

# **TOXICOLOGICAL PROFILE FOR MERCURY**

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

March 1999

## **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 Mercury—Draft for Public Comment was released in September 1997. 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.



Jeffrey P. Koplan, M.D., M.P.H.  
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 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 November 17, 1997 (62 FR 61332). For prior versions of the list of substances, see *Federal Register* notices dated April 29, 1996 (61 FR 18744); 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.

# QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

### ***Primary Chapters/Sections of Interest***

**Chapter 1: Public Health Statement:** The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.

**Chapter 2: Health Effects:** Specific health effects of a given hazardous compound are reported by *route of exposure*, by *type of health effect* (death, systemic, immunologic, reproductive), and by *length of exposure* (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.

**NOTE:** Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

**Pediatrics:** Four new sections have been added to each Toxicological Profile to address child health issues:

- Section 1.6      How Can (Chemical X) Affect Children?**
  - Section 1.7      How Can Families Reduce the Risk of Exposure to (Chemical X)?**
  - Section 2.6      Children's Susceptibility**
  - Section 5.6      Exposures of Children**

#### **Other Sections of Interest:**

- ## **Section 2.7 Biomarkers of Exposure and Effect**

## **Section 2.10 Methods for Reducing Toxic Effects**

## *ATSDR Information Center*

**Phone:** 1-800-447-1544 (to be replaced by 1-888-42-ATSDR in 1999)

or 404-639-6357

*Fax:* 404-639-6359

*E-mail:* [atsdric@cdc.gov](mailto:atsdric@cdc.gov)

**Internet:** <http://atsdr1.atsdr.cdc.gov:8080>

The following additional material can be ordered through the ATSDR Information Center:

*Case Studies in Environmental Medicine: Taking an Exposure History*—The importance of taking an exposure history and how to conduct one are described, and an example of a thorough exposure history is provided. Other case studies of interest include *Reproductive and Developmental Hazards*; *Skin Lesions and Environmental Exposures*; *Cholinesterase-Inhibiting Pesticide Toxicity*; and numerous chemical-specific case studies.

*Managing Hazardous Materials Incidents* is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—*Medical Management Guidelines for Acute Chemical Exposures*—is a guide for health care professionals treating patients exposed to hazardous materials.

*Fact Sheets (ToxFAQs)* provide answers to frequently asked questions about toxic substances.

---

## ***Other Agencies and Organizations***

*The National Center for Environmental Health* (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. *Contact:* NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 • Phone: 770-488-7000 • FAX: 770-488-7015.

*The National Institute for Occupational Safety and Health* (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. *Contact:* NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 • Phone: 800-356-4674 or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 • Phone: 800-35-NIOSH.

*The National Institute of Environmental Health Sciences* (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. *Contact:* NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 • Phone: 919-541-3212.

---

## ***Referrals***

*The Association of Occupational and Environmental Clinics* (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. *Contact:* AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976 • FAX: 202-347-4950 • e-mail: [aoec@dgs.dgssys.com](mailto:aoec@dgs.dgssys.com) • AOEC Clinic Director: <http://occ-env-med.mc.duke.edu/oem/aoec.htm>.

*The American College of Occupational and Environmental Medicine* (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. *Contact:* ACOEM, 55 West Seegers Road, Arlington Heights, IL 60005 • Phone: 847-228-6850 • FAX: 847-228-1856.

## CONTRIBUTORS

### **CHEMICAL MANAGER(S)/AUTHORS(S):**

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

Rob DeWoskin, 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 mercury. The panel consisted of the following members:

1. Mr. Harvey Clewell, K.S. Crump Group, ICF Kaiser International, Inc., Ruston, LA
2. Dr. Ingeborg Harding-Barlow, Private Consultant, Environmental and Occupational Toxicology, 3717 Laguna Ave., Palo Alto, California;
- Dr. Thomas Hinesly, Professor (Emeritus), Department of Natural Resources and Environmental Sciences, University of Illinois, Champaign-Urbana, Illinois;
4. Dr. Loren D. Koller, Professor, College of Veterinary Medicine, Oregon State University, Corvallis, Oregon; and
5. Dr. Kenneth Reuhl, Professor, Neurotoxicology Laboratory, Rutgers University, Piscataway, New York.

These experts collectively have knowledge of mercury'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 reviewer's comments and determined which comments will be included in the profile. A listing of the profile. A listing of the peer reviewers' comments not incorporated in the profile, with 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
QUICK REFERENCE FOR HEALTH CARE PROVIDERS .....	vii
CONTRIBUTORS .....	ix
PEER REVIEW .....	xi
LIST OF FIGURES .....	xvii
LIST OF TABLES .....	xix
1. PUBLIC HEALTH STATEMENT .....	1
1.1 WHAT IS MERCURY? .....	1
1.2 WHAT HAPPENS TO MERCURY WHEN IT ENTERS THE ENVIRONMENT? .....	4
1.3 HOW MIGHT I BE EXPOSED TO MERCURY? .....	6
1.4 HOW CAN MERCURY ENTER AND LEAVE MY BODY? .....	11
1.5 HOW CAN MERCURY AFFECT MY HEALTH? .....	12
1.6 HOW CAN MERCURY AFFECT CHILDREN? .....	16
1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO MERCURY? .....	19
1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO MERCURY? .....	25
1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH? .....	26
1.10 WHERE CAN I GET MORE INFORMATION? .....	27
2. HEALTH EFFECTS .....	29
2.1 INTRODUCTION .....	29
2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE .....	31
2.2.1 Inhalation Exposure .....	33
2.2.1.1 Death .....	34
2.2.1.2 Systemic Effects .....	43
2.2.1.3 Immunological and Lymphoreticular Effects .....	55
2.2.1.4 Neurological Effects .....	58
2.2.1.5 Reproductive Effects .....	67
2.2.1.6 Developmental Effects .....	69
2.2.1.7 Genotoxic Effects .....	72
2.2.1.8 Cancer .....	74
2.2.2 Oral Exposure .....	74
2.2.2.1 Death .....	75
2.2.2.2 Systemic Effects .....	105
2.2.2.3 Immunological and Lymphoreticular Effects .....	123
2.2.2.4 Neurological Effects .....	124
2.2.2.5 Reproductive Effects .....	138
2.2.2.6 Developmental Effects .....	140
2.2.2.7 Genotoxic Effects .....	152
2.2.2.8 Cancer .....	154

2.2.3	Dermal Exposure .....	155
2.2.3.1	Death .....	155
2.2.3.2	Systemic Effects .....	156
2.2.3.3	Immunological and Lymphoreticular Effects .....	159
2.2.3.4	Neurological Effects .....	160
2.2.3.5	Reproductive Effects .....	161
2.2.3.6	Developmental Effects .....	161
2.2.3.7	Genotoxic Effects .....	161
2.2.3.8	Cancer .....	161
2.3	TOXICOKINETICS .....	161
2.3.1	Absorption .....	162
2.3.1.1	Inhalation Exposure .....	163
2.3.1.2	Oral Exposure .....	164
2.3.1.3	Dermal Exposure .....	169
2.3.1.4	Other Routes of Exposure .....	170
2.3.2	Distribution .....	171
2.3.2.1	Inhalation Exposure .....	171
2.3.2.2	Oral Exposure .....	175
2.3.2.3	Dermal Exposure .....	180
2.3.2.4	Other Routes of Exposure .....	181
2.3.3	Metabolism .....	182
2.3.4	Elimination and Excretion .....	185
2.3.5	Physiologically based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models ..	193
2.3.5.1	Summary of PBPK Models .....	194
2.3.5.2	Mercury PBPK Model Comparison .....	194
2.3.5.3	Discussion of Models .....	196
2.4	MECHANISMS OF ACTION .....	207
2.4.1	Pharmacokinetic Mechanisms .....	207
2.4.2	Mechanisms of Toxicity .....	210
2.4.3	Animal-to-Human Extrapolations .....	219
2.5	RELEVANCE TO PUBLIC HEALTH .....	220
2.6	CHILDREN'S SUSCEPTIBILITY .....	301
2.7	Biomarkers of Exposure and Effect .....	310
2.7.1	Biomarkers Used to Identify or Quantify Exposure to Mercury .....	311
2.7.2	Biomarkers Used to Characterize Effects Caused by Mercury .....	317
2.8	INTERACTIONS WITH OTHER CHEMICALS .....	323
2.9	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE .....	327
2.10	METHODS FOR REDUCING TOXIC EFFECTS .....	329
2.10.1	Reducing Peak Absorption Following Exposure .....	330
2.10.2	Reducing Body Burden .....	331
2.10.3	Interfering with the Mechanism of Action for Toxic Effects .....	334
2.11	ADEQUACY OF THE DATABASE .....	335
2.11.1	Existing Information on Health Effects of Mercury .....	335
2.11.2	Identification of Data Needs .....	341
2.11.3	Ongoing Studies .....	357
3.	CHEMICAL AND PHYSICAL INFORMATION .....	363
3.1	CHEMICAL IDENTITY .....	363
3.2	PHYSICAL AND CHEMICAL PROPERTIES .....	363

4. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL .....	371
4.1 PRODUCTION .....	371
4.2 IMPORT/EXPORT .....	374
4.3 USE .....	375
4.4 DISPOSAL .....	377
5. POTENTIAL FOR HUMAN EXPOSURE .....	379
5.1 OVERVIEW .....	379
5.2 RELEASES TO THE ENVIRONMENT .....	380
5.2.1 Air .....	386
5.2.2 Water .....	391
5.2.3 Soil .....	396
5.3 ENVIRONMENTAL FATE .....	398
5.3.1 Transport and Partitioning .....	398
5.3.2 Transformation and Degradation .....	405
5.3.2.1 Air .....	406
5.3.2.2 Water .....	406
5.3.2.3 Sediment and Soil .....	409
5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT .....	410
5.4.1 Air .....	410
5.4.2 Water .....	413
5.4.3 Sediment and Soil .....	414
5.4.4 Other Environmental Media .....	416
5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE .....	431
5.6 EXPOSURES OF CHILDREN .....	454
5.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES .....	464
5.8 ADEQUACY OF THE DATABASE .....	476
5.8.1 Identification of Data Needs .....	476
5.8.2 Ongoing Studies .....	482
6. ANALYTICAL METHODS .....	487
6.1 BIOLOGICAL MATERIALS .....	488
6.2 ENVIRONMENTAL SAMPLES .....	495
6.3 ADEQUACY OF THE DATABASE .....	504
6.3.1 Identification of Data Needs .....	505
6.3.2 Ongoing Studies .....	506
7. REGULATIONS AND ADVISORIES .....	509
8. REFERENCES .....	525
9. GLOSSARY .....	611

**APPENDICES**

B. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS .....	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 Inorganic Mercury - Inhalation .....	40
2-2	Levels of Significant Exposure to Inorganic Mercury - Oral .....	84
2-3	Levels of Significant Exposure to Organic Mercury - Oral .....	101
2-4	Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance .....	195
2-5	Compartmental Flow Diagram for a Pharmacokinetic Model of Methylmercury in the Growing Rat .....	197
2-6	PBPK Model for Mercury in the Pregnant Rat .....	202
2-7	Model for Mercury Transport in the Pregnant Rat and Fetus .....	203
2-8	Existing Information on Health Effects of Metallic Mercury .....	336
2-9	Existing Information on Health Effects of Inorganic Mercury Salts .....	337
2-10	Existing Information on Health Effects of Methylmercuric Mercury .....	338
2-11	Existing Information on Health Effects of Phenylmercuric Mercury .....	339
5-1	Frequency of NPL Sites with Mercury (Elemental) Contamination .....	381
5-2	Frequency of NPL Sites with Mercuric Acetate Contamination .....	382
5-3	Frequency of NPL Sites with Mercuric Chloride Contamination .....	383
5-4	Frequency of NPL Sites with Mercurous Chloride Contamination .....	384
5-5	Frequency of NPL Sites with Dimethylmercury Contamination .....	385
5-6	Transformation of Mercury in Air, Water, and Sediment .....	407
5-7	National Listing of Fish and Wildlife Consumption Advisories for Mercury .....	470



## LIST OF TABLES

2-1	Levels of Significant Exposure to Inorganic Mercury - Inhalation .....	35
2-2	Levels of Significant Exposure to Inorganic Mercury - Oral .....	76
2-3	Levels of Significant Exposure to Organic Mercury - Oral .....	87
2-4	Half-lives of Inorganic Mercury in Humans .....	187
2-5	Elimination Constants for Methylmercury Measured in Blood and Hair .....	191
2-6	Intercompartmental Mass Transport Parameters Used to Model Methylmercury and Mercuric Mercury Pharmacokinetics in Rats .....	198
2-7	Linear Binding and Membrane Transfer Constants .....	204
2-8	Secretion/Reabsorption Constants .....	205
2-9	Available Data on Hair:Blood Ratio (total Hg) .....	250
2-10	Concentration of Total Mercury in Hair. ....	260
2-11	Genotoxicity of Mercury <i>In Vivo</i> .....	286
2-12	Genotoxicity of Mercury <i>In Vitro</i> .....	290
2-13	Health Effects Associated with Mercury Levels in Human Blood and Urine .....	318
2-14	Ongoing Studies on Health Effects of Mercury .....	358
3-1	Chemical Identity of Selected Inorganic and Organic Mercury Compounds .....	364
3-2	Physical and Chemical Properties of Selected Inorganic and Organic Mercury Compounds ...	367
4-1	Facilities That Manufacture or Process Mercury .....	372
4-2	U.S. Mercury Supply, Demand, Imports, and Exports .....	373
5-1	Releases to the Environment from Facilities That Manufacture or Process Mercury .....	387
5-2	Comparison of Environmental Releases of Mercury from Facilities That Manufacture or Process Mercury Reported to the Toxics Release Inventory (TRI) in 1991, 1994, and 1996 .....	388
5-3	Atmospheric Mercury Emission Inventory for the United States by Anthropogenic Source Type	392
5-4	Estimates of U.S. Mercury Emission Rates by Category .....	393
5-5	Estimated Discards of Mercury in Products in Municipal Solid Waste .....	397

5-6 Bioaccumulation of Various Mercury Compounds by Freshwater and Saltwater Organisms . . . . .	402
5-7 Comparison of the Biomagnification of Methylmercury and Inorganic Mercury in a Freshwater Food Chain (Little Rock Lake) . . . . .	403
5-8 Mercury Concentrations for Largemouth Bass Collected in Various States Throughout the United States (1990–1995) . . . . .	420
5-9 Mercury Concentrations for Channel Catfish Collected in Various States Throughout the United States (1990–1995) . . . . .	421
5-10 Combined Data on Mercury Levels in Selected Fish Species in the Northeast . . . . .	423
5-11 Total Mercury Concentrations in Tissues of Marine Mammals in Alaska and Canada . . . . .	426
5-12 Estimated Average Daily Intake and Retention of Total Mercury and Mercury Compounds in the General Population . . . . .	432
5-13 Mercury Concentrations in the Top 10 Types of Fish Consumed by the U.S. Population . . . . .	435
5-14 Fish Consumption Rates of Various Populations Including General Population and Recreational and Subsistence Fishers . . . . .	437
5-15 Estimated U.S. Population Consuming Fish, Excluding Alaska and Hawaii . . . . .	438
5-16 Estimates of Mean Daily Elemental Mercury Uptake from Dental Amalgam Restorations . . . . .	441
5-17 Total Mercury Concentrations in Human Breast Milk . . . . .	444
5-18 Mercury Concentrations in Hair from Residents of Various U.S. Communities . . . . .	447
5-19 Total Mercury Levels in Exposed Workers and Controls . . . . .	450
5-20 Estimated Number of Workers Potentially Exposed to Mercury and Various Mercury Compounds in the Workplace . . . . .	455
5-21 Calculated Mercury Absorption from Air . . . . .	456
5-22 Ongoing Research Relevant to Human Exposure to Mercury . . . . .	483
6-1 Analytical Methods for Determining Mercury in Biological Samples . . . . .	489
6-2 Analytical Methods for Determining Mercury in Environmental Samples . . . . .	496
6-3 Research on New Methods for the Detection of Mercury . . . . .	507
7-1 Regulations and Guidelines Applicable to Mercury . . . . .	515