

Toxicological Profile for Endrin

March 2021



ENDRIN

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.

ENDRIN iii

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

Stick Marga

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 ENDRIN in

*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.

ENDRIN v

VERSION HISTORY

Date	Description
March 2021	Final toxicological profile released
May 2019	Draft for public comment toxicological profile released
August 1996	Final toxicological profile released

ENDRIN vi

CONTRIBUTORS & REVIEWERS

CHEMICAL MANAGER TEAM

Susan Zells Ingber, AB, MSPP (Lead) Kimberly Zaccaria, Ph.D., D.A.B.T.

Lisa Ingerman, Ph.D., D.A.B.T.

ATSDR, Office of Innovation and Analytics,

Toxicology Section, Atlanta, GA

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.

PEER REVIEWERS

- 1. Jonathan Doorn, Ph.D., Associate Professor, College of Pharmacy, Division of Medicinal and Natural Products Chemistry, Division Head, Medicinal and Natural Products Chemistry, The University of Iowa, Iowa City, Iowa
- 2. J.E. Klaunig, Ph.D., Fellow ATS, Fellow IATP, Professor, Environmental Health, Professor, School of Public and Environmental Affairs, Indiana University Bloomington, Indiana
- 3. Debasis Bagchi, Ph.D., MACN, CNS, MAIChE, Chief Scientific Officer at Cepham Research Center, Industry Pharmaceuticals, San Francisco, California

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.

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	i
FOREWORD	ii
VERSION HISTORY	٠١
CONTRIBUTORS & REVIEWERS	v
CONTENTS	vi
LIST OF FIGURES	ix
LIST OF TABLES	У
CHAPTER 1. RELEVANCE TO PUBLIC HEALTH	1
1.1 OVERVIEW AND U.S. EXPOSURES	1
1.2 SUMMARY OF HEALTH EFFECTS	
1.3 MINIMAL RISK LEVELS (MRLs)	
CHAPTER 2. HEALTH EFFECTS	8
2.1 INTRODUCTION	
2.2 DEATH	
2.3 BODY WEIGHT	
2.4 RESPIRATORY	
2.5 CARDIOVASCULAR	47
2.6 GASTROINTESTINAL	
2.7 HEMATOLOGICAL	
2.8 MUSCULOSKELETAL	49
2.9 HEPATIC	
2.10 RENAL	
2.11 DERMAL	
2.12 OCULAR	
2.13 ENDOCRINE	
2.14 IMMUNOLOGICAL	
2.15 NEUROLOGICAL	57
2.16 REPRODUCTIVE	
2.17 DEVELOPMENTAL	61
2.18 OTHER NONCANCER	
2.19 CANCER	64
2.20 GENOTOXICITY	66
2.21 MECHANISMS OF TOXICITY	69
CHAPTER 3. TOXICOKINETICS, SUSCEPTIBLE POPULATIONS, BIOMARKERS, CHEMI	CAL
INTERACTIONS	
3.1 TOXICOKINETICS	71
3.1.1 Absorption	71
3.1.2 Distribution	72
3.1.3 Metabolism	73
3.1.4 Excretion	75
3.1.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models	7 6
3.1.6 Animal-to-Human Extrapolations	
3.2 CHILDREN AND OTHER POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBE	
3.3 BIOMARKERS OF EXPOSURE AND EFFECT	
3.3.1 Biomarkers of Exposure	
3.3.2 Biomarkers of Effect	80

3.4 INTERACTIONS WITH OTHER CHEMICALS	80
CHAPTER 4. CHEMICAL AND PHYSICAL INFORMATION	
4.1 CHEMICAL IDENTITY	
4.2 PHYSICAL AND CHEMICAL PROPERTIES	82
CHAPTER 5. POTENTIAL FOR HUMAN EXPOSURE	86
5.1 OVERVIEW	86
5.2 PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSA	
5.2.1 Production	87
5.2.2 Import/Export	88
5.2.3 Use	88
5.2.4 Disposal	88
5.3 RELEASES TO THE ENVIRONMENT	89
5.3.1 Air	89
5.3.2 Water	90
5.3.3 Soil	90
5.4 ENVIRONMENTAL FATE	
5.4.1 Transport and Partitioning	91
5.4.2 Transformation and Degradation	94
5.5 LEVELS IN THE ENVIRONMENT	
5.5.1 Air	98
5.5.2 Water	100
5.5.3 Sediment and Soil	101
5.5.4 Other Media	102
5.6 GENERAL POPULATION EXPOSURE	106
5.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSUR	ES109
CHAPTER 6. ADEQUACY OF THE DATABASE	111
6.1 Information on Health Effects	
6.2 Identification of Data Needs	
6.3 Ongoing Studies	
CHAPTER 7. REGULATIONS AND GUIDELINES	120
CHAPTER 8. REFERENCES	122
APPENDICES	
APPENDIX A. ATSDR MINIMAL RISK LEVELS AND WORKSH	EETSA-1
APPENDIX B. LITERATURE SEARCH FRAMEWORK FOR END	PRIN B-1
APPENDIX C. USER'S GUIDEAPPENDIX D. QUICK REFERENCE FOR HEALTH CARE PROV	IDERSD-1
APPENDIX E. GLOSSARY	E-1
APPENDIX F ACRONYMS ABBREVIATIONS AND SYMBOLS	F-1

ENDRIN ix

LIST OF FIGURES

1-1. Health Effects Found in Animals Following Oral Exposure to Endrin	2
1-2. Summary of Sensitive Targets of Endrin – Oral	6
2-1. Overview of the Number of Studies Examining Endrin Health Effects	11
2-2. Levels of Significant Exposure to Endrin – Inhalation	22
2-3. Levels of Significant Exposure to Endrin/Endrin Aldehyde/Endrin Ketone – Oral	38
3-1. Proposed Metabolism Scheme for Endrin in Mammals	74
5-1. Number of NPL Sites with Endrin, Endrin Aldehyde, or Endrin Ketone Contamination	86
6-1. Summary of Existing Health Effects Studies on Endrin By Route and Endpoint	112

ENDRIN

LIST OF TABLES

1-1.	Minimal Risk Levels (MRLs) for Endrin	7
2-1.	Health Effects in Humans Exposed to Endrin—Epidemiological Studies	12
2-2.	Levels of Significant Exposure to Endrin – Inhalation	21
2-3.	Levels of Significant Exposure to Endrin/Endrin Aldehyde/Endrin Ketone – Oral	23
2-4.	Levels of Significant Exposure to Endrin – Dermal	43
2-5.	Genotoxicity of Endrin In Vitro	66
2-6.	Genotoxicity of Endrin In Vivo	67
4-1.	Chemical Identity of Endrin, Endrin Aldehyde, and Endrin Ketone	83
4-2.	Physical and Chemical Properties of Endrin, Endrin Aldehyde, and Endrin Ketone	84
5-1.	Bioconcentration Data for Endrin	92
5-2.	Lowest Limit of Detection Based on Standards	98
5-3.	Endrin, Endrin Aldehyde and Endrin Ketone Levels in Water, Soil, and Air of National Priorities List (NPL) Sites	98
5-4.	Serum Endrin Levels (Lipid-Adjusted) in the NHANES U.S. Population	108
7-1.	Regulations and Guidelines Applicable to Endrin	120