# TOXICOLOGICAL PROFILE FOR 1,1,1-TRICHLOROETHANE

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

1,1,1-TRICHLOROETHANE

# **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.

1,1,1-TRICHLOROETHANE iii

## **UPDATE STATEMENT**

A Toxicological Profile for 1,1,1-Trichloroethane, Draft for Public Comment, was released in September 2004. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry
Division of Toxicology and Environmental Medicine/Applied Toxicology Branch
1600 Clifton Road NE
Mailstop F-32
Atlanta, Georgia 30333

1,1,1-TRICHLOROETHANE iv

## **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.

Julie Louise Gerberding M.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). This public law directed ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. The availability of the revised priority list of 275 hazardous substances was announced in the Federal Register on December 7, 2005 (70 FR 72840). For prior versions of the list of substances, see Federal Register notices dated April 17, 1987 (52 FR 12866); October 20, 1988 (53 FR 41280); October 26, 1989 (54 FR 43619); October 17,1990 (55 FR 42067); October 17, 1991 (56 FR 52166); October 28, 1992 (57 FR 48801); February 28, 1994 (59 FR 9486); April 29, 1996 (61 FR 18744); November 17, 1997 (62 FR 61332); October 21, 1999 (64 FR 56792); October 25, 2001 (66 FR 54014), and November 7, 2003 (68 FR 63098). Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

1,1,1-TRICHLOROETHANE vii

#### QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

## Primary Chapters/Sections of Interest

- **Chapter 1: Public Health Statement:** The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.
- **Chapter 2: Relevance to Public Health**: The Relevance to Public Health Section evaluates, interprets, and assesses the significance of toxicity data to human health.
- **Chapter 3: Health Effects**: Specific health effects of a given hazardous compound are reported by type of health effect (death, systemic, immunologic, reproductive), by route of exposure, and by length of exposure (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.

**NOTE**: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

**Pediatrics**: Four new sections have been added to each Toxicological Profile to address child health issues:

Section 1.6 How Can (Chemical X) Affect Children?

**Section 1.7** How Can Families Reduce the Risk of Exposure to (Chemical X)?

Section 3.7 Children's Susceptibility

Section 6.6 Exposures of Children

#### **Other Sections of Interest:**

Section 3.8 Biomarkers of Exposure and Effect Section 3.11 Methods for Reducing Toxic Effects

#### **ATSDR Information Center**

**Phone:** 1-888-42-ATSDR or (404) 498-0110 **Fax:** (770) 488-4178

The following additional material can be ordered through the ATSDR Information Center:

Case Studies in Environmental Medicine: Taking an Exposure History—The importance of taking an exposure history and how to conduct one are described, and an example of a thorough exposure history is provided. Other case studies of interest include Reproductive and Developmental

1,1,1-TRICHLOROETHANE viii

Hazards; Skin Lesions and Environmental Exposures; Cholinesterase-Inhibiting Pesticide Toxicity; and numerous chemical-specific case studies.

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—

Medical Management Guidelines for Acute Chemical Exposures—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs) provide answers to frequently asked questions about toxic substances.

#### Other Agencies and Organizations

The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015.

The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 • Phone: 800-356-4674 or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 • Phone: 800-35-NIOSH.

The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212.

#### Referrals

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact: AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: AOEC@AOEC.ORG • Web Page: http://www.aoec.org/.

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 25 Northwest Point Boulevard, Suite 700, Elk Grove Village, IL 60007-1030 • Phone: 847-818-1800 • FAX: 847-818-9266.

1,1,1-TRICHLOROETHANE

#### **CONTRIBUTORS**

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

Henry G. Abadin, M.S.P.H.
Daphne B. Moffett, Ph.D.
Alfred F. Dorsey, D.V.M.
ATSDR, Division of Toxicology and Environmental Medicine, Atlanta, GA

David W. Wohlers, Ph.D.
Sari J. Paikoff, Ph.D
Mona Singh, Ph.D.
Syracuse Research Corporation, North Syracuse, NY

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

- 1. 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.
- 2. 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.
- 3. Data Needs Review. The Research Implementation Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.
- 4. Green Border Review. Green Border review assures the consistency with ATSDR policy.

1,1,1-TRICHLOROETHANE x

1,1,1-TRICHLOROETHANE x

#### PEER REVIEW

A peer review panel was assembled for 1,1,1-trichloroethane for the pre-public draft. The panel consisted of the following members:

- 1. Dr. Bhupendra Kaphalia, Associate Professor, Department of Pathology, University of Texas Medical Branch, Galveston Texas;
- 2. Dr. Kannan Krishnan, Professor and Director, Human Toxicology Research Group, University of Montreal, Pierrefonds, PQ, Canada; and
- 3. Dr. Gary Stoner, Professor, Environmental Health Sciences, Ohio State University School of Public Health, Columbus, Ohio.

These experts collectively have knowledge of 1,1,1-trichloroethane'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.

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.

1,1,1-TRICHLOROETHANE xii

# **CONTENTS**

DISCLAI	MER	ii
<b>UPDATE</b>	STATEMENT	iii
	PRD	
QUICK R	EFERENCE FOR HEALTH CARE PROVIDERS	vii
CONTRIE	BUTORS	ix
PEER RE	VIEW	xi
<b>CONTEN</b>	TS	xiii
LIST OF I	FIGURES	xvii
LIST OF	TABLES	xix
	C HEALTH STATEMENT	
1.1	WHAT IS 1,1,1-TRICHLOROETHANE?	I
1.2	WHAT HAPPENS TO 1,1,1-TRICHLOROETHANE WHEN IT ENTERS THE	2
1.0	ENVIRONMENT?	
1.3	HOW MIGHT I BE EXPOSED TO 1,1,1-TRICHLOROETHANE?	
1.4	HOW CAN 1,1,1-TRICHLOROETHANE ENTER AND LEAVE MY BODY?	
1.5	HOW CAN 1,1,1-TRICHLOROETHANE AFFECT MY HEALTH?	
1.6	HOW CAN 1,1,1-TRICHLOROETHANE AFFECT CHILDREN?	6
1.7	HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO	_
1.0	1,1,1-TRICHLOROETHANE?IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSI	0
1.8	TO 1,1,1-TRICHLOROETHANE?	
1.9	WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO	/
1.9	PROTECT HUMAN HEALTH?	7
1.10	WHERE CAN I GET MORE INFORMATION?	
1.10	WHERE CANTOET MORE INFORMATION:	
2 RELEV	VANCE TO PUBLIC HEALTH	11
2.1	BACKGROUND AND ENVIRONMENTAL EXPOSURES TO	
	1,1,1-TRICHLOROETHANE IN THE UNITED STATES	11
2.2	SUMMARY OF HEALTH EFFECTS	
2.3	MINIMAL RISK LEVELS (MRLs)	
	, , , , , , , , , , , , , , , , , , , ,	
3. HEAL	TH EFFECTS	21
3.1	INTRODUCTION	21
3.2	DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	21
3.2.1	Inhalation Exposure	22
3.2	.1.1 Death	22
3.2		
3.2	.1.3 Immunological and Lymphoreticular Effects	69
3.2	.1.4 Neurological Effects	70
3.2	.1.5 Reproductive Effects	75
3.2	.1.6 Developmental Effects	76
3.2	1.7 Cancer	77
3.2.2	Oral Exposure	
3.2		
3.2	· · · · · · · · · · · · · · · · · · ·	
3.2	.2.3 Immunological and Lymphoreticular Effects	95

xiv

3.2.2.4 No	eurological Effects	95
	eproductive Effects	
	evelopmental Effects	
3.2.2.7 Ca	nncer	99
3.2.3 Dermal	Exposure	101
3.2.3.1 De	eath	101
3.2.3.2 Sy	stemic Effects	101
3.2.3.3 Im	nmunological and Lymphoreticular Effects	110
	eurological Effects	
	eproductive Effects	
3.2.3.6 De	evelopmental Effects	112
3.2.3.7 Ca	nncer	112
3.3 GENOTO	XICITY	112
3.4 TOXICOR	KINETICS	117
3.4.1 Absorpt	tion	118
3.4.1.1 În	halation Exposure	118
3.4.1.2 Or	al Exposure	119
	ermal Exposure	
	ıtion	
3.4.2.1 In	halation Exposure	121
	al Exposure	
	ermal Exposure	
	her Routes of Exposure	
	lism	
	tion and Excretion	
	halation Exposure	
	al Exposure	
	ermal Exposure	
	ogically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models	
	IISMS OF ACTION	
3.5.1 Pharma	cokinetic Mechanisms	132
3.5.2 Mechan	isms of Toxicity	134
	-to-Human Extrapolations	
	ES MEDIATED THROUGH THE NEUROENDOCRINE AXIS	
3.7 CHILDRE	EN'S SUSCEPTIBILITY	138
	KERS OF EXPOSURE AND EFFECT	
	kers Used to Identify or Quantify Exposure to 1,1,1-Trichloroethane	141
	kers Used to Characterize Effects Caused by 1,1,1-Trichloroethane	
	TIONS WITH OTHER CHEMICALS	
3.10 POPULAT	TIONS THAT ARE UNUSUALLY SUSCEPTIBLE	145
	S FOR REDUCING TOXIC EFFECTS	
3.11.1 Redu	cing Peak Absorption Following Exposure	147
	cing Body Burden	
	fering with the Mechanism of Action for Toxic Effects	
	CY OF THE DATABASE	
	ing Information on Health Effects of 1,1,1-Trichloroethane	
	ification of Data Needs	
	oing Studies	
	PHYSICAL INFORMATION	
4.1 CHEMICA	AL IDENTITY	163

1,1,1-TRICHLOROETHANE xv

4.2	PHYSICAL AND CHEMICAL PROPERTIES	163
5. PROD	OUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	167
5.1	PRODUCTION	167
5.2	IMPORT/EXPORT	170
5.3	USE	170
5.4	DISPOSAL	171
6. POTE	NTIAL FOR HUMAN EXPOSURE	175
6.1	OVERVIEW	
6.2	RELEASES TO THE ENVIRONMENT	178
6.2.1	Air	178
6.2.2	Water	181
6.2.3	Soil	186
6.3	ENVIRONMENTAL FATE	186
6.3.1		186
6.3.2	Transformation and Degradation	187
6.3	3.2.1 Air	187
6.3	3.2.2 Water	189
6.3	3.2.3 Sediment and Soil	190
6.4	LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	191
6.4.1	Air	191
6.4.2	Water	201
6.4.3	Sediment and Soil	204
6.4.4	Other Environmental Media	204
6.5	GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	210
6.6	EXPOSURES OF CHILDREN	214
6.7	POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	218
6.8	ADEQUACY OF THE DATABASE	219
6.8.1	Identification of Data Needs	219
6.8.2	Ongoing Studies	223
7. ANAI	LYTICAL METHODS	225
7.1	BIOLOGICAL MATERIALS	225
7.2	ENVIRONMENTAL SAMPLES	227
7.3	ADEQUACY OF THE DATABASE	230
7.3.1		
7.3.2		
8. REGU	JLATIONS AND ADVISORIES	233
9. REFE	RENCES	237
10. GLO	SSARY	319

1,1,1-TRICHLOROETHANE xvi

## **APPENDICES**

A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS	SA-:
B. USER'S GUIDE	B-
C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS	
D. INDEX	D-

1,1,1-TRICHLOROETHANE xvii

# **LIST OF FIGURES**

3-1.	Levels of Significant Exposure to 1,1,1-Trichloroethane–Inhalation	51
3-2.	Levels of Significant Exposure to 1,1,1-Trichloroethane–Oral	88
3-3.	Metabolic Scheme for 1,1,1-Trichloroethane	124
3-4.	Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance	130
3-5.	Scatter Diagram Relating Time-Weighted Average of Environmental Concentration and Urinary Concentration of 1,1,1-Trichloroethane in Exposed Workers	
3-6.	Existing Information on Health Effects of 1,1,1-Trichloroethane	151
6-1.	Frequency of NPL Sites with 1.1.1-Trichloroethane Contamination	176

1,1,1-TRICHLOROETHANE xviii

1,1,1-TRICHLOROETHANE xix

# **LIST OF TABLES**

3-1.	Levels of Significant Exposure to 1,1,1-Trichloroethane–Inhalation	25
3-2.	Levels of Significant Exposure to 1,1,1-Trichloroethane–Oral	80
3-3.	Levels of Significant Exposure to 1,1,1-Trichloroethane–Dermal	. 102
3-4.	Genotoxicity of 1,1,1-Trichloroethane <i>In Vivo</i>	. 113
3-5.	Genotoxicity of 1,1,1-Trichloroethane <i>In Vitro</i>	.114
3-6.	Parameters Used in the Physiologically Based Pharmacokinetic Model for 1,1,1-Trichloroethane Developed by Reitz et al. (1988)	
4-1.	Chemical Identity of 1,1,1-Trichloroethane	. 164
4-2.	Physical and Chemical Properties of 1,1,1-Trichloroethane	. 165
5-1.	Facilities that Produce, Process, or Use 1,1,1-Trichloroethane	. 168
5-2.	1,1,1-Trichloroethane in Common Household Products	. 172
6-1.	Releases to the Environment from Facilities that Produce, Process, or Use 1,1,1-Trichloroethane	. 180
6-2.	Detection of 1,1,1-Trichloroethane in Water and Sediments	. 182
6-3.	Detection of 1,1,1-Trichloroethane in Air	. 192
6-4.	Detection of 1,1,1-Trichloroethane in Effluent	. 202
6-5.	Detection of 1,1,1-Trichloroethane in Soils	. 205
6-6.	Detection of 1,1,1-Trichloroethane in Foods	. 206
6-7.	Detection of 1,1,1-Trichloroethane in Human Samples	.211
6-8.	Occupational Air Levels of 1,1,1-Trichloroethane	.215
7-1.	Analytical Methods for Determining 1,1,1-Trichloroethane in Biological Samples	. 226
7-2.	Analytical Methods for Determining 1,1,1-Trichloroethane in Environmental Samples	. 228
8-1.	Regulations and Guidelines Applicable to 1,1,1-Trichloroethane	. 234