

**TOXICOLOGICAL PROFILE FOR
ENDRIN**

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

August 1996

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 endrin was released in May 1989. This edition supersedes any previously released draft or final profile.

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 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 audience for the toxicological profiles is 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.



David Satcher, M.D., Ph.D.
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 Super-fund). 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 April 29, 1996 (61 FR 18744). 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); and February 28, 1994 (59 FR 9486). Section 104(I)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list.

CONTRIBUTORS

CHEMICAL MANAGER(S)/AUTHOR(S):

Jessilyn Taylor, M.S.
ATSDR, Division of Toxicology, Atlanta, GA

Jerry W. Spoo, DVM
Research Triangle Institute, Research Triangle Park, NC

Lorrene Buckley Kedderis, Ph.D., DABT
Research Triangle Institute, Research Triangle Park, NC

THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

1. Green Border Review. Green Border review assures consistency with ATSDR policy.
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.

PEER REVIEW

A peer review panel was assembled for endrin. The panel consisted of the following members:

- 1 . Dr. Gary Booth, Brigham Young University, Provo, Utah;
- 2 . Dr. Donald Morgan, Private Consultant, Iowa City, Iowa; and
- 3 . Dr. Martha J. Radike, Department of Environmental Health, University of Cincinnati, Cincinnati, Ohio.

These experts collectively have knowledge of endrin'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(1)(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 ENDRIN?	2
1.2 WHAT HAPPENS TO ENDRIN WHEN IT ENTERS THE ENVIRONMENT?	2
1.3 HOW MIGHT I BE EXPOSED TO ENDRIN?	3
1.4 HOW CAN ENDRIN ENTER AND LEAVE MY BODY?	4
1.5 HOW CAN ENDRIN AFFECT MY HEALTH?	4
1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO ENDRIN?	6
1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?	6
1.8 WHERE CAN I GET MORE INFORMATION?	7
2. HEALTH EFFECTS	9
2.1 INTRODUCTION	9
2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	9
2.2.1 Inhalation Exposure	11
2.2.1.1 Death	11
2.2.1.2 Systemic Effects	16
2.2.1.3 Immunological and Lymphoreticular Effects	17
2.2.1.4 Neurological Effects	17
2.2.1.5 Reproductive Effects	18
2.2.1.6 Developmental Effects	18
2.2.1.7 Genotoxic Effects	18
2.2.1.8 Cancer	18
2.2.2 Oral Exposure	19
2.2.2.1 Death	19
2.2.2.2 Systemic Effects	21
2.2.2.3 Immunological and Lymphoreticular Effects	45
2.2.2.4 Neurological Effects	46
2.2.2.5 Reproductive Effects	47
2.2.2.6 Developmental Effects	48
2.2.2.7 Genotoxic Effects	50
2.2.2.8 Cancer	50

2.2.3	Dermal Exposure	51
2.2.3.1	Death	52
2.2.3.2	Systemic Effects	52
2.2.3.3	Immunological and Lymphoreticular Effects	55
2.2.3.4	Neurological Effects	55
2.2.3.5	Reproductive Effects	56
2.2.3.6	Developmental Effects	56
2.2.3.7	Genotoxic Effects	56
2.2.3.8	Cancer	56
2.3	TOXICOKINETICS	56
2.3.1	Absorption	57
2.3.1.1	Inhalation Exposure	57
2.3.1.2	Oral Exposure	57
2.3.1.3	Dermal Exposure	57
2.3.2	Distribution	58
2.3.2.1	Inhalation Exposure	58
2.3.2.2	Oral Exposure	58
2.3.2.3	Dermal Exposure	60
2.3.3	Metabolism	60
2.3.4	Excretion	62
2.3.4.1	Inhalation Exposure	62
2.3.4.2	Oral Exposure	62
2.3.4.3	Dermal Exposure	63
2.4	MECHANISMS OF ACTION	63
2.5	RELEVANCE TO PUBLIC HEALTH	65
2.6	BIOMARKERS OF EXPOSURE AND EFFECT	72
2.6.1	Biomarkers Used to Identify or Quantify Exposure to Endrin	73
2.6.2	Biomarkers Used to Characterize Effects Caused by Endrin	74
2.7	INTERACTIONS WITH OTHER CHEMICALS	75
2.8	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	75
2.9	METHODS FOR REDUCING TOXIC EFFECTS	76
2.9.1	Reducing Peak Absorption Following Exposure	76
2.9.2	Reducing Body Burden	77
2.9.3	Interfering with the Mechanism of Action for Toxic Effects	78
2.10	ADEQUACY OF THE DATABASE	79
2.10.1	Existing Information on Health Effects of Endrin	79
2.10.2	Identification of Data Needs	81
2.10.3	Ongoing Studies	87
3.	CHEMICAL AND PHYSICAL INFORMATION	89
3.1	CHEMICAL IDENTITY	89
3.2	PHYSICAL AND CHEMICAL PROPERTIES	89
4.	PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	95
4.1	PRODUCTION	95
4.2	IMPORT/EXPORT	96
4.3	USE	96
4.4	DISPOSAL	96

5.1	OVERVIEW	99
5.2	RELEASES TO THE ENVIRONMENT	104
5.2.1	Air	104
5.2.2	Water	104
5.2.3	Soil	105
5.3	ENVIRONMENTAL FATE	105
5.3.1	Transport and Partitioning	105
5.3.2	Transformation and Degradation	110
5.3.2.1	Air	110
5.3.2.2	Water	111
5.3.2.3	Sediment and Soil	112
5.4	LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	114
5.4.1	Air	114
5.4.2	Water	115
5.4.3	Sediment and Soil	117
5.4.4	Other Environmental Media	119
5.5	GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	123
5.6	POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	126
5.7	ADEQUACY OF THE DATABASE	126
5.7.1	Identification of Data Needs	126
5.7.2	Ongoing Studies	131
6.	ANALYTICAL METHODS	133
6.1	BIOLOGICAL SAMPLES	133
6.2	ENVIRONMENTAL SAMPLES	135
6.3	ADEQUACY OF THE DATABASE	138
6.3.1	Identification of Data Needs	143
6.3.2	Ongoing Studies	144
7.	REGULATIONS AND ADVISORIES	145
8.	REFERENCES	161
9.	GLOSSARY	189

APPENDICES

A.	MINIMAL RISK LEVEL (MRL) WORKSHEET(S)	A-3
B.	USER'S GUIDE	B-1
C.	ACRONYMS, ABBREVIATIONS, AND SYMBOLS	C-1

LIST OF FIGURES

2-1	Levels of Significant Exposure to Endrin - Inhalation	14
2-2	Levels of Significant Exposure to Endrin - Oral	37
2-3	Proposed Metabolic Scheme for Endrin in Mammals	61
2-4	Existing Information on Health Effects of Endrin	80
5-1	Frequency of Sites with Endrin Contamination	102
5-2	Frequency of Sites with Endrin Ketone Contamination	103

LIST OF TABLES

2-1	Levels of Significant Exposure to Endrin - Inhalation	12
2-2	Levels of Significant Exposure to Endrin - Oral	22
2-3	Levels of Significant Exposure to Endrin - Dermal	53
2-4	Genotoxicity of Endrin <i>In Vitro</i>	71
2-5	Ongoing Research for Endrin, Endrin Aldehyde, or Endrin Ketone	80
3-1	Chemical Identity of Endrin, Endrin Aldehyde, and Endrin Ketone	90
3-2	Physical and Chemical Properties of Endrin	92
5-1	Bioconcentration Data for Endrin	108
6-1	Analytical Methods for Determining Endrin and Metabolites in Biological Samples	136
6-2	Analytical Methods for Determining Endrin and Transformation Products in Environmental Samples	139
7-1	Regulations and Guidelines Applicable to Endrin/Endrin Aldehyde/Endrin Ketone	147

