

# **Toxicological Profile for Disulfoton**

August 2022



### **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

#### \*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.

# **VERSION HISTORY**

Date	Description
August 2022	Final toxicological profile released
July 2021	Draft for public comment toxicological profile released
September 2011	Addendum to the toxicological profile released
August 1995	Final toxicological profile released

#### **CONTRIBUTORS & REVIEWERS**

#### **CHEMICAL MANAGER TEAM**

Melanie Buser, M.P.H. (Lead) Nickolette Roney, M.P.H. ATSDR, Office of Innovation and Analytics, Toxicology Section, Atlanta, GA Adriana Antezana, M.P.H. Hannah Derrick, B.S. Andrea Chiger, M.P.H. Lauren Brown, M.S., DABT Kaley Beins, M.P.H. Abt Associates, Rockville, MD

Bob Sonawane, Ph.D. Bruce Fowler, Ph.D. Toxicology and Risk Assessment Consulting Services, Maryland (subcontractor to Abt Associates)

Kimberly Zaccaria, Ph.D., D.A.B.T. Jenny Crisman, B.S. 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.

#### PEER REVIEWERS

- 1. Dr. Xiaozhong Yu, MD, MPH, Ph.D., Associate Professor, Environmental Health Science, College of Public Health, University of Georgia, Athens, Georgia
- 2. Dr. Lucio G. Costa, PharmD, Professor, Environmental Health Director, Toxicology Program, University of Washington, Seattle, Washington
- 3. Dr. Dale Hattis, Professor, Ph.D., The George Perkins Marsh Institute, Clark University, Worcester, Massachusetts

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.

DISULFOTON vii

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**

DISCLAIMER	ii
FOREWORD	iii
VERSION HISTORY	v
CONTRIBUTORS & REVIEWERS	vi
CONTENTS	viii
LIST OF FIGURES	
LIST OF TABLES	
CHAPTER 1. RELEVANCE TO PUBLIC HEALTH	
1.1 OVERVIEW AND U.S. EXPOSURES	
1.1 OVERVIEW AND U.S. EAPOSURES	
1.3 MINIMAL RISK LEVELS (MRLs)	
CHAPTER 2. HEALTH EFFECTS	
2.1 INTRODUCTION	
2.2 DEATH	
2.3 BODY WEIGHT	
2.4 RESPIRATORY	
2.5 CARDIOVASCULAR	
2.6 GASTROINTESTINAL	
2.8 MUSCULOSKELETAL	
2.9 HEPATIC	
2.10 RENAL	
2.11 DERMAL	
2.12 OCULAR	
2.13 ENDOCRINE	
2.14 IMMUNOLOGICAL	
2.15 NEUROLOGICAL	
2.16 REPRODUCTIVE	
2.17 DEVELOPMENTAL	
2.18 OTHER NONCANCER	
2.19 CANCER	85
2.20 GENOTOXICITY	86
CHAPTER 3. TOXICOKINETICS, SUSCEPTIBLE POPULATIONS, BIOMARKERS, CHEMICA	۱L
INTERACTIONS	92
3.1 TOXICOKINETICS	92
3.1.1 Absorption	92
3.1.2 Distribution	94
3.1.3 Metabolism	
3.1.4 Excretion	
3.1.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models	
3.1.6 Animal-to-Human Extrapolations	
3.2 CHILDREN AND OTHER POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	
3.3 BIOMARKERS OF EXPOSURE AND EFFECT	
3.3.1 Biomarkers of Exposure	103

3.3.2 Biomarkers of Effect	
3.4 INTERACTIONS WITH OTHER CHEMICALS	107
CHAPTER 4. CHEMICAL AND PHYSICAL INFORMATION	111
4.1 CHEMICAL IDENTITY	
4.2 PHYSICAL AND CHEMICAL PROPERTIES	
CHAPTER 5. POTENTIAL FOR HUMAN EXPOSURE	112
5.1 OVERVIEW	
5.2 PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	
5.2.1 Production	
5.2.2 Import/Export	
5.2.3 Use	
5.2.4 Disposal	116
5.3 RELEASES TO THE ENVIRONMENT	117
5.3.1 Air	
5.3.2 Water	
5.3.3 Soil	
5.4 ENVIRONMENTAL FATE	
5.4.1 Transport and Partitioning	
5.4.2 Transformation and Degradation	
5.5 LEVELS IN THE ENVIRONMENT	
5.5.1 Air	
5.5.2 Water	
5.5.3 Sediment and Soil	
5.5.4 Other Media	
5.6 GENERAL POPULATION EXPOSURE 5.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	
CHAPTER 6. ADEQUACY OF THE DATABASE	
6.1 INFORMATION ON HEALTH EFFECTS	
6.2 IDENTIFICATION OF DATA NEEDS	
6.3 ONGOING STUDIES	147
CHAPTER 7. REGULATIONS AND GUIDELINES	148
CHAPTER 8. REFERENCES	150
CHAFTER 6. REPERENCES	130
APPENDICES	
APPENDIX A. ATSDR MINIMAL RISK LEVEL WORKSHEETS	A-1
APPENDIX B. LITERATURE SEARCH FRAMEWORK FOR DISULFOTON	
APPENDIX C. FRAMEWORK FOR ATSDR'S SYSTEMATIC REVIEW OF HEALTH EFFEC	
DATA FOR DISULFOTON	C-1
APPENDIX D. USER'S GUIDE	D-1
APPENDIX E. QUICK REFERENCE FOR HEALTH CARE PROVIDERS	
APPENDIX F. GLOSSARY	F-1
APPENDIX G. ACRONYMS, ABBREVIATIONS, AND SYMBOLS	G-1

## **LIST OF FIGURES**

1-1. Health Effects Found in Animals Following Inhalation Expos	sure to Disulfoton
1-2. Health Effects Found in Animals Following Oral Exposure to	
1-3. Summary of Sensitive Targets of Disulfoton – Inhalation	
1-4. Summary of Sensitive Targets of Disulfoton – Oral	
2-1. Overview of the Number of Studies Examining Disulfoton H	ealth Effects1
2-2. Levels of Significant Exposure to Disulfoton – Inhalation	17
2-3. Levels of Significant Exposure to Disulfoton – Oral	4
3-1. Metabolic Pathways for Disulfoton	95
5-1. Number of NPL Sites with Disulfoton Contamination	113
6-1. Summary of Existing Health Effects Studies on Disulfoton B	y Route and Endpoint138

DISULFOTON xi

## **LIST OF TABLES**

1-1.	Minimal Risk Levels (MRLs) for Disulfoton	8
2-1.	Levels of Significant Exposure to Disulfoton – Inhalation	12
2-2.	Levels of Significant Exposure to Disulfoton – Oral	22
2-3.	Levels of Significant Exposure to Disulfoton – Dermal	52
2-4.	Genotoxicity of Disulfoton In Vivo	87
2-5.	Genotoxicity of Disulfoton In Vitro	88
4-1.	Chemical Identity of Disulfoton	111
4-2.	Physical and Chemical Properties of Disulfoton	112
5-1.	Lowest Limit of Detection for Disulfoton Based on Standards	125
5-2.	Summary of Environmental Levels of Disulfoton	125
5-3.	Disulfoton Levels in Water, Soil, and Air of National Priorities List (NPL) Sites	126
5-4.	Outdoor Air Monitoring Data for Disulfoton	127
5-5.	Surface Water Monitoring Data for Disulfoton	129
5-6.	Concentrations of Disulfoton in Soil and Sediment	131
5-7.	Concentrations of Disulfoton in Fish Tissues	132
7-1.	Regulations and Guidelines Applicable to Disulfoton	148