEA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosomethylethylamine (NMEA), *N*-nitrosopyrrolidine (NPYR) and *N*-nitrosopiperidine (NPIP) is one to two orders of magnitude lower than that for NDMA (Sacher et al., 2008). Data from UCMR 2 show that although the ranges of observed concentrations of individual nitrosamines are similar, NDMA is detected far more frequently than the others. Thus, this chapter focuses on formation of NDMA.

6.2 Nitrosamine Formation Potential

Many organic nitrogen-containing compounds can contribute to the formation of nitrosamines (Sacher et al., 2008). Although correlations between dissolved organic nitrogen (DON) concentration and NDMA precursors have been observed in some studies, they are absent in others (Lee et al., 2007a; Krasner et al., 2008; Mitch et al., 2009; Xu et al., 2011). The observed relationships between dissolved organic carbon (DOC) concentration and nitrosamine formation are also inconsistent (Gerecke and Sedlak, 2003; Hua et al., 2007; Lee et al., 2007a; Krasner et al., 2008; Mitch et al., 2009; Xu et al., 2011). Dimethylamine (DMA), a known NDMA precursor that has been widely used in laboratory studies, can be measured at relatively low concentrations (Mitch et al., 2003a). However, because DMA is not the only precursor responsible for NDMA formation in drinking water sources, its measurement has limited use in quantifying NDMA formation. Therefore, to evaluate the presence of nitrosamine precursors in a variety of water supplies, researchers have developed tests to determine nitrosamine FP. Nitrosamine FP tests serve as surrogate measures of nitrosamine precursors, and are analogous to the disinfection by-product (DBP) FP tests used to determine the level of other DBP precursors in source water.

Nitrosamine FP tests are performed in a variety of ways. For example, Mitch et al. (2003) added 2 mM monochloramine to a water phosphate-buffered at pH 6.8 with a reaction duration of up to 10 days. Krasner et al. (2009), on the other hand, formed chloramines *in situ* by adding ammonia

and then chlorine; samples were held for three days at room temperature at pH 8. Different experimental protocols, as well as different source waters and different types of precursors, mean that FP tests may not be directly comparable and should be interpreted with caution.

Although FP tests do not directly predict the concentrations of nitrosamines that will form in water under field operating conditions, as the tests are typically conducted using extreme chlorine doses, correlations can be found between FP tests and expected concentrations of NDMA (Mitch et al., 2003a). The results from FP tests should be carefully evaluated and may not be comparable across different waters due to varying water quality parameters (i.e., pH, bromide concentrations, etc.) or treatment (i.e., chlorine vs. chloramine). The FP test, however, is still a useful tool for estimating precursor concentrations in a drinking water source and evaluating various nitrosamine removal processes within a single treatment plant (Mitch et al., 2003a).

Krasner et al. (2011) presented results of a simulated distribution system test to mimic potential nitrosamine and regulated DBP formation under more realistic disinfection conditions. They validated simulated distribution system tests against full-scale occurrence for NDMA and halogenated DBPs (trihalomethanes [THMs] and haloacetic acids [HAAs]). Such a test may help utilities to determine optimal conditions for controlling a range of DBPs while meeting disinfection requirements.

6.3 Formation Pathways

As shown by the analysis of UCMR 2 data and other data in Appendix A, nitrosamine occurrence is generally associated with treated drinking water, rather than source water. Utilities treating surface waters affected by wastewater flows generally show higher nitrosamine formation compared to those treating ground water or more pristine surface waters (Padhye et al., 2010). Nitrosamines have been shown to form under many different disinfection techniques, including the application of free chlorine (Choi and Valentine, 2003; Schreiber and Mitch, 2007; Nawrocki and Andrzejewski, 2011; Shah and Mitch, 2012), chlorine dioxide (Andrzejewski and Nawrocki, 2007; Pozzi et al., 2011), ozone (Sedlak et al., 2005; Andrzejewski and Nawrocki, 2007; Andrzejewski et al., 2008; Schmidt and Brauch, 2008; Yang et al., 2009; Pozzi et al., 2011), ultraviolet (UV) light (Zhao et al., 2008) and advanced oxidation processes (AOPs) (Zhao et al., 2008). Krasner et al. (2013) provided a literature review to discuss the formation of nitrosamines under many of these scenarios. However, data from both the literature (Najm and Trussell, 2001; Andrzejewski et al., 2008; Krasner et al., 2008; Sacher et al., 2008; Zhao et al., 2008; Mitch et al., 2009; Krasner et al., 2013) and UCMR 2 indicate that formation via the chloramination pathway is the primary mechanism of interest for drinking water utilities. This section presents information on the chloramination pathway first, followed by a discussion on the chlorine-enhanced nitrosation pathway, the breakpoint chlorination pathway and other minor formation pathways. Nitrosamines formation due to use of disinfectants other than chlorine or chloramines is also discussed. In addition to the formation pathways that take place in water as discussed in this section, NDMA can be produced endogenously in humans via the interaction of nitrates and nitrites with amines in the stomach (Fristachi and Rice, 2007).

6.3.1 Chloramination Pathway

Findings from a wide range of laboratory and full-scale studies agree with the UCMR 2 findings: chloramination generally results in higher NDMA formation than other disinfection practices

(Najm and Trussell, 2001; Krasner et al., 2008; Sacher et al., 2008; Zhao et al., 2008; Mitch et al., 2009). This finding is especially relevant because many utilities have been switching from using chlorine to using alternative disinfectants, including chloramines, to reduce the formation of regulated THMs and HAAs and to comply with the Stage 2 Disinfectants and Disinfection By-Products Rule (Stage 2 D/DBPR) (Seidel et al., 2005). Such a change is also discussed in more detail in the agency's *Six-Year Review 3 Technical Support Document for Chlorate* (USEPA, 2016b).

Choi and Valentine (2002) first observed that the addition of monochloramine to a solution of DMA produced two orders of magnitude more NDMA than the addition of chlorine, and six times as much as the addition of nitrite. The use of isotopically labeled chloramines indicated that one of the nitrogens found in NDMA originated from chloramines, indicating that NDMA was a chloramination DBP (Choi and Valentine, 2002).

Initially, NDMA was thought to form primarily via a monochloramine pathway. The proposed pathway involved a nucleophilic substitution reaction between DMA and monochloramine, which creates unsymmetrical dimethylhydrazine (UDMH), which is then oxidized by chloramines to result in the formation of NDMA (Choi et al., 2002; Mitch and Sedlak, 2002). However, further research indicated that this mechanism did not fully explain the formation of NDMA. For example, experiments showed that at least two orders of magnitude higher NDMA concentrations formed following monochloramine application to DMA than to equivalent concentrations of UDMH (Schreiber and Mitch, 2006a). Also, studies showed that the presence of dichloramine significantly increased nitrosamine formation (Mitch et al., 2005; Schreiber and Mitch, 2005).

Under typical drinking water treatment conditions, monochloramine is the dominant chloramine species, though dichloramine is also present according to the following equilibrium:

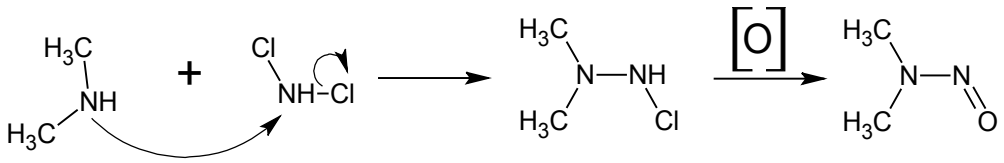
$$2NH_2Cl + H^+ \leftrightarrow NHCl_2 + NH_4^+$$

Dichloramine formation from the disproportionation of monochloramine is slow, such that its formation after the application of preformed monochloramine should be minimal (Schreiber and Mitch, 2006a). Chloramine speciation is impacted by both pH and the chlorine-to-ammonia (Cl_2:NH_3) molar ratio. At a Cl_2:NH_3 ratio of 1.5 and pH 7, monochloramine and dichloramine are present in approximately equal molar concentrations. Monochloramine predominates above pH 8.5, while dichloramine predominates below pH 5 (Schreiber and Mitch, 2006a). At Cl_2:NH_3 ratios less than or equal to 1.5, monochloramine is the dominant species. At Cl_2:NH_3 ratios greater than 1.5, dichloramine is the dominant species.

A revised mechanism was proposed that incorporated the more recent research findings, including results suggesting that the presence of dichloramine resulted in higher NDMA formation compared to monochloramine, and that formation of NDMA increased with increased dissolved oxygen (DO) concentration (Schreiber and Mitch, 2006a). The modified pathway involves a nucleophilic substitution reaction between DMA (or other secondary amines) and dichloramine, which creates a chlorinated-UDMH intermediate that is then oxidized by DO (Exhibit 6.1). The revised pathway has been shown to accurately model NDMA formation over a wide range of formation conditions (Schreiber and Mitch, 2006a). Schreiber and Mitch (2006a) also found that other nitrosamines (NDEA, NMEA, *N*-nitrosomorpholine [NMOR], NPIP, NPYR) formed along a parallel pathway from their respective secondary amine precursors. The

authors showed that nitrosamine formation is enhanced by higher DO concentrations. The kinetics of this pathway is such that nitrosamine precursors can react with chloramines over several days resulting in the continued formation of nitrosamines in the distribution system (Charrois and Hrudey, 2007; Goslan et al., 2009).

Exhibit 6.1: Mechanism of NDMA Formation via the Chloramination Pathway



Source: Adapted from Schreiber and Mitch, 2006a.

In general, all nitrosamines show relatively low molar conversions from their respective amines. Sacher et al. (2008) determined the following molar percent yields for a range of nitrosamines from the chloramination of their respective secondary amines (amine concentration of 1,000 ng/L, dosed with 0.4 mM chloramines at pH 7, 20 degrees C for 168 hours):

- NDBA: 0.69%
- NDEA: 0.53%
- NDMA: 0.49%
- NDPA: 0.02%
- NMOR: 0.07%
- NPIP: 1.35%
- NPYR: 1.84%

Selbes et al. (2013) tested 21 different amines for NDMA formation with 100 mg/L chloramine at pH 7.5. They found that aliphatic amines had low yields: for example, DMA had a yield of 1.2 percent, and dimethylbutylamine had a yield of 0.3 percent. Branched alkyl groups had higher yields, with dimethylisopropylamine (DMiPA) having a yield of 83.9 percent. They also found amines with aromatic rings one carbon away from the DMA functional group had higher yields: for example, dimethylbenzylamine (DMBzA) had a yield of 83.8 percent. The investigators also tested the formation of NDMA with an addition of extra ammonia to lower the concentration of dichloramine. They found that some amines reacted preferentially with dichloramine, while others reacted preferentially with monochloramine. Those amines with electron-withdrawing groups attached to the nitrogen of the DMA functional group reacted preferentially with monochloramine. Amines with electron-donating groups attached to the nitrogen of the DMA functional group preferentially reacted with dichloramine. The investigators proposed that this was due to the reaction occurring through a nucleophilic attack on the chloramine by the amine.

Nitrosamine formation may also occur via unintended chloramination: for example, when chlorine is applied to waters containing high concentrations of ammonia. Higher NDMA

concentrations were observed following the addition of chlorine to secondary municipal wastewater effluents than when equivalent doses of preformed monochloramine were added (Schreiber and Mitch, 2005). This unexpected result may be explained by dichloramine formation during chlorination of waters with high ammonia content, such that the majority of nitrosamine formation takes place via the chloramination pathway (Schreiber and Mitch, 2005).

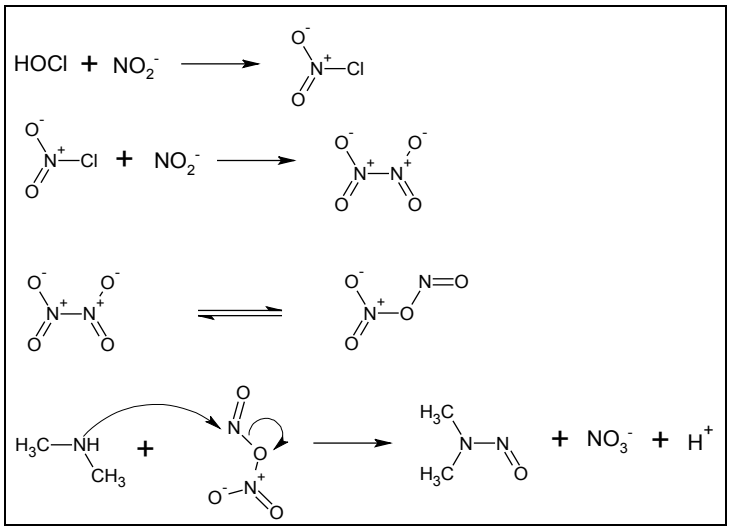
6.3.2 Chlorine Enhanced Nitrosation Pathway

The formation of NDMA from chlorination in the absence of ammonia, but in the presence of DMA, was described by Choi and Valentine (2003). The authors found that free chlorine added to a solution of nitrite and DMA created more NDMA than the solutions lacking free chlorine. The results were explained by the formation of the unstable intermediate dinitrogen tetroxide, a nitrosating agent. (A nitrosating agent reacts with amines to form nitrosoamines by a nitrosation reaction.) This mechanism is known as the chlorine enhanced nitrosation pathway and is shown in Exhibit 6.2. Under comparable conditions, formation of NDMA by enhanced nitrosation has been shown to be significantly lower than by chloramination (Schreiber and Mitch, 2007). Nawrocki and Andrzejewski (2011) state that the chlorine enhanced nitrosation reaction is slow and is not expected to contribute much in NDMA formation. Shah and Mitch (2012) note that the importance of the enhanced nitrosation pathway in drinking water treatment needs further clarification for drinking water where nitrite concentrations are typically relatively low.

Liu et al. (2014) proposed a nitrosation pathway involving chloramines and tertiary amines as well. In their mechanism, the chloramine forms a complex which then reacts by an elimination reaction, eliminating an ONX agent which is trapped by oxygen to form a nitrosating agent OONX where X is either hydrogen or chlorine. The nitrosating reagent further reacts to form NO+, which can react with the amine to form a nitrosamine. The model correctly predicts the relative yields of many tertiary amines. The model predicts that a strong electron-withdrawing group on the first carbon will lower NDMA yield, while an electron-donating group will increase yield. The model did not perform well with all tertiary amines; however, so it is likely multiple mechanisms are at work.

The enhanced nitrosation pathway may be more important for utilities chlorinating source waters impacted by nitrified wastewater effluents (Shah and Mitch, 2012). Chen and Young (2009) observed close to a 10-fold increase in the production of NDMA during the chlorination of diuron (an herbicide and known NDMA precursor) when 5 mg/L nitrate and/or nitrite was added. This pathway may also be relevant for utilities chlorinating ground water sources, as nitrate (and nitrite at relatively lower concentrations) is possibly the most widespread contaminant in ground water (Nolan et al., 2002). A recent report found persistent widespread contamination of nitrate in California's ground water resources in heavily agricultural areas, indicating that nitrate pollution will likely worsen over the next several decades (Harter et al., 2012).

Exhibit 6.2: NDMA Formation via the Enhanced Nitrosation Pathway



Source: Adapted from Choi and Valentine, 2003.

6.3.3 Breakpoint Chlorination

Breakpoint chlorination, the practice of adding enough chlorine to overcome the chlorine demand, results in a free chlorine residual. Schreiber and Mitch (2007) observed that maximum nitrosamine formation was observed close to the breakpoint (Cl_2:NH_3 molar ratio of 1.7) during chloramination of DMA over a range of Cl_2:NH_3 ratios. Initially, the authors hypothesized that nitrosamines were forming via a combination of chloramination and chlorine enhanced nitrosation pathways. However, experimental results indicated that the chlorine enhanced nitrosation pathway could not account for the rapid formation of nitrosamines observed at the breakpoint. Two concurrent pathways have been proposed during breakpoint chlorination (Schreiber and Mitch, 2007). For Cl_2:NH_3 molar ratios less than or equal to 1.5, nitrosamines form via the relatively slow chloramination reaction, described in Section 6.3.1. At Cl_2:NH_3 molar ratios greater than 1.5, an additional formation pathway occurs that involves reactive breakpoint chlorination intermediates and results in the rapid formation of nitrosamines. The authors propose that reactive breakpoint chlorination intermediates are involved in the direct nitrosation of DMA, though this pathway requires further verification.

Because treatment facilities typically operate with a sufficient chlorine residual, nitrosamine formation by this pathway (i.e., breakpoint chlorination with no significant free chlorine residual) is likely to be of minor importance (Shah and Mitch, 2012).

6.3.4 Other Formation Pathways

Though chlorination and chloramination are the main sources of nitrosamines in drinking water treatment, other treatment techniques have also been shown to result in the formation of nitrosamines.

In the absence of a disinfectant, activated carbon has been shown to catalyze the transformation of NDBA, NDEA, NDMA, NDPA and NMEA from di-*n*-butylamine (DBA), diethylamine (DEA), DMA, di-*n*-propylamine (DPA), and methylethylamine (MEA), respectively (Padhye et

al., 2010). Yields ranged from 0.05 to 0.29 percent (calculated by dividing the amount of nitrosamine formed by the amount of secondary amine adsorbed at pH 7.5) (Padhye et al., 2010). Nitrosamine formation was higher for experiments using wastewater in comparison to surface water or deionized water. These findings are relevant not only for drinking water treatment, but also for analytical methods, as activated carbon is used for nitrosamine extraction (Padhye et al., 2010).

Some studies have shown that oxidation of DMA may lead to the formation of NDMA, particularly at higher pH (Nawrocki and Andrzejewski, 2011). The application of strong oxidants such as ozone, chlorine dioxide, permanganate, UV and hydrogen peroxide to DMA in the presence and absence of ammonia has been shown to result in NDMA formation (Andrzejewski and Nawrocki, 2007). A study at 11 wastewater plants using ozone found NDMA formation with concentrations ranging from less than 10 ng/L to 143 ng/L. NDMA formation was less in nitrified wastewaters and when the ozone-to-DOC ratio was less than 0.5 (Gerrity et al., 2014). It is suspected that the reaction between DMA and strong oxidants is direct nitrosation involving the oxidation of DMA into nitrite and nitrates, though the yields from these reactions are generally small and pH-dependent (Nawrocki and Andrzejewski, 2011).

Other studies have also documented NDMA formation via ozonation of DMA, but yields were low and formation only occurred at specific ozone-to-DMA ratios (Andrzejewski et al., 2008; Yang et al., 2009). Likewise, ozonation of MEA and DEA at a 1-to-1 molar ratio formed NMEA and NDEA, although yields were low and experiments were performed at pH 10.5 (Andrzejewski et al., 2008). Ozonation of UDMH or select compounds with UDMH-like functional groups results in NDMA yields of greater than 50 percent, however (Schmidt and Brauch, 2008; Kosaka et al., 2009). Marti et al. (2015) found that reaction of ozone with UDMH, acetone dimethylhydrazone, 2-furaldehyde dimethylhydrazone, daminozide, tetramethyl-4,4'-(methylenedi-*p*-phenylene)disemicarbazide and a toluene-derived dimethyl semicarbazide in wastewater all formed NDMA at molar yields of greater than 40 percent. Molar yields in ultrapure water with and without varying levels of bromide were approximately 40–90 percent of those in wastewater.

Treatment of DMA with chlorine dioxide or hydrogen peroxide has been shown to form NDMA, but yields from chlorine dioxide were 0.2 percent and NDMA formation was only observed with hydrogen peroxide at pH values greater than 10 (Andrzejewski and Nawrocki, 2007). Chlorine dioxide has also been shown to cause nitrosamine formation in the presence of a number of pharmaceutical and personal care products but at molar yields ranging from 6.9×10^{-6} to 0.055 percent (Zhang et al., 2014). Exposure of DMA to permanganate can lead to NDMA formation, but only at permanganate doses much greater than those typically used for water treatment (Andrzejewski and Nawrocki, 2009). Gan et al. (2015) found that daminozide formed NDMA at molar yields of up to 5.01 percent in the presence of chlorine dioxide. The proposed formation mechanism involved oxidation of the compound to form a UDMH intermediate.

Pozzi et al. (2011) observed NDBA, NDEA, NDPA and NMOR concentrations of up to 11.0 ng/L, 30.7 ng/L, 8.1 ng/L, and 83.7 ng/L, respectively, in finished water gathered from seven surface water plants and two ground water plants that disinfect with ozone and chlorine dioxide.

Zhao et al. (2008) observed elevated NDMA concentrations (compared to untreated water) following an AOP (namely, hydrogen peroxide (H_2O_2)/UV) in the absence of disinfectant

addition in some surface waters. Chlorination following AOP also resulted in increased NDMA concentrations for some surface waters.

Trogolo et al. (2015) found that ozone could react with *N,N*-dimethylsulfamide, an herbicide metabolite, to form NDMA. They found that the reaction was effected by hypobromous acid/hypobromite formed by oxidation of bromide. The mechanism involved oxidation of bromide to hypobromous acid by ozone followed by bromination of the sulfamoyl nitrogen in the DMS, deprotonation of the resulting complex, and attack by ozone. Lv et al. (2015) found that the pharmaceutical chlorpheniramine formed DMA when reacted with ozone. The DMA could then be oxidized by hydroxyl radicals formed by ozone to form NDMA. The reaction was dependent on pH, with the reaction inhibited at lower pH.

While the reactions of DMA with oxidants like ozone have been found to have relatively low yields, it is possible that with sufficiently high concentrations of precursors significant amounts of NDMA may be formed. It is also possible that other precursors exist that produce higher yields.

Soltermann et al. (2013) examined the reaction of chlorinated DMA and chloramine when irradiated with UV light in pool water. They found the reaction could form NDMA. They found that at some UV doses, the formation of NDMA from chlorinated DMA and chloramines could offset the destruction of NDMA by UV light. They proposed a reaction pathway involving the reaction of nitric oxide (NO) with an aminyl radical. They also found that NDEA and NMOR could be formed from chlorinated DEA and morpholine, respectively, in the presence of chloramines and UV light. Experiments with NDEA and NMOR suggest that peroxynitrite may be responsible for some nitrosamine formation under UV light.

Some studies have found oxidation to decrease nitrosamine formation through the oxidation of precursors to varying degrees (Wilczak et al., 2003; Lee et al., 2007a, 2008; Chen and Valentine, 2008; Mitch et al., 2009; Russell et al., 2012). While these results may seem contradictory, it should be noted that conditions and experimental setups varied from study to study. Many of the studies finding NDMA formation through oxidation have only looked at oxidation of DMA as a model precursor. On the other hand, many of the precursor oxidation studies used more complex waters with natural precursors or mixtures of precursors. One possible explanation is suggested by Lee et al. (2007b). They found that while chlorine dioxide reduced NDMA FP, the reduction in NDMA formation was not always as large as would be suggested by the disappearance of the NDMA precursor. The study found that oxidation of precursors such as dimethylaminobenzene resulted in production of DMA, which reacted only slowly with chlorine dioxide (Lee et al., 2007b). It seems likely that the reactions of strong oxidants with NDMA precursors in natural waters is a complex reaction that yields differing results depending on the nature and concentration of precursors and other water quality parameters. Continued research into the effects of oxidants on NDMA formation may shed more light on the reactions of NDMA precursors and the formation of NDMA.

6.4 Precursors: Sources and Characterization

This section focuses on the precursors specifically associated with nitrosamine formation. For a characterization of precursors and their occurrence for a wider range of DBPs, see the Agency's *Six-Year Review 3 Technical Support Document for Disinfectants and Disinfection By-Products Rules* (USEPA, 2016a).

NDMA precursors are distinct from the precursors that form chlorinated DBPs, such as THMs and HAAs, which are regulated under the Stage 1 and Stage 2 D/DBPRs. While naturally occurring humic substances are widely accepted to be the primary precursors for the formation of THMs and HAAs, they are not substantial precursors of NDMA (Gerecke and Sedlak, 2003; Mitch and Sedlak, 2004). Nitrosamine precursors may be naturally occurring or anthropogenic in origin. Potential NDMA precursors include DMA, organic nitrogen from natural organic matter (NOM) (Gerecke and Sedlak, 2003; Mitch and Sedlak, 2004; Chen and Valentine, 2007; Dotson et al., 2009), tertiary and quaternary amines (Mitch et al., 2003a; Mitch and Schreiber, 2008; Kemper et al., 2010), cationic flocculants (Wilczak et al., 2003; Valentine et al., 2005), and anionic exchange resins (Najm and Trussell, 2001; Kemper et al., 2010).

Under UCMR 2, NDMA, NMEA and NPYR were detected primarily in surface water PWSs, NDBA was detected in ground water public water systems (PWSs) but not surface water PWSs, and NDEA was detected in surface and ground water PWSs at similar frequencies. (NDPA was not detected in any samples.) Although these observations are based on a very limited number of detections in the case of several nitrosamines, they suggest that precursors of different nitrosamine compounds may be associated with different types of source waters. For NDMA, potential precursor compounds are typically associated with waste-impacted waters, and evidence suggests that anthropogenic materials have a significant role in formation, though naturally occurring precursors may also contribute to formation.

6.4.1 Natural Precursors

DMA, which has been used as a model precursor in the majority of laboratory experiments on NDMA, was initially thought to be a significant precursor of NDMA. DMA is a component of biological waste of both animal and human origin. Nawrocki and Andrzejewski (2011) report that few studies describe the occurrence of DMA in natural waters. Available occurrence data indicate concentrations from 3 µg/L to over 200 µg/L (Sacher et al., 1997; Zhao et al., 2003). Waters affected by wastewater effluent have higher concentrations of DMA than more pristine waters. Studies by Gerecke and Sedlak (2003) and Mitch and Sedlak (2004) showed that 70 percent of the dissolved NDMA precursors in primary wastewater effluent could be accounted for by DMA; however, DMA contributed to only 14 percent of the dissolved precursors in secondary effluent and less than 25 percent of precursors in non-impacted waters. Moreover, cellular and biological constituents do not serve as significant NDMA precursors (Gerecke and Sedlak, 2003; Mitch et al., 2003a).

The yields of nitrosamines from DMA and other secondary amines vary, but are relatively low. Zhou et al. (2014) looked at yields of nitrosamines from the reaction of the secondary amine and chloramine. They found yields ranging from 0.32 to 2.32 percent. They found that the yield was the highest for NPYR, followed by *N*-nitrosodiphenylamine (NDPhA), NDMA, NPIP, NMEA, NMOR, NDEA, NDPA and NDBA.

A number of researchers have shown that chloramination of NOM may result in the formation of nitrosamines, though not to levels exceeding 10 ng/L (Gerecke and Sedlak, 2003; Chen and Valentine 2006, 2007). For Iowa River water, the hydrophilic fractions of NOM tended to form more NDMA than hydrophobic fractions, and basic fractions tended to form more NDMA than acid fractions when normalized to a carbon basis (Chen and Valentine, 2006). Several studies found that NDMA precursors are derived primarily from predominantly non-polar molecules that also contain cationic functional groups (Liao et al., 2015a; Chen et al., 2014). Dotson et al.

(2009) reported that nitrosamine precursors were found primarily in the nitrogen-rich colloidal, hydrophilic neutral and hydrophilic base fractions of organic matter. Chuang et al. (2013) found NDMA formation to be correlated with (DON) compounds in the hydrophilic and transphilic fractions of NOM. (The transphilic portion is the portion with a polarity between the hydrophobic and hydrophilic portions.) Selbes et al. (2013) also found that the transphilic portion of NOM produced more NDMA than the hydrophobic portion, although when specific precursors were spiked into the different portions of NOM, in most cases molar yields were higher in the hydrophobic portions.

DON is a component of NOM and consists of organic nitrogen-containing compounds that pass through a filter. Total dissolved nitrogen includes DON along with ammonia, nitrate, nitrite and other inorganic nitrogen compounds. Natural DON sources include autochthonous organic matter and soluble microbial products. The contribution of DON to total dissolved nitrogen varies widely in surface waters (27 to 91 percent), as reported by Westerhoff and Mash (2002). Algally influenced waters have been associated with elevated nitrosamine formation, though, in comparison, wastewater-impacted source waters are generally more prone to NDMA formation (Shah and Mitch, 2012). Wang et al. (2015a) found that ash from forest fires formed more than twice as much NDMA following chloramination as unburnt natural organic matter.

6.4.2 Anthropogenic Precursors

A variety of anthropogenic compounds, including wastewater-derived chemicals in source water and chemicals added during drinking water treatment, can serve as precursors to nitrosamines.

6.4.2.1 Wastewater Flows

Several studies have demonstrated the accumulation of nitrosamine precursors in surface water, a phenomenon which has been attributed to the addition of wastewater effluent flows (Schreiber and Mitch, 2006b; Charrois et al., 2007; Sacher et al., 2008). FP tests of ground water, lakes and reservoirs indicate maximum NDMA precursor concentrations of 58 ng/L, while wastewaters were shown to contain up to 1,300 ng/L of nitrosamine precursors (Gerecke and Sedlak, 2003; Pehlivanoglu-Mantas and Sedlak, 2006). Krasner et al. (2015) found a correlation between sucralose, which is considered an indicator of wastewater presence, and NDMA FP in some watersheds. Similarly, Uzun et al. (2015) found that in free-flowing rivers in the southeastern United States, NDMA FP depended on the ratio of wastewater effluent to river flow. The impact of wastewater was often found to increase as river flows decreased. Lee et al. (2015) sampled two wastewater treatment plant effluents as well as upstream and downstream of the two plants in the Sacramento-San Joaquin Delta. They found median increases in NDMA FP (from the upstream to downstream locations) of 5 to 17 ng/L at one plant and 16 to 40 ng/L at the other plant. NDMA and NPYR precursors were found in the plant effluent, as well as preformed NMOR. No nitrosamines were found in the river water, possibly because of dilution or photolysis.

High concentrations of NDMA precursors in municipal wastewater effluent may be explained by the contributions of DMA and related compounds from industrial, domestic and agricultural sources. Both direct waste flows and surface runoff may contribute to the precursor materials observed in wastewater flows. In addition to precursors, wastewater effluent may contain nitrosamines themselves. Nitrosamine concentrations in treated wastewater are affected by wastewater treatment processes, including nitrification and disinfection (Krasner et al., 2009).

Nitrosamines in wastewater effluents are a matter of concern for drinking water PWSs, as nitrosamines have been found in drinking water influents located downstream from wastewater plant discharge points (Krasner et al., 2005; Drewes et al., 2006).

Several researchers studied the effects of wastewater treatment on NDMA formation in wastewater. Qi et al. (2014) found between 300 and 600 ng/L of NDMA in secondary effluent of a Chinese wastewater plant; no advanced disinfection was in place at that plant. Sgroi et al. (2015) found that chlorinating wastewater from a wastewater treatment plant used for indirect potable use formed up to 248 ng/L NDMA. While reverse osmosis (RO) and UV treatment processes reduced the concentrations of NDMA, up to 16 ng/L was still observed in the plant effluent. This may have been due to the presence of small nonpolar molecules such as dimethylformamide, which can pass through RO membranes and form NDMA upon reaction with chloramines formed by reaction of chlorine with ammonia in the wastewater. Sgroi et al. (2015) also demonstrated that ozonating wastewater containing chloramines formed more NDMA than chloramines alone. Similarly, Gerrity et al. (2015) found both NDMA and NMOR at concentrations up to 89 ng/L for NDMA and 67 ng/L for NMOR in primary wastewater effluent. They also found ozone-induced formation of nitrosamines ranging from 10 to 143 ng/L in ten of eleven wastewater treatment plants examined, although biological filtration and/or UV after ozone was able to control the formed NDMA. Kosaka et al. (2014) found an NDMA precursor, 1,1,5,5-tetramethylcarbohydrazide, in industrial effluent-containing sewage in the Yodo River basin in Japan. The precursor reacted with ozone to form NDMA with a molecular yield of 140 percent. This precursor was found to account for between 42 and 72 percent of all NDMA in the sewage treatment plant effluent.

Several studies investigated the sources of nitrosamine precursors. Zeng and Mitch (2015) examined NDMA formation from chloramination or ozonation of various wastewater sources including shower, sink, toilet and laundry. They found that the laundry contributed 58 percent of NDMA precursors in chloraminated water and 99 percent of NDMA precursors in ozonated water. The shower was also a significant source of NDMA precursors in chloraminated water. Use of ranitidine pharmaceuticals significantly increased NDMA FP of urine although not enough to become a significant source of NDMA compared to other streams when volume is taken into account. Yoon and Tanaka (2014) performed laboratory experiments adding amines from pollutant inventories to wastewater samples from a Japanese wastewater plant. Samples were reacted with chloramine and ozone and nitrosamine formation was measured. All of the secondary and tertiary amines tested and many of the primary amines reacted with chloramine to form NDMA. Ozone produced NDMA from 1,1 dimethylhydrazine, formed NDEA from p-chloroaniline, and formed NMOR and NDBA from primary amines. Qi et al. (2014) found that NDMA FP in secondary effluents correlated best to low molecular weight DON fractions. Ma et al. (2015) examined nitrosamine formation from various wastewater microbial products. They found that microbial products associated with microbial utilization or decay formed twice as much NDMA as products associated with biomass or microbial growth.

Industrial Effluents

Though some secondary amines are found in the natural environment, many may also be industrial in origin. For example, DEA is used in the production of rubber, textiles, resins, dyes and insecticides and as a flame retardant. DPA, piperidine (precursor to NPIP), and pyrrolidine (precursor to NPYR) are used in the production of dyes, pesticides, lacquers, and rubber manufacturing.

Industrial effluents may be a significant source of NDMA precursors. Industrial discharges have been shown to contain up to 82,000 ng/L of NDMA precursors (Deeb et al., 2006). Yoon and Tanaka (2014) found that 15 amines that are common industrial emissions were precursors for nitrosamines when oxidized in a Japanese wastewater using either ozone or chloramines.

Parker et al. (2014) investigated the influence of hydraulic fracturing wastewater on NDMA formation. They diluted wastewater from a domestic wastewater treatment plant and from three hydraulic fracturing wastewaters with river water from Ohio and Pennsylvania and measured the formation of nitrosamines. Without either domestic wastewater or water from hydraulic fracturing wastewater, no NDMA was formed. Addition of 10 percent domestic wastewater led to formation of about 7 ng/L of NDMA. Adding just 0.1 percent of hydraulic fracturing wastewater led to a 50 percent increase in NDMA formation. NDMA formation was higher in waters with higher iodide levels.

Pharmaceuticals and Personal Care Products

Recent studies have shown that a number of pharmaceuticals and personal care products contain nitrosamine precursors. The pharmaceutical ranitidine (Zantac) has been shown to convert to NDMA at high yields (over 60 percent) under chloramination (Schmidt et al., 2006; Sacher et al., 2008; Le Roux et al., 2011; Shen and Andrews, 2011a, 2011b). Shen and Andrews (2011a) found that 20 different pharmaceuticals (including ranitidine) tested formed nitrosamines during chloramination, with eight pharmaceuticals demonstrating NDMA yields greater than 1 percent. Of the eight, ranitidine was the highest with 89.9 to 94.2 percent yield. The other seven all had single digit percentage yields.

Nitrosamine formation has also been associated with quaternary amines, which are significant constituents of consumer products, including shampoos, detergents and fabric softeners (Kemper et al., 2010). Kemper et al. (2010) chloraminated a range of model compounds and personal care products to determine their NDMA FP and found that polymeric and benzylated quaternary amines were stronger precursors than monomeric quaternary alkylamines. An NDMA FP test of Suave® Shampoo resulted in 0.00005 mass yield of NDMA while cocamidopropyl betaine, an ingredient found in Suave® Shampoo, resulted in 0.16 percent molar yield of NDMA. Dawn® detergent exhibited an NDMA FP 25 times higher than Suave® Shampoo (Kemper et al., 2010). Kemper et al. (2010) showed that the NDMA yields associated with personal care products indicate that those products could account for 2 to 3 percent of the total NDMA precursor loading at a wastewater treatment facility. Benzalkonium chloride, a quaternary amine surfactant found in antimicrobial soaps, gave a 2.1 percent molar yield of NDMA after 10 days of contact with a high dose of chloramines at pH 7 (Mitch et al., 2009). A likely tertiary amine breakdown product, DMBzA showed a 300 times higher yield under the same conditions (Mitch et al., 2009).

Amine-based pharmaceutical and personal care products have also been shown to form nitrosamines upon disinfection using chlorine or chlorine dioxide, although at much lower molar yields (Zhang et al., 2014). For example, molar yields for ranitidine with chlorine or chlorine dioxide were 0.050 and 0.055 percent, respectively, compared to 40.2–90.6 percent for chloramine. Ranitidine had the highest yield of ten pharmaceutical and personal care products examined (Zhang et al., 2014).

Pesticides and Herbicides

A number of pesticides and herbicides have also been shown to be NDMA precursors, with some compounds resulting in the formation of NDMA at relatively high yields. DMS, a degradate of the pesticide tolylfluanid, formed NDMA at 52 percent molar yield upon application of 6 mg/L ozone. Because DMS is not removed by riverbank filtration, flocculation or activated carbon, it can contribute significantly to the formation of NDMA in drinking waters. Depending on the treatment processes and degree of contamination at drinking water facilities, 73 to 100 percent of DMS can be transformed, resulting in NDMA concentrations ranging from 1.9 to 310 ng/L (Schmidt and Brauch, 2008).

Other pesticides have been shown to form NDMA upon addition of nitrite, ammonia, and free chlorine, including thiram, sodium dimethyldithiocarbamate, 1,1-dimethyl-3-(4-methoxyphenyl)-2-thiourea, and 1,1,3,3-tetramethyl-2-thiourea. These chemicals produced 5 to 30 times the NDMA formed from DMA under the same conditions (Valentine et al., 2005). Application of 6 mg/L of ozone for 30 minutes to 2 µg/L of the pesticide daminozide led to an 80 percent molar yield of NDMA (Sedlak et al., 2005). Twenty-two micrograms per liter (22,000 ng/L) of NDMA formed when 0.086 mM of the pesticide diuron was added to a well-mixed solution of 4.1 mM ammonia and 3.45 mM free chlorine, while the application of free chlorine alone formed 15.8 µg/L (15,800 ng/L) of NDMA. However, diuron is not expected to be a significant source of NDMA because at reactant concentrations more representative of water treatment operations, NDMA was not detected upon chloramination of diuron (Chen and Young, 2008, 2009). At the same time, this formation pathway is important because it can proceed without the addition of another nitrogen source such as ammonium or nitrate (Chen and Young, 2009). Chen et al. (2015a) found that chlorine or chloramine could react with five different phenylurea-based herbicides to produce NDMA or NPYR at molar yields between 0.003 and 0.99 percent. Dithiocarbamates have been found to form nitrosamines when exposed to chloramine, ozone, chlorine, or chlorine dioxide (Padhye et al., 2013). Fifty µM pesticide with 100 µM disinfectant yielded between 118 and 302 ng/L nitrosamines. Chloramine and ozone formed more nitrosamines from dithiocarbamate pesticides than did chlorine or chlorine dioxide. Hydrolysis of the pesticides to form amines, followed by oxidation of the amines by the disinfectant, likely contributed to nitrosamine formation.

During the application of fumigants containing dimethyldithiocarbamates for root control to sewer trunklines in residential and industrial areas, concentrations of NDMA were found to be 2,400 ng/L, and the concentration of NDMA precursors was found to be 89,000 ng/L in the collection area (Deeb et al., 2006). During the application of metam sodium, a dithiocarbamate used for root control, NDMA concentrations greater than 2,000 ng/L were detected in residential trunklines (Sedlak et al., 2005).

Dyes

Ozonation of dyes such as methylene blue, methyl orange, methyl violet B, Auramine, brilliant green, *N,N*-dimethylaminobenzene and *N,N*-dimethyl-p-phenylenediamine yielded NDMA ranging from 0.0001 to 0.043 percent upon treatment with ozone at a flow rate of 1 mL/min for 15 min at pH 7 in deionized water (Oya et al., 2008).

Anti-yellowing agents 4,4'-hexamethylenebis(1,1-dimethylsemicarbazide) and 1,1,1',1'-tetramethyl-4,4'-(methylenedi-p-phenylene)disemicarbazide contributed to 1.4 percent of the

NDMA formation formed from ozonation of a secondary wastewater effluent (Kosaka et al., 2009).

Nanomaterials

Verdugo et al. (2014) found that carbon nanotubes could act as both a source of NDMA contamination and a precursor to NDMA formation. They found that carbon nanotube powders with amine, amide, or other nitrogen-containing polymer groups leached up to 50 ng of NDMA per mg of nanotube powder before any reactions occurred. These nanotube powders formed additional NDMA upon disinfection with chlorine, monochloramine, or ozone. Formation yields of NDMA were approximately equivalent to yields from reactions of chloramine with NOM.

6.4.2.2 Treatment Additions

Polymer Addition

In addition to precursor material from source waters, NDMA formation has also been associated with flocculation polymers and ion exchange resins applied during the treatment process. A survey conducted in the United Kingdom indicates that ferric coagulant may be a source of NDMA (DEFRA, 2008). Numerous studies have shown that cationic polymers, including polyDADMAC and epichlorohydrin-dimethylamine (epi-DMA), may be sources of NDMA precursors (Kohut and Andrews, 2003; Valentine et al., 2005; Wilczak et al. 2003; Park et al., 2009).

PolyDADMAC is a cationic polymer widely used for primary coagulation (Montgomery, 1985). Several studies have shown correlations between polyDADMAC dose and NDMA formation in pilot- and full-scale water treatment plants using chloramines, indicating that polyDADMAC may be a source of NDMA precursors (Wilczak et al., 2003; Valentine et al., 2005; Mitch et al., 2009). Wilczak et al. (2003) observed enhanced NDMA formation when polyDADMAC was added prior to chloramination, but not for chlorination. For chloramination, the order of reagent addition was observed to be important, with the highest NDMA formation observed when polymer was added to the test water and followed immediately by chloramine formation. The authors suggest that NDMA formation could be reduced if chloramination occurred after filtration to allow for polymer removal. They also suggested allowing for a short free chlorine contact time before ammonia addition to allow for precursor oxidation to reduce NDMA formation. Mitch et al. (2009) also found that effluent NDMA concentrations at chloramine treatment plants generally increased with increased polymer dose.

Valentine et al. (2005) found a linear relationship between polyDADMAC dose and NDMA formation following chlorination, though NDMA concentrations were much less than those reported by Wilczak et al. (2003) for chloramination. This finding suggests that chlorine may be more efficient at breaking polymer bonds. However, Valentine et al. (2005) observed greater NDMA formation when polyDADMAC reacted with chlorine than with chloramine, indicating that other water quality parameters, such as the presence of nitrite, may impact which disinfectant contributes to NDMA formation. Experiments showed that polymer dose and the interaction of nitrite, polymer and chlorine were important to NDMA formation when polyDADMAC interacted with chlorine, while only polymer dose was found to be important when polyDADMAC reacted with chloramine (Valentine et al., 2005).

Padhye (2010) found in laboratory experiments that doses of 5–10 mg/L of polyDADMAC could yield up to 800 ng/L of NDMA upon ozonation of the polymer. The NDMA appeared to be formed as a result of oxidation of the polymer to release DMA, followed by oxidation of the DMA. Padhye (2010) also found that NDMA formation upon ozonation of polyDADMAC increased with higher pH.

Park et al. (2014) found that NDMA formation for polyDADMAC was the greatest when the chlorine-to-ammonia ratio was close to the breakpoint. Later experiments found that a chlorine-to-ammonia ratio of 1.4 formed the most from polyDADMAC polymers (Park et al., 2015). They also found that adding chloramine followed by free chlorine gave the highest NDMA formation. They found that chloramines were the mostly likely oxidant to form NDMA, followed by chlorine, ozone and chlorine dioxide. Pre-oxidation in some cases was able to lower NDMA formation by altering the polymer structure to make it less susceptible to reaction. With pre-oxidation using ozone, however, NDMA formation increased, possibly due to release and oxidation of DMA.

Other polymers, including polyamine, epi-DMA and epi-DMA with ethylenediamine (epi-DMA-co-ED), also showed elevated NDMA formation following reactions with chlorine and chloramines (Valentine et al., 2005; Park et al., 2015). Park et al. (2015) found that a chlorine-to-ammonia ratio of 1.8 maximized NDMA formation from polyamine polymers. Chlorination of epi-DMA has been shown to result in greater formation of NDMA than polyDADMAC (Valentine et al., 2005). NDMA has also been detected during application of free chlorine or chloramine to polyamines or when tap water containing polyamine was amended with nitrite (Bolto, 2005; Kohut and Andrews, 2003; Park et al., 2014). No difference in NDMA formation was seen between chlorine and chloramine reactions with polyamines (Valentine et al., 2005).

Through a series of purification experiments, Park et al. (2009) showed that the polymer itself, and not any impurities, is responsible for NDMA formation upon chloramination of polyDADMAC and polyamine polymers. Though free DMA may exist as an impurity in polymer stocks, Park et al. (2009) found that NDMA formation is more dependent on DMA released by polymer degradation following reactions with chloramine than by residual DMA present in the polymer. Ozonation of polyDADMAC has been shown to result in substantial release of DMA, such that increased NDMA formation may occur if chloramines are added subsequent to the ozonation process (Huang et al., 2011). Valentine et al. (2005) examined an experimental version of polyDADMAC reported by the manufacturer to have 20 times less free DMA than conventional polyDADMAC polymers. Upon chlorination the new polymer did show lower NDMA production, but the production was about a third of the original polymer, not a twentieth, as might be expected if free DMA impurities were largely responsible for NDMA formation (Valentine et al., 2005).

The age of polyDADMAC stocks does not appear to have a substantial impact on NDMA formation (Kohut and Andrews, 2003; Valentine et al., 2005). Valentine et al. (2005) reported that the age of polyDADMAC-prepared stock had a significant effect on NDMA over the 50-hour tested interval; however, the authors concluded that NDMA yields were most likely not affected by the age of polyDADMAC-prepared stock within the range applicable to coagulant use, because the stock is used in 48 hours or less. NDMA yields for epi-DMA did not increase over the entire 50-hour test interval, but did increase within the first five hours of aging, though NDMA formation reached a plateau as the age further increased (Kohut and Andrews, 2003; Valentine et al., 2005).

In a survey of 100 utilities (including 88 from UCMR 2 and 12 from the Ontario Drinking Water Surveillance Program), no significant difference was observed in NDMA concentrations between utilities that used cationic polymers and those that did not (Russell et al., 2012). However, a smaller study found that among plants employing coagulation there was a 43–82 percent increase in NDMA in plants using cationic polymers, compared to no increase in a plant not using cationic polymer (Krasner et al. 2012b). These findings suggest that multiple factors may influence the possibility of higher NDMA formation from cationic polymers. The results of the survey by Russell et al. (2012) suggest that the use of chloramines was a more important factor than polymer use in NDMA formation.

Sgroi et al. (2014) found that polyacrylamide polymers used to treat sludge at wastewater plants formed NDMA upon reaction with ozone. The polymer entered the wastewater plant through the recycle stream from the sludge treatment process and was the single largest source of NDMA precursors in the wastewater treatment plant.

Anion Exchange Resins

Anion exchange resins, which contain quaternary amines, have been found to release NDMA directly, as well as to release amines that can form NDMA upon reaction with chloramines (Kemper et al., 2009). Najm and Trussell (2001) examined four strong base anion exchange resins for NDMA formation. The resins were based on dimethyl-ethanol, trimethyl, triethyl, and tripropyl functional groups. They soaked the resins in three different unchlorinated waters: deionized water, ground water and buffered distilled water. They found that the dimethyl-ethanol and trimethyl functional groups both produced NDMA, with the dimethyl-ethanol quarternary amine forming the most NDMA. They postulated the triethyl and tripropyl functional groups may have formed NDEA and NDPA, respectively, but did not test this hypothesis (Najm and Trussell, 2001).

Kemper et al. (2009) conducted a series of column studies to examine the nitrosamine and nitrosamine precursors associated with two types of anion exchange resins. In the absence of any disinfectant, the authors found that NDMA was released by fresh alkylamine (trimethylamine (TMA) and tributylamine) and dialkylethanolamine anion exchange resins in the range of 2 to 10 ng/L and at up to 20 ng/L following regeneration. In the presence of feedwaters containing 2 mg/L free chlorine or 2 mg/L monochloramine, NDMA concentrations and NDMA precursor concentrations increased. For alkylamine resins, the NDMA concentration was approximately 300 ng/L when chlorine was applied upstream, and ranged from 10 to 100 ng/L when monochloramine was applied upstream. For the tributylamine resin, NDBA concentrations were less than 60 ng/L for both chlorine and monochloramine feedwaters. For the TMA resin, NDMA precursor concentrations initially spiked to approximately 16,000 and 20,000 ng/L in the presence of chlorine and chloramine feedwaters, respectively, but then rapidly declined. For the tributylamine resin, NDMA precursor concentrations were generally low, though NDBA precursors were observed at levels of 1,700 ng/L and 6,000 ng/L for chlorine and monochloramine, respectively, before rapidly declining to less than 500 ng/L. For the dialkylethanolamine resin, NDMA concentrations were similar for feedwaters containing free chlorine and monochloramine and ranged from 200 to 800 ng/L. NDMA precursor concentrations were less than 500 ng/L for chloramines and ranged from 1,500 to 3,500 ng/L for feedwaters containing free chlorine. Nitrosamine concentrations and precursor concentrations diminished after multiple regeneration cycles, indicating that releases may eventually subside (Kemper et al., 2009).

Flowers and Singer (2013) examined 21 different resins containing trialkylamine or dimethylethanolamine groups using both batch desorption and laboratory column flow-through experiments. They found that six resins desorbed nitrosamines in batch experiments where washed resins were exposed to clean water for an hour. The resins that released nitrosamines included A530E, A600E, CalRes 2103, PWA2, PWA5 and PWA15. A530E contained triethylamine and tributylamine groups, A600E contained trimethylamine, CalRes 2103 contained tripropylamine, PWA2 contained tributylamine, PWA5 contained triethylamine and PWA15 contained trimethylamine. Released nitrosamines included NDMA (from A530E, A600E, PWA2 and PWA15, at concentrations less than 10 ng/L), NDPA (from CalRes 2103 at a concentration of about 10 ng/L), NDEA (from PWA15 at a concentration of about 15 ng/L and A530E at a concentration of about 110 ng/L) and NDBA (from A530E at a concentration of 974 ng/L and PWA2 at a concentration of 592 ng/L). A flow-through column experiment with resin A300E released 223 ng/L NDMA in the first 10 bed volumes; that level dropped to 23 ng/L NDMA after 50 bed volumes. It took 240 bed volumes before the NDMA dropped below detection levels. The experiments with resin A300E also found the release of 1,402 ng/L of nitrosamine precursors in the initial 10 bed volumes, dropping down to 34 ng/L after 50 bed volumes. Regeneration of the column led to a temporary increase of 50 ng/L in precursor concentrations. When similar column experiments were performed with other resins, seven of the 15 resins were found to release quantifiable levels of nitrosamines, which declined over time, generally washing away after 100 bed volumes. Introducing 0.24 mg/L chlorine or chloramine to the feedwater increased the concentration of released nitrosamines, with chloramines producing more nitrosamines than chlorine. For example, resin PWA2 produced no detectable NDMA with chlorine, but 1,240 ng/L of NDMA with chloramines.

Magnetic ion exchange resin (MIEX) has also been found to form nitrosamines, especially when used in wastewater with chloramine exposure. Gan et al. (2013) found MIEX resin formed 36 ng/L NDMA when used to treat wastewater in combination with chloramines. If chlorine was used, NDMA formation was only 10 ng/L. If MIEX alone was used to treat drinking water, NDMA formation was 5 ng/L.

Use of Rubber Distribution System Components

Studies have also found that NDMA in drinking water may originate from rubber gaskets or sealing rings within the distribution system (Morran et al., 2011; Teefy et al., 2011). Morran et al. (2011) did not observe a trend between the amount of NDMA released and sealing ring size or age from bench-scale studies, and they suggested that the variability may be due to differences in the manufacturing process and/or in the leaching rates. During a distribution system extension project in South Australia, elevated NDMA concentrations were observed in a new polyvinyl chloride pipeline (Morran et al., 2011). NDMA concentrations in the new pipeline exceeded 100 ng/L, in comparison to concentrations of 9 to 34 ng/L for an existing concrete-lined pipe distributing water from the same source. Laboratory tests revealed that sealing gaskets used in the pipe were a substantial source of NDMA (~40 ng/L), while neither polyvinyl chloride nor lubricant released any measureable NDMA (Morran et al., 2011).

Though no changes had occurred in the water treatment process in a California plant, an elevated NDMA concentration (21 ng/L) was observed in the distribution system downstream from a temporary storage tank that contained rubber gaskets (Teefy et al., 2011). A bench-scale study found that NDBA, NDMA and NPIP were present in test water following the exposure of the gaskets to chloraminated system water for periods of 2 and 14 days. Concentrations of NDMA

and NPIP increased over time, while NDBA concentrations were similar for both test periods. New gasket material released higher concentrations of the measured nitrosamines than gaskets that had been in use. A comparison study conducted with water in the absence of chloramines resulted in NDMA concentrations similar to those measured for the chloraminated water, indicating that the NDMA leached directly from the gaskets, and did not form due to a reaction with chloramines (Teefy et al., 2011). A follow-up study (Teefy et al., 2014) found that the nitrosamines were present whether or not chloramines were used and that NDBA and NPIP were more prevalent in the newer gasket material, while NDMA was prevalent in the used gasket material. The results of this and other studies discussed previously show that NDMA levels may increase within the distribution system because of leaching of NDMA from rubber distribution system components, regardless of the disinfectant used at the treatment facility.

6.4.3 Precursor Characterization

Although specific precursors have not yet been identified, work with model precursors has shown that tertiary amines with DMA functional groups form NDMA at higher yields than amides with DMA functional groups (Mitch and Sedlak, 2004; Chen and Young, 2008). Amine-based nitrosamine precursors tend to be found in low molecular weight hydrophilic neutral or base fractions, which are poorly removed during conventional water treatment processes compared to the hydrophobic fractions that contain THM precursors (Dotson and Westerhoff, 2009, Chuang et al., 2013, Wang et al., 2013a). Amines are more reactive with oxidants, such as free chlorine, than are other major nitrogenous functional groups (Hawkins et al., 2003; Shah and Mitch, 2012).

Studies on the relationships between NDMA formation and bulk water quality parameters, such as DOC concentration and DON concentration, have shown inconsistent results, with relationships appearing to be water-specific. Ultraviolet absorbance (UVA) and fluorescence have also been studied as possible indicators.

One of the challenges of determining broadly applicable relationships for NDMA formation is that most studies aggregate data from different water types exhibiting different chemistry and NOM characteristics. For example, organic matter from algal and other sources may confound establishment of relationships between NDMA and organic matter of waste origin (Mitch et al., 2009).

Other properties in addition to DOC, DON and UVA have also been considered. Upon monitoring total organic carbon (TOC), pH, turbidity and color, Zhao et al. (2008) found no relationship between these factors and NDMA formation in surface waters. Yang et al. (2015) used fluorescence excitation emission to correlate NDMA formation to protein-like organic components.

6.4.3.1 Dissolved Organic Carbon (DOC) Concentration

Though DOC concentration has been used as a surrogate measure for the formation of other DBPs, the relationship between DOC concentration and nitrosamine formation is unclear. Gerecke and Sedlak (2003) found a strong linear relationship between DOC concentration and NDMA FP for Suwanee River NOM ($r^2 = 0.98$), but found only a weak correlation for other surface waters ($r^2 = 0.41$). Krasner et al. (2008) found a correlation between DOC and NDMA FP for a wastewater-impacted river. Zhao et al. (2008) did not find a significant relationship

between TOC (of which DOC is one component) and NDMA FP in a study of seven surface waters. Li et al. (2015) reported a linear correlation between DOC and total nitrosamine concentrations in raw water; however, similar relationships were not established between DOC and nitrosamine concentrations in finished water or distribution system water.

6.4.3.2 Dissolved Organic Nitrogen (DON) Concentration

Lee et al. (2007b) hypothesized that NDMA formation would increase for organic matter that was enriched in organic nitrogen. The authors found that NDMA formation increased as the DOC-to-DON ratio decreased (i.e., increasing nitrogen content of dissolved organic matter, or DOM). The authors also found that NDMA formation increased as the amino sugar-to-aromatic ratio of DOM increased.

Drinking water treatment plants with source waters impacted by algae and/or wastewater have higher DON concentrations than treatment plants with more pristine source waters (Mitch et al., 2009). Higher DON concentrations observed in algal and wastewater-influenced waters have also been associated with higher nitrosamine formation (Schreiber and Mitch, 2006b; Krasner et al., 2008; Chen et al., 2009). However, consistent relationships between DON concentration and nitrosamine formation have not been determined. The lack of clear relationship is highlighted by two case studies for wastewater-impacted rivers presented by Krasner et al. (2008). For the South Platte River, Colorado, a weak relationship between DON concentration and NDMA FP was found ($r^2 = 0.49$), while a strong linear relationship ($r^2 = 0.83$) was observed for the Santa Cruz River, Arizona. Mitch et al. (2009) found no correlation between DON concentration and NDMA FP from wastewater- or algal-impacted raw drinking water. Xu et al. (2011) showed that DON concentration correlated with NDMA FP for raw water in Shanghai, China ($r^2 = 0.77$). Wang et al. (2015b) noted an increase in nitrosamine concentrations in post-disinfection drinking water upon switching from the Luan River to the Yellow River over an 11-month period. Source water from the Luan River was used from June to October and the source was switched to the Yellow River for November to April. The authors cite higher levels of precursors in the Yellow River as a potential cause and note a correlation between DON and the formation of nitrosamines; however, the effect of the lower water temperatures that would have been present when the Yellow River was used as source water was not discussed at length. As discussed in Section 6.5.2, lower water temperatures may be associated with increases in the concentration of some nitrosamines and decreases in the concentration of other nitrosamines.

6.4.3.3 Ultraviolet Absorbance (UVA)

UVA and specific UVA (SUVA), which is the UV absorbance divided by the DOC concentration, have both been associated with the formation of other DBPs, though their use as surrogate measures for nitrosamine formation is less certain. Wastewater, which has been shown to be rich in nitrosamine precursors, generally has low SUVA values (Krasner et al., 2008). Chen and Valentine (2007) found an inverse linear relationship with NDMA FP and SUVA at 272 nm for Iowa River water. However, the authors did not observe a relationship between NDMA FP and SUVA at 254 nm or 272 nm for NOM fractions, indicating that SUVA may not be useful as a universal index for NDMA FP. Zhao et al. (2008) found no significant relationship between UVA at 254 nm and NDMA FP in a study of seven surface waters. Li et al. (2015) reported a linear correlation between UVA at 254 nm and 272 nm and total nitrosamine concentrations in raw water; however, similar relationships were not established between UVA at 254 nm and 272 nm and nitrosamine concentrations in finished water or distribution system water. Negative

correlations were observed between SUVA at 254 nm and 272 nm and total nitrosamine concentrations in raw water.

6.4.3.4 Fluorescence

A number of studies have found relationships between DOM fluorescence and regulated DBP concentrations (Marhaba and Kochar, 2000; Hua et al., 2007; Beggs et al., 2009; Kraus et al., 2010). Limited information is available regarding relationships between DOM fluorescence and nitrosamine formation. Lee et al. (2006) found a correlation between DON concentrations and protein-like (excitation 270–280 nm; emission 300–350 nm) fluorescence intensities ($r^2 = 0.71$). Hua et al. (2007) also found protein-like fluorescence (excitation 290–310 nm; emission 330–350 nm) to be associated with NDMA formation. Though no relationship was observed between DOC concentration and NDMA FP for a diverse group of 53 Missouri lakes, a correlation for a subset of the lakes with medium to high fluorescence intensity was observed ($r^2 = 0.63$).

Exhibit 6.3 provides a summary of reported correlations between nitrosamine FP and organic carbon and organic nitrogen.

Exhibit 6.3: Studies Correlating Organic Carbon and Organic Nitrogen to NDMA Formation Potential

Study	FP Conditions	Correlation of NDMA FP to Organic Carbon	Correlation of NDMA FP to Organic Nitrogen	Water Type
Gerecke and Sedlak, 2003	2 mM chloramines, pH 7, 25 °C, 10 days	Linear (r^2 = 0.41)	N/A	Reservoir water, ground water, and eutrophic lake
Gerecke and Sedlak, 2003	2 mM chloramines, pH 7, 10 days	Linear (r^2 = 0.98)	N/A	Suwannee River NOM
Hua et al., 2007	1 mM chloramines to 50 ml water sample in a brown bottle; sample allowed to react in dark for 7 days at room temperature	None	N/A	Surface waters
Hua et al., 2007	1 mM chloramines to 50 ml water sample in a brown bottle; sample allowed to react in dark for 7 days at room temperature	Linear (r^2 = 0.63)	N/A	Lakes with high protein-like fluorescence intensity
Lee et al., 2007b	0.634 mM chloramines per mg DOC, pH 7, 10 days	*	*	Raw drinking water
Krasner et al., 2008	Chloramines added to 3x weight of TOC, pH 8, 25 °C, 3 days	N/A	Linear (r^2 = 0.47)	Wastewater effluent, drinking water influent, ground water, and surface water
Krasner et al., 2008	Chloramines added to 3x weight of TOC, pH 8, 25 °C, 3 days	Linear (r^2 = 0.80)	Linear (r^2 = 0.83)	Santa Cruz River, Arizona (wastewater-impacted)
Krasner et al., 2008	Chloramines added to 3x weight of TOC, pH 8, 25 °C, 3 days	N/A	Linear (r^2 = 0.49)	South Platte River, Colorado (wastewater-impacted)
Mitch et al., 2009	2 mM chloramines, pH 7, 10 days	N/A	None	Waste- or algal- impacted raw drinking water
Xu et al., 2011	2 mM chloramines, pH 7, 25 °C, 7 days	N/A	Linear (r^2 = 0.77)	Raw water (from river in China)

* Non-linear correlation ($r^2 = 0.40$) found between DOC/DON ratio and NDMA.

6.5 Key Factors Impacting Formation

A range of factors influences the formation of nitrosamines in drinking water. In this section, the impacts of chloramination/chlorination conditions, along with water quality parameters such as DO, pH, temperature and bromide, are discussed.

6.5.1 The Impact of Chlorination and Chloramination

Utilities that switch their disinfectant from chlorine to chloramine may see an increase in the formation of NDMA depending on the availability of precursor material in the source water. Data from UCMR 2 show that over 34 percent of samples collected from chloraminating PWSs had NDMA concentrations greater than the MRL, compared to approximately 4 percent of samples from chlorinated PWSs. In addition to chloraminating PWSs, water recycling facilities and utilities adding chlorine to ammonia-containing source waters may also see elevated NDMA formation.

Dichloramine has been shown to contribute to NDMA formation rates at least an order of magnitude higher than monochloramine (Schreiber and Mitch, 2005, 2006a). Under typical drinking water treatment conditions, monochloramine is the dominant chloramine species, though dichloramine is also present. Chloramine speciation is impacted by both pH and the chlorine-to-ammonia (Cl_2:NH_3) molar ratio. For drinking water utilities that practice chloramination, research has shown that the use of preformed chloramines, formed under conditions that favor monochloramine (pH > 8.5 and Cl_2:NH_3 molar ratio <<1), helps to minimize NDMA formation by reducing the formation of dichloramine (Schreiber and Mitch, 2005; Mitch et al., 2005). Dichloramine formation from the disproportionation of monochloramine is slow, such that dichloramine formation after the application of preformed monochloramine should be minimal (Schreiber and Mitch, 2006a).

Schreiber and Mitch (2005) found that the order in which reagents are added during chloramination treatment may also play a role in nitrosamine formation. Based on experiments with wastewater, the authors proposed that greater NDMA formation occurs in drinking water when chlorine is added after ammonia for *in situ* chloramination than when ammonia is added after chlorine. This occurred even at molar Cl:N ratios of less than 1:1, because of localized dichloramine formation in areas where the molar Cl:N ratio exceeds 1:1 at the point of chlorine addition prior to complete mixing (Schreiber and Mitch, 2005). Also, under the right conditions, pre-chlorination of NDMA's precursor DMA will result in the formation of chlorinated DMA, which when exposed to ammonia forms almost an order of magnitude less NDMA than does DMA (Schreiber and Mitch, 2005).

Krasner et al. (2008) showed that nitrosamine formation increased after chlorination if the addition of chlorine resulted in the formation of chloramines. For example, at wastewater treatment plants with a Cl_2:N ratio of less than 10:1 (by weight), NDMA concentrations ranged from non-detection to 3,165 ng/L. When the Cl_2:N ratio exceeded 10:1 (by weight), NDMA ranged from non-detection to 8.2 ng/L. Other nitrosamines such as NDEA, NDPA and NPYR also showed increased formation in the presence of chloramines (Krasner et al., 2008).

Longer contact times with chloramines have been associated with increased nitrosamine concentrations because of the slow kinetics of the reaction (Mitch et al., 2003a). Therefore, measurements made at the treatment plant may not be representative of the maximum formation,

as nitrosamine formation may continue within the distribution system. UCMR 2 data provide evidence of this continuing reaction, as shown in Exhibit 6.4. The exhibit shows, for maximum residence (MR) time and entry point (EP) locations sampled in UCMR 2 where only chloramine disinfection was used, the number and percentage of those locations at which one or more samples exceeded various concentration thresholds for NDMA. At all concentration thresholds, the rate of threshold exceedance at MR time locations is approximately twice the rate of exceedance at the EP locations. Studies have shown that the reaction is typically limited by the amount of organic precursors, and not the monochloramine concentration (Mitch et al., 2003a).

Exhibit 6.4: Number and Percentage of Entry Points and Maximum Residence Time Locations in UCMR 2 Using Chloramine-Only Disinfection With At Least One Sample Exceeding the Indicated NDMA Thresholds

NDMA Thresholds (ng/L)	Count of Entry Points	Percentage of Entry Points (n = 572)	Count of Maximum Residence Time Locations	Percentage of Maximum Residence Time Locations (n = 394)
2	171	29.9%	246	62.4%
6	66	11.5%	93	23.6%
10	38	6.6%	50	12.7%
20	16	2.8%	23	5.8%
60	5	0.9%	5	1.3%
100	2	0.3%	3	0.8%
200	1	0.2%	2	0.5%
600	0	0.0%	1	0.3%

Increased chlorine contact time (before conversion to chloramines) has been associated with a decrease in NDMA formation (Wilczak et al., 2003; Lee et al., 2008; Chen and Valentine, 2008; Mitch et al., 2009; Russell et al., 2012), though this practice must be approached cautiously due to the potential for increasing regulated DBP concentrations.

Nitrification control strategies, including altering the Cl_2:NH_3 molar ratio and using breakpoint chlorination, may result in increased nitrosamine formation. Increasing the Cl_2:NH_3 molar ratio helps to control nitrification, but results in greater dichloramine and NDMA formation. Breakpoint chlorination may lead to the rapid formation of NDMA through reactions with breakpoint chlorination intermediates (Schreiber and Mitch, 2007).

6.5.2 The Impact of Water Quality Parameters

6.5.2.1 Dissolved Oxygen

Schreiber and Mitch (2005) showed that NDMA concentrations increased with increasing DO concentrations. Le Roux et al. (2011) found similar results when chloraminating the pharmaceutical ranitidine. In the absence of oxygen, little NDMA was formed, though under saturated DO conditions, the NDMA molar yield was 54 percent. Padhye et al. (2010) also found that the presence of oxygen was a critical factor in the activated carbon transformation of secondary amines, where adsorbed secondary amines exposed to air for longer periods of time exhibited significantly higher nitrosamine yields.

6.5.2.2 pH

Optimum conditions for NDMA formation from UDMH occur at pH 6 to 8 (Mitch and Sedlak, 2002). As use of dichloramines has been associated with high NDMA yields, the pH of chloramination is also important to consider. Most studies have found that NDMA formation increases with increasing pH (Mitch and Sedlak, 2002; Valentine et al., 2005; Schreiber and Mitch, 2006a; Sacher et al., 2008). Shen and Andrews (2013) examined the pH behavior of the reaction of chloramine with two pharmaceuticals, ranitidine and sumatriptan, and found the yields of NDMA peaked at pH 7 for ranitidine and pH 8 for sumatriptan, or about 1.2 to 1.6 pH units below their respective pKa values. The peak conversion was hypothesized to be a result of the reaction between dichloramine and the deprotonated amine. Because dichloramine is more prevalent at acid pH conditions and deprotonated amines are more prevalent at higher pH, this results in a maximum formation at intermediate pH levels.

6.5.2.3 Temperature and Seasonality

Temperature appears to have minimal impact on NDMA formation, though moderate increases in NDMA concentrations were observed with decreases in temperature (Mitch et al., 2003a). This result may be due to the reduction in monochloramine contact time with increasing temperature, as monochloramine is removed more rapidly by auto-decomposition at high temperatures (Mitch et al., 2003a). Krasner et al. (2010) found that at pH 8 the formation of NDMA was relatively unaffected by temperature. At pH 9 they found NDMA formation was greater at lower temperatures. Similar to the conclusions of Mitch et al. (2003a), the authors propose that the effect can be explained by chloramines being more stable at lower temperatures and the reaction rate of NDMA precursors being relatively temperature-independent, leading to more chloramines being available to react with NDMA precursors at lower temperature (Krasner et al., 2010). Woods et al. (2015) evaluated seasonal/temperature effects on NDMA formation at a water system in Denver, Colorado. The pH of the water at the water system was reported to be "generally greater than 8" during the study. A statistically significant negative correlation was established between water temperature and NDMA concentrations.

Seasonality appears to have a variable impact on nitrosamine formation. Li et al. (2015) also noted that the maximum concentration of NDMA in the distribution systems of nine drinking water treatment plants in East China was greater in the winter than in the summer. However, the opposite was observed for NPYR. Woods and Dickenson (2015) observed no seasonal trend in NDMA concentrations measured during EPA's monitoring during UCMR 2. Uzun et al. (2015) found no significant change in mean NDMA concentrations across the seasons at 12 monitoring sites in the southeastern United States.

6.5.2.4 Bromide Concentrations

Because bromine species are known to be more effective substitution agents than the equivalent chlorine species (Symons et al., 1993), waters containing bromide may demonstrate increases in NDMA formation where formation of bromamines is favorable. Although bromamines are more reactive, they decompose more rapidly than chloramines (Valentine et al., 2005), such that waters under the influence of 1 mg/L bromide are not expected to exhibit higher concentrations of NDMA than they would if only chloramines were present. Le Roux et al. (2012) found that the presence of 1 mM bromide enhanced the formation of NDMA during chloramination of DMA and DMA-containing compounds, which was thought to be related to the formation of

reactive brominated oxidants. Luh and Marinas (2012) performed experiments with 0.2 mM (10 mg/L) chloramine and 0.0005 mM (22.5 µg/L) DMA in either the presence or absence of 0.4 mM (32 mg/L) bromide. They performed experiments between pH 6 and 9. They found that above pH 7 the formation of NDMA increased significantly. At pHs between 6 and 7 the formation of NDMA decreased in the presence of bromide. They found that at lower pH a bromochloramine intermediate was formed. At higher pH they were unable to identify the intermediate responsible for enhanced NDMA formation. Bromamine, tribromide, hypobromite and hypobromous acid were tested and ruled out. Zha et al. (2014) found that after ozonation and chlorination of several model DBP precursors, NDMA formation generally decreased as bromide concentration increased. The pH used by Zha et al. (2014) was not reported.

6.6 Kinetics and Predictive Models

Various attempts have been made to develop models to predict NDMA formation. These models vary in sophistication ranging from "curve fitting" of relationships between NDMA and bulk properties to those incorporating rate equations for each elementary step in the hypothesized reaction mechanism (Choi and Valentine, 2002; Schreiber and Mitch, 2006a; Chen and Valentine, 2006, 2007; Kim and Clevinger, 2007; Chen and Westerhoff, 2010). The mechanistic models use DMA as a model precursor and do not take into account other precursors or real world water matrices. Using Iowa River water, Chen and Valentine (2006, 2007) found that the amount of NDMA formed could be predicted from the drop in SUVA, although the relationship was likely dependent on the source water. Chen and Westerhoff (2010) showed that predictive power law models had a reasonable fit for real world wastewater samples with high NDMA FP but did not transfer to drinking water sources with lower NDMA FP. The authors found that addition of an inorganic nitrogen parameter did not substantially improve the predictions (Chen and Westerhoff, 2010). Unfortunately, the models based on fitting laboratory data to predictive functions such as those of Chen and Valentine or Chen and Westerhoff tend to be source water-specific and cannot be applied in a broad way to accurately predict nitrosamine formation at water utilities or in distribution systems.

6.7 Summary

Data from UCMR 2 indicate that waters disinfected with chloramines have higher and more frequent detections of NDMA, a finding that is consistent with data from the literature that shows that chloramination leads to the highest formation of NDMA. UCMR 2 data also indicate that detection rates of NDMA are about 10 times higher at PWSs that use chloramines than those at PWSs that use chlorine. Therefore, utilities that switch from chlorine to chloramines may see an increase in NDMA and other nitrosamines formation. Because formation of nitrosamines continues in the distribution system, the highest NDMA concentrations generally occur at the MR locations of surface water PWSs using chloramines. (As noted in Chapter 5, UCMR 2 data may underestimate NDMA detections due to the exclusion in that study of consecutive PWSs, which may have very long residence times from the point of treatment in the system from which they purchase their water.)

Water utilities using surface water under the influence of wastewater are at a higher risk for nitrosamine formation during chloramination than those making use of water sources that are not so influenced. Chloramination of wastewater forms an order of magnitude more NDMA than chloramination of drinking water; thus, the precursors responsible for NDMA formation are likely to be found in wastewater and in surface waters impacted by wastewater flows. Because

DMA and biological material in wastewater are not significant NDMA precursors in secondary wastewater effluents, anthropogenic materials in wastewater are thought to be the primary source of precursors. These materials range from pesticides and dyes to personal care products such as pharmaceuticals, shampoos, and soaps. Additionally, the use of flocculation aides and anion exchange resins in drinking water and wastewater treatment may also contribute to NDMA formation and occurrence. Because these materials have a wide range of chemical structures, they will exhibit varying degrees of removal during conventional drinking water treatment. A data gap may exist for understanding the extent of the impact from different precursor sources, such as the percentage of NDMA detections that can be attributed to wastewater discharge, polymer addition, distribution system materials, etc. Furthermore, because the kinetics of NDMA formation from these materials reacting with chloramines is on the order of days, NDMA levels may continue to rise in the distribution system days after these NDMA formation conditions and processes are initiated.

NDMA precursors have been shown to be oxidized (i.e., removed) by strong oxidants such as ozone, permanganate and chlorine dioxide. Other studies, however, have shown that DMA can be oxidized by strong oxidants to form NDMA. A data gap may exist for understanding the interactions of strong oxidants and NDMA precursors and their effect on ultimate NDMA formation.

Though data from UCMR 2 and the literature have increased our understanding of nitrosamine formation, a number of important questions remain. Chloramination has been identified as the primary pathway leading to NDMA formation, but a data gap may exist for understanding how particular source water quality and chloramination operating conditions work together to contribute to NDMA occurrence. Also, as chlorination is the most widely used disinfection technique, and nitrosamine formation is observed in PWSs that are using chlorination and not chloramination, further studies focused on the water quality and treatment parameters that lead to high nitrosamine occurrence in chlorinating treatment systems may be needed. UCMR 2 data has shown that the highest NDMA levels are found in the distribution system at MR time sampling points, suggesting that NDMA formation reactions continue in the distribution system. Not known, however, is the extent to which distribution system effects such as biofilm growth and nitrification influence NDMA concentrations.

A variety of nitrogen-containing organics originating from a wide range of natural and anthropogenic sources have been identified as nitrosamine precursors, though it is unknown to what extent each of these potential sources specifically contributes to overall formation. Identification of additional precursors and information on co-occurrence of different nitrosamine precursors coupled with occurrence data on nitrosamines and other relevant water quality parameters may help to improve understanding of formation mechanisms. Occurrence data can also help determine whether similar reactions account for all nitrosamine formation or if there are competing mechanisms that favor production of one nitrosamine over another. Such precursor occurrence data may also help to predict concentrations of individual nitrosamines under given water quality and treatment conditions.

7 Treatment

7.1 Introduction

This chapter discusses potential strategies for nitrosamine treatment and control. For a discussion of treatment for a range of disinfection by-products (DBPs), including activities related to nitrosamines, see the Agency's *Six-Year Review 3 Technical Support Document for Disinfectants and Disinfection By-Products Rules* (USEPA, 2016a).

As mentioned in Chapter 5 of this document, nitrosamines are detected more frequently in public water systems (PWSs) using chloramines as a disinfectant. Chapter 6 discusses how chloramination of amine-containing precursors appears to be the major pathway for nitrosamine formation. However, not all chloraminating PWSs have elevated nitrosamine concentrations in their finished water, which suggests that there are ways to reduce nitrosamine formation during chloramination. There are several potential points along the drinking water treatment continuum where strategies can be employed to reduce nitrosamine formation. One strategy is to implement source water management strategies to reduce the amount of nitrosamine precursors entering the treatment plant (for example, reducing the influence of wastewater discharges on the source water used by the PWS). A second strategy is to remove nitrosamine precursors within the treatment plant itself prior to application of chloramines. A third strategy is to optimize the chloramination process to reduce nitrosamine formation. The final strategy is to remove or reduce nitrosamines after they have formed.

Each of the control strategies mentioned above may have other potential beneficial and detrimental effects on the treatment process and on overall public health protection. Precursor removal has the added benefit of reducing levels of other DBP precursors, such as precursors of trihalomethanes (THM) and haloacetic acids (HAA) and lowering chlorine demand (Karanfil et al., 2008; Templeton and Chen, 2010). However, source water management strategies often require cooperation of agencies and groups external to the PWS and can be complicated to implement. Adding treatment to remove nitrosamine precursors or remove nitrosamines after their formation can be challenging. Altering the chloramination process is a relatively simple strategy; however, it may result in an increase in the formation of other DBPs.

This chapter presents potential strategies for nitrosamine control in public drinking water. The chapter is based on literature published up to December 2015. This field is an area of active research, and new literature is being published that may further inform our understanding of nitrosamine control. Discussion of wastewater treatment technologies is included as, in some cases, it may be easier to prevent precursors from entering the drinking water plant through treatment at the wastewater plant than to undertake treatment at the drinking water plant. Also, in some cases, wastewater treatment technologies are similar to processes that are used in drinking water treatment plants. Processes that are used to prevent nitrosamine formation are discussed first, followed by processes that remove nitrosamines that have already formed. Similar to Chapter 6, the focus of this chapter is on NDMA, though other nitrosamines are also discussed when information is available.

7.2 Prevention of Nitrosamine Formation

This section discusses two general prevention strategies for nitrosamine formation prevention: precursor reduction/removal and modification of disinfection practices. Among the precursor

reduction/removal approaches, there are some that can be effectively implemented at wastewater treatment plants to reduce concentrations of precursors released to source water. However, mitigating nitrosamine precursors at wastewater treatment plants may not be an option available to utilities. Wastewater treatment for precursors would require cooperation between the drinking water and wastewater utilities.

7.2.1 Precursor Removal

As discussed in the previous chapter, numerous nitrosamine precursors may be present in drinking water sources, including natural and synthetic amines and other nitrogen-containing compounds. Many nitrosamine precursors have yet to be identified. Therefore, many treatment studies focusing on precursor removal use either nitrosamine formation potential (FP) or model precursors such as dimethylamine (DMA) to study removal by treatment processes. Precursor removal processes include: source management; physical removal processes such as coagulation, filtration and absorption; and processes which destroy precursors, such as pre-oxidation.

European water utilities may provide good models of precursor removal in action, as they tend to use practices that minimize chlorine usage (Karanfil et al., 2008). Templeton and Chen (2010) surveyed seven nitrosamines at selected UK drinking water supply systems employing a variety of disinfection techniques, such as hypochlorite, chloramination and chlorine gas. The authors found that NDMA was detected above the minimum detection level only once. The detected concentration was 1 ng/L; the detection occurred at the sampling point furthest into the distribution system. This utility treated organic-rich and nitrogen-rich waters and used amine-based polymers epi-DMA and polyDADMAC, which would appear to put it at risk of much greater and more frequent nitrosamine concentrations. One possible explanation as to why the occurrence of NDMA in this study was low relative to NDMA occurrence observed in the United States is that disinfectant concentrations in North America can be up to 4 mg/L of total chlorine and are often higher than the average of 0.5 mg/L typically applied in the UK. Additionally, none of the systems tested in this study were impacted by wastewater effluents (Templeton and Chen, 2010).

7.2.1.1 Source Water Management

Studies have shown that wastewater discharges are associated with occurrence of nitrosamine precursors (Schreiber and Mitch, 2006b; Chen et al. 2009). At the South Platte River, Krasner et al. (2008) showed that dissolved organic nitrogen (DON) increased downstream of wastewater discharges. Careful consideration of drinking water intake locations relative to wastewater discharges may reduce human exposure to NDMA through drinking water. Longer distances between wastewater discharges and drinking water intakes allow natural attenuation processes to occur, which can reduce levels of nitrosamine precursors.

While altering source water intake practices can be an effective method to control nitrosamine precursors, implementation can be complicated. Source water management strategies often require cooperation of outside groups such as wastewater utilities, permitting agencies, and other stakeholder groups.

7.2.1.2 Coagulation

While the combination of coagulation and flocculation is successfully used to remove chlorination DBP precursors, it is less effective for nitrosamine precursors. Bench-scale jar tests were performed on German river waters to investigate the effect of coagulation, flocculation and sedimentation on the fate of nitrosamine precursors. Iron and alum salts added at 5 and 10 mg/L lowered the nitrosamine FP by less than 10 percent, compared to the FP without coagulation (Sacher et al., 2008). Lime softening led to only a 12 percent decrease in nitrosamine FP at a drinking water treatment plant in Ann Arbor, Michigan (Mitch et al., 2009). However, the poor removal was confounded by the addition of DADMAC polymer, which is an NDMA precursor and may have offset removal by coagulation (Mitch et al., 2009).

According to Westerhoff et al. (2006), maximum DON removal by coagulation with aluminum salts was about 40 percent. Coagulation with aluminum salts in conjunction with low dosages of polyDADMAC improved DON removal by 15 to 20 percent. However, as noted above, polyDADMAC is a nitrosamine precursor, and although DON was removed, the final effect of polyDADMAC on nitrosamine removal was not measured. Coagulation preferentially removed higher molecular weight fractions of DON (Westerhoff et al., 2006). A survey of 16 full-scale drinking water treatment plants with water impacted by algal blooms or wastewater found an average removal of 30 percent of DON by coagulation (Dotson and Westerhoff, 2009). Pietsch et al. (2001) found that aliphatic amines cannot be completely removed using either aluminum or iron coagulants. They found removal rates of less than 10 percent for most aliphatic amines; the exceptions were ethanolamine and ethylenediamine, which showed 30 and 45 percent removal, respectively. Liao et al. (2015b) found that coagulation and sedimentation removed only 18 percent of nitrosamine FP in a Chinese pilot plant. A follow up study (Liao et al., 2015a) attributed poor removal to the fact that both coagulants and nitrosamine precursors tended to be cationic.

The use of amine polymers in the coagulation process may obscure benefits achieved through coagulation. Mitch et al. (2009) examined the removal of DBP precursors through different unit processes (including coagulation) for surveyed water treatment plants. They found a 21 percent removal of DON, but a 43 percent increase in NDMA FP, which was most likely due to the presence of certain polymers. Laboratory experiments with polyDADMAC polymer confirmed that ozonation of polyDADMAC polymers can produce NDMA (Padhye et al., 2011). Padhye found that doses of polyDADMAC polymer ranging from 5 to 10 mg/L yielded NDMA concentrations up to 800 ng/L upon ozonation (Padhye, 2010).

Cornwell et al. (2015) examined a number of natural polymers as potential substitutes for polyDADMAC. They tested polymers based on corn, potato, tapioca and shellfish (chitosan) on waters from nine different water treatment plants. None of the tested polymers formed reportable levels of nitrosamines. For each of the waters tested, at least one of the natural polymers performed as well or better than polyDADMAC in terms of turbidity removal. Some of the natural polymers performed worse in terms of headloss. The headloss problems were not present if the filters were backwashed with chlorinated water, leading to the hypothesis that added headloss was due to biological activity. Zeng et al. (2014) developed a phosphine based polymer as a substitute for polyDADMAC polymers. The phosphine polymer did not produce nitrosamine when reacted with chloramine. The polymer showed the ability to increase dissolved organic carbon (DOC) removal by 17 to 25 percent when compared to alum or ferric coagulants alone,

which was similar to polyDADMAC. Although the polymer shows potential for reducing nitrosamine formation from water treatment polymers, it is not yet commercially available.

7.2.1.3 Sorption

Powdered activated carbon (PAC) may remove some nitrosamine precursors via sorption processes. One laboratory study showed that a PAC dose of 5 mg/L lowered the NDMA, *N*-nitrosomorpholine (NMOR) and *N*-nitrosopyrrolidine (NPYR) FP of river water by a factor of two (Sacher et al., 2008). Increased doses resulted in modestly increased precursor removal, with a dose of 100 mg/L of PAC resulting in a lowering of the nitrosamine FP by 83 percent (Sacher et al., 2008). Westerhoff et al. (2006) found PAC could remove DON. A dose of 5 mg/L removed 20 percent of DON from surface water and 50 percent from finished drinking water (Westerhoff et al., 2006). Increasing the dose to 25 mg/L only lowered nitrosamine FP by an additional 5 to 10 percent (Westerhoff et al., 2006). Hanigan et al. (2012) performed several adsorption experiments using a secondary wastewater effluent blended with a river water source to simulate a drinking water source impacted by wastewater. They found removals of NDMA FP between 70 and 90 percent using doses of PAC ranging from 15 to 210 mg/L over a 4-hour contact time. In contrast, the PAC decreased DOC by less than 25 percent and UV-254 (a water quality parameter indicating the presence of UV-absorbing organic matter) by less than 50 percent.

Mixed results have been found for precursor removal by GAC. Hwang et al. (1994) found limited removal of DMA using GAC filters. Farre et al. (2011a) studied removal of NDMA FP at a wastewater plant using biologically active GAC. They found 85 percent removal of the NDMA FP. The differences in removal between these two studies may be that the GAC in the Farre et al. study was biologically active while the GAC in the Hwang et al. study was not. Hanigan et al. (2012) performed column studies using GAC and found 50 percent removal of NDMA FP even after 10,000 bed volumes, even though DOC and total dissolved nitrogen broke through much earlier. They also examined two full-scale GAC contactors and found NDMA FP removal ranging from 54 to 84 percent.

Krasner et al. (2015) examined GAC and PAC for nitrosamine precursor removal. GAC and PAC were effective at removing NDMA precursors and (with a sufficient dose) removed them more effectively than they removed DOC. PAC also removed NDMA precursors from polyamine use. PAC and GAC were not, however, effective at removing precursors from polyDADMAC. Magnetic ion exchange resin (MIEX) was found able to remove NDMA precursors; however, it also contributed NDMA precursors to the water. Chu et al. (2015) found that 20 mg/L PAC, plus conventional treatment, removed 37 percent more NDMA precursors than conventional treatment alone in a Chinese pilot treatment plant. PAC with 1 mg/L potassium permanganate, plus conventional treatment, was able to eliminate 86 percent more NDMA precursors than conventional treatment alone.

Wu et al. (2015) compared adsorption of seven secondary and tertiary amines onto zeolites and PAC using laboratory water. One particular zeolite called mordenite was able to remove over 90 percent of all the amine precursors except for 4-dimethylaminoantipyrine (DMAP) at a dose of 100 mg/L. The zeolites performed best removing small precursors which were positively charged under the experimental conditions. PAC performed better removing larger, less hydrophilic precursors such as DMAP. Performance of both the zeolites and the PAC was poorer when a raw surface water was used to dissolve the precursors instead of laboratory water.

Removal of NDMA precursors by activated carbon has been found to be highly pH dependent and site specific. Chen et al. (2015b) examined water from an Arizona river mixed with 20 percent wastewater effluent and found removal of NDMA precursors increased from 29 percent at pH 3 to 58 percent at pH 9.5. The opposite trend, however, was found when aquaculture-impacted Chinese lake water was tested. NDMA precursor removal decreased from 83 percent at pH 3 to 34 percent at pH 11, while NDEA precursor removal decreased from 89 percent at pH 3 to 51 percent at pH 11.

7.2.1.4 Biological Filtration and Related Techniques

Biological processes at both water and wastewater treatment plants have been shown to remove nitrosamine precursors. If a drinking water treatment plant uses biological treatment, downstream filtration and disinfection may be required to prevent sloughed biomass from colonizing the distribution system.

A study of wastewater treatment plants in California showed that secondary treatment led to only a small decrease in DON (24 percent) over a 20-day incubation period (Pehlivanoglu-Mantas and Sedlak, 2006). Krasner et al. (2009) conducted a survey of 23 advanced wastewater treatment plants in the Midwest and the far western United States. The authors found that partial nitrification (reduction of dissolved nitrogen in the form of ammonia to 2-10 mg/L) and complete nitrification (reduction to below 2 mg/L) reduced the level of precursors by approximately 61 percent and 50 percent, respectively. Partial denitrification (nitrate-nitrogen reduction to 5-10 mg/L) and complete denitrification (nitrate-nitrogen reduction to below 5 mg/L) decreased precursors by approximately 9 percent and 66 percent, respectively, compared to no treatment (Krasner et al., 2009).

On average, 50 to 70 percent removal of NDMA precursors was demonstrated at four wastewater treatment facilities using aerated lagoon, advanced biological treatment, conventional secondary treatment with activated sludge and a membrane bioreactor, respectively (Krasner et al., 2008). An anaerobic digester at a municipal wastewater treatment plant was able to completely biodegrade the model precursors pyrrolidine (PYR), diethylamine (DEA), DMA and MEA (Padhye et al., 2009).

A study of a biologically-active GAC filter (following ozonation) found removals of 99 percent or more for four pharmaceuticals (known NDMA precursors) at a tertiary treatment facility in Australia (Farre et al., 2011a). The authors found that pilot-scale biologically active sand filters did not remove nitrosamine precursors, implying that adsorption followed by biological degradation was key to the removal process by biologically active GAC.

Biologically-active filtration processes in drinking water treatment have also been shown to reduce nitrosamine precursor levels. Biologically-active GAC removed 67 percent of NDMA FP at a drinking water facility in Ann Arbor (Mitch et al., 2009). Krasner et al., (2015) found mixed results for removal of NDMA precursors by biologically-active filters in water treatment plants. Out of fourteen samples from biofilters, NDMA formation was lowered in four, remained the same in one and increased in nine. Liao et al. (2014, 2015b) examined the performance of a biofilter at a Chinese pilot plant consisting of ozonation, coagulation and sedimentation, further ozonation, biologically-active GAC filtration and sand filtration. The biologically active GAC filter removed 59 percent of NDMA precursors, 55 percent of NDEA precursors and more than 70 percent of NPYR precursors (Liao et al., 2015b). Biofiltration was found to remove the lower

molecular weight DOC better than higher molecular weight DOC (Liao et al., 2014) and the cationic portion preferentially (Liao et al., 2015a). Further examining the characteristics of nitrosamine precursors, this research team found that 70 percent of the NDMA FP was biodegradable but only 42 percent was adsorbable, while 45 percent of NDEA FP was biodegradable and 59 percent was adsorbable (Liao et al., 2015b). Liao et al. (2015c) studied the effects of backwashing on biomass and nitrosamine precursor removal in a biologically-active filter. The pilot biofilter showed an approximate 50 percent decrease in biomass on the filter immediately after backwashing. The biomass recovered to near original levels after 2 days. Nitrosamine removal was initially about 60 percent in the filter. It increased to 80 percent on backwashing and then returned to 60 percent over time.

During full-scale testing of water facilities, riverbank filtration removed secondary amine precursors to varying degrees: 76 percent removal for DMA, 66 percent for DEA, 52 percent for PYR and 80 percent for morpholine were observed. Riverbank filtration decreased NDMA FP by 93 percent and NPYR and NDEA FPs by 50 percent and 66 percent, respectively. Ground water recharge at a separate utility decreased NDMA FP by 88 percent and NPYR FP by 63 percent (Sacher et al., 2008). Krasner et al. (2012c) found a 64 percent reduction in NDMA FP at a plant using riverbank filtration in the United States. In a series of 5-day bench-scale biological sand filtration trials, NDMA precursor removal ranged from approximately 45 to 80 percent, NPYR precursor removal ranged from 0 to approximately 85 percent and NMOR precursor removal ranged from 0 to approximately 50 percent (Krasner et al., 2008).

Liao et al. (2015d) examined the ability of biofilters to degrade DMA specifically. They extracted a culture from a pilot-scale GAC biofilter and determined the effect of carbon and nitrogen amendments on degradation and bacterial community composition. By day 5, in the biofilter culture amended with carbon (in the form of glucose), nearly complete removal of DMA (initial concentration: 10 mg/L) was observed. Biofilter culture amended with nitrogen (i.e., ammonia) did not significantly differ from a culture with no amendments; at day 5, DMA levels were still approximately 1.5 mg/L, down from 10 mg/L. A rise in ammonia over time in all inoculated cultures confirmed earlier studies that had shown DMA could be broken down to ammonia by bioculture. The authors analyzed community composition from all cultures on day 0 and again on day 7 and found significant changes, particularly in the culture amended with glucose. *Brevundimonas* was dominant in the initial culture, the culture amended with ammonia, and the non-amended culture, but was not found in the glucose-amended culture. *Acinetobacter* was common in the glucose-amended culture but was not detected in the others. Except for *Bacillus* and *Pseudomonas*, the genera isolated from the cultures were not previously known to degrade DMA, although they have been shown to biodegrade other organic pollutants.

7.2.1.5 Membrane Filtration

Removal of nitrosamine precursors by membranes depends on the type of filter and the membrane pore size (microfiltration (MF), ultrafiltration (UF), nanofiltration (NF) and reverse osmosis (RO)). As expected, because NDMA precursors are associated with low molecular weight compounds, UF has been found to exhibit negligible removal (Pehlivanoglu-Mantas and Sedlak, 2008). On the other hand, Deeb et al. (2006) found that the fraction of NDMA precursors removed during MF ranged from 12 percent to as high as 95 percent at advanced water treatment facilities. Although media filtration was unsuccessful in removing NDMA precursors at selected wastewater treatment plants in California, RO demonstrated complete removal (Mitch and Sedlak, 2004). Steady-state rejections of nitrosamine precursors of concern (viz., di-*n*-

butylamine, DEA, DMA, di-*n*-propylamine, MEA and PYR) have been observed to exceed 98 and 99 percent by NF and RO membranes, respectively (Miyashita et al., 2009). Krasner et al. (2008) also found NPYR and NMOR precursors are well removed by RO membranes.

7.2.1.6 Oxidation of Precursors

NDMA precursors can be degraded by oxidation via chlorine, permanganate, hydrogen peroxide, ozone, chlorine dioxide and ferrate. Lee et al. (2007b) showed that NDMA precursors such as natural organic matter (NOM) can be oxidized by ozone and chlorine dioxide. A decrease in NDMA FP of between 32 and 94 percent was achieved when river waters were dosed with ozone or chlorine dioxide at concentrations of 1.9 mg/L and 2.7 mg/L, respectively, for a contact time of 5 minutes (Lee et al., 2007b). With natural waters they found chlorine dioxide and ozone to achieve similar removals. In laboratory experiments with model precursors, however, they found that ozone reduced NDMA FP more effectively, as chlorine dioxide produced DMA, which could react with chloramines to form NDMA (Lee et al., 2007b). For example, they found that ozone reduced NDMA production by DMA by 95 percent, but chlorine dioxide reduced NDMA formation by DMA by less than 10 percent (Lee et al., 2007b). Other studies have found slow oxidation of aliphatic amines by ozone. Only 20 percent decay was observed when 3.5 mg/L of ozone was added to a solution containing 1.6 mg/L trimethylamine (TMA), 3.2 mg/L DMA and 5.2 mg/L *n*-propylamine (NPA) for 100 minutes (Sacher et al., 2008). Temperature and pH were not specified in the report. Ozonation is more effective for removing cyclic amines, as rate constants for morpholine and piperazine are two orders of magnitude higher than for aliphatic amines (Sacher et al., 2008). Ozonation may have the additional benefit of reducing precursors of other halogenated DBPs such as THMs and HAAs. On the other hand, bromate formation is a concern with ozone use, and bromate must be monitored when ozone is used as an oxidant.

Liao et al. (2014) examined nitrosamine precursor removal in a Chinese pilot drinking water plant set up on a drinking water source known to be impacted by wastewater. Drinking water plants using this water source were known to have detected a wide variety of nitrosamines. The pilot plant consisted of coagulation, sedimentation, ozone, biologically-active GAC filtration and sand filtration. They found approximately 20 percent removal of nitrosamine precursors after the coagulation/sedimentation stage, 50 percent removal after mid-ozonation and 88 percent removal after GAC filtration. Further experiments found that ozonation preferentially removed nonpolar fractions of the precursors, removing 50 to 60 percent of this type of precursor (Liao et al., 2015a). Shah et al. (2012) found that ozone reduced NDMA formation by about 50 percent with exposure (measured as concentration × time, or CT) of 0.4 mg·min/L and chlorine achieved similar removal with exposure of about 60 mg·min/L. These exposure values are about 20 percent and 43 percent, respectively, of the CT required for *Giardia* control.

McCurry et al. (2015) examined the effect of preoxidation on NDMA formation, using 14 source water samples from 10 drinking water plants. Without pretreatment with oxidants, NDMA concentrations ranged from 5.6 to 58 ng/L upon chloramination of the water samples. The waters were treated with each oxidant (ozone, HOCl and UV) at two different CTs. For HOCl those represented 10 and 42 percent of the CT required for 3-log *Giardia* inactivation. For ozone the concentrations represented 10 and 50 percent of the CT required for 3-log *Giardia* inactivation. For UV (tested using both low-pressure and medium-pressure mercury lamps), fluence rates of 186 mJ/cm^2 and 1,000 mJ/cm^2 were used. At high doses, ozone, HOCl and medium-pressure UV were all fairly effective (median removal of NDMA FP over approximately 80 percent). At the lower doses ozone was still effective with 78 percent removal, while HOCl removal efficiency

was only 47 percent of the NDMA precursors and medium pressure UV removal efficiency was only 54 percent of the NDMA precursors. Low-pressure UV performed significantly worse than the other techniques at both the high and low doses. Reporting on the same set of experiments, Krasner et al. (2015) indicate that chlorine pre-oxidation was most effective at a pH between 8 and 9. Krasner et al. (2015) also report that although addition of a high dose of polyDADMAC polymer increased NDMA FP at the bench scale, addition of a low dose of polyDADMAC at full-scale plants did not appear to affect NDMA FP.

Chen and Valentine (2008) showed that NDMA formation decreased with increasing pre-chlorination contact time and dose. For example, NDMA concentrations decreased from 30 ng/L to 10 ng/L with 5.7 mg/L free chlorine contact time for 10 minutes before formation of chloramines as compared to use of preformed chloramines. Decreases in NDMA formation ranged from about 17 to 83 percent compared to preformed chloramines depending on chlorine dose and contact time (Chen and Valentine, 2008). Charrois and Hrudey (2007) also found a decrease in NDMA formation with increasing free chlorine contact time and dose at water treatment facilities in Alberta. Reductions of NDMA FP ranged from 68 to 93 percent for a free chlorine contact time of 2 hours prior to ammonia addition (Charrois and Hrudey, 2007). A review of several kinetic studies reported that chlorination of aliphatic amines was found to be considerably faster than ozonation, suggesting that prechlorination may be faster for oxidizing precursors (Sacher et al., 2008).

Although oxidation of precursors may be effective for nitrosamine control, it may produce other DBPs. Shah et al. (2012) found that chlorine produced THMs, HAAs and chloral hydrate, while ozone produced bromate, chloropicrin and chloral hydrate. In this study, doses of pre-oxidants high enough to remove NDMA precursors did not cause formation of DBPs to concentrations that exceeded regulatory levels. However, THM formation approached regulatory limits at the highest chlorine exposure, and bromate formation approached regulatory limits at the highest ozone exposure (Shah et al., 2012).

River water spiked with 21 mg/L of ferrate reduced between 46 and 84 percent of the NDMA FP within an hour (Lee et al., 2008). Ferrate, however, has neither been used in full-scale treatment plants, nor has it been widely studied in this context. Pre-oxidation with ferrate may be difficult due to the highly unstable nature of potassium and sodium salts (Sharma 2002).

Chen and Valentine (2008) studied precursor oxidation using Iowa River water. Application of either 10 mg/L of permanganate or 3 mg/L of hydrogen peroxide for one hour reduced NDMA formation by approximately 50 percent, while exposure to 7 mg/L of ozone reduced NDMA formation by 75 percent.

Sunlight may also oxidize nitrosamine precursors. Chen and Valentine (2008) found a 25 percent reduction in NDMA formation when Iowa River water was exposed to simulated sunlight. Mitch et al. (2003b) found, however, that most nitrosamine precursors were non-reactive with UV light.

It is important to note that some studies have shown that oxidation of DMA may actually lead to the formation of NDMA, particularly at higher pH (Nawrocki and Andrzejewski, 2011). The application of strong oxidants such as ozone, chlorine dioxide, permanganate and ferrate (IV) to DMA in the presence and absence of ammonia have been shown to form NDMA (Andrzejewski and Nawrocki, 2007). Lee et al. (2007b) found that NDMA FP remaining after pre-oxidation by ozone or chlorine dioxide could be largely attributed to DMA formation by the oxidants. The

DMA can then be oxidized to NDMA by the oxidants. Therefore, oxidation of precursors may not be a viable option in water with high pH (e.g., >8) and significant DMA concentration. Studies have also shown that chlorine can react quickly with DMA to form chlorinated DMA which may remain in solution to later react with chloramine to form NDMA (Selbes et al., 2015). Lv et al. (2015) found that oxidation of the pharmaceutical chlorpheniramine by ozone formed DMA, which was then oxidized by ozone to form NDMA. The concentration increased for about 20 minutes, after which it began to decrease as additional ozone contact time oxidized the NDMA.

Selbes et al. (2014) found complex relationships between oxidation of precursors (using chlorine, chlorine dioxide and ozone) and NDMA yield. They examined 15 NDMA precursors that contained a DMA structure and found that most precursors showed a decrease in yield of NDMA of about half upon exposure to 3 mg/L of chlorine. Water treatment polymers such as polyDADMAC, polyacryl and polyamine and the pesticide diuron, however, did not show a reduced yield of NDMA in the presence of chlorine. With some precursors, such as TMA and ranitidine, the yield of NDMA decreased with increased chlorine contact time, while with others, such as DMA, increased contact time did not further lower NDMA formation.

Chlorine dioxide was found to significantly decrease the NDMA FP of precursors that had high NDMA yields such as dimethylisopropylamine (DMiPA), ranitidine and dimethylbenzylamine (DMBzA). For these precursors, NDMA yields dropped from initial values of around 80 percent to a yield of 15 percent after a 5-minute contact time and dropped to a yield of 4 percent after a contact time of 15 minutes. Precursors that had low NDMA yields, such as DMA and TMA, showed little change in NDMA formation upon exposure to chlorine dioxide. Polymers such as polyDADMAC showed a slight decrease in NDMA yield of about 5 to 10 percent on exposure to chlorine dioxide (Selbes et al., 2014). Selbes et al. (2015) conclude that chlorine dioxide would be more appropriate in waters with high wastewater content than in waters with a low level of reactivity precursors. Gan et al. (2015) found that pre-oxidation with chlorine dioxide led to a lower yield of NDMA after chloramination in the case of 10 out of 13 amine precursors. The counterexamples were the precursors DMA, *N,N*-Dimethyl-p-phenylenediamine and daminozide.

For ozone, a slight initial increase of NDMA formation with DMA was noted, followed by a decrease with increased contact time (Selbes et al., 2014). The authors performed further experiments to demonstrate that oxidation of DMA by ozone could produce NDMA, but then the NDMA was oxidized by hydroxyl radicals created from the ozone. Similarly, ozone also increased NDMA formation initially for precursors such as methylene blue, dimethylaniline, polyDADMAC and dimethylphenetylamine, but overall NDMA formation decreased with increased contact time. Ozone also significantly reduced NDMA formation from TMA and high-NDMA-yielding compounds such as DMiPA, ranitidine and DMBzA. The authors identified effects of pH on oxidation of precursors as well. They found that the reactions proceeded faster with deprotonated amines. For chlorine, this resulted in an optimum pH of about 8.5 for pre-oxidation (about halfway between the pKa for hypochlorous acid and the pKa for the respective amine). For ozone and chlorine dioxide, a pH above the pKa of the amine generally produced the greatest reduction in yield of NDMA.

Wang et al. (2015c) documented precursor-specific differences in the effects of oxidants on NDMA FP. They examined four pharmaceutical precursors (ranitidine, doxylamine, nizatidene and carbinoaxime) and four oxidants (chlorine, ozone, permanganate and chlorine dioxide). Ozone was the most effective oxidant. The highest concentration of ozone removed

approximately 90 percent of all the pharmaceuticals and approximately 90 percent of NDMA FP from all the pharmaceuticals. Ozone removed doxylamine and carbinoaxime more effectively than ratinidine and nizatidine. Chlorine dioxide and chlorine were effective at breaking down the pharmaceuticals, but did not perform as well at reducing NDMA FP. NDMA FP even increased when nizatidine was oxidized with chlorine and when carbinoxamine was oxidized with chlorine dioxide (at certain doses). . While permanganate could oxidize the pharmaceuticals, it was too slow to be effective in lowering NDMA FP.

Exhibit 7.1 summarizes selected information about the studies cited in this section.

Exhibit 7.1: Oxidation of Nitrosamine Precursors

Oxidant	Study	Precursor	Reduction in NDMA FP	Potential Issues
Ozone	Lee et al., 2007b	NOM	32–94%	Bromate formation
Ozone	Lee et al., 2007b	DMA	95%	Bromate formation
Ozone	Sacher et al. 2008	DMA, TMA, NPA	20%	Bromate formation
Ozone	Chen and Valentine, 2008	NOM	75%	Bromate formation
Ozone	Liao et al., 2014	NDMA FP	45%	Bromate formation
Ozone	McCurry et al. 2015	NDMA FP	78+%	Bromate formation
Chlorine Dioxide	Lee et al., 2007b	NOM	32–94%	Potential DMA formation, chlorite formation
Chlorine Dioxide	Lee et al., 2007b	DMA	<10%	Potential DMA formation, chlorite formation
Chlorine	Chen and Valentine, 2008	NOM	17–83%	THM and HAA formation
Chlorine	Charrois and Hrudey, 2007	NOM	68–93%	THM and HAA formation
Chlorine	McCurry et al., 2015	NDMA FP	47+%	THM and HAA formation
Ferrate	Lee et al., 2008	NOM	46–84%	Oxidation of DMA
Permanganate	Chen and Valentine, 2008	NOM	50%	Oxidation of DMA
Hydrogen Peroxide	Chen and Valentine, 2008	NOM	50%	Oxidation of DMA
UV	Chen and Valentine, 2008	NOM	25%	No residual
UV	McCurry et al., 2015	NDMA FP	29+%	No residual

As can be seen from Exhibit 7.1, oxidation of precursors can be effective but effectiveness can vary significantly depending on precursors, oxidant dose and water quality. Potential issues associated with use of this approach include considerations related to the potential for formation of THMs and HAAs, bromate and NDMA.

7.2.2 Modification of Disinfection Practice

As nitrosamines are DBPs, nitrosamine formation can be reduced by changing disinfection practices. Possible modifications include modification of the chloramination technique or conversion from chloramination to another form of disinfection.

7.2.2.1 Modification of Chloramination Techniques

Because NDMA is mainly formed from the reaction of amine precursors with dichloramine, NDMA can be reduced by minimizing dichloramine formation (Mitch et al., 2005; Schreiber and

Mitch, 2005). This is done by chloraminating at chlorine to ammonia ratios of much less than 1, with a pH greater than 8.5. Farre et al. (2011b) found in bench-scale experiments on wastewater that using preformed monochloramine instead of adding chlorine to the ammonia in-line reduced NDMA concentrations from 310 ng/L to 16 ng/L at a dose of 10 mg/L with a 24-hour contact time. The practice of using low chlorine-to-ammonia ratios may become problematic, however, as ammonia-oxidizing bacteria may proliferate when high concentrations of ammonia are present, resulting in nitrification. To control nitrification episodes at low chlorine-to-ammonia ratios, utilities have used several strategies. Breakpoint chlorination eliminates free ammonia. Breakpoint chlorination, however, promotes a series of undefined reactions and chemical intermediates which can also increase NDMA concentrations up to an order of magnitude (Charrois and Hrudey, 2007; Schreiber and Mitch 2007). Other ways to limit nitrification include raising pH to above 9, reducing exposure to sunlight, and changing operations to reduce water age.

Bench-scale experiments at a wastewater treatment plant have also shown that reducing contact time between disinfectant and wastewater can reduce nitrosamine concentrations (Farre et al., 2011b). At a contact time of 8 hours or less, NDMA was not detected when the authors used preformed chloramine doses up to 15 mg/L. No NDMA was detected using chloramines formed in-line by addition of chlorine to ammonia or by dichloramine, with disinfectant doses of 4 mg/L and contact times of 8 hours. Disinfectant concentrations of 10 mg/L did yield 18 ng/L NDMA for in-line chloramines and 25 ng/L for dichloramines. A 24-hour contact time yielded 16 ng/L NDMA for a preformed chloramines dose of 10 mg/L, 310 ng/L NDMA for an in-line chloramines dose of 10 mg/L and 530 ng/L NDMA for a dichloramine dose of 10 mg/L. Of course, any reduction in contact time would need to be balanced with disinfection requirements to ensure that disinfection capabilities were not reduced below what is required by regulation (Farre et al., 2011b).

These studies indicate that using preformed chloramines and limiting contact time may reduce nitrosamine formation on par with precursor oxidation. However, there are other important considerations, including maintaining sufficient contact time to achieve disinfection goals, relative amounts of other DBP formation, and nitrification potential in the distribution system.

7.2.2.2 Conversion from Chloramination to Other Disinfection Practices

Because nitrosamines are found primarily in chloraminated distribution systems, eliminating chloramination may reduce nitrosamine formation. Switching to a different residual disinfectant, however, may increase the formation of other DBPs. Free chlorine can result in THM and HAA formation, ozone can result in bromate formation, and chlorine dioxide can result in chlorite (and chlorate) formation. Also, the use of free chlorine in ammonia-containing waters may result in unintended chloramination, such that nitrosamines may still be formed. Also, other oxidants such as chlorine dioxide and ozone may form NDMA if DMA is present in the source water (Nawrocki and Andrzejewski, 2011).

7.3 Nitrosamine Removal

Treatment processes placed after the point of disinfectant application can remove or reduce concentrations of nitrosamines formed as DBPs. Furthermore, treatment processes can remove or reduce concentrations of nitrosamines that may be present in the drinking water treatment plant influent.

Nitrosamines such as NDMA have low vapor pressures, low Henry's Law Constants and low octanol-water partitioning coefficients (Mhlongo et al., 2009), meaning they are not highly volatile and are hydrophilic. Therefore, they are expected to be mobile in water and will tend to remain in the aqueous phase in contrast to volatilizing to air or sorbing to carbon or soils. From a treatment standpoint, although some volatilization of nitrosamines may occur, the degree of volatilization is likely not sufficient to make a treatment process that relies on partitioning from water to air viable. Enhanced coagulation, adsorption, membranes, metal catalysis, UV, advanced oxidation and electrochemical techniques can remove nitrosamines and are discussed briefly in the following sections.

7.3.1 Enhanced Coagulation

Enhanced coagulation uses increased coagulant doses to remove organic compounds from drinking water. However, conventional alum and ferric coagulants dosed at up to 12 mg/L achieved minimal NDMA removal (<7 percent) from raw drinking water (Sacher et al., 2008). Enhanced coagulation would also only remove nitrosamines that entered with raw water or that were formed before disinfection. Because of its typical placement in a treatment plant (i.e., before filtration and final disinfection), enhanced coagulation would not be able to remove nitrosamines formed during the final disinfection step. Thus, application of enhanced coagulation is very limited for NDMA removal.

7.3.2 Adsorption

Adsorption can remove nitrosamines to varying degrees. Dosing raw water with 50 mg/L of PAC for 24 hours resulted in 17 percent NDMA removal (Chung et al., 2009). Although a contact time of between 1 and 24 hours had little effect, a dose of 200 mg/L of PAC for 60 hours removed 45 percent of NDMA (Chung et al., 2009). Gunnison et al. (2000) demonstrated that GAC units have limited effectiveness in removing NDMA from the North Boundary Containment System near Denver, Colorado, which is designed to treat munitions-contaminated alluvial aquifers. GAC units in this system decreased NDMA from 350 ng/L to 200 ng/L. Additionally, results from sequential desorption tests of the soil showed that nearly all adsorbed NDMA desorbed after one cycle. Since NDMA sorbs poorly onto soil irrespective of soil properties, riverbank filtration is not likely to be an effective remediation technology for formed nitrosamines (Mohanty et al., 2006).

Wang et al. (2013b) did laboratory experiments with nanoparticles of activated carbon. They tested three types of activated carbon (bamboo, charcoal and coconut shell) and found coconut shell activated carbon had the same or better removal efficiency of the nitrosamine and precursor compounds than the other carbon types. Removal of 50 percent of most targeted compounds in lab reagent water was achieved with a typical dosage (from 1 to 20 mg/L) of the activated carbon nanoparticles and a contact time of 4 hours. Removal rates generally increased with time. For some nitrosamine compounds, coconut shell-based carbon had much better removal efficiencies than the other carbon sources. Generally, the removal efficiency was lower in prefiltered natural river than in reagent water (presumably due to competitive adsorption), while the study's two pH conditions (6.6 and 8.6) did not significantly affect removal efficiency.

Zhu et al. (2001) attempted to sorb NDMA onto a zeolite, which has a large surface area. The authors reported higher sorption efficiencies than alumina and silica, but the laboratory

conditions used for adsorption were at much higher concentrations than would be found in typical drinking water plants.

Chen et al. (2015c) adsorbed NDMA onto biochar made from bamboo, rice straw and wood sawdust. Batch experiments were performed in the laboratory using concentrations of NDMA ranging from 0.5 to 20 mg/L, much higher than typically present in drinking water. The researchers found that with a 61.68 percent removal efficiency, biochar from bamboo manufactured at 500 degrees C was more effective than biochar from wood or rice or from bamboo prepared at other temperatures. Solution chemistry (e.g., pH, metal ions) did not significantly affect biochar performance.

Dai et al. (2009) showed that activated carbon made from petroleum coke and coconut shell had NDMA sorption capacities of 24 mg/g when batch experiments were performed over 24 hours in deionized water, compared to 17 mg/g demonstrated for zeolites. Modification of the surface by heat treatment and coating with titanium dioxide nanoparticles increased sorption capacity Fleming et al. (1996) showed a similar superiority of activated carbon over zeolites. Batch studies performed with ground water showed 99 percent removal of NDMA using activated carbon, compared to 15 to 20 percent removal using zeolite, silica or XAD resins. Addition of silica to zeolite showed little removal of NDMA, but when the combined silica and zeolite were treated with copper, removal increased to 26 percent. The authors concluded that the best sorbents for NDMA are carbonaceous resins, such as Ambersorb 572 and 563, both of which exhibited 99 percent removal of 100 µg/L NDMA spiked into ground water after 1 hour (Fleming et al., 1996). Although removal of NDMA by activated carbon has been proven to be very efficient, it is important to note that the studies presented above were batch experiments, and other experiments in full-scale facilities have shown less promising results. It is likely that removal rates will depend on the specific type of adsorbent used, as well as water quality parameters.

7.3.3 Membrane Filtration

As discussed in Section 7.2.1.5, membrane filtration can remove nitrosamine precursors. It may be able to remove nitrosamines as well. As membranes are typically placed before final disinfection in the treatment train, they would not remove nitrosamines formed during final disinfection. They could, however, remove nitrosamines entering with the raw water or formed during pre-disinfection with chlorine or another oxidant such as ozone.

Nitrosamine removal by membranes has been studied at several wastewater treatment plants. For example, an advanced wastewater treatment facility in Southern California using MF and RO was studied to discern the effects of membrane treatment on NDMA removal. MF was not effective in removing NDMA. In fact, NDMA increased as a result of the chlorination installed ahead of the filters in order to prevent membrane fouling. RO, however, exhibited removal efficiencies of between 24 and 56 percent (Plumlee et al., 2008). Additional experiments performed with deionized water showed that NDMA was removed by RO in the range of 54 to 70 percent, depending on the membrane used. Nitrosamines of higher molecular weight were removed more effectively (Steinle-Darling et al., 2007). A strong correlation was found between the molecular weight of the tested nitrosamine and rejection rates. The authors tested *N*-nitroso-n-dibutylamine (NDBA), NDEA, NDMA, *N*-nitrosomethylethylamine (NMEA), *N*-nitrosopiperidine (NPIP), *N*-nitroso-n-dipropylamine (NDPA) and NPYR. Nitrosamines exhibited higher removal in the order: NDBA = NDPA = NPIP > NDEA > NPYR > NMEA >

NDMA. When alginate was spiked into the influent to simulate biofouling, a drop in NDMA rejection from 55 to 38 percent rejection was observed (Steinle-Darling et al., 2007).

Khan and McDonald (2010) studied RO rejection at an advanced wastewater treatment facility in Australia. NDMA was poorly removed and variable, with 5th and 95th percentile values of 26 percent and 35 percent, respectively. As with other studies, nitrosamines of higher molecular weight had better removal rates. NDEA was rejected with 5th and 95th percentile values both around 91 percent. Removal of NDPA was higher, with 5th and 95th percentile values of 97 percent and 98 percent (Khan and McDonald, 2010). Another advanced water treatment facility in Australia averaged 10 percent removal of NDMA by RO (Poussade et al., 2009). Miyashita et al. (2009) also found rejection by membranes correlated to molecular weight for both NF and RO membranes. They performed bench-scale tests with polyamide thin-film composite membranes in deionized water buffered at pH 7 to study the rejection of NDMA, NDEA, NMEA, NDPA, NDBA and NPYR. Rejection of nitrosamines by NF membranes varied from 9 to 55 percent. Rejection by RO membranes ranged from 54 to 97 percent (Miyashita et al., 2009).

Hatzinger et al. (2011) studied NDMA removal in a membrane bioreactor. The bioreactor combines biological reactions with membrane filtration. The bench-scale study found stable NDMA removal of 99.95 percent over a 70-day period. Cessation of biological activity by addition of trichloroethylene resulted in an increase in NDMA in the effluent, indicating that biological degradation was an important component of the overall removal. Chon et al. (2015) examined the effectiveness of a laboratory scale system for wastewater reclamation involving a membrane bioreactor and NF membrane. They found the removal efficiency in the membrane bioreactor was 73-84 percent for NDMA, 58-61 percent for NPYR, 76-77 percent for NDEA, 57-76 percent for NPIP, 45-57 percent for NMOR, 75-78 percent for NDBA and 53-54 percent for NDPhA. Removal by NF membranes correlated relatively well with molecular size and was 8-59 percent for NDMA, 38-60 percent for NPYR, 43-75 percent for NDEA, 39-72 percent for NPIP, 51-74 percent for NMOR, 61-71 percent for NDBA and 69-80 percent for NDPhA.

Fujioka et al. have done several experiments involving removal of NDMA and NMEA by NF and RO membranes. They found removal highly variable—from 8 to 82 percent for NDMA and 23 to 94 percent for NMEA. For nitrosamines with higher molecular weights, removal was more consistent, with 90 percent removal for NDPA and NDBA (Fujioka et al. 2013a). For the nitrosamines with lower molecular weights, removal was correlated with membrane permeability; an RO membrane designed for boron removal gave the best removal of nitrosamines, with up to 71 percent removal of NDMA. Their work also showed the importance of membrane permeability for removal of low molecular weight nitrosamines, showing that membrane fouling could increase NDMA removal (Fujioka et al., 2013b) and that cleaning the membranes could actually reduce removal (Fujioka et al., 2014). The same team also examined the rejection of 7 nitrosamines (including NDMA, NDEA, NMEA, NDPA and NPYR) using hollow fiber cellulose triacetate RO membranes as a substitute for traditional polyamide membranes. They found rejection rates ranging from 25 percent (for NDMA) to 78 percent (for NPIP). Rejection appeared to be influenced by both molecular size and hydrophobicity (Fujioka et al., 2015).

7.3.4 Metal Catalysis

A number of metal catalysts have been examined for the catalytic reduction of NDMA and other nitrosamines. Nitrosamine reduction can produce the corresponding amine as a product;

therefore, if the reaction does not go to completion, nitrosamines can re-form if the product water is exposed to an oxidant. Iron and nickel-enhanced iron column flow-through reactors were found to be capable of destroying NDMA at half-lives of 13 hours and 2 minutes, respectively, but accumulation of surface oxides caused rapid decreases in rates (Gui et al., 2000; Odziemkowski et al., 2000). Conversion of nitrosamines to their respective amines was achieved by porous nickel catalysts under a hydrogen atmosphere. Catalyst concentrated at 500 mg/L in deoxygenated water buffered at pH 7 under 1 atm of hydrogen pressure gave rate constants of 0.51/min, 0.49/min, 0.42/min, 0.28/min and 0.26/min for NDMA, NDPhA, NDEA, NDPA and NDBA, respectively. In these experiments, catalysts were sensitive to matrix effects, as nitrate and sulfide severely inhibited reactivity. Calcium, magnesium, chloride, sulfate, bicarbonate and NOM decreased rates by a factor of 2.2. However, the use of hydrogen gas and pyrophoric catalysts at water utilities poses a safety hazard. Additionally, nickel and aluminum leaching may occur (Frierdich et al., 2007).

Lee et al. (2005a) achieved successful photocatalytic degradation of NDMA by titanium dioxide (TiO_2); however, experiments were performed under conditions far removed from those found at treatment plants. Davie et al. (2008) found that addition of indium to 5 percent palladium on aluminum oxide transformed NDMA to DMA and ammonia. An iridium loading of 1 percent transformed NDMA at a rate of 0.25/hour. Although this technology exhibits favorable kinetics, the catalyst is prone to sulfide poisoning and may be cost-prohibitive.

Davie et al. (2006) studied a number of metals for potential catalytic properties. Iron, nickel, nickel-enhanced iron and magnesium resulted in NDMA half-lives of 533 ± 218 hours, 8.4 ± 2.2 hours, 107±2 hours and 990 ± 220 hours, respectively, for 10 mg/L of metal. Metal-catalyzed reduction of NDMA by hydrogen gas resulted in half-lives of 6.0 ± 0.4 hours, 1.0 ± 0.1 hours and 0 hours for palladium, copper-enhanced palladium and copper, respectively. All experiments were performed in deionized water. Thus, the feasibility of these techniques at PWSs is unknown (Davie et al., 2006). However, studies performed using a ground water-soil matrix showed that nickel and zero-valent iron were ineffective catalysts (Schaefer and Fuller, 2007).

7.3.5 Sunlight Photolysis

Natural sunlight has been found to be effective for nitrosamine removal. When nitrosamines (NDBA, NDEA, NDMA, NDPA, NMEA, NPYR, NPIP and NMOR) in organic-free water were exposed to natural sunlight exhibiting intensity ranging from 1150 to 1300 W/m^2, 99 percent of total nitrosamines were photolyzed in one hour (Chen et al., 2010). Removal for the various nitrosamines corresponded to half-lives ranging from 8 to 10 minutes, with a rate constant of approximately 4.9/hour. Indoor tests using simulated sunlight at 1325 W/m^2 exhibited slightly faster photolysis with half-lives ranging from 3 to 9 minutes. Nitrosamines with cyclic side groups (i.e., NMOR, NPYR and NPIP) had the highest rate constants of the nitrosamines, whereas the three nitrosamines with only methyl and/or ethyl side groups had the lower rate constants. When nitrosamines were spiked into water containing secondary effluent from a wastewater facility, first-order rate constants were approximately 50 percent less than those for nitrosamines spiked into organic-free water, indicating that the presence of NOM may decrease the performance of UV photolysis (Chen et al., 2010).

Direct photolysis studies were carried out in deionized water using a photosimulator that emitted light with wavelengths between 290 and 800 nm at 765 watts per square meter (W/m^2) (Plumlee and Reinhard, 2007). The authors calculated half-lives of less than 20 minutes for all

nitrosamines tested (NDBA, NDEA, NDMA, NDPA, NMEA, NPYR and NPIP). Methylamine and nitrite were the dominant products of NDMA degradation. It is possible these products could be reoxidized to re-form the nitrosamine. Addition of dissolved organic matter (DOM) led to a decrease in the photodecay rate due to light screening. Further decreases in efficiency are seen with increasing depth of water. For example, if the depth of the water is reduced to 10 cm from 1 m the half-lives are reduced by a factor of approximately ten (Plumlee and Reinhard, 2007).

Organic-free water buffered at pH 7.2 and amended with 10,000 ng/L NDMA was exposed to sunlight at an intensity of 1150–1300 W/cm^2 (Chen et al., 2010). NDMA was rapidly photolyzed with a half-life of approximately 8 to 10 minutes. The efficiency of NDMA photolysis was shown to be sensitive to the water matrix. Experiments done in biologically treated wastewater effluent and filtered effluent exhibited first-order rate constants 50 percent and 11 percent, respectively, below those observed in organic-free water (Chen et al., 2010). At the Orange County Water District of California, shallow sunlit basins with residence times of approximately 1 day resulted in removal of approximately 50 percent of NDMA (Mitch et al., 2003b).

7.3.6 UV Photolysis

Although UV doses required for NDMA degradation are approximately an order of magnitude higher than those typically used for disinfection purposes, the high efficiency of UV makes it an attractive option for removal of nitrosamines at drinking water and wastewater utilities (Mitch et al., 2003b). NDMA exhibits strong absorption bands at 228 and 332 nm, resulting in the breakdown of the nitrogen-nitrogen bond (Liang et al., 2003). Placement of the UV units after disinfection may facilitate removal of nitrosamines formed during the disinfection process.

Lee et al. (2005b, 2005c) investigated NDMA photolysis using a low-pressure mercury lamp emitting at 253.7 nm. Photolysis experiments were performed in phosphate-buffered distilled water containing 1 mM NDMA. The authors found the efficiency of photolysis to be dependent on DO; decay rates under oxygen saturation conditions were higher than nitrogen saturation conditions. This phenomenon only occurred at light irradiation >300 nm. Quantum yields (the number of molecules reacting per photon) were found to be constant, at 0.31, regardless of pH. However, product yields of DMA and methylamine were dependent on pH, with methylamine and nitrate dominating at pH >9.

In an ambient water study, photolysis of NDPA spiked into lake water exhibited fast degradation independent of pH and initial concentration (Berkowitz, 2008; Sacher et al., 2008). Products were propylamine and dipropylamine. Nitrosamines such as NDMA and NDEA also converted to their parent amines upon UV treatment with a high-pressure mercury lamp (Berkowitz, 2008; Sacher et al., 2008).

Shah et al. (2013) found that UV light at an intensity of 1000 mJ/cm^2 achieved 90 percent removal of nitrosamines from a pilot plant treating amine-based solutions from carbon capture and storage.

Xu et al. (2008) found that NDEA can be degraded in deionized water by a low-pressure mercury lamp with an emission at 253.7 nm (1000 µW/cm^2). NDEA degraded to below the detection limit (DL) in 20 minutes at an initial concentration of 0.01 mM (1.02 mg/L) in deionized water at pH 6. Reaction rates decreased slightly with increasing pH. To investigate the effect of NOM on degradation efficiency, humic acid was added at various concentrations.

Addition of 2.9 mg/L humic acid decreased the degradation rate by approximately a factor of 2 (from 0.74/min to 0.40/min). Degradation products were methylamine, DMA, DEA and nitrite (Xu et al., 2008).

Xu et al. (2009a) investigated the photolysis of NPYR and NPIP. Deionized water was spiked with NPYR or NPIP to achieve a final concentration of 1 µM (100 µg/L and 114 µg/L respectively). Solutions were irradiated with a low-pressure mercury lamp (8 W, 1000 $\mu W/cm^2$). Ninety-nine percent removal was observed for both nitrosamines after 5 minutes of irradiation. While pH had little effect on NPYR, it had a large effect on NPIP degradation; when the solution pH was increased from 3.1 to 10.5, the reaction rate constant decreased by 95 percent. Addition of NOM had little effect on degradation efficiency for both nitrosamines. NPYR and NPIP degradation products were similar, as both produced a mixture of aliphatic amines, nitrate and nitrite.

Genuino et al. (2011) investigated the use of metal photocatalysts to enhance the photodegradation of NDMA. Their lab-scale experiments found that a platinum-manganese catalyst and an amorphous manganese oxide resulted in 95 percent and 100 percent removal of 7.4 mg/L NDMA within 3 hours of irradiation.

The intensities required for UV photolysis of nitrosamines are greater than those typically used for disinfection. Another consideration is that the byproducts of UV photolysis can react with disinfectants to re-form NDMA. For example, although irradiation of 100 µM (7.4 mg/L) NDMA in distilled water by a low-pressure mercury lamp provided 99 percent removal within 20 minutes, subsequent application of 1 mg/L chlorine resulted in formation of 51.8 µg/L NDMA (Xu et al., 2009b). Nawrocki and Andrzejewski, (2011) postulate that the re-formation is a result of DMA and nitrite being formed as products of the photolysis of NDMA.

Using another oxidant with the UV to form an advanced oxidation process (AOP) has been found to lower NDMA re-formation, probably through oxidation of nitrite and DMA. Regeneration of NDMA was less than 1 µg/L, compared to the initial concentration of 7.4 mg/L, upon application of UV combined with 6.6 mg/L ozone (Xu et al., 2009b). AOPs, such as UV/ozone and UV/peroxide, do not enhance NDMA destruction relative to UV alone, as the decay is primarily driven by photolysis, but rather inhibit its re-formation (Kruithof et al., 2007; Swaim et al., 2008). Although the chemistry is complex and involves solvated electrons, hydroxyl radicals and hydrogen atoms, the ultimate goal is to decrease DMA and nitrite byproducts of UV treatment so as to preclude NDMA re-formation (Liang et al., 2003; Sharpless and Linden, 2003). However, it has been demonstrated that high doses of peroxide can inhibit NDMA photolysis by competing for light absorption (Kruithof et al., 2007; Swaim et al., 2008).

7.3.7 Advanced Oxidation Processes (AOP)

AOPs (e.g., UV/ozone, UV/hydrogen peroxide and ozone/hydrogen peroxide) have the common feature of forming hydroxyl radicals to oxidize contaminants. Their effectiveness in removing nitrosamines will depend on their placement in the treatment train. The reaction rates of radical species with nitrosamines are high, such that the use of AOPs for nitrosamine removal may be feasible.

Hydroxyl radicals and hydrated electrons were introduced into nitrogen-sparged deionized water by pulse radiolysis in a study conducted by Mezyk et al. (2006). Hydroxyl radical rate constants

for NMEA and NDEA were 4.95 x 10^8 and 6.99 x 10^8 M/sec, respectively. Reaction of hydroxyl radicals with nitrosamines led to a hydrogen abstraction from the alkyl group leading to subsequent nitrosamine degradation. Although reactions with hydrated electrons were faster, the electron-nitrosamine adduct led to re-formation of the parent nitrosamine (Mezyk et al., 2006).

Xu et al. (2010) compared UV and UV/ozone AOPs for NDEA removal using a low-pressure mercury lamp. Addition of 0.1 mM (10.2 mg/L) NDEA to deionized water buffered at pH 6 and containing 6.64 mg/L ozone led to only 10 percent removal of the nitrosamine. NDEA removal reached 99 percent when exposed to UV radiation over 10 minutes, and a similar removal rate was seen for combined UV/ozone. While the addition of ozone did not enhance the rate of NDEA decay, it did affect the product ratio. The yield of DEA and nitrite produced in the UV/ozone process was less than that in the UV process. This difference ranged from 22 percent to 54 percent, depending on the pH, with higher difference at lower pH (Xu et al., 2010).

Hydroxyl radicals formed through AOPs react quickly with nitrosamines, with rate constants on the order of 10^8 to 10^9 moles per liter per second (Landsman et al., 2007). Nitrosamines with higher molecular weights have higher rate constants. Reaction rates determined by Landsman et al. (2007) may be overestimated for drinking water, because experiments were performed in deionized water containing high concentrations of nitrosamines (1 mM). In real waters, reaction with NOM and carbonate consumes most hydroxyl radicals (Landsman et al., 2007).

A pilot study (Liang et al., 2003) was performed with Colorado River water and Southern California ground water to investigate the degradation of NDMA via pulsed-UV processes, including UV/hydrogen peroxide as one study condition. A pulsed-UV dose of 5.2 kilowatt-hours per 1,000 gallons resulted in an NDMA pseudo-first-order rate constant of 4.1/min for ground water and 1.4/min for river water. The discrepancy between the rates suggests competition for light between NDMA and organic constituents in the water matrix. NDMA concentrations did not change when UV/hydrogen peroxide was substituted for UV alone. NDMA concentrations more than doubled, however, when water treated with UV was chlorinated (Liang et al., 2003). In a separate study, two water treatment plants in Asia exhibited similar influent NDMA levels, but the plant using peroxide/UV advanced oxidation had lower effluent NDMA levels (<5 ng/L) than the plant using UV alone (>15 ng/L) (Valentine et al., 2005). A field study performed at the Bundama advanced water treatment plant in Australia demonstrated a 1.6 log removal of NDMA by UV/peroxide treatment, with most NDMA values below 5 ng/L after treatment with a dose of 4–5 mg/L peroxide (Poussade et al., 2009).

In batch experiments performed in deionized water buffered at pH 7, the addition of excess ozone at concentrations of up to 160 µM oxidized 13 percent of the initial 74 µg/L of NDMA, whereas 85 percent of NDMA was oxidized by 40 µM ozone combined with 80 µM peroxide. Hydroxyl scavengers, such as carbonate, reduced the rate and percent of NDMA oxidation. For example, higher oxidant doses were required for the same levels of NDMA oxidation in Lake Zurich water, with an alkalinity of 2.6 mM as bicarbonate (Lee et al., 2007c). Conventional ozonation with 160 µM ozone led to 25 percent NDMA oxidation, whereas the AOP ozone/peroxide resulted in 55 percent NDMA oxidation. Reaction products consisted of methylamine and ammonia, with ammonia increasing with hydroxyl radical production. Although this AOP was effective, its use (as, presumably, is the case with the use of any AOP involving ozone) may increase bromate such that it exceeds the drinking water maximum contaminant level of 10 µg/L. For example, the maximum dose of ozone that can be applied

without exceeding 10 µg/L bromate in Lake Zurich water is approximately 80 µM, which corresponds to 39 percent NDMA oxidation (Lee et al., 2007c).

7.3.8 Electrochemical Techniques

Oxidation and reduction of NDMA by boron-doped diamond film electrodes has been studied by Chaplin et al. (2010a,b). While rates were sufficient to remove up to 97 percent of 37 mg/L of NDMA, the process was tested on RO concentrates having much higher NDMA concentrations than typical of drinking water. The rates would be expected to be slower at lower concentrations.

7.3.9 Biological Techniques

Webster et al. (2013) examined the removal of NDMA in a laboratory-scale biological fluidized bed reactor. The reactor used *Rhodococcus ruber* bacteria supported on an activated carbon media with propane as a food source for the bacteria. The reactor treated contaminated ground water with initial NDMA concentrations of 10 to 20 µg/L. With a 20-minute contact time, the reactor achieved 90 percent removal of NDMA. Increasing the contact time to 30 minutes and increasing propane and oxygen flow enabled 99 percent removal. Homme and Sharp (2013) examined laboratory reaction of nitrosamines by the bacteria *Rhodococcus jostii* grown on propane and found degradation of NDMA, NDEA, NDPA, NPYR and to a smaller extent, NMOR. They found the order of reactivity of the different nitrosamines was NDMA>NDEA>NDPA>NPYR>NMOR. Wang et al. (2015d) examined the effects of nitrosamine digestion on a biofilter's microbial community. Exposure of the microbial community to low levels of nitrosamines led to an increase in proteobacteria relative to other phyla. After assimilation for 10 days, biofilters removed between 8 and 40.7 percent of various nitrosamine species (including all six that are the subject of this document), with smaller nitrosamines being removed more efficiently. The research team was able to isolate a species *Rhodococcus cercidiphylli* that was able to reduce 5 of 9 nitrosamines studied. In separate trials using the isolated bacteria, the following removals were obtained after 10 days: NDMA (85.4 percent), NDPA (78.8 percent), NDEA (47.7 percent), NPYR (48.5 percent) and NDBA (38.1 percent).

7.4 Summary

A variety of strategies are available to control and/or reduce nitrosamine concentrations in drinking water. Each strategy has its advantages and limitations. Exhibit 7.2 provides a summary of the treatment strategies discussed in this chapter along with ranges of removal efficiencies and other potential benefits and issues identified for each technology.

Source water management can be an effective strategy for controlling nitrosamines in drinking water. Longer distances between wastewater discharges and drinking water intakes will allow natural attenuation processes such as photolysis and biological degradation of organic matter from wastewater discharges (including nitrosamine precursors) to occur. While source water management can be an effective way to control nitrosamine formation, it can be a challenging undertaking because it involves the cooperation of groups outside the control of the drinking water utility.

Removing nitrosamine precursors during drinking water treatment is also a viable and sometimes advantageous strategy. A significant advantage of tighter precursor control is that less chlorine is required for primary and secondary disinfection.

Achieving nitrosamine precursor removal through sorption may be difficult because of the hydrophilicity of NDMA precursors. Sorption can achieve substantial removal of NDMA precursors under conventional flow-through operating conditions, but it requires large doses of activated carbon. Customized sorbents may prove more effective but are likely to be more costly. Current data gaps involve the properties and performance of specific sorbents and results from full-scale studies of nitrosamine precursor removal.

Biodegradation of NDMA has been shown to occur at widely varying rates depending on site-specific conditions. Biological reaction often requires adsorption of the compound for the process to occur efficiently. Also, larger nitrosamines do not degrade as quickly as NDMA, so this treatment technique may not be effective for all nitrosamines. On the other hand, riverbank filtration has been shown to provide precursor removal in several cases. Data gaps involve the effectiveness of biological filtration for reducing nitrosamine formation and the applicability of riverbank filtration and biologically active filtration for nitrosamine reduction. If a drinking water treatment plant decides to add biological treatment, downstream filtration and disinfection may be required to prevent sloughed biomass from colonizing the distribution system.

Exhibit 7.2: Summary of Removal Efficiencies of Precursors, NDMA and Other Nitrosamines

Technology	Precursor Removal	Reference(s)	NDMA Removal	Reference(s)	Other Nitrosamine Removal	Reference(s)	Other Potential Benefits	Issues
Enhanced Coagulation	10–18% (full-scale and lab-scale NDMA FP removal) 30–45% (full-scale and lab-scale DON removal)	Sacher et al., 2008 Mitch et al., 2009 Westerhoff et al., 2006 Dotson and Westerhoff, 2009 Liao et al. 2015b	< 7% (lab-scale NDMA FP removal)	Sacher et al., 2008	N/A	N/A	Often an existing process; Also removes THM and HAA precursors	Not very effective for precursor or nitrosamine removal; Must be careful with selection of coagulation polymers
Sorption	29–90% (using PAC lab-scale FP removal) 54–84% (full-scale GAC FP removal) >90% (bench scale removal of select amines)	Sacher et al., 2008 Hanigan et al., 2012 Chu et al., 2015 Krasner et al., 2015 Wu et al., 2015 Chen et al., 2015b	AC: 17–99%[1] (lab-scale NDMA removal) Zeolite: 15–26% (bench-scale NDMA removal) Carbonaceous resins: 99% (bench-scale NDMA removal) Activated carbon nanoparticles (lab-scale NDMA removal) 20%	Fleming et al., 1996 Wang et al., 2013b	N/A	N/A	Also removes THM and HAA precursors and other contaminants	Removal is dependent on sorbent, CT and concentration; Removal is dependent on the structure of the compound and on water quality parameters; Sorbent may have to be regenerated frequently; Desorption from GAC may be problematic
Biological Processes	67% (DW full-scale NDMA FP removal) 59%, 55%, >70% (DW pilot scale removal of NDMA FP, NDEA FP and NPYR FP, respectively)	Mitch et al., 2009 Liao et al., 2015b	90–99% (laboratory scale NDMA removal) 85.4% (NDMA removal laboratory using isolated bacteria)	Webster et al., 2013 Wang et al. 2015d	78.8%, 47.7%, 48.5%, 38.1% (respective removal of NDPA, NDEA, NPYR and NDBA using laboratory isolated bacteria)	Wang et al., 2015d	Also removes other *N*-DBP precursors	Limited drinking water information available; Rate of degradation is too slow for drinking water treatment (Health Canada 2011)

Technology	Precursor Removal	Reference(s)	NDMA Removal	Reference(s)	Other Nitrosamine Removal	Reference(s)	Other Potential Benefits	Issues
Riverbank Filtration	50–93% (full-scale removal of precursors)	Sacher et al., 2008	N/A	N/A	N/A	N/A	Also removes other *N*-DBP precursors	Limited drinking water information available; Rate of degradation is too slow for drinking water treatment (Health Canada 2011)
Slow Sand Filtration	23–83% (lab-scale precursor removal)	Krasner et al., 2008	N/A	N/A	N/A	N/A	Good removal at full scale	Requires large surface area
Membrane Filtration	MF: 12–95% (removal of precursors) RO: 98-99%	Deeb et al., 2006 Miyashita et al., 2009	MF/UF: negligible NF: 8-59% (WW lab scale) RO: 25 - 84% (WW lab and full scale)	Plumlee et al., 2008, Steinle-Darling et al., 2007 Fujioka et al., 2013a Chon et al. 2015 Fujioka et al. 2015	23–97% (DW lab scale) (NDEA, NMEA, NDPA, NDBA and NPYR)	Miyashita et al., 2009 Fujioka et al., 2013a Fujioka et al., 2015 Chon et al., 2015	Also removes THM and HAA precursors and other contaminants	Results are membrane-specific; Typical membrane placement in process would not remove nitrosamines formed during final disinfection; To avoid membrane fouling, additional chlorine may be added, which can result in increased DBP formation
AOPs (UV/Hydrogen Peroxide or UV/Ozone)	N/A	N/A	25–97 (lab scale and full scale)	Poussade et al., 2009 Lee et al., 2007c	99% (lab scale) (NDEA)	Xu et al., 2010	May remove other contaminants, prevents NDMA re-formation	Can contribute to the formation of other DBPs and can be expensive
Oxidation by Ozone, Permanganate, or Chlorine Dioxide	20–94% (lab-scale NDMA FP removal) 88% (full-scale NDMA FP removal when combined with biological GAC filters)	Lee et al., 2007b Sacher et al., 2008 Liao et al., 2014 McCurry et al., 2015 Krasner et al., 2015 Wang et al., 2015c	N/A	N/A	N/A	N/A	May remove other contaminants	May form other DBPs; may oxidize DMA to NDMA

Technology	Precursor Removal	Reference(s)	NDMA Removal	Reference(s)	Other Nitrosamine Removal	Reference(s)	Other Potential Benefits	Issues
Pre-Oxidation with Chlorine	17–93% (lab scale and full scale)	Charrois and Hrudey, 2007 Chen and Valentine, 2008 McCurry et al. 2015 Krasner et al., 2015	N/A	N/A	N/A	N/A	Simple to use; May remove other contaminants	May form chlorination DBPs (THMs and HAAs)
Sunlight Photolysis	25% (lab-scale NDMA FP removal)	Chen and Valentine, 2008	50–99% (full scale and lab scale)	Mitch et al., 2003b Chen et al., 2010 Plumlee and Reinhard, 2007	99% (lab scale) (NDBA, NDEA, NDMA, NDPA, NMEA, NPYR, NPIP)	Chen et al., 2010 Plumlee and Reinhard, 2007	Effective and inexpensive	Performance decreases in presence of NOM; Byproducts of photolysis can react with chlorine to re-form nitrosamines; Longer contact time needed for natural sunlight exposures
UV Photolysis	54+% (MP UV pilot scale NDMA FP removal) 29+% (LP UV pilot scale NDMA FP removal)	McCurry et al,. 2015	>99%, or 95–100% (lab scale)	Mitch et al. (2003b) Lee et al. (2005b,c) Genuino et al. (2011) Xu et al. (2009b)	>99% (lab scale)(NDEA, NDPA, NPYR, NPIP)	Berkowitz, 2008 Sacher et al., 2008 Xu et al., 2008 Xu et al. (2009a)	Can provide additional disinfection and may remove other contaminants	Requires higher doses; Byproducts of UV photolysis can react with chlorine to re-form nitrosamines

Note:

1) These Activated Carbon (AC) sorption trials were batch experiments, far removed from normal flow-through operating conditions at water facilities.

The small size of NDMA molecules makes MF and UF less effective for nitrosamine control. RO has been shown to eliminate almost all NDMA precursors. NF and RO can also remove nitrosamines, with nitrosamines of higher molecular weight exhibiting higher removal rates. Therefore, not all nitrosamines will be removed with equal effectiveness. NDMA, however, has the lowest molecular weight of the nitrosamines, so a membrane that can remove it will likely be adequate for all nitrosamines.

Research has shown that use of pre-oxidants can also be an effective strategy for controlling nitrosamine formation. Pre-oxidants, however, will form DBPs of their own. Pre-oxidation with ferrate may be difficult due to the highly unstable nature of potassium and sodium salts. Ferrate has not been extensively used in drinking water treatment. Data gaps exist regarding the use of ferrate for nitrosamine control. Permanganate is an easy-to-use pre-oxidant. Chlorine is already available at most drinking water utilities. However, the pre-oxidation dose and contact time must be monitored closely so that maximum contaminant levels for other DBPs such as THMs and MAAs are not exceeded. While pre-oxidation of NDMA precursors could be a practical treatment technique for utilities to control NDMA formation, waters with high concentrations of DMA or other precursors may see less net reduction because of the simultaneous formation of NDMA by oxidation of these precursors. Data gaps exist regarding the optimization of oxidation processes for nitrosamine control, including examining multiple categories of DBP formation by oxidation.

Removal of nitrosamines after they have formed is often more difficult than controlling source water or removing precursors. Generally, nitrosamine removal requires more advanced technologies. Degradation of nitrosamines by sunlight, however, has been shown to be effective. It is dependent on water depth, water quality and available sunlight and may not be effective for all waters. UV photolysis is effective for reducing all nitrosamines and produces few regulated DBPs and is less dependent on water depth or available sunlight. However, it requires higher doses. An advantage is that UV photolysis may also be effective in removing other contaminants. Re-formation of NDMA from disinfection with chlorine or chloramines can be a limiting factor, although a degree of re-formation generally results in much lower concentrations than the original nitrosamine concentration. Data gaps exist regarding ways to reduce nitrosamine re-formation.

Control of nitrosamines can be achieved through a wide array of possible strategies ranging from traditional technologies to advanced treatment processes. Most treatment technologies discussed in this chapter are not completely new. Many of these technologies are also discussed in the *Six Year Review 3 Technical Support Document for Disinfectants and Disinfection By-Products Rules* (USEPA, 2016a) and the *Simultaneous Compliance Guidance Manual for the Long-Term 2 and Stage 2 DBP Rules* (USEPA, 2007d).

8 References

Aiub, C.A., L.F.R. Pinto, and I. Felzenszwalb. 2003. *N*-Nitrosodiethylamine mutagenicity at low concentrations. Toxicology Letters. 145(1): 36-45.

Aiub, C.A., J.L. Mazzei, L.R.F. Pinto, and I. Felzenszwalb. 2006. Evaluation of nitroreductase and acetyltransferase participation in *N*-nitrosodiethylamine genotoxicity. Chemico-Biological Interactions. 161(2): 146-154.

Aleksandrov, V.A. 1968. Blastomogenic effect of dimethylnitrosamine on pregnant rats and their offspring. Nature. 218: 280 (as cited in Health Canada, 2010).

Althoff, J. and C. Grandjean. 1979. *In vivo* studies in Syrian golden hamsters: A transplacental bioassay of ten nitrosamines. National Cancer Institute Monograph. 51: 251-255.

Althoff, J., P. Pour, C. Grandjean, and S. Marsh. 1977. Transplacental effects of nitrosamines in Syrian hamsters. Zeitschrift für Krebsforschung und Klinische Onkologie. 90: 79-86 (as cited in IPCS, 2002).

Amacher, D.E. and S.C. Paillet. 1983. The activation of procarcinogens to mutagens by cultured rat hepatocytes in the L5178Y/TK mutation assay. Research/Environmental Mutagenesis and Related Subjects. 113:77-88 (as cited in ATSDR, 1989).

Amelizad, S., K.E. Appel, M. Schoepke, C.S. Rühl, and F. Oesch. 1989. Enhanced demethylation and denitrosation of N-nitrosodimethylamine by human liver microsomes for alcoholics. Cancer Letters. 46(1): 43-49.

American Conference of Governmental Industrial Hygienists (ACGIH). 1991. *Documentation of the TLV and biological exposure indices*. 6th ed., vol. 2. Cincinnati, Ohio.

Anderson, L.M., L.J. Priest, and J.M. Budinger. 1979. Lung tumorigenesis in mice after chronic exposure in early life to a low dose of dimethylnitrosamine. Journal of the National Cancer Institute. 62(6): 1553-1555 (as cited in CalEPA, 2006).

Anderson, L.M., G.W. Harrington, H.M. Pylypiw, Jr., A. Hagiwara, and P.N. Magee. 1986. Tissue levels and biological effects of *N*-nitrosodimethylamine in mice during chronic low or high dose exposure with or without ethanol. Drug Metabolism and Disposition. 14(6): 733-739 (as cited in IPCS, 2002; CalEPA, 2006; ATSDR, 1989).

Anderson, L.M., A. Hagiwara, R.M. Kovatch, S. Rehm, and J.M. Rice. 1989. Transplacental initiation of liver, lung, neurogenic and connective tissue tumors by *N*-nitroso compounds. Toxicological Sciences. 12: 604-620 (as cited in CalEPA, 2006; Health Canada, 2010).

Anderson, L.M., J.P. Carter, C.L. Driver, D.L. Logsdon, R.M. Kovatch, and A. Giner-Sorolla. 1993. Enhancement of tumorigenesis by *N*-nitrosodiethylamine, *N*-nitrosopyrrolidine and N6-(methylnitroso)-adenosine by ethanol. Cancer Letters. 68: 61–66.

Andrews, A.W. and W. Lijinsky. 1980. The mutagenicity of 45 nitrosamines in the *Salmonella typhimurium*. Teratogenesis, Carcinogenesis, and Mutagenesis. 1(3): 295-303.

Andrzejewski, P. and J. Nawrocki. 2007. *N*-nitrosodimethylamine formation during treatment with strong oxidants of dimethylamine containing water. Water Science & Technology. 56(12): 125-131.

Andrzejewski, P. and J. Nawrocki. 2009. *N*-nitrosodimethylamine (NDMA) as a product of potassium permanganate reaction with aqueous solutions of dimethylamine (DMA). Water Research. 43(5): 1219-1228.

Andrzejewski, P., B. Kasprzyk-Hordern, and J. Nawrocki. 2008. *N*-nitrosodimethylamine (NDMA) formation during ozonation of dimethylamine-containing waters. Water Research. 42(4-5): 863-870.

Araki, A., M. Muramatsu, and T. Matsushima. 1984. Comparison of mutagenicities of *N*-nitrosamines on *Salmonella typhimurium* Ta100 and *Escherichia coli* Wp2 Uvra/Pkm101 using rat and hamster liver. Journal of Cancer Research. 75: 8-16.

Agency for Toxic Substances and Disease Registry (ATSDR). 1989a. Toxicological profile for *N*-nitroso-di-n-propylamine. U.S. Department of Health and Human Services, Public Health Service. December 1989. Available online at: https://www.atsdr.cdc.gov/ToxProfiles/tp142.pdf.

ATSDR. 1989b. Toxicological profile for *N*-nitrosodimethylamine. U.S. Department of Health and Human Services, Public Health Service. Available online at: https://www.atsdr.cdc.gov/toxprofiles/tp141.pdf.

ATSDR. 2010. Addendum to the toxicological profile for *N*-nitroso-di-n-propylamine. U.S. Department of Health and Human Services. Public Health Service, Agency for Toxic Substances and Disease Registry. Available online at: http://www.atsdr.cdc.gov/toxprofiles/n_nitrosodi_n_propylamine_addendum.pdf.

Australia National Health and Medical Research Council (NHMRC). 2013. Australian drinking water guidelines paper 6 (2011). National water quality management strategy. Version 2.0. Updated December 2013. Canberra, Australia: National Health and Medical Research Council, National Resource Management Ministerial Council.

Aze, Y., K. Toyoda, F. Furukawa, K. Mitsumori, and M. Takahashi. 1993. Enhancing effect of ethanol on esophageal tumor development in rats by initiation of diethylnitrosamine. Carcinogenesis. 14: 37-40 (as cited in IARC, 2010).

Bansal, A.K., R. Trivedi, G.L. Soni, and D. Bhatnagar. 2000. Hepatic and renal oxidative stress in acute toxicity of *N*-nitrosodiethylamine in rats. Indian Journal of Experimental Biology. 38(9): 916-920.

Bednar A.J., A.K. Kam, C.R. Mao, D.E. Splichal, D.B. Taggart, and K.H. Coats. 2009. Determination of low level NDMA in soils. U.S. Army Corps of Engineers. ERDC TN-EQT-09-01.

Beggs, K.M.H., R.S. Summers, and D.M. McKnight. 2009. Characterizing chlorine oxidation of dissolved organic matter and disinfection by-product formation with fluorescence spectroscopy and parallel factor analysis. Journal of Geophysical Research-Biogeosciences. 114: G04001.

Berger, M.R., D. Schmähl, and H. Zerban. 1987. Combination experiments with very low doses of three genotoxic *N*-nitrosamines with similar organotropic carcinogenicity in rats. Carcinogenesis. 8(11): 1635-1643.

Berkowitz, B. 2008. Abiotic contaminant transformations in subsurface water. In *Contaminant geochemistry: Transport and fate*, pp. 273-293. Berlin: Springer.

Bertram, J.S. and A.W. Craig. 1970. Induction of bladder tumours in mice with dibutylnitrosamine. British Journal of Cancer. 24: 352-359.

Bhattacharyya, K. 1965. Fetal and neonatal responses to hepatotoxic agents. The Journal of Pathology and Bacteriology. 90: 151-161 (as cited in ATSDR, 1989).

Bolto, B. 2005. Reaction of chlorine with organic polyelectrolytes in water treatment: A review. Journal of Water Supply: Research and Technology. 54(8): 531-544.

Brambilla, G., M. Cavanna, A. Pino, and L. Robbiano. 1981. Quantitative correlation among DNA damaging potency of six *N*-nitroso compounds and their potency in inducing tumor growth and bacterial mutations. Carcinogenesis. 2(5): 425-9.

Brambilla, G., P. Carl, R. Finollo, and L. Sciabà. 1987. Dose-response curves for liver DNA fragmentation induced in rats by sixteen *N*-nitroso compounds as measured by viscometric and alkaline elution analyses. Cancer Research. 47(13): 3485-3491.

Brendler, S.Y., A. Tompa, K.F. Hutter, R. Preussmann, and B.L. Pool-Zobel. 1992. *In vivo* and *in vitro* genotoxicity of several *N*-nitrosamines in extrahepatic tissues of the rat. Carcinogenesis. 13(12): 2435-2441.

California Department of Public Health (CDPH). 2013. NDMA and other nitrosamines – Drinking water issues. Available online at: http://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/NDMA.shtml.

California Environmental Protection Agency (CalEPA). 2006. Public health goal for N-nitrosodimethylamine in drinking water. Office of Environmental Health Hazard Assessment, Pesticide and Environmental Toxicology Branch. Available online at: http://oehha.ca.gov/water/phg/pdf/122206NDMAphg.pdf.

Chaplin, B.P., G. Schrader, and J. Farrell. 2010a. Electrochemical destruction of *N*-nitrosodimethylamine in reverse osmosis concentrates using boron-doped diamond film electrodes. Environmental Science & Technology. 44(11):4264-4269.

Chaplin, B.P., G. Schrader, and J. Farrell. 2010b. Electrochemical oxidation of *N*-nitrosodimethylamine with boron-doped diamond film electrodes. Environmental Science & Technology. 43(21): 8302-8307.

Charrois, J.W.A. and S.E. Hrudey. 2007. Breakpoint chlorination and free-chlorine contact time: Implications for drinking water *N*-nitrosodimethylamine concentrations. Water Research. 41(3): 674-682.

Charrois, J.W.A., J.M. Boyd, K.L. Froese, and S.E. Hrudey. 2007. Occurrence of *N*-nitrosamines in Alberta public drinking-water distribution systems. Journal of Environmental Engineering Science. 6: 103-114

ChemIDPlus. 2010. Toxicology Data Network. Available online at: http://chem.sis.nlm.nih.gov/chemidplus/. Accessed August 27, 2010.

Chen, Z. and R.L. Valentine. 2006. Modeling the formation of *N*-nitrosodimethylamine (NDMA) from the reaction of natural organic matter (NOM) with monochloramine. Environmental Science & Technology. 40(23): 7290-7297.

Chen, Z. and R.L. Valentine. 2007. Formation of *N*-nitrosodimethylamine (NDMA) from humic substances in natural water. Environmental Science & Technology. 41(17): 6059-6065.

Chen, Z. and R.L. Valentine. 2008. The influence of the pre-oxidization of natural organic matter on the formation of *N*-nitrosodimethylamine (NDMA). Environmental Science & Technology. 42(14): 5062-5067.

Chen, B. and P. Westerhoff. 2010. Predicting disinfection by-product formation potential in water. Water Research. 44(13): 3755-3762.

Chen, W. and T.M. Young. 2008. NDMA formation during chlorination and chloramination of aqueous diuron solutions. Environmental Science & Technology. 42(4): 1072-1077.

Chen, W. and T.M. Young. 2009. Influence of nitrogen source on NDMA formation during chlorination of diuron. Water Research. 43(12): 3047-3056.

Chen, B., S. Nam, P. Westerhoff, S.W. Krasner, and G. Amy. 2009. Fate of effluent organic matter and DBP precursors in an effluent-dominated river: a case study of wastewater impact on downstream water quality. Water Research. 43(6): 1755-1765.

Chen, B., W. Lee, P. Westerhoff, S.W. Krasner, and P. Herckes. 2010. Solar photolysis kinetics of disinfection byproducts. Water Research. 44(11): 3401-3409.

Chen, C., S. Leavey, S.W. Krasner, and I.H. Suffet. 2014. Applying polarity rapid assessment method and ultrafiltration to characterize NDMA precursors in wastewater effluents. Water Research. 57: 115-126.

Chen, W., Y. Yang, Y. Wang, C. Li, K. Lin, and J. Lou. 2015a. Effect of molecular characteristics on the formation of nitrosamines during chloramination of phenylurea herbicides. Environmental Science Processes and Impacts. 17: 2092-2100.

Chen, C., D. Hanigan, X. Liao, J. Wang, X. Zhang, I.H. Suffet, S.W. Krasner, and P. Westerhoff. 2015b. pH Effect on Nitrosamine Prescursor Removal by Activated Carbon Adsorption. In *Recent Advances in Disinfection By-Products*, ed. Karanfil et al, Chapter 10. ACS Symposium Series.

Chen, C., W. Zhou, and D. Lin. 2015c. Sorption characteristics of n-nitrosodimethylamine onto biochar from aqueous solution. Bioresource Technology. 179: 359-366.

Chhabra, S.K., V.L. Souliotis, J.W. Harbaugh, S.W. Krasnow, A.B. Jones, L.M. Anderson, and S.A. Kyrtopoulos. 1995. O^6-methylguanine DNA adduct formation and modulation by ethanol in placenta and fetal tissues after exposure of pregnant patas monkeys to N-nitrosodimethylamine. Cancer Research. 55(24): 6017-6020.

Choi, J. and R.L. Valentine. 2002. Formation of *N*-nitrosodimethylamine (NDMA) from reaction of monochloramine: a new disinfection by-product. Water Research. 36(4): 817-824.

Choi, J. and R.L. Valentine. 2003. *N*-nitrosodimethylamine formation by free-chlorine enhanced nitrosation of dimethylamine. Environmental Science & Technology. 37(21): 4871-4876.

Choi, J., S.E. Duirk, and R.L. Valentine. 2002. Mechanistic studies of *N*-nitrosodimethylamine (NDMA) formation in chlorinated drinking water. Journal of Environmental Monitoring. 4(2): 249-252.

Chon, K., S.H. Kim, and J. Cho. 2015. Removal of *N*-nitrosamines in a membrane bioreactor and nanofiltration hybrid system for municipal wastewater reclamation: process efficiency and mechanisms. Bioresource Technology. 170: 490-507.

Chu, W., D. Yao, N. Gao, T. Bond, and M.R. Templeton. 2015. The enhanced removal of carbanaceous and nitrogenous disinfection by-product precursors using integrated permanganate oxidation and powdered activated carbon adsorption pretreatment. Chemosphere. 141: 1-6.

Chuang, Y.H., A.Y. Lin, X.H. Wang., and H.H. Tung. 2013. The contribution of dissolved organic nitrogen and chloramines to nitrogenous disinfection byproduct formation from natural organic matter. Water Research. 47(3): 1308-1316.

Chung, F.L., T. Tanaka, and S.S. Hecht. 1986. Induction of liver tumors in F344 rats by crotonaldehyde. Cancer Research. 46(3): 1285-1289.

Chung, J. Y., Y. Yoon, M. Kim, S.B. Lee, H.J. Kim, and C.K. Choi. 2009. Removal of radio *N*-nitrosodimethylamine from drinking water by coagulation and powdered activated carbon (PAC) adsorption. Drinking Water Engineering and Science. 2(2): 49-55.

Clapp, N.K., A.W. Craig, and R.E. Toya, Sr. 1968. Pulmonary and hepatic oncogenesis during treatment of male RF mice with dimethylnitrosamine. Journal of the National Cancer Institute. 41: 1213-1227.

Clapp, N.K., R.L. Tyndall, and J.A. Otten. 1971. Differences in tumor types and organ susceptibility in BALB/c and Rf mice following dimethylnitrosamine and diethylnitrosamine. Cancer Research. 31: 196-198.

Cooper, S.W. and R.D. Kimbrough. 1980. Acute dimethylnitrosamine poisoning outbreak. Journal of Forensic Science. 25(4): 874-882.

Cornwell, D.A., S.W. Krasner, W.A. Mitch, and J.J. Pignatello. 2015. Investigating coagulant aid alternatives to polyDADMAC polymers. Water Resarch Foundation. Project #4452.

Dai, N and W.A. Mitch 2013. Relative importance of *N*‑nitrosodimethylamine compared to total *N*‑nitrosamines in drinking water. Environmental Science & Technology. 47: 3648-3656.

Dai, N. and W.A. Mitch. 2015. Controlling nitrosamines, nitramines, and amines in amine-based CO_2 Capture Systems with continuous ultraviolet and ozone treatment of washwater. Environmental Science & Technology. 49(7): 8878-8886

Dai, X., L. Zou, Z. Yan, and M. Millikan. 2009. Adsorption characteristics of N-nitrosodimethylamine from aqueous solution on surface-modified activated carbons. Journal of Hazardous Materials. 168(1): 51-56.

Dai, N., A.D. Shah, L. Hu, M.J. Plewa, B. McKague, and W.A. Mitch. 2012. Measurement of nitrosamine and nitramine formation from NOx reactions with amines during amine-based carbon dioxide capture for postcombustion carbon sequestration. Environmental Science & Technology. 46: 9793-9801.

Davie, M.G., M. Reinhard, and J.R. Shapley. 2006. Metal-catalyzed reduction of *N*-nitrosodimethylamine with hydrogen in water. Environmental Science & Technology. 40(23): 7329-7335.

Davie, M.G., K. Shih, F.A. Pacheco, J.O. Lickie, and M. Reinhard. 2008. Palladium-indium catalyzed reduction of *N*-nitrosodimethylamine: Indium as a promoter metal. Environmental Science & Technology. 42(8): 3040-3046.

De Stefani, E., H. Deneo-Pellegrini, J.C. Carzoglio, A. Ronco, and M. Mendilaharsu. 1996. Dietary nitrosodimethylamine and the risk of lung cancer: a case-control study from Uruguay. Cancer Epidemiology Biomarkers & Prevention. 5: 679-682 (as cited in IPCS, 2002).

Dean, B.J. and K.R. Senner. 1977. Detection of chemically induced somatic mutations in Chinese hamsters. Mutation Research/Environmental Mutagenesis and Related Subjects. 46: 403-407 (as cited in Kuroki et al., 1980).

Deeb, R., E. Hawley, D. Sedlak, J. Loveland, and M. Kavanaugh. 2006. Removal and destruction of NDMA and precursors during wastewater treatment. Proceedings of the Water Environment Federation. WEFTEC Session 11-20:1468-1477.

Department of Environment Food and Rural Affairs (DEFRA). 2008. NDMA – concentrations in drinking water and factors affecting its formation, final report, DEFRA 7348. Available online at: http://dwi.defra.gov.uk/research/completed-research/reports/DWI70_2_210.pdf.

Desjardins, R., M. Fournier, F. Denizeau, and K. Krzstyniak. 1992. Immunosuppression by chronic exposure to *N*-nitrosodimethylamine (NDMA) in mice. Journal of Toxicology and Environmental Health, Part A Current Issues. 37(3): 351-361.

Diaz Gomez, M.I., D. Tamayo, and J.A. Castro. 1986. Administration of *N*-nitrosodimethylamine, *N*-nitrosopyrrolidine, or N'-nitrosonornicotine to nursing rats: their interactions with liver and kidney nucleic acids from sucklings. Journal of the National. Cancer Institute. 76(6): 1133-1136.

Donovan, P. J. and G.T. Smith. 2008. Urethane and *N*-nitrosodiethylamine are mutagenic for the Syrian hamster fetus. Mutation Research/Genetic Toxicology and Environmental Mutagenesis. 657(2): 160-163.

Dotson, A. and P. Westerhoff. 2009. Occurrence and removal of amino acids during drinking water treatment. Journal American Water Works Association. 101(9): 101-116.

Dotson, A., P. Westerhoff, and S.W. Krasner. 2009. Nitrogen enriched dissolved organic matter (DOM) isolates and their affinity to form emerging disinfection by-products. Water Science & Technology. 60(1): 135-143.

Drabik-Markiewicz, G., K. Van den Maagdenberg, E. De May, S. Deprez, T. Kowalska, and H. Paelinck. 2009. Role of proline and hydroxyproline in *N*-nitrosamine formation during heating in cured meat. Meat Science. 81: 479-486.

Drewes, J.E., T. Harfelder, and C. Hoppe. 2006. Sustainable removal of micropollutants through riverbank filtration (RBF) and aquifer recharge and recovery (ARR). WQTC 2006 Conference Proceedings.

Druckrey, H., R. Preussmann, S. Ivankovic, and D. Schmähl. 1967. Organotropic carcinogenic effects of 65 various *N*-nitroso- compounds on BD rats. Zeitschrift für Krebsforschung. 69(2): 103-201 (as cited in USEPA, 1987; CalEPA, 2006)

Farre, J.F., J. Reungoat, F.X. Argaud., M. Rattier, J. Keller, and W. Gernjak. 2011a. Fate of *N*-nitrosodimethylamine, trihalomethane, and haloacetic acid precursors in tertiary treatment including biofiltration. Water Research. 45(8): 5695-5704.

Farre, J.F., K. Doderer, L. Hearn, Y. Poussade, J. Keller, and W. Gernjak. 2011b. Understanding the operational parameters affecting NDMA formation at advanced water treatment plants. Journal of Hazardous Materials. 185: 1575-1581.

Faust, S.D. and O.M. Aly. 1998. *Chemistry of water treatment.* 2nd edition. Boca Raton, FL: CRC Press.

Fine, D.H., R. Ross, D.P. Rounbehler, A. Silvergleid, and L. Song. 1977. Formation *in vivo* of volatile *N*-nitrosamines in many after ingestion of cooked bacon and spinach. Nature. 265: 753-755.

Fleming, E., J. Pennington, B. Wachob, R. Howe, and D. Hill. 1996. Removal of *N*-nitrosodimethylamine from waters using physical-chemical techniques. Journal of Hazardous Materials. 51(1-3): 151–164.

Flowers, R.C., and P.C. Singer. 2013. Anion exchange resins as a source of nitrosamines and nitrosamine precursors. Environmental Science & Technology. 47: 7365-7372.

Frierdich, A. J., J.R. Shapley, and T.J. Strathmann. (2007). Rapid reduction of *N*-nitrosamine disinfection byproducts in water with hydrogen and porous nickel catalysts. Environmental Science & Technology. 42(1): 262-269.

Fristachi, A. and G. Rice. 2007. Estimation of the total daily oral intake of NDMA attributable to drinking water. Journal of Water and Health 5(3): 341-355.

Fujii, K., S. Odashima, and M. Okada. 1977. Induction of tumours by administration of N-dibutylnitrosamine and derivatives to infant mice. British Journal of Cancer. 35(5): 610-4.

Fujioka, T., S.J. Khan, J.A. McDonald, A. Roux, Y. Poussade, J.E. Drewes, and L.D. Nghiem. 2013a. *N*-nitrosamine rejection by nanofiltration and reverse osmosis membranes: The importance of membrane characteristics. Desalination. 316: 67-75.

Fujioka, T., S.J. Khan, J.A. McDonald, R.K. Henderson, Y. Poussade, J.E. Drewes, and L.D. Nghiem. 2013b. Effects of membrane fouling on *N*-nitrosamine rejection by nanofiltration and reverse osmosis membranes. Journal of Membrane Science. 427: 311-319.

Fujioka, T., S.J. Khan, J.A. McDonald, A. Roux, Y. Poussade, J.E. Drewes, and L.D. Nghiem. 2014. *N*-nitrosamine rejection by reverse osmosis: effects of membrane exposure to chemical cleaning reagents. Desalination. 343: 60-66.

Fujioka, T., S.J. Khan, J.A. McDonald, and L.D. Nghiem. 2015. Rejection of trace organic chemicals by a hollow fiber cellulose triacetate reverse osmosis membrane. Desalination. 368: 69-75

Fujita, K and T. Kamataki. 2001. Role of human cytochrome P450 (CYP) in the metabolic activation of N-alkylnitrosamines: application of genetically engineered Salmonella typhimurium YG7108 expressing each form of CYP together with human NADPH-cytochrome P450 reductase. Mutation Research/Fundamental and Molecular Mechanisms. 483(1-2): 35-41.

Gan, X., T. Karanfil, S. Sule Kaplan Bekaroglu, and J. Shan. 2013. The control of N-DBP and C-DBP precursors with MIEX. Water Research. 47: 1344-1352.

Gan, W., T. Bond, X. Yang, and P. Westerhoff. 2015. Role of chlorine dioxide in *N*-nitrosodimethylamine formation from oxidation of model amines. Environmental Science & Technology. 49: 11429−11437.

Genuino, H.C., E.C. Njagi, E.M. Benbow, G.E. Hoag, J.B. Collins, and S.L. Suib. 2011. Enhancement of the photodegradation of *N*-nitrosodimethylamine in water using amorphous and platinum manganese oxide catalysts. Journal of Photochemistry and Photobiology A: Chemistry. 217: 284-292.

Gerecke, A.C. and D.L. Sedlak. 2003. Precursors of *N*-nitrosodimethylamine in natural waters. Environmental Science & Technology. 37(7): 1331-1336.

Gerrity, D., A.N. Pisarenko, E. Marti, R.A. Trenholm, F. Gerringer, J. Reungoat, and E. Dickenson. 2014. Nitrosamines in pilot-scale and full-scale wastewater treatment plants with ozonation. Water Research. In press.

Gerrity, D., A.N. Pisarenko, E. Marti, R.A. Trenholm, F. Gerringer, J. Reungoat, and E. Dickenson. 2015. Nitrosamines in pilot-scale and full-scale wastewater treatment plants with ozonation. Water Research. 72: 251-261.

Gibel, W. 1967. Experimental studies on syncarcinogenesis in esophageal carcinoma. Archiv fur Geschwulstforsch. 30: 181-189 (as cited in IARC, 2010).

Gilbert, P.J., B. Rollmann, F.D. de Valkeneer, J. Rondelet, M. Mercier, and F. Poncelet. 1984. Quantitative correlation between the metabolism and the mutagenic activity of *N*-nitrosopyrrolidine. Toxicology. 29(3): 261-270.

Giles, G.G., J.J. McNeil, G. Donnon, C. Webley, M.P. Staples, P.D. Ireland, S.F. Hurley, and M. Salzberg. 1994. Dietary factors and the risk of glioma in adults: results of a case-control study in Melbourne, Australia. International Journal of Cancer. 59: 357-362 (as cited in Health Canada, 2010).

Gollapudi, B.B., K.M. Jackson, and W.T. Scott. 1998. Hepatic lacI and cII mutation in transgenic ([lambda]LIZ) rats treated with dimethylnitrosamine. Mutation Research. 419: 131-135.

González, C.A., E. Riboli, J. Badosa, T. Cardona, S. Pita, J.M. Sanz, M. Torrent, and A. Agudo. 1994. Nutritional factors and gastric cancer in Spain. American Journal of Epidemiology. 139: 466-473 (as cited in IPCS, 2002; Health Canada, 2010).

Goodman, M.T., J.H. Hankin, L.R. Wilkens, and L.N. Kolonel. 1992. High-fat foods and the risk of lung cancer. Epidemiology. 3: 288-299 (as cited in IPCS, 2002).

Goslan, E.H., S.W. Krasner, M. Bower, S.A. Rocks, P. Holmes, L.S. Levy, and S.A. Parsons. 2009. A comparison of disinfection by-products found in chlorinated and chloraminated drinking waters in Scotland. Water Research. 43(18): 4698-4706.

Goto, Y., T. Matsuda, and K. Ito. 1999. Mutagenicities of *N*-nitrosodimethylamine and *N*-nitrosodiethylamine in Drosophila and their relationship to the levels of O-alkyl adducts in DNA. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis. 425(1): 125-134.

Gray, R., R. Peto, P. Brantom, and P. Grasso. 1991. Chronic nitrosamine ingestion in 1040 rodents: the effect of the choice of nitrosamines, the species studied and the age of starting exposure. Cancer Research. 51: 6470-6491 (as cited in Verna et al., 1996).

Greenblatt, M. and W. Lijinsky. 1972a. Nitrosamine studies: Neoplasms of liver and genital mesothelium in nitrosopyrrolidine-treated MRC rats. Journal of the National Cancer Institute. 48(6): 1687-1696.

Greenblatt, M. and W. Lijinsky. 1972b. Failure to induce tumors in Swiss mice after concurrent administration of amino acids and sodium nitrite. Journal of the National Cancer Institute. 48(5): 1389-1392.

Griciute, L. and S.V. Barauskaĭte. 1989. The carcinogenic activity of *N*-nitrosodipropylamine administered perorally to C57BL6I mice. Eksperimentalnaia Onkologgiia. 11(3): 10-11 (as cited in ATSDR, 2010).

Griciute L., M. Castegnaro, and J.C. Béréziat. 1982. Influence of ethyl alcohol on the carcinogenic activity of *N*-nitrosodi-n-propylamine. In *N-Nitroso compounds: Occurrence and Biological Effects*, IARC Scientific Publications No. 41, eds. Bartsch, H., M. Castegnaro, I.K. O'Neill, and M. Okada, pp. 643-648. Lyon: International Agency for Research on Cancer (IARC) (as cited in IARC, 2010).

Gui, L., R.W. Gillham, and M.S. Odziemkowski. 2000. Reduction of *N*-nitrosodimethylamine with granular iron and nickel-enhanced iron. 1. Pathways and kinetics. Environmental Science & Technology. 34(16): 3489-3494.

Gunnison, D., M.E. Zappi, C. Teeter, J.C. Pennington, and R. Bajpai. 2000. Attenuation mechanisms of *N*-nitrosodimethylamine at an operating intercept and treat groundwater remediation system. Journal of Hazardous Materials. 73(2): 179-197.

Guttenplan, J.B. 1987. Structure-activity relationships in oxidation and mutagenicities of N-nitrosamines. IARC publication on N-nitroso compounds. IARC Sci Publ. 1987(84): 129-31.

Hanigan, D., J. Zhang, P. Herckes, S.W. Krasner, C. Chen, and P. Westerhoff. 2012. Adsorption of *N*-nitrosodimethylamine precursors and granular activated carbon. Environmental Science & Technology. 46: 12630-12639.

Hannson, J. 1992. Inherited defects in DNA repair and susceptibility to DNA-damaging agents. Toxicology Letters. 64/65: 141-148.

Harter, T., J.R. Lund, J. Darby, G.E. Fogg, R. Howitt, K.K. Jessoe, G.S. Pettygrove, J.F. Quinn, J.H. Viers, D.B. Boyle, H.E. Canada, N. DeLaMora, K.N. Dzurella, A. Fryjoff-Hung, A.D. Hollander, K.L. Honeycutt, M.W. Jenkins, V.B. Jensen, A.M. King, G. Kourakos, D. Liptzin, E.M. Lopez, M.M. Mayzelle, A. McNally, J. Medellin-Azuara, and T.S. Rosenstock. 2012. Addressing nitrate in California's drinking water with a focus on Tulare Lake Basin and Salinas Valley groundwater. Report for the State Water Resources Control Board Report to the Legislature. Center for Watershed Sciences, University of California, Davis. Available online at: http://groundwaternitrate.ucdavis.edu.

Hatzinger, P.B., C. Condee, K.R. McClay., and A.P. Togna. 2011. Removal of *N*-nitrosodimethylamine in a propane-fed membrane bioreactor. Water Research. 45: 254-262.

Hawkins, C.L., D.I. Pattison, and M.J. Davies. 2003. Hypochlorite induced oxidation of amino acids, peptides and proteins. Amino Acids. 25(3-4): 259–274.

Hazardous Substances Data Bank (HSDB). 2003. *N*-Nitrosodi-n-propylamine. Available online at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

HSDB. 2010. Toxicology Data network. Available online at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB. Accessed on August 27, 2010.

He, Z., W. Kosinska, Z. Lin-Zhao, X.R. Wu, and J.B. Guttenplan. 2012. Tissue-specific mutagenesis by *N*-butyl[*N*-(4-hydroxybutyl)nitrosamine as the basis for urothelial carcinogenesis. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis. 742: 92-95.

Health Canada. 2010. *N*-nitrosodimethylamine (NDMA) in drinking water: Document for public comment.

Health Canada. 2011. Guidelines for Canadian drinking water quality: Guideline technical document N-nitrosodimethylamine (NDMA). Available online at: http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/ndma/index-eng.php#a2

Homme, C.L., and J.O. Sharp. 2013. Differential microbial transformation of nitrosamines by an inducible propane monooxygenase. Environmental Science & Technology. 47: 7388-7395.

Howard, P.H., R.S. Boethling, W.F. Jarvis, W.M. Meylan, and E.M. Michalenko. 1991. *Handbook of environmental degradation rates*. Chelsea, MI: Lewis Publishers (as cited in Siddiqui and Atasi, 2004).

Hua, B., K. Veum, A. Koirala, J. Jones, T. Clevenger, and B. Deng. 2007. Fluorescence fingerprints to monitor total trihalomethanes and *N*-nitrosodimethylamine formation potentials in water. Environmental Chemistry Letters. 5(2): 73-77.

Huang, C.H., L.P. Padhye, and S.H. Park. 2011. PolyDADMAC and dimthylamine as precurosrs of *N*-nitrosodimethylamine during ozonation. WQTC Conference Proceedings.

Hwang, Y., T. Matsuo, K. Hanaki, and N. Suzuki. 1994. Removal of odorous compounds in wastewater by using activated carbon, ozonation, and aerated biofilter. Water Research. 28(11): 2309-2319.

International Agency for Research on Cancer (IARC). 1978. Some *N*-nitroso compounds. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans,* vol. 17: 125-175 (as cited in HSDB, 2003).

IARC. 2010. Alcohol Consumption and Ethyl Carbamate. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans,* vol. 96. Available online at: http://monographs.iarc.fr/ENG/Monographs/vol96/index.php.

International Occupational Safety and Health Information Centre. 2001. *N*-nitrosodimethylamine, CAS 62-75-9. Geneva, Switzerland (March 2001).

International Programme on Chemical Safety (IPCS). 2002. N-Nitrosodimethylamine. Concise International Chemical Assessment Document 38. Available online at: http://www.inchem.org/documents/cicads/cicads/cicad38.htm.

Irving, C.C., W.M. Murphy, and D.S. Daniel. 1984. Comparative carcinogenicity of N-butyl-N-(3-carboxypropyl)-nitrosamine and *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine for the urinary bladder of (C57BL/6 X DBA/2)F1 mice. Journal of the National Cancer Institute. 73(3): 753-6.

Jakszyn, P. and C.A. González. 2006. Nitrosamine and related food intake and gastric and oesophageal cancer risk: A systematic review of the epidemiological evidence. World Journal of Gastroenterology. 12(27): 4296-4303.

Jakszyn, P., S. Bingham, G. Pera, A. Agudo, R. Luben, A. Welch, H. Boeing, G. Del Giudice, D. Palli, C. Saieva, V. Krogh, C. Sacerdote, R. Tumino, S. Panico, G. Berglund, H. Simán, G. Hallmans, M.J. Sanchez, N. Larrañaga, A. Barricarte, M.D. Chirlaque, J.R. Quirós, T.J. Key, N. Allen, E. Lund, F. Carneiro, J. Linseisen, G. Nagel, K. Overvad, A. Tionneland, A. Olsen, H.B. Bueno-de-Mesquita, M.O. Ocké, P.H. Peeters, M.E. Numans, F. Clavel-Chapelon, A. Trichopoulou, C. Fenger, R. Stenling, P. Ferrari, M. Jenab, T. Norat, E. Riboli, and C.A. Gonzalez. 2006. Endogenous versus exogenous exposure to N-nitroso compounds and gastric cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST) study. Carcinogenesis. 27(7): 1497-1501.

Jakszyn, P., C.A. González, and L.L. Lujan-Barroso. 2011. Red meat, dietary nitrosamines and heme iron and risk of bladder cancer in the European prospective investigation into cancer and nutrition (EPIC). Cancer Epidemiology Biomarkers and Prevention. 20(3): 555-559.

Janzowski, C., D. Jacob, I. Henn, H. Zankl, B.L. Poole-Zobel, and G. Eisenbrand. 1989. Investigations on organ-specific metabolism and genotoxic effects of the urinary bladder carcinogen N-nitrosobutyl-3-carboxypropylamine (BCPN) and its analogs N-nitrosodibutylamine (NDBA) and N-nitrosobutyl-4-hydroxybutylamine (4-OH-NDBA). Toxicology. 59(2): 195-209.

Janzowski, C., R. Landsiedel, P. Gölzer P, and G. Eisenbrand. 1994. Mitochondrial formation of beta-oxopropyl metabolites from bladder carcinogenic omega-carboxyalkylnitrosamines. Chemico-Biological Interactions. 90(1): 23-33.

Jarabek, A.M., L.H. Pottenger, L.S, Andrews, D. Casciano, M.R. Embry, J.H. Kim, R.J. Preston, M.V. Reddy, R. Schoeny, D. Shuker, J. Skare, J. Swenberg, G.M. Williams, and E. Zeiger. 2009. Creating context for the use of DNA adduct data in cancer risk assessment: I. Data organization. Critical Reviews in Toxicology. 39(8): 659-678.

Kadmi, Y., L. Favier, M. Lofti, N. Nasrallah, and D. Wolbert. 2014. A highly sensitive liquid chromatography-tandem mass spectrometry method for analysis of a toxic wastewater disinfection by-product, *N*-nitrosomethylethylamine. Analytical Methods. 6: 3231.

Kamataki, T., K. Fujita, K. Nakayama, Y. Yamazaki, M. Miyamoto, and N. Ariyoshi. 2002. Role of human cytochrome P450 (CYP) in the metabolic activation of nitrosamine derivatives: Application of genetically engineered Salmonella expressing human CYP. Drug Metabolism Reviews. 34(3): 667-676.

Kanki, K., A. Nishikawa, K. Masumura, T. Umemura, T. Imazawa, Y. Kitamura, T. Nohmi, and M. Hirose. 2005. In vivo mutational analysis of liver DNA in GPT delta transgenic rats treated with the hepatocarcinogens *N*-nitrosopyrrolidine, 2-amino-3-methylimidazo[4,5-f]quinoline, and di(2-ethylhexyl)phthalate. Molecular Carcinogenesis. 42(1): 9-17.

Karanfil, T. K., S.W. Krasner, P. Westerhoff, and Y. Xie. 2008. Recent advances in disinfection by-product formation, occurrence, control, health effects, and regulations. In *Disinfection By-Products in Drinking Water*. ACS Symposium Series, 995.

Kemper, J.M., P. Westerhoff, A. Dotson, and W.A. Mitch. 2009. Nitrosamine, dimethylnitramine, and chloropicrin formation during strong base anion-exchange treatment. Environmental Science & Technology. 43(2): 466-472.

Kemper, J.M., S.S. Walse, and W.A. Mitch. 2010. Quaternary amines as nitrosamine precursors: A role for consumer products? Environmental Science & Technology. 44(4): 1224-1231.

Kerklaan, P., S. Bouter, J.A. Zijlstra, and G.R. Mohn. 1986. The effect of mixed-function oxidase and amine oxidase inhibitors on the activation of dialkylnitrosamines and 1 2 dimethylhydrazine to bacterial mutagens in mice. Journal of Cancer Research and Clinical Oncology. 111(3): 196-202.

Ketkar, M.B., P. Schneider, R. Preussmann, Ch. Plass, and U. Mohr. 1982. Carcinogenic effect of low doses of nitrosopyrrolidine administered in drinking water to Syrian golden hamsters. Journal of Cancer Research and Clinical Oncology. 104(1-2): 75-79.

Khan, S. J. and J.A. McDonald. (2010). Quantifying human exposure to contaminants for multiple-barrier water reuse systems. Water Science & Technology. 61(1): 77-83.

Kim, J. and T.E. Clevinger. 2007. Prediction of *N*-nitrosodimethylamine (NDMA) formation as a disinfection by-product. Journal of Hazardous Materials. 145(1-2): 270-276.

Knekt, P., R. Järvinen, J. Dich, and T. Hakulinen. 1999. Risk of colorectal and other gastro-intestinal cancers after exposure to nitrate, nitrite and N -nitroso compounds: a follow-up study. International Journal of Cancer. 80: 852-856 (as cited in IPCS, 2002; CalEPA, 2006).

Kohut, K.D.A. and S. Andrews. 2003. Polyelectrolyte age and *N*-nitrosodimethylamine formation in drinking water treatment. Water Quality Research Journal Canada. 38(4): 719-735.

Kosaka, K., M. Asami, Y. Konno, M. Oya, and S. Kunikane. 2009. Identification of antiyellowing agents as precursors of *N*-nitrosodimethylamine production on ozonation from sewage treatment plant influent. Environmental Science & Technology. 43(14): 5236-5241.

Korsrud, G.O., H.G. Grice, and T.K. Goodman. 1973. Sensitivity of several serum enzymes for the detection of thioacetamide, dimethylnitrosamine- and diethanolamine-induced liver damage in rats. Toxicology and Applied Pharmacology. 26: 299-313.

Kosaka, K., M. Asami, K. Ohkubo, T. Iwamoto, Y. Tanaka, H. Koshino, S. Echigo, and M. Akiba. 2014. Identification of a new N-nitrosodimethylamine precursor in sewage containing industrial effluents. Environmental Science & Technology. 48: 11243-11250.

Krasner, S.W., P. Westerhoff, B. Chen, G. Amy, and S.N. Nam. 2005. Contribution of wastewater to DBP formation: Case study of an effluent-impacted river. WQTC 2005 Conference Proceedings.

Krasner, S.W., P. Westerhoff, B. Chen, G. Amy, S. Nam, Z. Chowdhury, S. Sinha, and B.E. Rittmann. 2008. Contribution of wastewater to DBP formation. Water Research Foundation, Project #2948.

Krasner, S.W., P. Westerhoff, B. Chen, B.E. Rittmann, S. Nam, and G. Amy. 2009. Impact of wastewater treatment processes on organic carbon, organic nitrogen, and DBP precursors in effluent organic matter. Environmental Science & Technology. 43(8): 2911-2918.

Krasner, S.W., M.S. Dale, C.F.T. Lee, E.A. Garcia, W. Mitch, and U. von Gunten. 2010. Effect of water quality and operational parameters during chloramination: NDMA versus halogenated dbps. AWWA Annual Conference & Exposition.

Krasner, S.W., C.F.T. Lee, E.A. Garcia, and W. Mitch. 2011. A simulated distribution system test to predict the formation of nitrosamines, THMs, and HAAs in drinking water. WQTC Conference Proceedings.

Krasner, S.W, M.J Sclimenti, and C.F.T. Lee. 2012a. Occurrence and formation of NDMA in consecutive systems in a major metropolitan area. WQTC 2012 Conference Proceedings.

Krasner, S.W., W.A. Mitch, P. Westerhoff, and A. Dotson. 2012b. Formation and control of emerging C- and N-DBPs in drinking water. Journal of the American Water Works Assoication. 104 (11): 33e34.

Krasner, S.W., P. Westerhoff, W.A. Mitch, and J. Skadsen. 2012c. Case studies on nitrosamine formation and control at fullscale drinking water treatment plants. WQTC 2012 Conference Proceedings (as cited in Krasner et al., 2013).

Krasner, S.W., W.A. Mitch, D.L. McCurry, D. Hanigan, and P. Westerhoff. 2013. Formation, precursors, control, and occurrence of nitrosamines in drinking water: A review. Water Research. 47: 4433-4450.

Krasner, S.W., R. Shirkani, P. Westerhoff, D. Hanigan, W.A. Mitch, D.L. McCurry, C. Chen, J. Skadsen, and U. von Gunten. 2015. Controlling the formation of nitrosamines during water treatment. Water Research Foundation, Project #4730.

Kraus, T.E.C., C.A. Anderson, K. Morgenstern, B.D. Downing, B.A. Pellerin, and B.A. Bergamaschi. 2010. Determining sources of dissolved organic carbon and disinfection byproduct precursors to the McKenzie River, Oregon. Journal of Environmental Quality. 39(6): 2100-2112.

Kruithof, J.C., P.C. Kamp, and B.J. Martijn. 2007. UV/H_2O_2 Treatment: A practical solution for organic contaminant control and primary disinfection. Ozone: Science & Engineering: The Journal of the International Ozone Association. 29(4): 273-280.

Kulshrestha, P., K.C. McKinstry, B.O. Fernandez, M. Feelisch, and W. Mitch. 2010. Application of an optimized total *N*-nitrosamine (TONO) assay to pools: placing *N*-nitrosodimethylamine (NDMA) into perspective. Environmental Science & Technology. 44(9): 3369-3375.

Kuroki, T., C. Drevon, and R. Montesano. 1977. Microsome-mediated mutagenesis in V79 Chinese hamster cells by various nitrosamines. Cancer Research. 37: 1044-1050.

Kuroki, T., A. Abbondandolo, C. Drevon, E. Huberman, and F. Laval. 1980. Mutagenesis assays with mammalian cells.. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans.* Supplement 2: 107-133.

Kushida, H., K. Fujita, A. Suzuki, M. Yamada, T. Endo, T. Nohmi, and T. Kamataki. 2000. Metabolic activation of *N*-alkylnitrosamines in genetically engineered *Salmonella typhimurium* expressing CYO2E1 or CYP2A6 together with human NADPH-cytochrome P450 reductase. Carcinogenesis. 21(6): 1227-1232.

La Vecchia, C., B. D'Avanzo, L. Airoldi, C. Braga, and A. Decarli. 1995. Nitrosamine intake and gastric cancer. European Journal of Cancer Prevention. 4: 469-474 (as cited in IPCS, 2002).

Landsman, N.A., K.L. Swancutt, C.N. Bradford, C.R. Cox, J.J. Kiddle, and S.P. Mezyk. 2007. Free radical chemistry of advanced oxidation process removal of nitrosamines in water. Environmental Science & Technology. 41(16): 5818-5823.

Langenbach, R. 1986. Mutagenic activity and structure-activity relationships of short-chain dialkyl *N*-nitrosamines in a hamster hepatocyte v79 cell-mediated system. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis. 163(3): 303-11.

Larsson, S.C., L. Bergkvist, and A. Wolk. 2006. Processed meat consumption, dietary nitrosamines and stomach cancer risk in a cohort of Swedish women. International Journal of Cancer. 915-919.

Le Roux, J., H. Gallard, and J.P. Croué. 2011. Chloramination of nitrogenous contaminants (pharmaceuticals and pesticides): NDMA and halogenated DBPs formation. Water Research. 45(10): 3164-3174

Le Roux, J., H. Gallard, and J.P. Croué. 2012. Formation of NDMA and halogenated DBPs by chloramination of tertiary amines: The influence of bromide ion. Environmental Science & Technology. 46(3): 1581-1589.

Lee, J., W. Choi, and J. Yoon. 2005a. Photocatalytic degradation of *N*-nitrosodimethylamine: mechanism, product distribution, and TiO_2 surface modification. Environmental Science & Technology. 39(17): 6800-6807.

Lee, C., W. Choi, and J. Yoon. 2005b. UV photolytic mechanism of *N*-nitrosodimethylamine in water: Roles of dissolved oxygen and solution pH. Environmental Science & Technology. 39(24): 9702-9709.

Lee, C., W. Choi, Y.G. Kim, and J. Yoon. 2005c. UV photolytic mechanism of *N*-nitrosodimethylamine in water: Dual pathways to methylamine versus dimethylamine. Environmental Science & Technology. 39(7): 2101-2106.

Lee, W., P. Westerhoff, and M. Esparza-Soto. 2006. Occurrence and removal of dissolved organic nitrogen in U.S. water treatment plant. Journal of the American Water Works. 98(10): 102-110.

Lee, W., P. Westerhoff, and J. Croué. 2007a. Dissolved organic nitrogen as a precursor for chloroform, dichloroacetonitrile, *N*-nitrosodimethylamine, and trichloronitromethane. Environmental Science & Technology. 41(15): 5485-5490.

Lee, C., C. Schmidt, J. Yoon, and U. von Gunten. 2007b. Oxidation of *N*-nitrosodimethylamine (NDMA) precursors with ozone and chlorine dioxide: Kinetics and effect on NDMA formation potential. Environmental Science & Technology. 41(6): 2056-2063.

Lee, C., J. Yoon, and U. von Gunten. 2007c. Oxidative degradation of *N*-nitrosodimethylamine by conventional ozonation and the advanced oxidation process ozone/hydrogen peroxide. Water Research. 41(3): 581-590.

Lee, C., Y. Lee, C. Schmidt, J. Yoon, and U. von Gunten. 2008. Oxidation of suspected *N*-nitrosodimethylamine (NDMA) precursors by ferrate (VI) kinetics and effect on NDMA formation potential of natural waters. Water Research. 42(1-2): 433–441.

Lee, M., Y. Lee F. Soltermann, and U. von Gunten. 2013. Analysis of *N*-nitrosamines and other nitro(so) compounds in water by high performance liquid choromatography with post column UV photolysis/Griess reaction. Water Research. 47: 4893-4903.

Lee, C-F.T., S.W. Krasner, M.J. Sclimenti, M. Prescott, and Y.C. Guo. 2015. Nitrosamine precursors and wastewater indicators in discharges in the Sacramento-San Joaquin Delta. In *Advances in Disinfection Byproducts*, Chapter 7, pp. 119–133. ACS Symposium Series, 1190.

Lewis, R.J. Sr. 1981. *Hawley's condensed chemical dictionary*. 13th edition. New York, NY: Van Nostrand Reinhold.

Li, T., D. Yu, Q. Xian, A. Li, and C. Sun. 2015. Variation of levels and distribution of *N*-nitrosamines in different seasons in drinking waters of East China. Environmental Science and Pollution Research. 22: 11792-11800.

Liang, S., H.M. Joon, M.K. Davis, J.F. Green, and D.S. Remer. 2003. Use of pulsed-UV processes to destroy NDMA. Journal of the American Water Works Association. 95(9): 121-131.

Liao, X., Wang, C., Wang, J., Zhang, X., Chen, C., Krasner, S.W., and I.H. Suffet. 2014. Nitrosamine precursor and DOM control in an effluent-affected drinking water. Journal of the American Water Works Association. 106(7): E307-E318.

Liao, X., E. Bei, S. Li, Y Ouyang, J. Wang, C. Chen, X. Zhang, S.W. Krasner, and I.H. Suffet. 2015a. Applying the polarity rapid assessment method to characterize nitrosamine precursors and to understand their removal by water treatment processes. Water Research. 87: 292-298.

Liao, X., C. Chen, S. Xie, D. Hanigan, J. Wang, X. Zhang, P. Westerhoff, and S.W. Krasner. 2015b. Nitrosamine precursor removal by BAC: A Case study of adsorption versus biotreatment. Journal of the American Water Works Association. 107(9): E454-E463.

Liao, X., C. Chen, J. Zhang, Y. Dai, X. Zhang, and S. Xie. 2015c. Operational performance, biomass, and microbial community structure: Impacts of backwashing on drinking water biofilter. Environmental Science Pollution Research. 22: 546-554.

Liao, X., C. Chen, J. Zhang, and S. Xie. 2015d. Dimethylamine biodegradation by mixed culture enriched from drinking water biofilter. Chemosphere. 119: 935-940

Lide, D.R. 1995-96. *CRC handbook of chemistry and physics*. 76th Edition. New York, NY: CRC Press.

Lijinsky, W. 1983. Species specificity in nitrosamine carcinogenesis. Basic Life Science. 24: 63-75 (as cited in CalEPA, 2006).

Lijinsky, W. 1987a. Carcinogenicity and mutagenicity of N-nitroso compounds. Molecular Toxicology. 1(1): 107-119.

Lijinsky, W. 1987b. Structure-activity relations in carcinogenesis by N-nitroso compounds. Cancer and Metastasis Reviews. 6(3): 301-356

Lijinsky, W. and M.D. Reuber. 1980. Carcinogenicity in rats of nitrosomethylethylamines labeled with deuterium in several positions. Cancer Research. 40(1): 19-21.

Lijinsky, W. and M.D. Reuber. 1981. Comparative carcinogenesis by some aliphatic nitrosamines in Fischer rats. Cancer Letters. 14(3): 297-302.

Lijinsky, W. and M.D. Reuber. 1983. Carcinogens in Fischer rats by nitrosodipropylamine, nitrosodibutylamine and nitrosobis(2-oxopropyl)amine given by gavage. Cancer Letters. 19: 207-213.

Lijinsky, W. and H.W. Taylor. 1978. Comparative carcinogenicity of some derivatives of nitrosodi-n-propylamine in rats. Ecotoxicology and Environmental Safety. 2: 421-426.

Lijinsky, W. and H.W. Taylor. 1979. Carcinogenicity of methylated derivatives of *N*-nitrosodiethylamine and related compounds in Sprague-Dawley rats. Journal of the National Cancer Institute. 62: 407-410 (as cited in USEPA, 1987).

Lijinsky, W., R.M. Kovatch, and C.W. Riggs. 1987. Carcinogenesis by nitrosodialkylamines and azoxyalkanes given by gavage to rats and hamsters. Cancer Research. 47: 3968-3972.

Liu, Y.X. and J.B. Guttenplan. 1992. Mutational specificities of *N*-nitrosamines in a host-mediated assay: comparison with direct-acting N-nitroso compounds *in vitro* and an approach to deducing the nature of ultimate mutagens *in vivo*. Molecular Carcinogenesis. 6: 232-237.

Liu, Y.D., M. Selbes, C. Zeng, R. Zhong, and T. Karanfil. 2014. Formation mechanism of NDMA from ranitidine, trimethylamine, and other tertiary amines during chloramination: A computational study. Environmental Science & Technology. 48: 8653-8663

Löfberg, B. and H. Tjälve. 1986. Perinatal metabolism of N-nitrosodibutylamine in Syrian golden hamsters. Cancer Lett. 31: 153-161.

Loh, Y.H., P. Jakszyn, R.N. Luben, A.A. Mulligan, P.N. Mitrou and K.T. Khaw. 2011. N-Nitroso compounds and cancer incidence: The European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk Study. The American Journal of Clinical Nutrition. 93(5): 1053-61.

Luh, J., and B. Marinas. 2012. Bromide ion effect on *N*-nitrosodimethylamine formation by monochloramine. Environmental Science & Technology. 46(9): 5085-5092.

Lv, J., L. Wang, Y. Song, and Y. Li. 2015. *N*-nitrosodimethylamine formation from ozonation of chlorpheniramine: Influencing factors and transformation mechanism. Journal of Hazardous Materials. 299: 484-494.

Ma, D., Y. Meng, C. Xia, B. Gao, and Y. Wang. 2015. Fractionation, characterization, and C-, N-disinfection byproduct formation of soluble microbial products in MBR processes. Bioresource Technology. 98: 380-387.

Maduagwu, E.N. and O. Bassir. 1980. A comparative assessment of toxic effects of dimethylnitrosamine in six different species. Toxicology and Applied Pharmacology. 53: 211-219.

Marhaba, T. F. and I.H. Kochar. 2000. Rapid prediction of disinfection by-product formation potential by fluorescence. Environmental Engineering and Policy. 2(1): 29-36.

Martelli, A., L. Robbiano, G.M. Gazzaniga, and G. Brambilla. 1988. Comparative study of DNA damage and repair induced by ten *N*-nitroso compounds in primary cultures of human and rat hepatocytes. Cancer Research. 48(15): 4144-52.

Marti, E.J., A.N. Pisarenko, J.R. Peller, and E.R.V. Dickenson. 2015. *N*-nitrosodimethylamine (NDMA) formation from the ozonation of model compounds. Water Research. 72: 262-270.

Massachusetts Department of Environmental Protection (DEP). 2004. Current regulatory limit: N-nitrosodimethylamine (NDMA). Available online at: http://www.mass.gov/eea/agencies/massdep/water/drinking/standards/n-nitrosodimethylamine-ndma.html.

McCann, J., E. Choi, E. Yamasaki, and B.N. Ames. 1975. Detection of carcinogens as mutagens in the Salmonella/microsome test: assay of 300 chemicals. Proceedings of the National Academy of Sciences., U.S.A. 72: 5135-5139 (as cited in Aiub et al., 2003).

McCoy, G.D., S.S. Hecht, and K. Furuya. 1986. The effect of chronic ethanol consumption on the tumorigenicity of *N*-nitrosopyrrolidine in male Syrian golden hamsters. Cancer Letters. 33(2): 151-159.

McCurry, D.L., Krasner, S.W., Von Gunten, U. and W.A. Mitch. 2015. Determinants of disinfectant pretreatment efficacy for nitrosamine control in chloraminated drinking water. Water Research. 84: 161-170.

Mezyk, S. P., D.B. Ewing, J.J. Kiddle, and K.P. Madden. 2006. Kinetics and mechanisms of the reactions of hydroxyl radicals and hydrated electrons with nitrosamines and nitramines in water. The Journal of Physical Chemistry A. 110(14): 4732-4737.

Mhlongo, S.H., B.B. Mamba, and R.W. Krause. 2009. Nitrosamines: A review on their prevalence as emerging pollutants and potential remediation options. Water SA. 35(5): 735-740.

Michejda, C.J., M.B. Krueger-Koepke, and R.M. Kovatch. 1986. Carcinogenic effects of sequential administration of two nitrosamines to rats. Cancer Research. 25: 126.

Mirvish, S. S. 1974. Formation of *N*-nitroso compounds: Chemistry, kinetics, and in vivo occurrence. Toxicology and Applied Pharmacology. 31: 325-351.

Mirvish, S. S. 1992. In vivo formation of *N*-nitroso compounds: Formation from nitrite and nitrogen dioxide, and relation to gastric cancer. In *Nitrosamines and human cancer, Banbury Report 12*, ed. P.N. Magee, pp. 227-241. New York, NY: Cold Spring Harbor Laboratory, New York.

Mitch, W.A. and I.M. Schreiber. 2008. Degradation of tertiary alkylamines during chlorination/chloramination: implications for formation of aldehydes, nitriles, halonitroalkanes, and nitrosamines. Environmental Science & Technology. 42(13): 4811-4817.

Mitch, W.A. and D.L. Sedlak. 2002. Formation of *N*-nitrosodimethylamine (NDMA) from dimethylamine during chlorination. Environmental Science & Technology. 36(4): 588-595.

Mitch, W.A. and D.L. Sedlak. 2004. Characterization and fate of *N*-nitrosodimethylamine precursors in municipal wastewater treatment plants. Environmental Science & Technology. 38(5): 1445-1454.

Mitch, W.A., A.C. Gerecke, and D.L. Sedlak. 2003a. A *N*-nitrosodimethylamine (NDMA) precursor analysis for chlorination of water and wastewater. Water Research. 37(15): 3733-3741.

Mitch, W.A., J.O. Sharp, R.D Trussell, R.L. Valentine, L. Alvarez-Cohen, and D.L. Sedlak. 2003b. *N*-nitrosodimethylamine (NDMA) as a drinking water contaminant: A review. Environmental Engineering Science. 20(5): 389-404.

Mitch, W.A., G.L. Oelker, E.L. Hawley, R.A. Deeb, and D.L. Sedlak. 2005. Minimization of NDMA formation during chlorine disinfection of municipal wastewater by application of pre-formed chloramines. Environmental Engineering Science. 22(6): 882-890.

Mitch, W.A., S.W. Krasner, P. Westerhoff, and A. Dotson. 2009. Occurrence and formation of nitrogenous disinfection by-products. Water Research Foundation, Project #3014.

Miyashita, Y., S. Park, H. Hyung, C. Huang, and J. Kim. 2009. Removal of *N*-nitrosamines and their precursors by nanofiltration and reverse osmosis membranes. Journal of Environmental Engineering. 135(9): 788-795.

Mochizuki, M., T. Anjo, K. Takeda, E. Suzuki, N. Sekiguchi, G.F. Huang, and M. Okada. 1986. Chemistry and mutagenicity of alpha hydroxy nitrosamines. IARC Sci. PubL. 41: 553-559.

Mohanty, S.K., M. Snehota, and C. Ray. 2006. Transport of selected contaminants in recycled water through a Hawaii soil. Proceedings of the World Environmental and Water Resources Congress.

Mohr, U. and J. Althoff. 1965. The transplacental effect of the carcinogen diethylnitrosamine in the mouse. Zeitschrift für Krebsforschung. 67: 152-155. (English translation).

Mohr, U., J. Althoff, and A. Authaler. 1966. Diaplacental effect of the carcinogen diethylnitrosamine in the golden hamster. Cancer Research. 26: 2349-2352.

Montesano, R. and H. Bartsch. 1976. Mutagenic and carcinogenic *N*-nitroso compounds: possible environmental hazards. Mutation Research/Reviews in Genetic Toxicology. 32: 179-228 (as cited in Verna et al., 1996).

Montgomery, J.M. 1985. *Water treatment principles and design*. New York, NY: John Wiley and Sons.

Morita, T., N. Asano, T. Awogi, Y.F. Sasaki, S. Sato, H. Shimada, S. Sutou, A. Wakata, T. Sofuni, and M. Hayashi. 1997. Evaluation of the rodent micronucleus assay in the screening of IARC carcinogens (Groups 1, 2A and 2B): The summary report of the 6th collaborative study by CSGMT/JEMS – MOA. Mutation Research/Reviews in Genetic Toxicology. 389: 3-122.

Morran, J., M. Whittle, R.B. Fabris, M. Harris, J.S. Leach, G. Newcombe, and M. Drikas. 2011. Nitrosamines from pipeline materials in drinking water distribution systems. Journal of the American Water Works Association. 103(10): 76-83.

Nagao, M., E. Suzuki, K. Yasuo, T. Yahagi, and Y. Seino. 1977. Mutagenicity of *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine, a bladder carcinogen, and related compounds. Cancer Research. 37: 399-407.

Najm, I. and R.R. Trussell. 2001. NDMA formation in water and wastewater. Journal of the American Water Works Association. 93(2): 92-99.

Napalkov, N.P. and V.A. Aleksandrov. 1968. On the effects of blastomogenic substances during embryogenesis. Zeitschrift für Krebsforschung. 71: 195-205 (as cited in IPCS, 2002).

National Toxicology Program (NTP). 2011. Report on carcinogens. 12th edition. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service.

Nawrocki, J. and P. Andrzejewski. 2011. Nitrosamines and water. Journal of Hazardous Materials. 189(1-2): 1-18.

Negishi, T. and H. Hayatsu. 1980. The pH-dependent response of *Salmonella typhimurium* TA100 to mutagenic *N*-nitrosamines. Mutation Research/Reviews in Genetic Toxicology.79(3): 223-230.

Negishi, T., T. Shiotani, K. Fujikawa, and H. Hayatsu. 1991. The genotoxicities of *N*-nitrosamines in *Drosophila melanogaster* in vivo: the correlation of mutagenicity in the wing spot test with the DNA damages detected by the DNA-repair test. Mutation Research/Reviews in Genetic Toxicology. 252(2): 119-28.

New Jersey Department of Environmental Protection (NJDEP). 2014. N.J.A.C. 7:9C; Ground water quality standards. Available online at: http://www.nj.gov/dep/rules/rules/njac7_9c.pdf. Last amended July 22, 2010.

Nishie, K. 1983. Comparison of the effects of *N*-nitrosodimethylamine on pregnant and nonpregnant Holtzman rats. Food and Chemical Toxicology. 21(4): 453-462.

Nishikawa, T., E.I. Salim, K. Morimura, M. Kaneko, M. Ogawa, A. Kinoshita, H. Osugi, H. Kinoshita, and S. Fukushima. 2003. High susceptibility of p53 knockout mice to esophageal and urinary bladder carcinogenesis induced by N, N-dibutylnitrosamine. Cancer Letters. 194(1): 45-54.

Nolan, B.T., K.J. Hitt, and B.C. Ruddy. 2002. Probability of nitrate contamination of recently recharged groundwaters in the conterminous United States. Environmental Science & Technology. 36(10): 2138-2145.

Occupational Safety and Health Administration (OSHA). 2006. Chemical sampling information: *N*-Nitrosodimethylamine. Washington, DC: U.S. Department of Labor, Occupational Safety and Health Administration. Available online at: http://www.osha.gov/dts/chemicalsampling/data/CH_258000.html#health.

O'Day, R., J. Rench, R. Oen, and A. Castro. 1998. Demographic Distribution of Sensitive Populations Groups. U.S. Environmental Protection Agency, Office of Water, Office of Science and Technology, Health and Ecological Criteria Division. Contract No. 68-C6-0036. SRA 557-05/14.

Odziemkowski, M.S., L. Gui, and R.W. Gillham. 2000. Reduction of *N*-nitrosodimethylamine with granular iron and nickel-enhanced iron. 2. Mechanistic studies. Environmental Science & Technology. 34(16): 3495-3500.

Olajos, E.J., N. Maverakis, and H.H. Cornish. 1978. Mutagenicity of alkyl-(omega-hydroxyalkyl) nitrosamines related to dibutylnitrosamine. Mutation Research/Reviews in Genetic Toxicology. 56(3): 219-23.

O'Neil, M.J., A. Smith, and P.E. Heckelman (eds). 2001. *The Merck index: An encyclopedia of chemicals, drugs, and biologicals*. 13th edition. Whitehouse Station, NJ: Merck and Co., Inc.

Otsuka, H. and A. Kuwahara. 1971. Hemangiomatous lesions of mice treated with nitrosodimethylamine. Gann. 62: 147-156 (as cited in CalEPA, 2006).

Oya, M., K. Kosaka, M. Asami, and S. Kunikane. 2008. Formation of *N*-nitrosodimethylamine (NDMA) by ozonation of dyes and related compounds. Chemosphere. 73(11): 1724-1730.

Padhye, L. 2010. Roles of polydadmacs, dithiocarbamates and activated carbons in formation of n-nitrosamine contaminants in water. Dissertation, Georgia Institute of Technology School of Civil and Environmental Engineering.

Padhye, L., U. Tezel, W.A. Mitch, S.G. Pavlostathis, and C. Huang. 2009. Occurrence and fate of nitrosamines and their precursors in municipal sludge and anaerobic digestion systems. Environmental Science & Technology. 43(9): 3087-3093.

Padhye, L., P. Wang, T. Karanfil, and C. Huang. 2010. Unexpected role of activated carbon in promoting transformation of secondary amines to *N*-nitrosamines. Environmental Science & Technology. 44(11): 4161-4168.

Padhye, L., Y. Luzinova, M. Cho, B. Mizaikhoff, J. Kim, and C. Huang. 2011. PolyDADMAC and dimethylamine as precursors of *N*-nitrosodimethylamine during ozonation: Reaction kinetics and mechanisms. Environmental Science & Technology. 45: 4353-4359.

Padhye, L., Kim, J-H., and C-H. Huang. 2013. Oxidation of dithiocarbamates to yield *N*-nitrosamines by water disinfection oxidants. Water Research. 47: 725-736.

Park, S., S. Wei, B. Mizaikoff, A.E. Taylor, C. Favero, and C. Huang. 2009. Degradation of amine-based water treatment polymers during chloramination as *N*-nitrosodimethylamine (NDMA) precursors. Environmental Science & Technology. 43(5): 1360-1366.

Park, S.H., L.P. Padhye, P. Wang, M. Cho, J.H. Kim, and C.H. Huang. 2014. *N*-nitrosodimethylamine (NDMA) formation potential of amine-based water treatment polymers: Effects of in-situ chloramination, breakpoint chlorination, and pre-oxidation. Journal of Hazardous Materials. In press.

Park, S.H., L.P. Padhye, P. Wang, M. Cho, J-H. Kim, and C-H. Huang. 2015. *N*-nitrosodimethylamine (NDMA) formation potential of amine-based water treatment polymers: Effect of in-situ chloramination, breakpoint chlorination, and pre-oxidation. Journal of Hazardous Materials. 282: 133-140.

Parker, K., T. Zeng, J. Harkness, A. Vengosh, and W. Mitch. 2014. Enhanced formation of disinfection byproducts in shale gas wastewater-impacted drinking water supplies. Environmental Science & Technology. 48: 11161−11169.

Parodi, S., A. Zunino, L. Ottaggio, and L. Santi. 1983. Quantitative correlation between carcinogenicity and sister chromatid exchange induction in vivo for a group of 11 *N*-nitroso derivatives. Journal of Toxicology and Environmental Health, Part A Current Issues. 11(3): 337-46.

PBT Profiler. 2010. U.S. Environmental Protection Agecy, Office of Chemical Safety and Pollution Prevention, Environmental Health Analysis Center. Available online at: http://www.pbtprofiler.net/.

Pedal, I., K. Bresserer, and K. Goerttler. 1982. Fatal nitrosamine poisoning. Archives of Toxicology. 50(2): 101-112.

Pehlivanoglu-Mantas, E. and D.L. Sedlak. 2006. The fate of wastewater-derived NDMA precursors in the aquatic environment. Water Research. 40(6): 1287-1293.

Pehlivanoglu-Mantas, E. and D. L. Sedlak 2008. Measurement of dissolved organic nitrogen forms in wastewater effluents: Concentrations, size distribution and NDMA formation potential. Water Research. 42(14): 3890-3898.

Pérez, D.M., G.G. Alatorre, E.B. Álvarez, E.E. Silva, and J.F.J. Alvarado. 2008. Solid-phase microextraction of *N*-nitrosodimethylamine in beer. Food Chemistry. 107: 1348-1352.

Peto, R., R. Gray, P. Brantom, and P. Grasso. 1984. Nitrosamine carcinogenesis in 5120 rodents: chronic administration of sixteen different concentrations of NDEA, NDMA, NPYR and NPIP in the water of 4440 inbred rats, with parallel studies on NDEA alone of the effect of age of starting (3, 6 or 20 weeks) and of species (rats, mice or hamsters) (as cited in O' Neill et al., 1984).

Peto, R., R. Gray, P. Brantom, and P. Grasso. 1991a. Dose and time relationships for tumor induction in the liver and esophagus of 4080 inbred rats by chronic ingestion of *N*-nitrosodiethylamine or *N*-nitrosodimethylamine. Cancer Research. 51(23 Pt 2): 6452-6469.

Peto R, R. Gray, P. Brantom, and P. Grasso. 1991b. Effects on 4080 rats of chronic ingestion of *N*-nitrosodiethylamine or *N*-nitrosodimethylamine: a detailed dose-response study. Cancer Research. 51(23 Pt 2): 6415-6451.

Phillipson, C.E., and C. Ioannides. 1985. Metabolic activation of nitrosamines to mutagens by various animal species including man. Biochemical Pharmacology. 34(3): 441-442.

Pietsch, J., F. Sacher, W. Schmidt, and H-J Bauch. 2001. Polar nitrogen compounds and their behavior in the drinking water treatment process. Water Research. 35(15): 3537-3544.

Plumlee, M.H. and M. Reinhard. 2007. Photochemical attenuation of *N*-nitrosodimethylamine (NDMA) and other nitrosamines in surface water. Environmental Science & Technology. 41(17): 6170-6176.

Plumlee, M.H., M. López-Mesas, A. Heidlberger, K.P. Ishida, and M. Reinhard. 2008. *N*-nitrosodimethylamine (NDMA) removal by reverse osmosis and UV treatment and analysis via LC-MS/MS. Water Research. 42(1-2): 347-355.

Pobel, D., E. Riboli, J. Cornée, B. Hémon, and M. Guyader. 1995. Nitrosamine, nitrate and nitrite in relation to gastric cancer: A case-control study in Marseille, France. European Journal of Epidemiology.11: 67-73 (as cited in IPCS, 2002).

Pool, B.L., J. Gottfried-Anacker, G. Eisenbrand, and C. Janzowski. 1988. *N*-Nitroso-butyl-3-carboxypropylamine (BCPN), a urinary bladder carcinogen, non mutagenic in *S. typhimurium.* Mutation Research/Reviews in Genetic Toxicology. 209: 79-83.

Poussade, Y., A. Roux, T. Walker, and V. Zavlanos. 2009. Advanced oxidation for indirect potable reuse: a practical application in Australia. Water Science & Technology. 60(9): 2419-2424.

Pozzi, R., P. Bocchini, F. Pinelli, and G.C. Galletti. 2011. Determination of nitrosamines in water by gas chromatography/chemical/ionization/selective ion trapping mass spectrometry. Journal of Chromatography A. 1218(14): 1808-1814.

Preston-Martin, S. 1989. Epidemiological studies of perinatal carcinogenesis. IARC Scientific. Publications. 96: 289-314.

Preussmann, R. and B.W. Stewart. 1984. *N*-Nitroso carcinogens. In *Chemical Carcinogens (2nd ed.), Monograph 182*, ed. Searle, C.E., pp. 643-828. Washington, D.C.: American Chemical Society (as cited in CalEPA, 2006).

Preussmann, R., D. Schmahl, and G. Eisenbrand. 1977. Carcinogenicity of *N*-nitrosopyrrolidine: Dose-response study in rats. Zeitschrift für Krebsforschung. 90: 161-166.

Prival, M.J., V.D. King, and A.T. Sheldon, Jr. 1979. The mutagenicity of dialkyl nitrosamines in the Salmonella plate assay. Environmental Mutagenesis. 1(2): 95-104.

Qi, W., L.F. Yee, and H. Jiangyong. 2014. Relationship between organic precursors and *N*-nitrosodimethylamine (NDMA) formation in tropical water sources. Journal of Water and Health. 12(4): 736-746.

Quillardet, P. and M. Hofnung. 1985. The SOS chromotest: a review. Mutation Research/Reviews in Genetic Toxicology. 297: 235-279 (as cited in Aiub et al., 2003).

Rajat, S. 2008. Kinetics of NDMA (N-nitrosodimethylamine) oxidation by permanganate under a range of pH and temperature conditions. Dissertation, University of Colorado at Boulder. Abstract only.

Registry of Toxic Effects of Chemical Substances (RTECS). 2002. Dimethylamine, *N*-nitroso-. (as cited in CalEPA, 2006; Health Canada, 2010).

Risch, H.A., M. Jain, N.W. Choi, J.G. Fodor, C.J. Pfeiffer, G.R. Howe, L.W. Harrison, K.J. Craib, and A.B. Miller. 1985. Dietary factors and the incidence of cancer of the stomach. American Journal of Epidemiology. 122: 947-957 (as cited in CalEPA, 2006).

Risk Assessment Information System (RAIS). 2009. "RAIS Toxicity and Properties." Available online at: http://rais.ornl.gov/cgi-bin/tools/TOX_search?select=chem. Accessed on August 10, 2009.

Robbiano, L., E. Mereto, C. Corbu, and G. Brambilla. 1996. DNA damage induced by seven N-nitroso compounds in primary cultures of human and rat kidney cells. Mutation Research. 368(1): 41-47.

Rogers, M.A.M., T.L. Vaughn, S. Davis, and D.B. Thomas. 1995. Consumption of nitrate, nitrite, and nitrosodimethylamine and the risk of upper aerodigestive tract cancer. Cancer Epidemiology Biomarkers & Prevention. 4: 29-36 (as cited in CalEPA, 2006).

Russell, C. G., N.K. Blute, S. Via, X. Wu, and Z. Chowdhury. 2012. Nationwide assessment of nitrosamine occurrence and trends. Journal of the American Water Works Association. 104(3): E205-E217.

Sacher, F.S., S. Lenz, and H.-J. Brauch. 1997. Analysis of primary and secondary aliphatic amines in waste water and surface water by gas chromatography-mass spectrometry after derivatization with 2,4-dinitrofluorobenzene or benzene-sulfonyl chloride. Journal of Chromatography A. 764(1): 85-93.

Sacher, F. S., C.K. Schmidt, C. Lee, and U. von Gunten. 2008. Strategies for minimizing nitrosamine formation during disinfection. Water Research Foundation Project, #2729.

Schaefer, C.E., C. Topoleski, and M.E. Fuller. 2007. Effectiveness of zerovalent iron and nickel catalysts for degrading chlorinated solvents and *N*-nitrosodimethylamine in natural groundwater. Water Environment Research. 79(1): 57-62.

Schmidt, C. K. and H. Brauch. 2008. *N,N*-dimethylsulfamide as precursor for *N*-nitrosodimethylamine (NDMA) formation upon ozonation and its fate during drinking water treatment. Environmental Science & Technology. 42(17): 6340-6346.

Schmidt, C.K., F. Sacher, and H. Brauch. 2006. Strategies for minimizing formation of NDMA and other nitrosamines during disinfection of drinking water. WQTC 2006 Conference Proceedings.

Schreiber, I.M. and W.A. Mitch. 2005. Influence of the order of reagent addition on NDMA formation during chloramination. Environmental Science & Technology. 39(10): 3811-3818.

Schreiber, I.M. and W.A. Mitch. 2006a. Nitrosamine formation pathway revisited: The importance of chloramine speciation and dissolved oxygen. Environmental Science & Technology. 40(19): 6007-6014.

Schreiber, I.M. and W.A. Mitch. 2006b. Occurrence and fate of nitrosamines and nitrosamine precursors in wastewater-impacted surface waters using boron as a conservative tracer. Environmental Science & Technology. 40(10): 3203-3210.

Schreiber, I.M. and W.A. Mitch. 2007. Enhanced nitrogenous disinfection byproduct formation near the breakpoint: implications for nitrification control. Environmental Science & Technology. 41(20): 7039-7046.

Sedlak, D.L., R.A. Deeb, E.L. Hawley, W.A. Mitch, T.D. Durbin, S. Mowbray, and S. Carr. 2005. Sources and fate of nitrosodimethylamine and its precursors in municipal wastewater treatment plants. Water Environment Research. 77(1): 32-39.

Seidel, C. J., M.J. McGuire, R.S. Summers, and S. Via. 2005. Have utilities switched to chloramines? Journal of the American Water Works Association. 97(10): 87-97.

Selbes, M., D. Kim, N. Ates, and T. Karanfil. 2013. The roles of tertiary amine structure, backround organic matter and chloramine species on NDMA formation. Water Research. 47: 945-953.

Selbes, M., D. Kim, and T. Karanfil. 2014. The effect of pre-oxidation on NDMA formation and the influence of pH. Water Research. 66: 169-179.

Selbes, M., Glenn M., and T. Karanfil. 2015. The Role of Pre-oxidation in Controlling NDMA Formation: A Review. In: *Recent Advances in Disinfection By-Products*, eds. Karanfil, T., B. Mitch, P. Westerhoff, and Y. Xie, Chapter 9. ACS Symposium Series, 1190.

Sgroi, M., P. Roccaro, G.L. Oelker, and S.A. Snyder. 2014. *N*-nitrosodimethylamine formation upon ozonation and identification of precursors source in a municipal wastewater treatment plant. Environmental Science & Technology. In press.

Sgroi, M., P. Roccaro, G.L. Oelker, and S.A. Snyder. 2015. *N*-nitrosodimethylamine (NDMA) formation at an indirect potable reuse facility. Water Research. 70: 174-183.

Shah, A.D. and W.A. Mitch. 2012. Halonitroalkanes, halonitriles, haloamides, and *N*-nitrosamines: a critical review of nitrogenous disinfection byproduct formation pathways. Environmental Science & Technology. 46(1): 119-131.

Shah, A.D., S.W. Krasner, C.F.T. Lee, U. von Gunten, and W.A. Mitch. 2012. Trade-offs in disinfection byproduct formation associated with precursor pre-oxidation for control of *N*-nitrosodimethylamine formation. Environmental Science & Technology. 46(9): 4809-4818.

Shah, A.D., N. Dai, and W.A. Mitch. 2013. Application of ultraviolet, ozone, and advanced oxidation treatments to washwaters to destroy nitrosamines, amines, and aldehydes formed during amine based carbon capture. Environmental Science & Technology. 47: 2799-2808.

Sharma, V. K. 2002. Potassium ferrate(VI): an environmentally friendly oxidant. Advances in Environmental Research. 6: 143-156.

Sharpless, C. M. and K. G. Linden. 2003. Experimental and model comparisons of low- and medium-pressure Hg lamps for the direct and H_2O_2 assisted UV photodegradation of *N*-nitrosodimethylamine in simulated drinking water. Environmental Science & Technology. 37(9): 1933-1940.

Shen, R. and S. Andrews. 2011a. Demonstration of 20 pharmaceuticals and personal care products (PPCPs) as nitrosamine precursors during chloramine disinfection. Water Research. 45(2): 944-952.

Shen, R. and S. Andrews. 2011b. NDMA formation kinetics from three pharmaceuticals in four water matrices. Water Research. 45(17): 5687-5694.

Shen, R. and S. Andrews. 2013. Formation of NDMA from ranitidine and sumatriptan: The role of pH. Water Research. 47: 802–810.

Shu, L. and P.F. Hollenberg. 1996. Role of cytochrom P450 in DNA damage induced by *N*-nitrosodialkylamines in cultured rat hepatocytes. Carcinogenesis. 17(3): 569-576 (as cited in Shu and Hollenberg, 1997).

Shu, L. and P.F. Hollenberg. 1997. Alkylation of cellular macromolecules and target specificity of carcinogenic nitrosodialkylamines: metabolic activation by cytochromes P450 2B1 and 2E1. Carcinogenesis. 18(4): 801-810.

Standard Methods (SM). 2012a. SM 6450B. Carbonaceous-resin solid-phase extraction GC/MS method. In *Standard methods for the examination of water and wastewater*, 22nd edition. Washington, DC: American Public Health Association.

SM. 2012b. SM 6450C. Micro liquid-liquid extraction GC/MS method. In *Standard methods for the examination of water and wastewater*, 22nd edition. Washington, DC: American Public Health Association.

SM. 2012c. SM 6410B. Extractable base/neutrals and acids. In *Standard methods for the examination of water and wastewater*, 22nd edition. Washington, DC: American Public Health Association.

Soltermann, F., M. Lee, S. Canonica, and U. von Gunten. 2013. Enhanced *N*-nitrosamine formation in pool water by UV irradiation of chlorinated secondary amines in the presence of monochloramine. Water Research. 47: 79-90.

Souliotis, V.L., J.H. van Delft, M.J. Steenwinkel, R.A. Baan, and S.A. Kyrtopoulos. 1998. DNA adducts, mutant frequencies and mutation spectra in lambda lacZ transgenic mice treated with N-nitrosodimethylamine. Carcinogenesis. 19(5): 731-739.

Steinle-Darling, E., M. Zedda, M.H. Plumlee, H.F. Ridgway, and M. Reinhard. 2007. Evaluating the impacts of membrane type, coating, fouling, chemical properties and water chemistry on reverse osmosis rejection of seven nitrosoalklyamines, including NDMA. Water Research. 41(17): 3959-3967.

Straif, K., D. Taeger, D. Holthenrich, Y. Sun, M. Bungers, and S.K. Weiland. (2000). Exposure to N-nitrosamines, carbon black, asbestos, and talc and mortality from stomach, lung, and laryngeal cancer in a cohort of rubber workers. American Journal of Epidemiology. 152(4): 297-306 (as cited in CalEPA, 2006).

Swaim, P., A. Royce, T. Smith, T. Maloney, D. Ehlen, and B. Carter. 2008. Effectiveness of UV advanced oxidation for destruction of micro-pollutants. Ozone: Science & Engineering: The Journal of the International Ozone Association. 30(1): 34-42.

Symons, J.M., S.W. Krasner, L.A. Simms, and M. Sclimenti. 1993. Measurement of THM and precursor concentrations revisited – the effect of bromide ion. Journal of the American Water Works Association. 85(1): 51-62.

Takada, A., J. Nei, S. Takase, and Y. Matsuda. 1986. Effects of ethanol on experimental hepatocarcinogenesis. Hepatology. 6: 65-72 (as cited in IARC, 2010).

Takayama, S. and K. Oota. 1965. Induction of malignant tumors in various strains of mice by oral administration of *N*-nitrosodimethylamine and *N*-nitrosodiethylamine. Gann. 56: 189-199 (as cited in ATSDR, 1989).

Tang, H., P.C. Choy, and H. Chen. 1992. Changes in lipid content and composition during the development of *N*-nitrosodiethylamine induced hepatocarcinoma. Molecular and Cellular Biochemistry. 109(1): 83-87.

Teefy, S., C.C. Chan, W. Wong, and L. Work. 2011. NDMA formation from gaskets used in water storage tanks. WQTC 2011 Conference Proceedings.

Teefy, S., C.C. Chan, W. Wong, and L. Work. 2014. NDMA formation from gaskets used in water storage tanks. Journal of the American Water Works Association. 106: 408-418.

Templeton, M. R., and Z. Chen. 2010. NDMA and seven other nitrosamines in selected UK drinking water supply systems. Journal of Water Supply: Research and Technology-AQUA. 59(4): 277-283.

Terracini, B., G. Palestro, M.R. Gigliardi, G. Montesano, and R. Montesano. 1966. Carcinogenicity of dimethylnitrosamine in Swiss mice. British Journal of Cancer. 20: 871-876 (as cited in ATSDR, 1989).

Terracini, B., P.N. Magee, and J.M. Barnes. 1967. Hepatic pathology in rats on low dietary levels of dimethylnitrosamine. British Journal of Cancer. 21: 559-565.

Tinwell, H., P.A. Lefevre, and J. Ashby. 1994. Mutation studies with dimethyl nitrosoamine in young and old lac I transgenic mice. Mutation Research. 307: 501-508.

Tomatis, L. 1973. Transplacental carcinogenesis. In *Modern trends in oncology. Part I*, ed. Raven, R.W. London, England: Butterworths (as cited in CalEPA, 2006).

Tomatis, L, P.N. Magee, and P. Shubik. 1964. Induction of liver tumors in the Syrian golden hamster by feeding dimethylnitrosamine. Journal of the National Cancer Institute. 33: 341-345 (as cited in CalEPA, 2006).

Tricker, A.R., B. Pfundstein, and R. Preussmann. 1994. Nitrosatable secondary amines: Exogenous and endogenous exposure and nitrosation in-vivo. In *Nitrosamines and related N-nitro compounds: chemistry and biochemistry*, eds. Leoppky, R.N. and C.J. Michejda, pp. 93-101. Washington, DC: American Chemical Society.

Trogolo, D., B.K. Mishra, M.B. Heeb, U. von Gunten, and J.S. Arey. 2015. Molecular mechanism of NDMA formation from *N,N*-dimethylsulfamide during ozonation: Quantum chemical insights into bromide-catalyzed pathway. Environmental Science & Technology. 49: 4163-4175.

Tsuda H., Y. Mera, K. Seki, T. Aoki, S. Fukushima, and N. Ito. 1987. Induction of tumors in the liver, urinary bladder, esophagus and forestomach by short-term treatment with different doses of N,N'-dibutylnitrosamine in rats. Japanese Journal of Cancer Research GANN. 78(3): 227-34.

United States Department of Energy (USDOE). 1997. Method OM100R, Analysis of Semivolatile Organic Compounds Using Capillary Gas Chromatography with Ion Trap Mass Spectrometric Detection. United States Department of Energy, Oak Ridge National Laboratory. Available online at: https://www.nemi.gov/apex/f?p=237:38:3157202209350950::::P38_METHOD_ID:4795.

United States Environmental Protection Agency (USEPA). 1987. *N*-Nitrosodimethylamine. IRIS (Integrated risk information system). Cincinnati, OH: U.S. EPA, Office of Research and Development (ORD). Available online at: http://www.epa.gov/iris/subst/0045.htm.

USEPA. 1996a. 1996 Toxics Release Inventory: Public data release report. Chapter 3: Year-to-Year Comparison of Toxics Release Inventory Data.

USEPA. 1996b. EPA Method 8260B, Volatile Organic Compounds by Gas Chromatography/mass Spectrometry (GC/MS), SW-846 Online: Test Methods for Evaluating Solid Waste, Physical/chemical Methods. Available online at: https://www.epa.gov/sites/production/files/2015-12/documents/8260b.pdf.

USEPA. 1996c. EPA Method 5031, Volatile, Nonpurgeable, Water-soluble Compounds by Azeotropic Distillation, SW-846. Available online at: https://www.epa.gov/hw-sw846/sw-846-test-method-5031-volatile-nonpurgeable-water-soluble-compounds-azeotropic.

USEPA. 2001a. EPA Method 1625, Semivolatile Organic Compounds by Isotope Dilution GCMS. 40 CFR 136, Appendix A.

USEPA. 2001b. EPA Method 607—Nitrosamines. 40 CFR 136, Appendix A.

USEPA. 2001c. EPA Method 625, Base/Neutrals and Acids. 40 CFR 136, Appendix A.

USEPA. 2003. Occurrence Estimation Methodology and Occurrence Findings for the Six-Year Review of National Primary Drinking Water Regulations. EPA 815-R-03-006. June 2003.

USEPA 2004a. The Toxics Release Inventory (TRI) and Factors to Consider When Using TRI Data. Available online at: https://www.epa.gov/sites/production/files/2015-06/documents/factors_to_consider_6.15.15_final.pdf .

USEPA. 2004b. EPA Method 521, Version 1.0, Determination of Nitrosamines in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionization Tandem Mass Spectrometry (CI-MS/MS). EPA 600-R-05-054. September 2004.

USEPA. 2005a. Guidelines for Carcinogen Risk Assessment. Risk Assessment Forum, Washington, DC. EPA 630-P-03-001B. March 2005.

USEPA. 2005b. Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. Risk Assessment Forum, Washington, DC. EPA 630-R-03-003F. March 2005.

USEPA. 2005c. Unregulated Contaminant Monitoring Regulation (UCMR) for Public Water Systems Revisions; Proposed Rule. 70 FR 49094. August 22, 2005.

USEPA. 2005d. Economic Analysis for the Final Stage 2 Disinfectants and Disinfection Byproducts Rule. EPA 815-R-05-010. December 2005.

USEPA. 2007a. EPA Method 8015C, Nonhalogenated Organics Using GC/FID, SW-846 Revision 3. Available online: https://www.epa.gov/sites/production/files/2015-12/documents/8015c.pdf.

USEPA. 2007b. EPA Method 8270D, Semivolatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS), SW-846, Revision 4.

USEPA. 2007c. Unregulated Contaminant Monitoring Regulation (UCMR) for Public Water Systems Revisions; Final Rule. 72 FR 367. January 4, 2007.

USEPA. 2007d. Simultaneous Compliance Guidance Manual for the Long-Term 2 and Stage 2 DBP Rules. EPA 815-R-07-017. March 2007.

USEPA. 2009. Final Contaminant Candidate List 3 Chemicals: Classification of the PCCL to CCL. Office of Water. EPA 815-R-09-008.

USEPA. 2010. Technical Description of the Statistical Model of Perchlorate Occurrence in Drinking Water. Peer reviewed draft report.

USEPA. 2011. Age Dependent Adjustment Factor Application. Washington, DC: Office of Water Policy Document. Office of Science and Technology. Office of Water. Draft.

USEPA. 2012. Toxic Release Inventory (TRI) Explorer: Trends. Available online at: http://www.epa.gov/triexplorer/trends.htm. Accessed March 9, 2012.

USEPA. 2014a. Announcement of Preliminary Regulatory Determinations for Contaminants on the Third Drinking Water Contaminant Candidate List. 79 FR 62716. October 20, 2014.

USEPA. 2014b. Occurrence data from the second unregulated contaminant monitoring regulation (UCMR 2). EPA 815-R-14-004. April 2014

USEPA. 2016a. Six-Year Review 3 Technical Support Document for Disinfectants/Disinfection Byproducts Rules. EPA 810-R-16-012.

USEPA. 2016b. Six-Year Review 3 Technical Support Document for Chlorate. EPA 810-R-16-013.

United States Geological Survey (USGS). 1983. Method O-3118-83, Base/Neutral Extractable Compounds, Total Recoverable, Gas Chromatographic/Mass Spectrometric. Available online at: https://www.nemi.gov/apex/f?p=237:38:3157202209350950:::P38_METHOD_ID:8963 .

Uzun, H., D. Kim, and T. Karanfil. 2015. Seasonal and temporal patterns of NDMA formation potentials in surface waters. Water Research. 69: 162-172.

Valentine, R.L., J. Choi, Z. Chen, S.E. Barrett, C. Hwang, Y. Guo, M. Wehner, S. Fitzsimmons, S.A. Andrews, A.G. Werker, C. Brubacher, and K. Kohut. 2005. Factors affecting the formation of NDMA in water and occurrence. Water Research Foundation, Project # 2678..

Verdugo, E.M., C. Krause, Y. Han, T.E. Mattes, R.L. Valentine, and D.M. Cwiertny. 2014. N-functionalized carbon nanotubes as a source and precursor of *N*-nitrosodimethylamine: Implications for environmental fate, transport, and toxicity. Environmental Science & Technology. 48: 9279-9287.

Verna, L., J. Shysner, and G.M. Williams. 1996. N-nitrosodiethylamine mechanistic data and risk assessment: Bioactivation, DNA-adduct formation, mutagenicity, and tumor initiation. Pharmacology and Therapeutics. 71(1-2): 57-81.

Verscheuren, K. 1996. *Handbook of Environmental Data on Organic Chemicals*. 3rd edition, pp. 829-830. New York, NY: Van Nostrand Reinhold.

Vesselinovitch, S.D., M. Koka, N. Mihailovich, and K.V. Rao. 1984. Carcinogenicity of diethylnitrosamine in newborn, infant, and adult mice. Journal of Cancer Research and Clinical Oncology. 108: 60-65.

Vogel, E.W. and M. J.M. Nivard. 1993. Performance of 181 chemicals in a Drosophila assay predominantly monitoring interchromosomal mitotic recombination. Mutagenesis. 8(1): 57-81.

Wang, M., Y. Lao, G. Cheng, Y. Shi, P.W. Villalta, A. Nishikawa, and S.S. Hecht. 2007. Analysis of adducts in hepatic DNA of rats treated with *N*-nitrosopyrrolidine. Chemical Research in Toxicology. 20(4): 634-640.

Wang, C., X. Zhang, J. Wang, S. Liu, C. Chen, and Y. Xie. 2013a. Effects of organic fractions on the formation and control of *N*-nitrosamine precursors during conventional drinking water treatment processes. Science of the Total Environment. 449: 295-301

Wang, C., H. Shi, C.D. Adams, T. Timmons, and Y. Ma. 2013b. Investigation of removal of *N*-nitrosamines and their precursors in water treatments using activated carbon nanoparticles. International Journal of Environmental Technology and Management. 16(1-2): 34-48.

Wang, J., R.A. Dahlgren, M.S. Ersan, T. Karanfil, and A.T. Chow. 2015a. Wildfire altering terrestrial precursors of disinfection byproducts in forest detritus. Environmental Science & Technology. 49(10): 5921–5929

Wang, C., S. Liu, J. Wang, X. Zhang, and C. Chen. 2015b. Monthly survey of *N*-nitrosamine yield in a conventional water treatment plant in North China. Journal of Environmental Sciences. 38: 142-149.

Wang, X., H. Yang, B. Zhou, X. Wang, and Y. Xie. 2015c. Effect of Oxidation on Amine Based Pharmaceutical Degradation and N-Nitrosodimethylamine Formation. Water Research. 87: 403-411.

Wang, W., Y. Guo, Q. Yang, Y. Huang, C. Zhu, J. Fan, and F. Pan. 2015d. Characterization of the microbial community structure and nitrosamine-reducing isolates in drinking water biofilters. Science of the Total Environment. 521-522: 219-225.

Webster, T.S., C. Condee, and P.B. Hatzinger. 2013. Ex situ treatment of *N*-nitrosodimethylamine (NDMA) in groundwater using a fluidized bed reactor. Water Research. 47 :811-820.

Westerhoff, P. and H. Mash. 2002. Dissolved organic nitrogen in drinking water supplies: A review. Journal of Water Supply Research and Technology – AQUA. 41(8): 415-448.

Westerhoff, P., W. Lee, J. Croue, H. Gallard, and G. Amy. 2006. Organic nitrogen in drinking water and reclaimed wastewater. AWWARF. 91116.

Wilczak, A., A. Assadi-Rad, H.H. Lai, L.L. Hoover, J.F. Smith, R. Berger, F. Rodigari, J.W. Beland, L.J. Lazzelle, E.G. Kincannon, H. Baker, and C.T. Heaney. 2003. Formation of NDMA in chloraminated water coagulated with DADMAC cationic polymer. Journal of the American Water Works Association. 95(9): 94- 106.

Woods, G.C. and E.R.V. Dickenson. 2015. Evaluation of the final UCMR2 database: Nationwide trends in NDMA. Journal of the American Water Works Association. 107(1): E58-E68.

Woods, G.C., R.A. Trenholm, B. Hale, Z. Campbell, and E.R.V. Dickenson. 2015. Seasonal and spatial variability of nitrosamines and their precursor sources at a large-scale urban drinking water system. Science of the Total Environment. 520: 120-126.

World Health Organization (WHO). 2002. Concise international chemical assessment document 38, *N*-nitrosodimethylamine. Geneva, Switzerland: World Health Organization. Available online at: http://www.inchem.org/documents/cicads/cicads/cicad38.htm.

WHO. 2008. N-Nitrosodimethylamine in drinking water. Background document for development of WHO guidelines for drinking-water quality. Geneva, Switzerland: World Health Organization. Available online at: http://www.who.int/water_sanitation_health/dwq/chemicals/ndma_2add_feb2008.pdf

Wu, Q., H. Shi, Y. Ma, C. Adams, H. Jiang, J. Wang, T. Eichholz, and T. Timmons. 2015. Removal of N-nitrosamine precursors in drinking water system using adsorption methods. Separation and Purification Technology. 156: 972-979.

Xu, B., Z. Chen, F. Qi, and L. Yang. 2008. Photodegradation of *N*-nitrosodiethylamine in water with UV irradiation. Chinese Science Bulletin. 53(21): 3395-3401.

Xu, B., Z. Chen, F. Qi, J. Ma, and F. Wu. 2009a. Rapid degradation of new disinfection by-products in drinking water by UV irradiation: *N*-nitrosopyrrolidine and *N*-nitrosopiperidine. Separation and Purification Technology. 69: 126-133.

Xu, B., Z. Chen, F. Qi, J. Ma, and F. Wu. 2009b. Inhibiting the regeneration of *N*-nitrosodimethylamine in drinking water by UV photolysis combined with ozonation. Journal of Hazardous Materials. 168(1): 108-114.

Xu, B., Z. Chen, F. Qi, J. Ma, and F. Wu. 2010. Comparison of *N*-nitrosodiethylamine degradation in water by UV irradiation and UV/O_3: Efficiency, product and mechanism. Journal of Hazardous Materials. 179(1-3): 976-982.

Xu, B., T. Ye, D.P-. Li, C.-Y. Hu, Y.-L. Lin, S.-J. Xia, F.-X. Tiang, and N.-Y. Gao. 2011. Measurement of dissolved organic nitrogen in a drinking water treatment plant: Size fraction, fate, and relation to water quality parameters. Science of the Total Environment. 409(6): 1116-1122.

Yahagi, T., M. Nagao, Y. Seino, T. Matsushima, and T. Sugimura. 1977. Mutagenicities of *N*-nitrosamines on Salmonella. Mutat. Res. 48: 121-130 (as cited in Aiub et al., 2003).

Yamazaki, H., Y. Inui, C.H. Yun, F.P. Guengerich, and T. Shimada. 1992a. Cytochrome P4502E1 and 2A6 enzymes as major catalysts for metabolic activation of *N*-nitrososdialkylamines and tobacco-related nitrosamines to human liver and microsomes. Carcinogenesis. 13: 1789-1794 (as cited in Verna et al., 1996).

Yamazaki, H., Y. Oda, Y. Funai, S. Imaoka Y. Inui, F.P. Guengerich, and T. Shimada. 1992b. Participation of rat liver cytochrome P4502E1 in the activation of *N*-nitrosodimethylamine and *N*-nitrosodiethylamine to products genotoxic in an acetyltransferase-overexpressing *Salmonella typhimurium* strain (NM2009). Carcinogenesis. 13: 979-985 (as cited in Verna et al., 1996).

Yang, L., Z. Chen, J. Shen, Z. Xu, H. Liang, J. Tian, Y. Ben, X. Zhai, W. Shi, and G. Li. 2009. Reinvestigation of the nitrosamine-formation mechanism during ozonation. Environmental Science & Technology. 43(14): 5481-5487.

Yang, L., D. Kim, H. Uzun, T. Karnfil, and J. Hur. 2015. Assessing trihalomethanes (THMs) and *N*-nitrosodimethylamine formation potentials in drinking water treatment plants using fluorescence spectroscopy and parallel factor analysis. Chemosphere. 121: 84-91.

Yoon, S., and H. Tanaka. 2014. Formation of *N*-nitrosamines by chloramination of amines listed in pollutant release and transfer registers. Chemosphere. 95: 88-95.

Yurchenko, S. and U. Mölder. 2007. The occurrence of volatile *N*-nitrosamines in Estonian meat products. Food Chemistry. 100: 1713-1721.

Zeiger, E., B. Anderson, S. Haworth, T. Lawlor, K. Mortelmans, and W. Speck. 1987. Salmonella mutagenicity tests. III. Results from the testing of 255 chemicals. Environmental Mutagenesis. 9: 1-110 (as cited in Aiub et al., 2003).

Zeng. T. and W.A. Mitch. 2015. Contribution of *N*-nitrosamines and their precursors to sewage by greywaters and blackwaters. Environmental Science & Technology. 49: 13158–13167.

Zeng, T., J.J. Pignatello, R.J. Li, and W.A. Mitch. 2014. Synthesis and Application of a Quaternary Phosphonium Polymer to Avoid N-Nitrosamine Formation. Environmental Science & Technology. 48: 13392-13401.

Zha, X., Y. Liu, Q. Zhang, R. Dai, L. Ying, J. Wu, J. Wang, and L. Ma. 2014. Effects of bromide and iodide ions on the formation of disinfection byproducts during ozonation and subsequent chlorination of water containing biological source matters. Environmental Science Pollution Research. 22: 2714-2723.

Zhang, A., Y. Li, Y. Song, J. Lv, and J. Yang. 2014. Characterization of pharmaceuticals and personal care products as *N*-nitrosodimethylamine precursors during disinfection processes using free chlorine and chlorine dioxide. Journal of Hazardous Materials. 276: 499–509.

Zhao, Y., L.-S. Cai, Z. Jing, H. Wang, J.X. Yu, and H.-S. Zhang. 2003. Determination of aliphatic amines using *N*-succinimidyl benzoate as a new derivatization reagent in gas chromatography combined with solid-phase microextraction. Journal of Chromatography A. 1021(1-2): 175-181.

Zhao, Y., J.M. Boyd, M. Woodbeck, R.C. Andrews, F. Qin, S.E. Hrudey, and X. Li. 2008. Formation of *N*-nitrosamines from eleven disinfection treatments of seven different surface waters. Environmental Science & Technology. 42(13): 4857-4862.

Zhou, W., C. Chen, L. Lou, Q. Yang, and L. Zhu. 2014. Formation potential of nine nitrosamines from corresponding secondary amines by chloramination. Chemosphere. 95: 81-87.

Zhu, J. H., D. Yan, J.R. Xai, L.L. Ma, and B. Shen. 2001. Attempt to adsorb *N*-nitrosamines in solution by use of zeolites. Chemosphere. 44(5): 949-956.

Zielenska, M., A. Ahmed, and B.W. Glickman. 1990. Mutational specificities of environmental carcinogens in the Lac I gene of *Escherichia coli* (III). The cyclic nitrosamine *N*-nitrosopyrrolidine is a complex mutagen. Molecular Carcinogenesis. 3(3): 122-125.