TOXICOLOGICAL PROFILE FOR
DICHLOROPROPENES

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

September 2008
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

A Toxicological Profile for 1,3-Dichloropropene, Draft for Public Comment, was released in 2006. 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
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.

Howard Frumkin M.D., Dr.P.H.  
Director  
National Center for Environmental Health/  
Agency for Toxic Substances and Disease Registry

Julie Louise Gerberding, M.D., M.P.H.  
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.
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: 1-800-CDC-INFO (800-232-4636) or Fax: (770) 488-4178
E-mail: cdcinfo@cdc.gov
Internet: http://www.atsdr.cdc.gov

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
**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.
CONTRIBUTORS

CHEMICAL MANAGER(S)/AUTHOR(S):

Annette Ashizawa, Ph.D.
Sharon Wilbur, M.A.
Heraline Hicks, Ph.D.
ATSDR, Division of Toxicology and Environmental Medicine, Atlanta, GA

Julie M. Klotzbach, Ph.D.
Daniel J. Plewak, B.S.
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 Applied Toxicology Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

This page is intentionally blank.
PEER REVIEW

A peer review panel was assembled in 2006 for dichloropropenes. The panel consisted of the following members:

1. Dr. Mary Davis, Professor, Department of Physiology and Pharmacology, West Virginia University Medical Center, Morgantown, West Virginia;

2. Dr. Rogene Henderson, Senior Scientist (retired), Lovelace Respiratory Research Institute, Albuquerque, New Mexico; and

3. Dr. Lisa M. Kamendulis, Assistant Professor, Department of Pharmacology and Toxicology, Indiana University School of Medicine, Indianapolis, Indiana.

These experts collectively have knowledge of 1,3-dichloropropene'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.
This page is intentionally blank.
## CONTENTS

- DISCLAIMER ............................................................................................................................... ii
- UPDATE STATEMENT ..................................................................................................................... iii
- FOREWORD ....................................................................................................................................... v
- QUICK REFERENCE FOR HEALTH CARE PROVIDERS .................................................................. vii
- CONTRIBUTORS ................................................................................................................................. ix
- PEER REVIEW .................................................................................................................................... xi
- CONTENTS .......................................................................................................................................... xiii
- LIST OF FIGURES ............................................................................................................................. xvii
- LIST OF TABLES ............................................................................................................................... xix

### 1. PUBLIC HEALTH STATEMENT

1.1 WHAT ARE DICHLOROPROPENES? ............................................................................................. 1
1.2 WHAT HAPPENS TO DICHLOROPROPENES WHEN THEY ENTER THE ENVIRONMENT? ........ 1
1.3 HOW MIGHT I BE EXPOSED TO DICHLOROPROPENES? ......................................................... 2
1.4 HOW CAN DICHLOROPROPENES ENTER AND LEAVE MY BODY? ....................................... 2
1.5 HOW CAN DICHLOROPROPENES AFFECT MY HEALTH? ....................................................... 3
1.6 HOW CAN DICHLOROPROPENES AFFECT CHILDREN? .......................................................... 4
1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO DICHLOROPROPENES? ............ 4
1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO DICHLOROPROPENES? ............................................................................................................. 5
1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH? ......................................................................................................................... 5
1.10 WHERE CAN I GET MORE INFORMATION? ........................................................................... 6

### 2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO DICHLOROPROPENES IN THE UNITED STATES ................................................................................................................................. 7
2.2 SUMMARY OF HEALTH EFFECTS ........................................................................................ 8
2.3 MINIMAL RISK LEVELS (MRLs) ............................................................................................. 15

### 3. HEALTH EFFECTS

3.1 INTRODUCTION ......................................................................................................................... 33
3.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE ........................................... 35
3.2.1 Inhalation Exposure ................................................................................................................. 36
3.2.1.1 Death .................................................................................................................................. 60
3.2.1.2 Systemic Effects .................................................................................................................. 61
3.2.1.3 Immunological and Lymphoreticular Effects ..................................................................... 70
3.2.1.4 Neurological Effects ........................................................................................................... 71
3.2.1.5 Reproductive Effects .......................................................................................................... 72
3.2.1.6 Developmental Effects ...................................................................................................... 73
3.2.1.7 Cancer .............................................................................................................................. 73
3.2.2 Oral Exposure ......................................................................................................................... 74
3.2.2.1 Death .................................................................................................................................. 75
3.2.2.2 Systemic Effects .................................................................................................................. 97
3.2.2.3 Immunological and Lymphoreticular Effects ..................................................................... 104
APPENDICES

A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS ............................................................. A-1
B. USER’S GUIDE.......................................................................................................................... B-1
C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS................................................................. C-1
D. INDEX ........................................................................................................................................ D-1
LIST OF FIGURES

3-1. Levels of Significant Exposure to 1,3-Dichloropropene – Inhalation .................................................. 48
3-2. Levels of Significant Exposure to 2,3-Dichloropropene – Inhalation .................................................. 58
3-3. Levels of Significant Exposure to 1,3-Dichloropropene – Oral .............................................................. 91
3-4. Levels of Significant Exposure to 2,3-Dichloropropene – Oral .............................................................. 96
3-5. Proposed Metabolic Pathway for 1,3-Dichloropropene in the Rat ......................................................... 131
3-6. Correlation of Exposure to 1,3-Dichloropropene with Urinary Excretion of the N-Acetyl Cysteine Metabolite .......................................................................................................................... 132
3-7. Proposed Metabolic Pathway for 2,3-Dichloropropene in the Rat ......................................................... 135
3-8. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance .................................................................................................... 141
3-9. Kinetic Model for Uptake and Elimination of 1,3-Dichloropropene ...................................................... 142
3-10. Existing Information on Health Effects of 1,1-Dichloropropene .......................................................... 155
3-11. Existing Information on Health Effects of 3,3-Dichloropropene .......................................................... 156
3-12. Existing Information on Health Effects of 1,2-Dichloropropene .......................................................... 157
3-13. Existing Information on Health Effects of 2,3-Dichloropropene .......................................................... 158
3-14. Existing Information on Health Effects of 1,3-Dichloropropene .......................................................... 159
6-1. Frequency of NPL Sites with 1,1-Dichloropropane Contamination .......................................................... 194
6-2. Frequency of NPL Sites with 1,2-Dichloropropene Contamination .......................................................... 195
6-3. Frequency of NPL Sites with 1,3-Dichloropropene Contamination .......................................................... 196
6-4. Frequency of NPL Sites with 2,3-Dichloropropene Contamination .......................................................... 197
This page is intentionally blank.
LIST OF TABLES

2-1. Summary of Minimum Risk Levels (MRLs) Derived for Dichloropropenes................................. 17
2-2. Incidence of Significant Lesions in Fischer 344 Rats and B6C3F1 Mice Exposed to 2,3-Dichloropropene (>99%) Vapor 6 Hours/Day, for 9/11 Days ................................................................. 28
3-1. Trade Names and Components of Pure 1,3-Dichloropropene Formulations.................................. 34
3-2. Levels of Significant Exposure to 1,3-Dichloropropene – Inhalation ........................................... 37
3-3. Levels of Significant Exposure to 2,3-Dichloropropene – Inhalation ........................................... 53
3-4. Levels of Significant Exposure to 1,3-Dichloropropene – Oral .................................................... 76
3-5. Levels of Significant Exposure to 2,3-Dichloropropene – Oral .................................................... 95
3-6. Levels of Significant Exposure to 1,3-Dichloropropene – Dermal ............................................... 108
3-7. Levels of Significant Exposure to 2,3-Dichloropropene – Dermal ............................................... 111
3-8. Genotoxicity of Dichloropropenes In Vivo .................................................................................. 116
3-9. Genotoxicity of Dichloropropenes In Vitro ................................................................................ 118
4-1. Chemical Identity of the Isomers of Dichloropropene ................................................................. 180
4-2. Physical and Chemical Properties of the Isomers of Dichloropropene ......................................... 183
5-1. Facilities that Produce, Process, or Use 1,3-Dichloropropene ..................................................... 189
5-2. Facilities that Produce, Process, or Use 2,3-Dichloropropene ..................................................... 190
5-3. Compositions of Actively Registered Commercial Products Containing 1,3-Dichloropropene ..... 191
6-1. Releases to the Environment from Facilities that Produce, Process, or Use 1,3-Dichloropropene ............................................................................................................................... 201
6-2. Releases to the Environment from Facilities that Produce, Process, or Use 2,3-Dichloropropene ............................................................................................................................... 202
6-3. Maximum Concentrations (24-Hour Time-Weighted Average) of 1,3-Dichloropropene in Air at Varying Distances from Treated Fields ................................................................. 204
6-4. Estimated Annual Use of 1,3-Dichloropropene in the United States ............................................ 207
6-5. Exposure Levels of Employees to 1,3-Dichloropropene Measured During Loading and Application ............................................................................................................................. 222
7-1. Analytical Methods for Determining cis- and trans-1,3-Dichloropropene and Metabolites in Biological Materials .......................................................... 233
7-2. Analytical Methods for Determining 1,3-Dichloropropene in Environmental Materials .............. 236
7-3. Analytical Methods for Determining 1,1-Dichloropropene in Environmental Materials .............. 238
8-1. Regulations and Guidelines Applicable to Dichloropropenes ..................................................... 244