

**TOXICOLOGICAL PROFILE FOR
N-NITROSODIMETHYLAMINE**

Agency for Toxic Substances and Disease Registry (ATSDR)
U.S. Public Health Service

In collaboration with
U.S. Environmental Protection Agency (EPA)

December 1989

DISCLAIMER

Mention of company name or product does not constitute endorsement by the Agency for Toxic Substances and Disease Registry.

FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the most significant hazardous substances were published in the Federal Register on April 17, 1987, and on October 20, 1988.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

(A) An examination, summary and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects,

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, or chronic health effects, and

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The original guidelines were published in the Federal Register on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every 3 years, as required by SARA.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that

describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the front of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public. We plan to revise these documents as additional data become available.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, EPA, the Centers for Disease Control, and the National Toxicology Program. It has also been reviewed by a panel of nongovernment peer reviewers and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



Walter R. Dowdle, Ph.D.
Acting Administrator
Agency for Toxic Substances and
Disease Registry

CONTENTS

FOREWORD	iii
LIST OF FIGURES	ix
LIST OF TABLES	xi
1. PUBLIC HEALTH STATEMENT	1
1.1 WHAT IS N-NITROSODIMETHYLAMINE?	1
1.2 HOW MIGHT I BE EXPOSED TO N-NITROSODIMETHYLAMINE?	1
1.3 HOW CAN N-NITROSODIMETHYLAMINE ENTER AND LEAVE MY BODY?	2
1.4 HOW CAN N-NITROSODIMETHYLAMINE AFFECT MY HEALTH?	2
1.5 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO N-NITROSODIMETHYLAMINE?	3
1.6 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?	3
1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?	3
1.8 WHERE CAN I GET MORE INFORMATION?	3
2. HEALTH EFFECTS	9
2.1 INTRODUCTION	9
2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	9
2.2.1 Inhalation Exposure	10
2.2.1.1 Death	10
2.2.1.2 Systemic Effects	13
2.2.1.3 Immunological Effects	14
2.2.1.4 Neurological Effects	14
2.2.1.5 Developmental Effects	14
2.2.1.6 Reproductive Effects	14
2.2.1.7 Genotoxic Effects	15
2.2.1.8 Cancer	15
2.2.2 Oral Exposure	16
2.2.2.1 Death	16
2.2.2.2 Systemic Effects	29
2.2.2.3 Immunological Effects	33
2.2.2.4 Neurological Effects	34
2.2.2.5 Developmental Effects	34
2.2.2.6 Reproductive Effects	35
2.2.2.7 Genotoxic Effects	35
2.2.2.8 Cancer	36
2.2.3 Dermal Exposure	38
2.2.3.1 Death	38
2.2.3.2 Systemic Effects	38
2.2.3.3 Immunological Effects	39
2.2.3.4 Neurological Effects	39
2.2.3.5 Developmental Effects	39
2.2.3.6 Reproductive Effects	39

2.2.3.7	Genotoxic Effects.	39
2.2.3.8	Cancer	39
2.3	RELEVANCE TO PUBLIC HEALTH	39
2.4	LEVELS IN HUMAN TISSUES AND FLUIDS ASSOCIATED WITH HEALTH EFFECTS.	46
2.5	LEVELS IN THE ENVIRONMENT ASSOCIATED WITH LEVELS IN HUMAN TISSUES AND/OR HEALTH EFFECTS.	47
2.6	TOXICOKINETICS	47
2.6.1	Absorption.	47
2.6.1.1	Inhalation Exposure.	47
2.6.1.2	Oral Exposure.	47
2.6.1.3	Dermal Exposure.	48
2.6.2	Distribution.	48
2.6.2.1	Inhalation Exposure.	48
2.6.2.2	Oral Exposure.	48
2.6.2.3	Dermal Exposure.	49
2.6.3	Metabolism.	49
2.6.3.1	Inhalation Exposure.	49
2.6.3.2	Oral Exposure.	49
2.6.3.3	Dermal Exposure.	51
2.6.4	Excretion	51
2.6.4.1	Inhalation Exposure.	51
2.6.4.2	Oral Exposure.	51
2.6.4.3	Dermal Exposure.	51
2.7	INTERACTIONS WITH OTHER CHEMICALS.	51
2.8	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	52
2.9	ADEQUACY OF THE DATABASE	52
2.9.1	Existing Information on Health Effects of N-Nitrosodimethylamine.	53
2.9.2	Data Needs.	53
2.9.3	On-going Studies.	58
3.	CHEMICAL AND PHYSICAL INFORMATION.	59
3.1	CHEMICAL IDENTITY.	59
3.2	PHYSICAL AND CHEMICAL PROPERTIES	59
4.	PRODUCTION, IMPORT, USE, AND DISPOSAL.	63
4.1	PRODUCTION	63
4.2	IMPORT	63
4.3	USE.	63
4.4	DISPOSAL	63
4.5	ADEQUACY OF THE DATA BASE.	64
4.5.1	Data Needs.	64
5.	POTENTIAL FOR HUMAN EXPOSURE	65
5.1	OVERVIEW	65
5.2	RELEASES TO THE ENVIRONMENT.	66
5.2.1	Air	66
5.2.2	Water	66

5.2.3	Soil	67
5.3	ENVIRONMENTAL FATE	67
5.3.1	Transport and Partitioning	67
5.3.2	Transformation and Degradation	68
5.3.2.1	Air	68
5.3.2.2	Water	68
5.3.2.3	Soil	68
5.4	LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	69
5.4.1	Air	69
5.4.2	Water	69
5.4.3	Soil	70
5.4.4	Other Media	70
5.5	GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	73
5.6	POPULATIONS WITH POTENTIALLY HIGH EXPOSURE	74
5.7	ADEQUACY OF THE DATABASE	74
5.7.1	Data Needs	75
5.7.2	On-going Studies	76
6.	ANALYTICAL METHODS	77
6.1	BIOLOGICAL MATERIALS	77
6.2	ENVIRONMENTAL SAMPLES	77
6.3	ADEQUACY OF THE DATABASE	81
6.3.1	Data Needs	81
6.3.2	On-going Studies	82
7.	REGULATIONS AND ADVISORIES	83
8.	REFERENCES	87
9.	GLOSSARY	115
	APPENDIX	119

LIST OF FIGURES

2-1.	Levels of Significant Exposure to N-Nitrosodimethylamine - Inhalation	12
2-2.	Levels of Significant Exposure to N-Nitrosodimethylamine - Oral. .	25
2-3.	Metabolism of N-Nitrosodimethylamine	50
2-4.	Existing Information on Health Effects of N-Nitrosodimethylamine .	54

LIST OF TABLES

1-1.	Human Health Effects from Breathing N-Nitrosodimethylamine	4
1-2.	Animal Health Effects from Breathing N-Nitrosodimethylamine. . . .	5
1-3.	Human Health Effects from Eating or Drinking N-Nitroso- dimethylamine.	6
1-4.	Animal Health Effects from Eating or Drinking N-Nitroso- dimethylamine.	7
2-1.	Levels of Significant Exposure to N-Nitrosodimethylamine - Inhalation	11
2-2.	Levels of Significant Exposure to N-Nitrosodimethylamine - Oral. .	17
2-3.	Genotoxicity of N-Nitrosodimethylamine In Vitro.	43
2-4.	Genotoxicity of N-Nitrosodimethylamine In Vivo	45
3-1.	Chemical Identity of N-Nitrosodimethylamine.	60
3-2.	Physical and Chemical Properties of N-Nitrosodimethylamine	61
5-1.	Detection of N-Nitrosodimethylamine in Food.	71
6-1.	Analytical Methods for Determining N-Nitrosodimethylamine in Biological Samples	78
6-2.	Analytical Methods for Determining N-Nitrosodimethylamine in Environmental Samples.	79
7-1.	Regulations and Guidelines Applicable to N-Nitrosodi- methylamine.	84

