TOXICOLOGICAL PROFILE FOR DI-*n*-OCTYLPHTHALATE

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.

mosch-

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):

Jessilynn B. Taylor, M.S. ATSDR, Division of Toxicology, Atlanta, GA

Patricia M. Bittner, M.S. 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 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 di-*n*-octylphthalate. The panel consisted of the following members:

- 1. Bernard D. Astill, Ph.D., Independent Consultant, Spencerport, New York
- 2. W. Homer Lawrence, Ph.D., Professor, University of Tennessee, Memphis, Tennessee
- 3. David E. Moody, Ph.D., Research Associate Professor, University of Utah, Salt Lake City, Utah

These experts collectively have knowledge of di-*n*-octylphthalate'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.

ix

CONTENTS

FC	REW	ORD			v
CC	ONTR	IBUTO	RS		vii
PE	ER R	EVIEW	,		ix
LI	ST OF	F FIGU	RES		xv
LI	ST OF	F TABL	ES	X	vii
1.	PUB 1.1 1.2	WHA' WHA'	Г IS DI- <i>n</i> Г НАРРЕ	TATEMENT -OCTYLPHTHALATE?	1
	1.3			NT?	
	1.4			-n-OCTYLPHTHALATE ENTER AND LEAVE MY BODY?	
	1.5			-n-OCTYLPHTHALATE AFFECT MY HEALTH?	
	1.6	IS TH	ERE A N	IEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN	
		EXPO	SED TO	DI- <i>n</i> -OCTYLPHTHALATE?	5
	1.7	WHAT	Г RECON	MMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO	
				MAN HEALTH?	
	1.8	WHE	RE CAN	I GET MORE INFORMATION?	5
~	T T T T A		eeroma		-
2.	неа 2.1				7
	2.1 2.2			OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	-
	2.2	2.2.1		on Exposure	
		2.2.1	2.2.1.1	Death	
			2.2.1.1	Systemic Effects	
			2.2.1.2	Immunological and Lymphoreticular Effects	
			2.2.1.3	Neurological Effects	9 9
			2.2.1.4	Reproductive Effects	
			2.2.1.5	Developmental Effects	
			2.2.1.7	Genotoxic Effects	
			2.2.1.8	Cancer	
		2.2.2			10
			2.2.2.1	-	10
			2.2.2.2		10
			2.2.2.3		28
			2.2.2.4	• • • •	30
			2.2.2.5		30
			2.2.2.6		32
			2.2.2.7		33
			2.2.2.8		33
		2.2.3	Dermal		34
			2.2.3.1	Death	34

		2.2.3.2 Systemic Effects	34
			35
		- · · ·	35
		6	35
		1	35
		1	35
			35
	2.3		35
	2.5		36
		1	36
		1	36
		*	30 37
		1	37 37
			37 37
		Ĩ	37 37
		I	
		1	38
			38
			40
		1	40
		1	40
	. /	1	40
	2.4		40
	2.5		41
	2.6		51
			52
			52
	2.7		52
	2.8		52
	2.9		53
		U I U I	53
			54
			54
	2.10	ADEQUACY OF THE DATABASE	54
		2.10.1 Existing Information on Health Effects of Di-n-octylphthalate	55
		2.10.2 Identification of Data Needs	55
		2.10.3 On-going Studies	63
3.	CHE	EMICAL AND PHYSICAL INFORMATION	55
	3.1	CHEMICAL IDENTITY	55
	3.2	PHYSICAL AND CHEMICAL PROPERTIES	55
4.	PRO	DUCTION, IMPORT, USE, AND DISPOSAL	59
	4.1		59
	4.2		73
	4.3		73
	4.4		73
			. 5
5.	POT	ENTIAL FOR HUMAN EXPOSURE	75
~ ·	5.1	OVERVIEW	

	5.2		76 76
			76
			31
	5.3		32
			32
			33
			33 33
			3 <i>3</i> 34
	5.4		34
		5.4.1 Air	35
			35
			36
	~ ~		36
	5.5		36 37
	5.6 5.7		37 37
	5.1		38
			91
(4 NT 4		22
0.	6.1		€ €
	6.2))3
	6.3		99
		5.3.1 Identification of Data Needs 10)0
		5.3.2 On-going Studies)0
7.	REG	LATIONS AND ADVISORIES 10)1
0	רובובו		<u>י</u> ר
8.	KEFI	$RENCES \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots $	כנ
9.	GLO	SARY	15
Ał	PPENI	ICES	
	A. 1	INIMAL RISK LEVEL WORKSHEETS A-	-1
	В. U	SER'S GUIDE B-	-1
	C. A	CRONYMS, ABBREVIATIONS, AND SYMBOLS C-	-1

· •••

LIST OF FIGURES

2-1.	Levels of Significant Exposure to Di-n-octylphthalate - Oral	19
2-2.	Major Metabolic Pathway of Di-n-octylphthalate	39
2-3.	Existing Information on Health Effects of Di-n-octylphthalate	56
5-1.	Frequency of NPL Sites with Di-n-octylphthalate Contamination	77

LIST OF TABLES

2-1.	Levels of Significant Exposure to Di-n-octylphthalate - Oral	11
2-2.	Genotoxicity of Di-n-octylphthalate In Vitro	50
3-1.	Chemical Identity of Di- <i>n</i> -octylphthalate	66
3-2.	Physical and Chemical Properties of Di-n-octylphthalate	67
4-1.	Facilities That Manufacture or Process Di-n-octylphthalate	70
5-1.	Releases to the Environment from Facilities That Manufacture or Process Di- <i>n</i> -octylphthalate	78
6-1.	Analytical Methods for Determining Di-n-octylphthalate in Biological Materials	94
6-2.	Analytical Methods for Determining Di-n-octylphthalate in Environmental Samples	95
7-1.	Regulations and Guidelines Applicable to Di-n-octylphthalate	102