

**TOXICOLOGICAL PROFILE FOR  
CHLORPYRIFOS**

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

September 1997

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 chlorpyrifos was released in August 1995 for public comment. 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 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.



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 Super-fund 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 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)/AUTHORS(S):

John F. Risher, Ph.D.  
ATSDR, Division of Toxicology, Atlanta, GA

Heman A. Navarro, Ph.D.  
Research Triangle Institute, Research Triangle Park, NC

### 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 Research Implementation Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.





## PEER REVIEW

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

- 1 . Dr. William Buck, Professor of Toxicology, University of Illinois, Tolono, IL 61880;
- 2 . Dr. Joel Coats, Professor, Department of Entomology, Iowa State University, Ames, IA 50011;  
and
- 3 . Dr. Frederick Oehme, Professor, Comparative Toxicology Laboratories, Kansas State University,  
Manhattan, KS 66506-5606

These experts collectively have knowledge of chlorpyrifos' 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 addressed 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 CHLORPYRIFOS? .....	1
1.2 WHAT HAPPENS TO CHLORPYRIFOS WHEN IT ENTERS THE ENVIRONMENT? .....	2
1.3 HOW MIGHT I BE EXPOSED TO CHLORPYRIFOS? .....	2
1.4 HOW CAN CHLORPYRIFOS ENTER AND LEAVE MY BODY? .....	3
1.5 HOW CAN CHLORPYRIFOS AFFECT MY HEALTH? .....	4
1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO CHLORPYRIFOS? .....	4
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 .....	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 .....	12
2.2.1.3 Immunological and Lymphoreticular Effects .....	20
2.2.1.4 Neurological Effects .....	20
2.2.1.5 Reproductive Effects .....	23
2.2.1.6 Developmental Effects .....	23
2.2.1.7 Genotoxic Effects .....	23
2.2.1.8 Cancer .....	24
2.2.2 Oral Exposure .....	24
2.2.2.1 Death .....	24
2.2.2.2 Systemic Effects .....	25
2.2.2.3 Immunological and Lymphoreticular Effects. ....	43
2.2.2.4 Neurological Effects .....	44
2.2.2.5 Reproductive Effects .....	48
2.2.2.6 Developmental Effects .....	49
2.2.2.7 Genotoxic Effects .....	50
2.2.2.8 Cancer .....	51

2.2.3	Dermal Exposure	52
2.2.3.1	Death	52
2.2.3.2	Systemic Effects	52
2.2.3.3	Immunological and Lymphoreticular Effects	59
2.2.3.4	Neurological Effects	60
2.2.3.5	Reproductive Effects	62
2.2.3.6	Developmental Effects	62
2.2.3.7	Genotoxic Effects	63
2.2.3.8	Cancer	63
2.3	TOXICOKINETICS	63
2.3.1	Absorption	64
2.3.1.1	Inhalation Exposure	64
2.3.1.2	Oral Exposure	64
2.3.1.3	Dermal Exposure	65
2.3.2	Distribution	65
2.3.2.1	Inhalation Exposure	65
2.3.2.2	Oral Exposure	66
2.3.2.3	Dermal Exposure	66
2.3.3	Metabolism	67
2.3.4	Elimination and Excretion	69
2.3.4.1	Inhalation Exposure	69
2.3.4.2	Oral Exposure	69
2.3.4.3	Dermal Exposure	69
2.3.5	Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Model	70
2.4	MECHANISMS OF ACTION	71
2.4.1	Pharmacokinetic Mechanisms	71
2.4.2	Mechanisms of Toxicity	74
2.4.3	Animal-to-Human Extrapolations	74
2.5	RELEVANCE TO PUBLIC HEALTH	75
2.6	BIOMARKERS OF EXPOSURE AND EFFECT	88
2.6.1	Biomarkers Used to Identify or Quantify Exposure to Chlorpyrifos	89
2.6.2	Biomarkers Used to Characterize Effects Caused by Chlorpyrifos	90
2.7	INTERACTIONS WITH OTHER CHEMICALS	90
2.8	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	90
2.9	METHODS FOR REDUCING TOXIC EFFECTS	91
2.9.1	Reducing Peak Absorption Following Exposure	92
2.9.2	Reducing Body Burden	92
2.9.3	Interfering with the Mechanism of Action for Toxic Effects	92
2.10	ADEQUACY OF THE DATABASE	93
2.10.1	Existing Information on Health Effects of Chlorpyrifos	93
2.10.2	Identification of Data Needs	95
2.10.3	Ongoing Studies	99
3.	CHEMICAL AND PHYSICAL INFORMATION	101
3.1	CHEMICAL IDENTITY	101
3.2	PHYSICAL AND CHEMICAL PROPERTIES	101

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL .....	105
4.1 PRODUCTION .....	105
4.2 IMPORT/EXPORT .....	105
4.3 USE .....	105
4.4 DISPOSAL .....	107
5. POTENTIAL FOR HUMAN EXPOSURE .....	109
5.1 OVERVIEW .....	109
5.2 RELEASES TO THE ENVIRONMENT .....	110
5.2.1 Air .....	110
5.2.2 Water .....	110
5.2.3 Soil .....	112
5.3 ENVIRONMENTAL FATE .....	112
5.3.1 Transport and Partitioning .....	112
5.3.2 Transformation and Degradation .....	116
5.3.2.1 Air .....	116
5.3.2.2 Water .....	116
5.3.2.3 Sediment and Soil .....	119
5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT .....	120
5.4.1 Air .....	121
5.4.2 Water .....	122
5.4.3 Sediment and Soil .....	123
5.4.4 Other Environmental Media .....	123
5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE .....	124
5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES .....	127
5.7 ADEQUACY OF THE DATABASE .....	127
5.7.1 Identification of Data Needs .....	127
5.7.2 Ongoing Studies .....	130
6. ANALYTICAL METHODS .....	133
6.1 BIOLOGICAL SAMPLES .....	133
6.2 ENVIRONMENTAL SAMPLES .....	144
6.3 ADEQUACY OF THE DATABASE .....	146
6.3.1 Identification of Data Needs .....	146
6.3.2 Ongoing Studies .....	148
7. REGULATIONS AND ADVISORIES .....	149
8. REFERENCES .....	153
9. GLOSSARY .....	177
APPENDICES	
A. ATSDR MINIMAL RISK LEVEL .....	A-1
B. USER'S GUIDE .....	B-1
C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS .....	C-1



## LIST OF FIGURES

2-1	Levels of Significant Exposure to Chlorpyrifos - Inhalation . . . . .	14
2-2	Levels of Significant Exposure to Chlorpyrifos - Oral . . . . .	35
2-3	Organophosphorus Compounds in Serum and Urine of Persons Poisoned by Chlorpyrifos . . .	68
2-4	Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance . . . . .	72
2-5	Existing Information on Health Effects of Chlorpyrifos . . . . .	94
5-1	Frequency of NPL Sites With Chlorpyrifos Contamination . . . . .	111
5-2	Environmental Degradation Pathways of Chlorpyrifos . . . . .	117





## LIST OF TABLES

2-1	Levels of Significant Exposure to Chlorpyrifos - Inhalation	13
2-2	Levels of Significant Exposure to Chlorpyrifos - Oral	26
2-3	Levels of Significant Exposure to Chlorpyrifos - Dermal	53
2-4	Genotoxicity of Chlorpyrifos <i>in Vivo</i>	86
2-5	Genotoxicity of Chlorpyrifos <i>in Vitro</i>	87
3-1	Chemical Identity of Chlorpyrifos	102
3-2	Physical and Chemical Properties of Chlorpyrifos	103
6-1	Analytical Methods for Determining Chlorpyrifos and Metabolites in Biological Samples	134
6-2	Analytical Methods for Determining Chlorpyrifos and Transformation Products in Environmental Samples	136
7-1	Regulations and Guidelines Applicable to Chlorpyrifos	150

