TOXICOLOGICAL PROFILE FOR TRICHLOROETHYLENE

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

September 1997

TRICHLOROETHYLENE

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.

TRICHLOROETHYLENE ii

UPDATE STATEMENT

An update Toxicological Profile for Trichloroethylene was released in April 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 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

The toxicological profiles are developed in response to the Super-fund 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 April 29, 1996 (61 FR 18744). 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); and February 28, 1994 (59 FR 9486). Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

TRICHLOROETHYLENE vii

CONTRIBUTORS

CHEMICAL MANAGER(S)/AUTHOR(S):

Mildred Williams-Johnson, Ph.D., D.A.B.T. ATSDR, Division of Toxicology, Atlanta, GA

Carol J. Eisenmann, Ph.D. Sciences International, Inc., Alexandria, VA

Steven G. Donkin, Ph.D. Sciences International, Inc., Alexandria, VA

The Chemical Manager and Authors acknowledge the contribution of Dr. Ted W. Simon, U.S. EPA, in applying physiologically-based pharmacokinetic modeling to the development of minimal risk levels for trichloroethylene.

THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

- 1. Green Border Review. Green Border review assures 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.

TRICHLOROETHYLENE ix

PEER REVIEW

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

- 1. Herbert Cornish, Ph.D., Private Consultant, Ypsilanti, MI
- 2. James Klaunig, Ph.D., Indiana University School of Medicine, Indianapolis, IN
- 3. Norbert Page, Ph.D., Private Consultant, Gaithersburg, MD

These experts collectively have knowledge of trichloroethylene's physical and chemical properties, toxico-kinetics, 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.

FOREW	ORD			v
CONTR	IBUTOF	RS		vii
PEER R	EVIEW			ix
LIST OF	FIGUR	ES		хv
LIST OF	TABLE	ES	X	vii
1. PUBI			ATEMENT	
1.1			CHLOROETHYLENE?	1
1.2			NS TO TRICHLOROETHYLENE WHEN IT ENTERS THE	
			TT?	
1.3			BE EXPOSED TO TRICHLOROETHYLENE?	
1.4			CHLOROETHYLENE ENTER AND LEAVE MY BODY?	
1.5			CHLOROETHYLENE AFFECT MY HEALTH?	4
1.6			EDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED	
			OETHYLENE?	6
1.7			IMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO	
			MAN HEALTH?	
1.8	WHER	E CAN I	GET MORE INFORMATION?	7
2. HEA	LTH EF	FECTS .		9
2.1			ON	
2.2			OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	
	2.2.1		on Exposure	
		2.2.1.1	Death	
		2.2.1.2	Systemic Effects	
		2.2.1.3	Immunological and Lymphoreticular Effects	
		2.2.1.4	Neurological Effects	
		2.2.1.5	Reproductive Effects	
		2.2.1.6	Developmental Effects	
		2.2.1.7	Genotoxic Effects	
		2.2.1.8	Cancer	
	2.2.2	Oral Ex	posure	49
		2.2.2.1	Death	
		2.2.2.2	Systemic Effects	
		2.2.2.3	Immunological and Lymphoreticular Effects	80
		2.2.2.4	Neurological Effects	
		2.2.2.5	Reproductive Effects	
		2.2.2.6	Developmental Effects	
		2.2.2.7	Genotoxic Effects	
		2.2.2.8	Cancer	

	2.2.3	Dermal 1	Exposure	93
		2.2.3.1	Death	93
		2.2.3.2	Systemic Effects	94
		2.2.3.3	Immunological and Lymphoreticular Effects	95
		2.2.3.4	Neurological Effects	95
		2.2.3.5	Reproductive Effects	96
		2.2.3.6	Developmental Effects	96
		2.2.3.7	Genotoxic Effects	96
		2.2.3.8	Cancer	96
2.3	TOXIC	COKINET	TCS	96
	2.3.1	Absorpti	on	97
		2.3.1.1	Inhalation Exposure	97
		2.3.1.2	Oral Exposure	98
		2.3.1.3	Dermal Exposure	
	2.3.2	Distribut	ion	. 100
		2.3.2.1	Inhalation Exposure	. 101
		2.3.2.2	Oral Exposure	. 102
		2.3.2.3	Dermal Exposure	. 102
	2.3.3	Metabol	ism	. 102
	2.3.4	Eliminat	ion and Excretion	. 108
		2.3.4.1	Inhalation Exposure	. 108
		2.3.4.2	Oral Exposure	. 109
		2.3.4.3	Dermal Exposure	
	2.3.5	Physiolo	gically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models	. 110
2.4	MECH	IANISMS	OF ACTION	. 118
	2.4.1	Pharmac	okinetic Mechanisms	. 118
	2.4.2	Mechani	sms of Toxicity	. 120
	2.4.3	Animal-	to-Human Extrapolations	. 125
2.5			O PUBLIC HEALTH	
2.6	BIOM	ARKERS	OF EXPOSURE AND EFFECT	. 153
	2.6.1	Biomark	ers Used to Identify or Quantify Exposure to Trichloroethylene	. 154
	2.6.2	Biomark	ers Used to Characterize Effects Caused by Trichloroethylene	. 157
2.7	INTER	ACTION	S WITH OTHER SUBSTANCES	. 158
2.8			S THAT ARE UNUSUALLY SUSCEPTIBLE	. 161
2.9	METH		R REDUCING TOXIC EFFECTS	. 102
	2.9.1	Reducing	g Peak Absorption Following Exposure	. 162
	2.9.2		g Body Burden	
	2.9.3	Interferi	ng with the Mechanism of Action for Toxic Effects	. 164
2.10			F THE DATABASE	
			Information on Health Effects of Trichloroethylene	
	2.10.2	Identific	ation of Data Needs	. 167
	2.10.3	On-goin	g Studies	. 179
3 CHEN	ЛСΔΙ	AND PE	YSICAL INFORMATION	191
3.1			ENTITY	
3.1			D CHEMICAL PROPERTIES	
ع.د	111101	CUL III	D CHEMICALI MOLLMILD	. 101

TRICHLOROETHYLENE

4.		DUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	
	4.1	PRODUCTION	
	4.2	IMPORT/EXPORT	
	4.3	USE	
	4.4	DISPOSAL	189
5.	POTE	INTIAL FOR HUMAN EXPOSURE	191
	5.1	OVERVIEW	
	5.2	RELEASES TO THE ENVIRONMENT	193
		5.2.1 Air	193
		5.2.2 Water	
		5.2.3 Soil	
	5.3	ENVIRONMENTAL FATE	
		5.3.1 Transport and Partitioning	
		5.3.2 Transformation and Degradation	
		5.3.2.1 Air	
		5.3.2.2 Water	
		5.3.2.3 Sediment and Soil	
	5.4	LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	
		5.4.1 Air	
		5.4.2 Water	
		5.4.3 Sediment and Soil	
		5.4.4 Other Environmental Media	
	5.5	GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	
	5.6	POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	
	5.7	ADEQUACY OF THE DATABASE	
		5.7.1 Identification of Data Needs	
		5.7.2 On-going Studies	
6	ANAI	LYTICAL METHODS	219
•	6.1	BIOLOGICAL MATERIALS	
	6.2	ENVIRONMENTAL SAMPLES	
	6.3	ADEQUACY OF THE DATABASE	
	0.5	6.3.1 Identification of Data Needs	
		6.3.2 On-going Studies	
		0.3.2 On-going studies	232
7.	REGU	JLATIONS AND ADVISORIES	233
8.	REFE	RENCES	241
0	വ റ	SSARV	205

TRICHLOROETHYLENE

APPENDICES

A. MINIMAL RISK LEVEL	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 Trichloroethylene - Inhalation	. 24
2-2	Levels of Significant Exposure to Trichloroethylene - Oral	. 68
2-3	Metabolic Pathways of Trichloroethylene	104
2-4	Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance	112
2-5	Existing Information on Health Effects of Trichloroethylene	166
5-1	Frequency of NPL Sites with Trichloroethylene Contamination	192

**					•
		•			
	•				
		•			
				~	

LIST OF TABLES

2-1	Levels of Significant Exposure to Trichloroethylene - Inhalation
2-2	Levels of Significant Exposure to Trichloroethylene - Oral
2-3	Parameters Used in Two Human PBPK Models
2-4	Genotoxicity of Trichloroethylene In Vivo
2-5	Genotoxicity of Trichloroethylene In Vitro
3-1	Chemical Identity of Trichloroethylene
3-2	Physical and Chemical Properties of Trichloroethylene
4-1	Facilities That Manufacture or Process Trichloroethylene
5-1	Releases to the Environment from Facilities That Manufacture or Process Trichloroethylene 194
6-1	Analytical Methods for Determining Trichloroethylene in Biological Materials
6-2	Analytical Methods for Determining Trichloroethylene in Environmental Samples
7-1	Regulations and Guidelines Applicable to Trichloroethylene