

**TOXICOLOGICAL PROFILE FOR  
HYDRAZINES**

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Agency for Toxic Substances and Disease Registry**

**September 1997**

**DISCLAIMER**

The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

**UPDATE STATEMENT**

Toxicological profiles are revised and republished as necessary, but no less than once every three years. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry  
Division of Toxicology/Toxicology Information Branch  
1600 Clifton Road NE, E-29  
Atlanta, Georgia 30333



## FOREWORD

This toxicological profile is prepared in accordance with guidelines\* developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is 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.

The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning 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 are identified by ATSDR and EPA.

Each profile includes the following:

- (A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance 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 that present a significant risk to human health of acute, subacute, and chronic health effects; and
- (C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

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.

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



David Satcher, M.D., Ph.D.  
Administrator  
Agency for Toxic Substances and  
Disease Registry

**\*Legislative Background**

The toxicological profiles are developed in response to the Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) which amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). Section 211 of SARA also amended Title 10 of the U. S. Code, creating the Defense Environmental Restoration Program. Section 2704(a) of Title 10 of the U. S. Code directs the Secretary of Defense to notify the Secretary of Health and Human Services of not less than 25 of the most commonly found unregulated hazardous substances at defense facilities. Section 2704(b) of Title 10 of the U. S. Code directs the Administrator of the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare a toxicological profile for each substance on the list provided by the Secretary of Defense under subsection (b).

**CONTRIBUTORS****CHEMICAL MANAGER(S)/AUTHOR(S):**

Gangadhar Choudhary, Ph.D.

ATSDR, Division of Toxicology, Atlanta, GA

Hugh Hansen, Ph.D.

ATSDR, Division of Toxicology, Atlanta, GA

Steve Donkin, Ph.D.

Sciences International, Inc., Alexandria, VA

Mr. Christopher Kirman

Life Systems, Inc., Cleveland, OH

**THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:**

1. Green Border Review. Green Border review assures the consistency with ATSDR policy.
2. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.
3. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific minimal risk levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.





## PEER REVIEW

A peer review panel was assembled for hydrazines. The panel consisted of the following members:

1. Dr. Emerich Fiala, Chief, Division of Biochemical Pharmacology, American Health Foundation, Valhalla, NY
2. Dr. Bela Toth, Professor, University of Nebraska Medical Center, Omaha, NE
3. Dr. Raghbir Sharma, Fred C. Davison Professor, University of Georgia, College of Veterinary Medicine, Athens, GA

These experts collectively have knowledge of hydrazines's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.



## CONTENTS

FOREWORD .....	v
CONTRIBUTORS .....	vii
PEER REVIEW .....	ix
LIST OF FIGURES .....	xv
LIST OF TABLES .....	xvii
1. PUBLIC HEALTH STATEMENT .....	1
1.1 WHAT ARE HYDRAZINES? .....	1
1.2 WHAT HAPPENS TO HYDRAZINES WHEN THEY ENTER THE ENVIRONMENT? .....	3
1.3 HOW MIGHT I BE EXPOSED TO HYDRAZINES? .....	4
1.4 HOW CAN HYDRAZINES ENTER AND LEAVE MY BODY? .....	5
1.5 HOW CAN HYDRAZINES AFFECT MY HEALTH? .....	5
1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO HYDRAZINES? .....	7
1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH? .....	8
1.8 WHERE CAN I GET MORE INFORMATION? .....	8
2. HEALTH EFFECTS .....	11
2.1 INTRODUCTION .....	11
2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE .....	11
2.2.1 Inhalation Exposure .....	13
2.2.1.1 Death .....	13
2.2.1.2 Systemic Effects .....	15
2.2.1.3 Immunological and Lymphoreticular Effects .....	33
2.2.1.4 Neurological Effects .....	33
2.2.1.5 Reproductive Effects .....	34
2.2.1.6 Developmental Effects .....	34
2.2.1.7 Genotoxic Effects .....	34
2.2.1.8 Cancer .....	35
2.2.2 Oral Exposure .....	36
2.2.2.1 Death .....	36
2.2.2.2 Systemic Effects .....	36
2.2.2.3 Immunological and Lymphoreticular Effects .....	52
2.2.2.4 Neurological Effects .....	52
2.2.2.5 Reproductive Effects .....	53
2.2.2.6 Developmental Effects .....	53
2.2.2.7 Genotoxic Effects .....	54
2.2.2.8 Cancer .....	54
2.2.3 Dermal Exposure .....	56
2.2.3.1 Death .....	56

2.2.3.2	Systemic Effects . . . . .	56
2.2.3.3	Immunological and Lymphoreticular Effects . . . . .	60
2.2.3.4	Neurological Effects . . . . .	60
2.2.3.5	Reproductive Effects . . . . .	61
2.2.3.6	Developmental Effects . . . . .	61
2.2.3.7	Genotoxic Effects . . . . .	61
2.2.3.8	Cancer . . . . .	61
2.3	TOXICOKINETICS . . . . .	61
2.3.1	Absorption . . . . .	62
2.3.1.1	Inhalation Exposure . . . . .	62
2.3.1.2	Oral Exposure . . . . .	62
2.3.1.3	Dermal Exposure . . . . .	63
2.3.2	Distribution . . . . .	63
2.3.2.1	Inhalation Exposure . . . . .	63
2.3.2.2	Oral Exposure . . . . .	63
2.3.2.3	Dermal Exposure . . . . .	64
2.3.2.4	Other Routes of Exposure . . . . .	64
2.3.3	Metabolism . . . . .	65
2.3.4	Excretion . . . . .	70
2.3.4.1	Inhalation Exposure . . . . .	70
2.3.4.2	Oral Exposure . . . . .	70
2.3.4.3	Dermal Exposure . . . . .	70
2.3.4.4	Other Exposure . . . . .	71
2.4	MECHANISMS OF ACTION . . . . .	72
2.5	RELEVANCE TO PUBLIC HEALTH . . . . .	74
2.6	BIOMARKERS OF EXPOSURE AND EFFECT . . . . .	90
2.6.1	Biomarkers Used to Identify or Quantify Exposure to Hydrazines . . . . .	91
2.6.2	Biomarkers Used to Characterize Effects Caused by Hydrazines . . . . .	92
2.7	INTERACTIONS WITH OTHER SUBSTANCES . . . . .	93
2.8	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE . . . . .	93
2.9	METHODS FOR REDUCING TOXIC EFFECTS . . . . .	94
2.9.1	Reducing Peak Absorption Following Exposure . . . . .	94
2.9.2	Reducing Body Burden . . . . .	95
2.9.3	Interfering with the Mechanism of Action for Toxic Effects . . . . .	95
2.10	ADEQUACY OF THE DATABASE . . . . .	97
2.10.1	Existing Information on Health Effects of Hydrazines . . . . .	97
2.10.2	Identification of Data Needs . . . . .	98
2.10.3	On-going Studies . . . . .	106
3.	CHEMICAL AND PHYSICAL INFORMATION . . . . .	109
3.1	CHEMICAL IDENTITY . . . . .	109
3.2	PHYSICAL AND CHEMICAL PROPERTIES . . . . .	109
4.	PRODUCTION, IMPORT, USE, AND DISPOSAL . . . . .	113
4.1	PRODUCTION . . . . .	113
4.2	IMPORT/EXPORT . . . . .	114
4.3	USE . . . . .	114
4.4	DISPOSAL . . . . .	118

5. POTENTIAL FOR HUMAN EXPOSURE .....	119
5.1 OVERVIEW .....	119
5.2 RELEASES TO THE ENVIRONMENT .....	119
5.2.1 Air .....	121
5.2.2 Water .....	126
5.2.3 Soil .....	126
5.3 ENVIRONMENTAL FATE .....	127
5.3.1 Transport and Partitioning .....	127
5.3.2 Transformation and Degradation .....	128
5.3.2.1 Air .....	128
5.3.2.2 Water .....	129
5.3.2.3 Sediment and Soil .....	130
5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT .....	131
5.4.1 Air .....	131
5.4.2 Water .....	131
5.4.3 Sediment and Soil .....	131
5.4.4 Other Environmental Media .....	131
5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE .....	132
5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES .....	133
5.7 ADEQUACY OF THE DATABASE .....	133
5.7.1 Identification of Data Needs .....	134
5.7.2 On-going Studies .....	136
6. ANALYTICAL METHODS .....	137
6.1 BIOLOGICAL MATERIALS .....	137
6.2 ENVIRONMENTAL SAMPLES .....	138
6.3 ADEQUACY OF THE DATABASE .....	143
6.3.1 Identification of Data Needs .....	143
6.3.2 On-going Studies .....	145
7. REGULATIONS AND ADVISORIES .....	147
8. REFERENCES .....	155
9. GLOSSARY .....	183
APPENDICES	
A. MINIMAL RISK LEVEL WORKSHEETS .....	A-1
B. USER'S GUIDE .....	B-1
C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS .....	C-1



## LIST OF FIGURES

2-1	Levels of Significant Exposure to Hydrazines - Inhalation .....	25
2-2	Levels of Significant Exposure to Hydrazines - Oral .....	48
2-3	Existing Information on Health Effects of Hydrazines .....	99
5-1	Frequency of NPL Sites with Hydrazines Contamination .....	120





**LIST OF TABLES**

2-1	Levels of Significant Exposure to Hydrazines - Inhalation	16
2-2	Levels of Significant Exposure to Hydrazines - Oral	38
2-3	Levels of Significant Exposure to Hydrazines - Dermal	57
2-4	Genotoxicity of Hydrazines <i>In Vivo</i>	85
2-5	Genotoxicity of Hydrazines <i>In Vitro</i>	87
2-6	On-going Studies on the Health Effects of Hydrazines	107
3-1	Chemical Identity of Hydrazines	110
3-2	Physical and Chemical Properties of Hydrazines	111
4-1	Facilities That Manufacture or Process Hydrazine	115
4-2	Facilities That Manufacture or Process 1,1-Dimethylhydrazine	117
5-1	Releases to the Environment from Facilities That Manufacture or Process Hydrazine	122
5-2	Releases to the Environment from Facilities That Manufacture or Process 1,1-Dimethylhydrazine	125
6-1	Analytical Methods for Determining Hydrazines In Biological Materials	139
6-2	Analytical Methods for Determining Hydrazines In Environmental Samples	141
7-1	Regulations and Guidelines Applicable to Hydrazines	148
7-2	Regulations and Guidelines Applicable to 1,1-Dimethylhydrazine	151
7-3	Regulations and Guidelines Applicable to 1,2-Dimethylhydrazine	153

