TOXICOLOGICAL PROFILE FOR
DISULFOTON

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

August 1995
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

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 ATSDR and 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 being described. Each profile identifies and reviews the key literature (that has been peer-reviewed) that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but 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.

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 protect public health will be identified by ATSDR and EPA. The focus of the profiles is on health and toxicologic information; therefore, we have included this information in the beginning of the document.

Each profile must include the following:

(A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance in order 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.

(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.

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 the Agency for Toxic Substances and Disease Registry (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 Environmental Protection Agency (EPA). The availability of the revised priority list of 275 hazardous substances was announced in the Federal Register on February 28, 1994 (59 FR 9486). 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); and October 17, 1991 (56 FR 52166); and October 28, 1992 (57 FR 48801).
Foreword

Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

This profile reflects our assessment of all relevant toxicologic testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, the Centers for Disease Control and Prevention (CDC), and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers 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
CONTRIBUTORS

CHEMICAL MANAGERS(S)/AUTHOR(S):

Nickolette Roney
ATSDR, Division of Toxicology, Atlanta, GA

Sharon Wilbur, M.A.
Research Triangle Institute, Research Triangle Park, NC

THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:


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.

4. Quality Assurance Review. The Quality Assurance Branch assures that consistency across profiles is maintained, identifies any significant problems in format or content, and establishes that Guidance has been followed.
A peer review panel was assembled for disulfoton. The panel consisted of the following members:

1. Dr. William Buck, Private Consultant, Consul-Tox, Inc., Tolono, Illinois;

2. Dr. Lucia Costa, Professor and Director, Toxicology Program, School of Public Health and Community Medicine, Department of Environmental Health, University of Washington, Seattle, Washington; and

3. Dr. Casey Robinson, Professor of Pharmacodynamics and Toxicology, College of Pharmacy, Health Science Center, University of Oklahoma, Oklahoma City, Oklahoma.

These experts collectively have knowledge of disulfoton’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. 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.
CONTENTS

FOREWORD ........................................................................................................ v

CONTRIBUTORS .............................................................................................. vii

PEER REVIEW ..................................................................................................... ix

LIST OF FIGURES .............................................................................................. xv

LIST OF TABLES ................................................................................................. xvii

1. PUBLIC HEALTH STATEMENT ......................................................................... 1
   1.1 WHAT IS DISULFOTON? .......................................................................... 1
   1.2 WHAT HAPPENS TO DISULFOTON WHEN IT ENTERS THE ENVIRONMENT? . 2
   1.3 HOW MIGHT I BE EXPOSED TO DISULFOTON? ...................................... 2
   1.4 HOW CAN DISULFOTON ENTER AND LEAVE MY BODY? ......................... 3
   1.5 HOW CAN DISULFOTON AFFECT MY HEALTH? ....................................... 4
   1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO DISULFOTON? .................................................... 5
   1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH? ................................................ 5
   1.8 WHERE CAN I GET MORE INFORMATION? ........................................... 6

2. HEALTH EFFECTS ........................................................................................... 7
   2.1 INTRODUCTION ..................................................................................... 7
   2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE .............. 7
      2.2.1 Inhalation Exposure ........................................................................... 9
         2.2.1.1 Death ....................................................................................... 9
         2.2.1.2 Systemic Effects ..................................................................... 9
         2.2.1.3 Immunological and Lymphoreticular Effects .................. 20
         2.2.1.4 Neurological Effects ................................................................ 20
         2.2.1.5 Reproductive Effects ................................................................ 24
         2.2.1.6 Developmental Effects ......................................................... 24
         2.2.1.7 Genotoxic Effects ................................................................... 24
         2.2.1.8 Cancer ................................................................................... 24
      2.2.2 Oral Exposure .................................................................................... 25
         2.2.2.1 Death ...................................................................................... 25
         2.2.2.2 Systemic Effects ..................................................................... 51
         2.2.2.3 Immunological and Lymphoreticular Effects .................. 59
         2.2.2.4 Neurological Effects ................................................................ 59
         2.2.2.5 Reproductive Effects ......................................................... 64
         2.2.2.6 Developmental Effects ......................................................... 65
         2.2.2.7 Genotoxic Effects ................................................................... 66
         2.2.2.8 Cancer ................................................................................... 67
      2.2.3 Dermal Exposure ................................................................................ 67
         2.2.3.1 Death ...................................................................................... 67
         2.2.3.2 Systemic Effects ..................................................................... 68
LIST OF FIGURES

2-1 Levels of Significant Exposure to Disulfoton - Inhalation ........................................ 16
2-2 Levels of Significant Exposure to Disulfoton - Oral .................................................. 46
2-3 Metabolic Pathways for Disulfoton ............................................................................. 81
2-4 Existing Information on Health Effects of Disulfoton ............................................. 125
5-1 Frequency of NPL Sites with Disulfoton Contamination ........................................ 149
# LIST OF TABLES

2-1 Levels of Significant Exposure to Disulfoton - Inhalation ........................................ 10

2-6 Levels of Significant Exposure to Disulfoton - Oral .................................................. 26

2-3 Levels of Significant Exposure to Disulfoton - Dermal .............................................. 69

2-4 Genotoxicity of Disulfoton *In Vivo* .............................................................................. 107

2-5 Genotoxicity of Disulfoton *In Vitro* .............................................................................. 109

3-1 Chemical Identity of Disulfoton ....................................................................................... 140

3-2 Physical and Chemical Properties of Disulfoton ......................................................... 141

6-1 Analytical Methods for Determining Disulfoton in Biological Samples ......................... 168

6-2 Analytical Methods for Determining Disulfoton in Environmental Samples ................. 170

7-1 Regulations and Guidelines Applicable to Disulfoton ................................................. 177