

**TOXICOLOGICAL PROFILE FOR
2,4,6-TRINITROTOLUENE**

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

June 1995

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 ATSDR and the Environmental Protection Agency (EPA) and in support of Department of Defense information needs. 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 being described. Each profile identifies and reviews the key literature (that has been peer-reviewed) that describes a hazardous substance's toxicologic properties. Other pertinent literature is also 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 public health statement is information concerning levels of significant human exposure and, when 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 significant to protect public health will be identified by ATSDR and the EPA. The focus of the profiles is on health and toxicologic information; therefore, we have included this information in the beginning of the document.

Each profile must include the following:

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

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).

Foreword

This profile reflects our assessment of all relevant toxicologic testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, the Centers for Disease Control and Prevention (CDC), and other federal agencies. 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.



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

CONTRIBUTORS

CHEMICAL MANAGER(S)/AUTHORS(S):

Patricia Richter-Torres, Ph.D.
ATSDR, Division of Toxicology, Atlanta, GA

Alfred Dorsey, D.V.M.
ATSDR, Division of Toxicology, Atlanta, GA

Colette S. Hodes, Ph.D.
Sciences International, Inc., Alexandria, VA

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 endpoints.
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.
4. Quality Assurance Review. The Quality Assurance Branch assures that consistency across profiles is maintained, identifies any significant problems in format or content, and establishes that Guidance has been followed.

PEER REVIEW

A peer review panel was assembled for 2,4,6-trinitrotoluene. The panel consisted of the following members:

1. Dr. Lawrence Martin Holland, Private Consultant, Los Alamos, New Mexico
2. Dr. Thomas McKone, Engineer, Environmental Science Division, Lawrence Livermore National Laboratory, Livermore, California
3. Dr. Ronald Spangord, Director Bio-Analytical Chemistry, Associate Director, Pharmaceutical Analysis Department, SRI International, Menlo Park, California
4. Dr. William George, Professor, Department of Pharmacology, Tulane University, New Orleans, Louisiana

These experts collectively have knowledge of 2,4,6-trinitrotoluene'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 IS 2,4,6-TRINITROTOLUENE?	2
1.2 WHAT HAPPENS TO 2,4,6-TRINITROTOLUENE WHEN IT ENTERS THE ENVIRONMENT?	2
1.3 HOW MIGHT I BE EXPOSED TO 2,4,6-TRINITROTOLUENE?	2
1.4 HOW CAN 2,4,6-TRINITROTOLUENE ENTER AND LEAVE MY BODY?	3
1.5 HOW CAN 2,4,6-TRINITROTOLUENE AFFECT MY HEALTH?	4
1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO 2,4,6-TRINITROTOLUENE?	5
1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?	5
1.8 WHERE CAN I GET MORE INFORMATION?	6
2. HEALTH EFFECTS	7
2.1 INTRODUCTION	7
2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	7
2.2.1 Inhalation Exposure	10
2.2.1.1 Death	10
2.2.1.2 Systemic Effects	10
2.2.1.3 Immunological and Lymphoreticular Effects	14
2.2.1.4 Neurological Effects	14
2.2.1.5 Reproductive Effects	15
2.2.1.6 Developmental Effects	15
2.2.1.7 Genotoxic Effects	15
2.2.1.8 Cancer	17
2.2.2 Oral Exposure	17
2.2.2.1 Death	17
2.2.2.2 Systemic Effects	18
2.2.2.3 Immunological and Lymphoreticular Effects	33
2.2.2.4 Neurological Effects	34
2.2.2.5 Reproductive Effects	35
2.2.2.6 Developmental Effects	35

2.2.2.7	Genotoxic Effects	35
2.2.2.8	Cancer	37
2.2.3	Dermal Exposure	38
2.2.3.1	Death	38
2.2.3.2	Systemic Effects	39
2.2.3.3	Immunological and Lymphoreticular Effects	41
2.2.3.4	Neurological Effects	41
2.2.3.5	Reproductive Effects	41
2.2.3.6	Developmental Effects	42
2.2.3.7	Genotoxic Effects	42
2.2.3.8	Cancer	42
2.3	TOXICOKINETICS	42
2.3.1	Absorption	43
2.3.1.1	Inhalation Exposure	43
2.3.1.2	Oral Exposure	44
2.3.1.3	Dermal Exposure	45
2.3.2	Distribution	46
2.3.2.1	Inhalation Exposure	46
2.3.2.2	Oral Exposure	47
2.3.2.3	Dermal Exposure	47
2.3.3	Metabolism	48
2.3.3.1	Inhalation Exposure	48
2.3.3.2	Oral Exposure	48
2.3.3.3	Dermal Exposure	50
2.3.4	Excretion	51
2.3.4.1	Inhalation Exposure	51
2.3.4.2	Oral Exposure	51
2.3.4.3	Dermal Exposure	52
2.3.5	Mechanisms of Action	52
2.4	RELEVANCE TO PUBLIC HEALTH	53
2.5	BIOMARKERS OF EXPOSURE AND EFFECT	68
2.5.1	Biomarkers Used to Identify or Quantify Exposure to 2,4,6-Trinitrotoluene	69
2.5.2	Biomarkers Used to Characterize Effects Caused by 2,4,6-Trinitrotoluene	70
2.6	INTERACTIONS WITH OTHER CHEMICALS	72
2.7	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	72
2.8	METHODS FOR REDUCING TOXIC EFFECTS	73
2.8.1	Reducing Peak Absorption Following Exposure	74
2.8.2	Reducing Body Burden	74
2.8.3	Interfering with the Mechanism of Action for Toxic Effects	75
2.9	ADEQUACY OF THE DATABASE	76
2.9.1	Existing Information on Health Effects of 2,4,6-Trinitrotoluene	76
2.9.2	Identification of Data Needs	78
2.9.3	On-going Studies	86
3.	CHEMICAL AND PHYSICAL INFORMATION	87
3.1	CHEMICAL IDENTITY	87

3.2	PHYSICAL AND CHEMICAL PROPERTIES	87
4.	PRODUCTION, IMPORT, USE, AND DISPOSAL	91
4.1	PRODUCTION	91
4.2	IMPORT/EXPORT	92
4.3	USE	92
4.4	DISPOSAL	92
5.	POTENTIAL FOR HUMAN EXPOSURE	95
5.1	OVERVIEW	95
5.2	RELEASES TO THE ENVIRONMENT	97
5.2.1	Air	97
5.2.2	Water	97
5.2.3	Soil	98
5.3	ENVIRONMENTAL FATE	98
5.3.1	Transport and Partitioning	98
5.3.2	Transformation and Degradation	100
5.3.2.1	Air	100
5.3.2.2	Water	101
5.3.2.3	Soil	103
5.4	LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	106
5.4.1	Air	106
5.4.2	Water	106
5.4.3	Soil	107
5.4.4	Other Environmental Media	107
5.5	GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	107
5.6	POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	110
5.7	ADEQUACY OF THE DATABASE	110
5.7.1	Identification of Data Needs	110
5.7.2	On-going Studies	113
6.	ANALYTICAL METHODS	115
6.1	BIOLOGICAL MATERIALS	115
6.2	ENVIRONMENTAL SAMPLES	120
6.3	ADEQUACY OF THE DATABASE	130
6.3.1	Identification of Data Needs	130
6.3.2	On-going Studies	131
7.	REGULATIONS AND ADVISORIES	133
8.	REFERENCES	139
9.	GLOSSARY	173

APPENDICES

A. USER'S GUIDE	A-1
B. ACRONYMS, ABBREVIATIONS, AND SYMBOLS	B-1

LIST OF FIGURES

2-1. Levels of Significant Exposure to 2,4,6-Trinitrotoluene - Oral	25
2-2. Schematic Presentation for Some Possible Biotransformation Products of 2,4,6-Trinitrotoluene	49
2-3. Existing Information on Health Effects of 2,4,6-Trinitrotoluene	77
5-1. Frequency of NPL Sites with 2,4,6-Trinitrotoluene Contamination	96

LIST OF TABLES

2-1. Levels of Significant Exposure to 2,4,6-Trinitrotoluene - Oral	19
2-2. Genotoxicity of 2,4,6-Trinitrotoluene <i>In Vitro</i>	65
2-3. Genotoxicity of 2,4,6-Trinitrotoluene <i>In Vivo</i>	66
3-1. Chemical Identity of to 2,4,6-Trinitrotoluene	88
3-2. Physical and Chemical Properties of 2,4,6-Trinitrotoluene	89
6-1. Analytical Methods for Determining 2,4,6-Trinitrotoluene in Biological Samples	116
6-2. Analytical Methods for Determining 2,4,6-Trinitrotoluene in Environmental Samples	121
7-1. Regulations and Guidelines Applicable to 2,4,6-Trinitrotoluene	134

