

Toxicological Profile for 1-Bromopropane

August 2017



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.

UPDATE STATEMENT

A Toxicological Profile for 1-Bromopropane, Draft for Public Comment was released in January 2016. 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 Human Health Sciences Environmental Toxicology Branch 1600 Clifton Road NE Mailstop F-57 Atlanta, Georgia 30329-4027

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 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 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 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. 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.

Jahole Bragne

Patrick N. Breysse, Ph.D., CIH Director, National Center for Environmental Health and Agency for Toxic Substances and Disease Registry Centers for Disease Control and Prevention

*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 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 National Priorities List, 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.

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 may 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 (e.g., 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:

Chapter 1	How Can (Chemical X) Affect Children?
Chapter 1	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 3.8Biomarkers of Exposure and EffectSection 3.11Methods for Reducing Toxic Effects

ATSDR Information Center

Phone: 1-800-CDC-INFO (800-232-4636) or 1-888-232-6348 (TTY) *Internet*: http://www.atsdr.cdc.gov

The following additional materials are available online:

Case Studies in Environmental Medicine are self-instructional publications designed to increase primary health care providers' knowledge of a hazardous substance in the environment and to aid in the evaluation of potentially exposed patients (see https://www.atsdr.cdc.gov/csem/csem.html).

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 (see https://www.atsdr.cdc.gov/MHMI/index.asp). 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*TM) provide answers to frequently asked questions about toxic substances (see https://www.atsdr.cdc.gov/toxfaqs/Index.asp).

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 • Web Page: https://www.cdc.gov/nceh/.
- *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, 395 E Street, S.W., Suite 9200, Patriots Plaza Building, Washington, DC 20201 Phone: 202-245-0625 or 1-800-CDC-INFO (800-232-4636) Web Page: https://www.cdc.gov/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 Web Page: https://www.niehs.nih.gov/.

Clinical Resources (Publicly Available Information)

- 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 • Web Page: http://www.acoem.org/.
- *The American College of Medical Toxicology* (ACMT) is a nonprofit association of physicians with recognized expertise in medical toxicology. Contact: ACMT, 10645 North Tatum Boulevard,

Suite 200-111, Phoenix AZ 85028 • Phone: 844-226-8333 • FAX: 844-226-8333 • Web Page: http://www.acmt.net.

- *The Pediatric Environmental Health Specialty Units* (PEHSUs) is an interconnected system of specialists who respond to questions from public health professionals, clinicians, policy makers, and the public about the impact of environmental factors on the health of children and reproductive-aged adults. Contact information for regional centers can be found at http://pehsu.net/findhelp.html.
- *The American Association of Poison Control Centers* (AAPCC) provide support on the prevention and treatment of poison exposures. Contact: AAPCC, 515 King Street, Suite 510, Alexandria VA 22314 Phone: 701-894-1858 Poison Help Line: 1-800-222-1222 Web Page: http://www.aapcc.org/.

CONTRIBUTORS

CHEMICAL MANAGER(S)/AUTHOR(S):

Nickolette Roney, M.P.H. Melanie Buser, M.P.H. Susan Zells Ingber, A.B., M.S.P.P. ATSDR, Division of Toxicology and Human Health Sciences, Atlanta, GA

Fernando Llados, Ph.D. Peter McClure, Ph.D., D.A.B.T. Kimberly Zaccaria, Ph.D. Courtney Hard, B.A. SRC, Inc., 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 Environmental Toxicology 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.

PEER REVIEW

A peer review panel was assembled for 1-bromopropane. The panel consisted of the following members:

- 1. Xiaozhong (John) Yu MD, Ph.D., Department of Environmental Health Science, College of Public Health, University of Georgia, Athens, Georgia;
- 2. James V. Bruckner, Ph.D., Professor of Pharmacology and Toxicology, Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, University of Georgia, Athens, Georgia; and
- 3. Gaku Ichihara, M.D., Ph.D., Department of Occupational and Environmental Health Faculty of Pharmaceutical Sciences, Tokyo University of Science, Japan.

These experts collectively have knowledge of 1-bromopropane'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.

CONTENTS

DISCLAIM	ER	ii
UPDATE S	TATEMENT	iii
FOREWOR	D	v
QUICK RE	FERENCE FOR HEALTH CARE PROVIDERS	vii
CONTRIBU	JTORS	xi
PEER REV	IEW	xiii
CONTENT	S	xv
LIST OF FI	GURES	xix
LIST OF TA	ABLES	xxi
1. PUBLIC	HEALTH STATEMENT FOR 1-BROMOPROPANE	1
	ANCE TO PUBLIC HEALTH	
	ACKGROUND AND ENVIRONMENTAL EXPOSURES TO 1-BROMOPROPANE I	
	IE UNITED STATES	
	MMARY OF HEALTH EFFECTS	
2.3 MI	NIMAL RISK LEVELS (MRLs)	10
	H EFFECTS	
	TRODUCTION	
	SCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	
3.2.1	Inhalation Exposure	
3.2.1		
3.2.1		
3.2.1		
3.2.1	0	
3.2.1	1 A A A A A A A A A A A A A A A A A A A	
3.2.1	L Contraction of the second seco	
3.2.1		
3.2.2	Oral Exposure	
3.2.2		
3.2.2		
3.2.2		
3.2.2		
3.2.2		
3.2.2	1 I	
3.2.2		
3.2.3	Dermal Exposure	
	DXICOKINETICS	
3.4.1	Absorption	
3.4.2	Distribution	
3.4.3	Metabolism	
3.4.4	Elimination and Excretion.	
3.4.5	Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models	
	ECHANISMS OF ACTION	
3.5.1	Pharmacokinetic Mechanisms	
3.5.2	Mechanisms of Toxicity	
3.5.3	Animal-to-Human Extrapolations	109

	OXICITIES MEDIATED THROUGH THE NEUROENDOCRINE AXIS	
	HILDREN'S SUSCEPTIBILITY	
3.8 B	IOMARKERS OF EXPOSURE AND EFFECT	
3.8.1	Biomarkers Used to Identify or Quantify Exposure to 1-Bromopropane	
3.8.2	Biomarkers Used to Characterize Effects Caused by 1-Bromopropane	117
	TERACTIONS WITH OTHER CHEMICALS	
3.10 PC	OPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	118
3.11 M	ETHODS FOR REDUCING TOXIC EFFECTS	119
3.11.1	Reducing Peak Absorption Following Exposure	
3.11.2		
3.11.3		
	DEQUACY OF THE DATABASE	
3.12.1	Existing Information on Health Effects of 1-Bromopropane	
3.12.2		
3.12.3	Ongoing Studies	
	CAL AND PHYSICAL INFORMATION	
	HEMICAL IDENTITY	
4.2 PI	HYSICAL AND CHEMICAL PROPERTIES	133
		105
	JCTION, IMPORT/EXPORT, USE, AND DISPOSAL	
	RODUCTION	
	APORT/EXPORT	
	SE	
5.4 D	ISPOSAL	139
6 POTEN	TIAL FOR HUMAN EXPOSURE	141
	VERVIEW	
	ELEASES TO THE ENVIRONMENT	
6.2.1	Air	
6.2.2	Water	
6.2.3	Soil	
	NVIRONMENTAL FATE	
6.3.1	Transport and Partitioning	
6.3.2	Transformation and Degradation	
	2.1 Air	
6.3.2		
6.3.2		
6.3.2		
	EVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	
6.4.1	Air	
6.4.2	Water	
6.4.3	Sediment and Soil	
6.4.4	Other Environmental Media	
	ENERAL POPULATION AND OCCUPATIONAL EXPOSURE	
	XPOSURES OF CHILDREN	
	OPULATIONS WITH POTENTIALLY HIGH EXPOSURES	
	DEQUACY OF THE DATABASE	
0.8 A 6.8.1	Identification of Data Needs	
6.8.1 6.8.2	Ongoing Studies	
0.0.2		

7. ANALYTICAL METHODS	
7.1 BIOLOGICAL MATERIALS	
7.2 ENVIRONMENTAL SAMPLES	
7.3 ADEQUACY OF THE DATABASE	
7.3.1 Identification of Data Needs	
7.3.2 Ongoing Studies	
8. REGULATIONS, ADVISORIES, AND GUIDELINES	
9. REFERENCES	167
10. GLOSSARY	
APPENDICES	
A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS	A-1
B. USER'S GUIDE	B-1
C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS	C-1

LIST OF FIGURES

3-1.	Levels of Significant Exposure to 1-Bromopropane – Inhalation	.46
3-2.	Levels of Significant Exposure to 1-Bromopropane – Oral	. 81
3-3.	Formation of N-Acetyl-S-(n-propyl)-L-cysteine from 1-Bromopropane via Conjugation with Reduced Glutathione (GSH)	.92
3-4.	Mercapturic Acid Metabolites with a Sulfoxide Group or a Hydroxyl or Carbonyl Group on the Propyl Residue Identified in Urine Samples of 1-Bromopropane-Exposed Workers	.93
3-5.	1-Bromopropane Metabolism in Male F-344 Rats and B6C3F1 Mice Following Inhalation Exposure or Tail Vein Injection	.94
3-6.	Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance	01
3-7.	Existing Information on Health Effects of 1-Bromopropane	22

LIST OF TABLES

3-1.	Levels of Significant Exposure to 1-Bromopropane – Inhalation	20
3-2.	Levels of Significant Exposure to 1-Bromopropane – Oral	79
3-3.	Genotoxicity of 1-Bromopropane In Vivo	86
3-4.	Genotoxicity of 1-Bromopropane In Vitro	87
4-1.	Chemical Identity of 1-Bromopropane1	34
4-2.	Physical and Chemical Properties of 1-Bromopropane1	35
7-1.	Analytical Methods for Determining 1-Bromopropane in Biological Samples	56
7-2.	Analytical Methods for Determining 1-Bromopropane in Environmental Samples1	58
8-1.	Regulations, Advisories, and Guidelines Applicable to 1-Bromopropane	63