

**TOXICOLOGICAL PROFILE FOR
DIETHYL PHTHALATE**

**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

A Toxicological Profile for Diethyl Phthalate was released on November 1993. This edition supersedes any previously released draft or final profile.

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):

Malcolm Williams, Ph.D.
ATSDR, Division of Toxicology, Atlanta, GA

Charles Shore, 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 diethyl phthalate. The panel consisted of the following members:

1. Dr. Martin Alexander, Cornell University, Department of Agronomy, Ithaca, NY
2. Dr. Fumio Matsumura, University of California, Davis, CA
3. Dr. John Lech, Medical College of Wisconsin, Department of Pharmacology and Toxicology, Milwaukee, WI

These experts collectively have knowledge of diethyl phthalate'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 DIETHYL PHTHALATE?	2
1.2 WHAT HAPPENS TO DIETHYL PHTHALATE WHEN IT ENTERS THE ENVIRONMENT?	2
1.3 HOW MIGHT I BE EXPOSED TO DIETHYL PHTHALATE?	3
1.4 HOW CAN DIETHYL PHTHALATE ENTER AND LEAVE MY BODY?	4
1.5 HOW CAN DIETHYL PHTHALATE AFFECT MY HEALTH?	4
1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO DIETHYL PHTHALATE?	5
1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?	6
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	8
2.2.1.1 Death	8
2.2.1.2 Systemic Effects	8
2.2.1.3 Immunological and Lymphoreticular Effects	8
2.2.1.4 Neurological Effects	9
2.2.1.5 Reproductive Effects	9
2.2.1.6 Developmental Effects	9
2.2.1.7 Genotoxic Effects	9
2.2.1.8 Cancer	9
2.2.2 Oral Exposure	9
2.2.2.1 Death	9
2.2.2.2 Systemic Effects	9
2.2.2.3 Immunological and Lymphoreticular Effects	19
2.2.2.4 Neurological Effects	19
2.2.2.5 Reproductive Effects	19
2.2.2.6 Developmental Effects	21

2.2.2.7	Genotoxic Effects	22
2.2.2.8	Cancer	22
2.2.3	Dermal Exposure	22
2.2.3.1	Death	22
2.2.3.2	Systemic Effects	22
2.2.3.3	Immunological and Lymphoreticular Effects	29
2.2.3.4	Neurological Effects	30
2.2.3.5	Reproductive Effects	30
2.2.3.6	Developmental Effects	30
2.2.3.7	Genotoxic Effects	30
2.2.3.8	Cancer	31
2.3	TOXICOKINETICS	31
2.3.1	Absorption	31
2.3.1.1	Inhalation Exposure	31
2.3.1.2	Oral Exposure	31
2.3.1.3	Dermal Exposure	32
2.3.2	Distribution	33
2.3.2.1	Inhalation Exposure	33
2.3.2.2	Oral Exposure	33
2.3.2.3	Dermal Exposure	33
2.3.2.4	Other Routes of Exposure	34
2.3.3	Metabolism	34
2.3.4	Excretion	36
2.3.4.1	Inhalation Exposure	36
2.3.4.2	Oral Exposure	36
2.3.4.3	Dermal Exposure	36
2.3.4.4	Other Routes of Exposure	37
2.3.5	Mechanisms of Action	37
2.4	RELEVANCE TO PUBLIC HEALTH	37
2.5	BIOMARKERS OF EXPOSURE AND EFFECT	50
2.5.1	Biomarkers Used to Identify or Quantify Exposure to Diethyl Phthalate	51
2.5.2	Biomarkers Used to Characterize Effects Caused by Diethyl Phthalate	52
2.6	INTERACTIONS WITH OTHER CHEMICALS	52
2.7	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	52
2.8	METHODS FOR REDUCING TOXIC EFFECTS	53
2.8.1	Reducing Peak Absorption Following Exposure	53
2.8.2	Reducing Body Burden	54
2.8.3	Interfering with the Mechanism of Action for Toxic Effects	54
2.9	ADEQUACY OF THE DATABASE	54
2.9.1	Existing Information on Health Effects of Diethyl Phthalate	55
2.9.2	Identification of Data Needs	55
2.9.3	On-going Studies	63
3.	CHEMICAL AND PHYSICAL INFORMATION	65
3.1	CHEMICAL IDENTITY	65
3.2	PHYSICAL AND CHEMICAL PROPERTIES	65

4. PRODUCTION, IMPORT, USE, AND DISPOSAL	69
4.1 PRODUCTION	69
4.2 IMPORT/EXPORT	69
4.3 USE	70
4.4 DISPOSAL	70
5. POTENTIAL FOR HUMAN EXPOSURE	71
5.1 OVERVIEW	71
5.2 RELEASES TO THE ENVIRONMENT	73
5.2.1 Air	73
5.2.2 Water	74
5.2.3 Soil	74
5.3 ENVIRONMENTAL FATE	74
5.3.1 Transport and Partitioning	74
5.3.2 Transformation and Degradation	77
5.3.2.1 Air	77
5.3.2.2 Water	77
5.3.2.3 Soil	80
5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	81
5.4.1 Air	81
5.4.2 Water	81
5.4.3 Soil	84
5.4.4 Other Environmental Media	84
5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	85
5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	87
5.7 ADEQUACY OF THE DATABASE	87
5.7.1 Identification of Data Needs	88
5.7.2 On-going Studies	90
6. ANALYTICAL METHODS	91
6.1 BIOLOGICAL MATERIALS	91
6.2 ENVIRONMENTAL SAMPLES	92
6.3 ADEQUACY OF THE DATABASE	95
6.3.1 Identification of Data Needs	100
6.3.2 On-going Studies	100
7. REGULATIONS AND ADVISORIES	101
8. REFERENCES	105
9. GLOSSARY	127

LIST OF FIGURES

2-1. Levels of Significant Exposure to Diethyl Phthalate - Oral	15
2-2. Existing Information on Health Effects of Diethyl Phthalate	56
5-1. Frequency of NPL Sites with Diethyl Phthalate Contamination	72

LIST OF TABLES

2-1. Levels of Significant Exposure to Diethyl Phthalate - Oral	11
2-2. Levels of Significant Exposure to Diethyl Phthalate - Dermal	23
2-3. Genotoxicity of Diethyl Phthalate <i>In Vitro</i>	48
3-1. Chemical Identity of Diethyl Phthalate	66
3-2. Physical and Chemical Properties of Diethyl Phthalate	67
6-1. Analytical Methods for Determining Diethyl Phthalate in Biological Materials	93
6-2. Analytical Methods for Determining Diethyl Phthalate in Environmental Samples	96
7-1. Regulations and Guidelines Applicable to Diethyl Phthalate	102

