

Toxicological Profile for 1,2,3-Trichloropropane

August 2021



1,2,3-TRICHLOROPROPANE

DISCLAIMER

Use of trade names is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry, the Public Health Service, or the U.S. Department of Health and Human Services.

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 these toxic substances described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a 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 relevance to public health discussion which would allow a public health professional to make a real-time determination of whether the presence of a particular substance in the environment poses a potential threat to human health. 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 the protection of public health are identified by ATSDR.

Each profile includes the following:

- (A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a toxic substance to ascertain the levels of significant human exposure for the substance due to associated acute, intermediate, and chronic exposures;
- (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, intermediate, 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. Staffs 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.

Patrick N. Breysse, Ph.D., CIH

atich Mergs

Director, National Center for Environmental Health and Agency for Toxic Substances and Disease Registry Centers for Disease Control and Prevention Christopher M. Reh, Ph.D. Associate Director

Agency for Toxic Substances and Disease Registry Centers for Disease Control and Prevention 1,2,3-TRICHLOROPROPANE

*Legislative Background

The toxicological profiles are developed under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended (CERCLA or Superfund). CERCLA section 104(i)(1) directs the Administrator of ATSDR to "...effectuate and implement the health related authorities" of the statute. This includes the preparation of toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL) and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. In addition, ATSDR has the authority to prepare toxicological profiles for substances not found at sites on the NPL, in an effort to "...establish and maintain inventory of literature, research, and studies on the health effects of toxic substances" under CERCLA Section 104(i)(1)(B), to respond to requests for consultation under section 104(i)(4), and as otherwise necessary to support the site-specific response actions conducted by ATSDR.

1,2,3-TRICHLOROPROPANE

VERSION HISTORY

Date	Description
August 2021	Final toxicological profile released
May 2019	Draft for public comment toxicological profile released
August 2011	Addendum to the toxicological profile released
September 1992	Draft for public comment toxicological profile released

1,2,3-TRICHLOROPROPANE v

CONTRIBUTORS & REVIEWERS

CHEMICAL MANAGER TEAM

Malcolm Williams, D.V.M., Ph.D. Lisa Ingerman, Ph.D., DABT

Jenny S. Crisman, B.S. Laura McIlroy, B.A.

ATSDR, Office of Innovation and Analytics, Toxicology Section, Atlanta, GA

SRC, Inc., North Syracuse, NY

REVIEWERS

Interagency Minimal Risk Level Workgroup:

Includes ATSDR; National Center for Environmental Health (NCEH); National Institute for Occupational Safety and Health (NIOSH); U.S. Environmental Protection Agency (EPA); National Toxicology Program (NTP).

Additional reviews for science and/or policy:

ATSDR, Office of Community Health and Hazard Assessment; ATSDR, Office of Capacity Development and Applied Prevention Science; ATSDR, Office of Science; NCEH, Division of Laboratory Science; NCEH, Division of Environmental Health Science and Practice; EPA, National Center for Environmental Assessment.

PEER REVIEWERS

- 1. Ghulam Ahmad Shakeel Ansari, Ph.D., The University of Texas Medical Branch at Galveston, Galveston, Texas
- 2. Dale Hattis, Ph.D., Research Professor, George Perkins Marsh Institute, Clark University, Worcester, Massachusetts
- 3. Helmut Zarbl, Ph.D., Professor in the Rutgers School of Public Health, Department of Environmental & Occupational Health, Director of the National Institute of Environmental Health Sciences (NIEHS), Piscataway, New Jersey

These experts collectively have knowledge of toxicology, chemistry, and/or health effects. All reviewers were selected in conformity with Section 104(I)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

ATSDR scientists review peer reviewers' comments and determine whether changes will be made to the profile based on comments. The peer reviewers' comments and responses to these comments are part of the administrative record for this compound.

The listing of peer reviewers should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with ATSDR.

CONTENTS

DISCL	AIMER	ii
FOREV	WORD	iii
VERSI	ON HISTORY	v
CONTI	RIBUTORS & REVIEWERS	vi
CONTI	ENTS	vii
LIST O	OF FIGURES	ix
LIST O	OF TABLES	X
CHAPT	FER 1. RELEVANCE TO PUBLIC HEALTH	
1.1	OVERVIEW AND U.S. EXPOSURES	1
1.2	SUMMARY OF HEALTH EFFECTS	1
1.3	MINIMAL RISK LEVELS (MRLs)	5
CHAPT	TER 2. HEALTH EFFECTS	8
2.1	INTRODUCTION	8
2.2	DEATH	36
2.3	BODY WEIGHT	37
2.4	RESPIRATORY	37
2.5	CARDIOVASCULAR	38
2.6	GASTROINTESTINAL	38
2.7	HEMATOLOGICAL	39
2.8	MUSCULOSKELETAL	40
2.9	HEPATIC	40
2.10	RENAL	41
2.11	DERMAL	42
2.12	OCULAR	42
	ENDOCRINE	
	IMMUNOLOGICAL	
	NEUROLOGICAL	
	REPRODUCTIVE	
	DEVELOPMENTAL	
	OTHER NONCANCER	
	CANCER	
2.20	GENOTOXICITY	47
CHAPT	TER 3. TOXICOKINETICS, SUSCEPTIBLE POPULATIONS, BIOMARKERS, CHEMICA	
	INTERACTIONS	
3.1	TOXICOKINETICS	
	1.1 Absorption	
	1.2 Distribution	
	1.3 Metabolism	
	.4 Excretion	
	.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models	
	1.6 Animal-to-Human Extrapolations	55
3.2	CHILDREN AND OTHER POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	
3.3	BIOMARKERS OF EXPOSURE AND EFFECT	
	3.1 Biomarkers of Exposure	
	3.2 Biomarkers of Effect	
3 4	UNIEKACIUNS WITH OTHEK CHEMICALS	58

CHAPTER 4. CHEMICAL AND PHYSICAL INFORMATION	59
4.1 CHEMICAL IDENTITY	59
4.2 PHYSICAL AND CHEMICAL PROPERTIES	59
CHAPTER 5. POTENTIAL FOR HUMAN EXPOSURE	61
5.1 OVERVIEW	
5.2 PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	62
5.2.1 Production	62
5.2.2 Import/Export	62
5.2.3 Use	63
5.2.4 Disposal	
5.3 RELEASES TO THE ENVIRONMENT	63
5.3.1 Air	64
5.3.2 Water	65
5.3.3 Soil	
5.4 ENVIRONMENTAL FATE	66
5.4.1 Transport and Partitioning	66
5.4.2 Transformation and Degradation	67
5.5 LEVELS IN THE ENVIRONMENT	68
5.5.1 Air	69
5.5.2 Water	70
5.5.3 Sediment and Soil	70
5.5.4 Other Media	
5.6 GENERAL POPULATION EXPOSURE	
5.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	72
CHAPTER 6. ADEQUACY OF THE DATABASE	73
6.1 Information on Health Effects	73
6.2 Identification of Data Needs	73
6.3 Ongoing Studies	80
CHAPTER 7. REGULATIONS AND GUIDELINES	81
CHAPTER 8. REFERENCES	83
APPENDICES	
APPENDIX A. ATSDR MINIMAL RISK LEVEL WORKSHEETS	
APPENDIX B. LITERATURE SEARCH FRAMEWORK FOR 1,2,3-TRICHLOROPROPANE	
APPENDIX C. USER'S GUIDE	
APPENDIX D. QUICK REFERENCE FOR HEALTH CARE PROVIDERS	
APPENDIX E. GLOSSARY	
APPENDIX E ACRONYMS ARREVIATIONS AND SYMBOLS	F. 1

1,2,3-TRICHLOROPROPANE b

LIST OF FIGURES

1-1.	Health Effects Found in Animals Following Inhalation Exposure to 1,2,3-Trichloropropane	2
1-2.	Health Effects Found in Animals Following Oral Exposure to 1,2,3-Trichloropropane	3
1-3.	Summary of Sensitive Targets of 1,2,3-Trichloropropane – Inhalation	5
1-4.	Summary of Sensitive Targets of 1,2,3-Trichloropropane – Oral	6
2-1.	Overview of the Number of Studies Examining 1,2,3-Trichloropropane Health Effects	11
2-2.	Levels of Significant Exposure to 1,2,3-Trichloropropane – Inhalation	16
2-3.	Levels of Significant Exposure to 1,2,3-Trichloropropane – Oral	29
3-1.	Possible Metabolic Pathways for the Formation of ACPC, CPC, and GMA from 1,2,3-Trichloropropane	53
5-1.	Number of NPL Sites with 1,2,3-Trichloropropane Contamination	61
6-1.	Summary of Existing Health Effects Studies on 1,2,3-Trichloropropane By Route and Endpoint	74

1,2,3-TRICHLOROPROPANE x

LIST OF TABLES

1-1.	Minimal Risk Levels (MRLs) for 1,2,3-Trichloropropane	7
2-1.	Levels of Significant Exposure to 1,2,3-Trichloropropane – Inhalation	12
2-2.	Levels of Significant Exposure to 1,2,3-Trichloropropane – Oral	20
2-3.	Levels of Significant Exposure to 1,2,3-Trichloropropane – Dermal	34
2-4.	Possible Associations Between Maternal Residential Proximity to 1,2,3-Trichloropropane Air Emissions and Birth Defects	46
2-5.	Genotoxicity of 1,2,3-Trichloropropane In Vitro	48
2-6.	Genotoxicity of 1,2,3-Trichloropropane In Vivo	49
4-1.	Chemical Identity of 1,2,3-Trichloropropane	59
4-2.	Physical and Chemical Properties of 1,2,3-Trichloropropane	60
5-1.	Facilities that Produce, Process, or Use 1,2,3-Trichloropropane	62
5-2.	Releases to the Environment from Facilities that Produce, Process, or Use 1,2,3-Trichloro-propane	64
5-3.	Lowest Limit of Detection Based on Standards	68
5-4.	1,2,3-Trichloropropane Levels in Water, Soil, and Air of National Priorities List (NPL) Sites	69
7-1.	Regulations and Guidelines Applicable to 1,2,3-Trichloropropane	81