

TOXICOLOGICAL PROFILE FOR NICKEL

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

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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 Nickel, Draft for Public Comment was released in September 2004. This edition supersedes any previously released draft or final profile.

Toxicological profiles are revised and republished as necessary. For information regarding the update status of previously released profiles, contact ATSDR at:

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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.

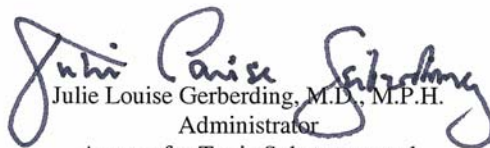
The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels 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.


Julie Louise Gerberding, M.D., M.P.H.
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*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: Relevance to Public Health: The Relevance to Public Health Section evaluates, interprets, and assesses the significance of toxicity data to human health.

Chapter 3: Health Effects: Specific health effects of a given hazardous compound are reported by type of health effect (death, systemic, immunologic, reproductive), by route of exposure, 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 3.7	Children's Susceptibility
Section 6.6	Exposures of Children

Other Sections of Interest:

Section 3.8	Biomarkers of Exposure and Effect
Section 3.11	Methods for Reducing Toxic Effects

ATSDR Information Center

Phone: 1-888-42-ATSDR or (404) 498-0110	Fax: (770) 488-4178
E-mail: atsdric@cdc.gov	Internet: http://www.atsdr.cdc.gov

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@AOEC.ORG • Web Page: <http://www.aoec.org/>.

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: 847-818-1800 • FAX: 847-818-9266.

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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.
4. Green Border Review. Green Border review assures the consistency with ATSDR policy.

PEER REVIEW

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

1. George Daston, Ph.D., Research Fellow, Miami Valley Laboratories, The Procter & Gamble Company, Cincinnati, OH;
2. A. Phillip Leber, Ph.D., DABT, Consultant in Toxicology, Akron, OH; and
3. Sam Kacew, Ph.D., ATS, Professor, Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, ON, Canada.

These experts collectively have knowledge of nickel'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.

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

DISCLAIMER	ii
UPDATE STATEMENT	iii
FOREWORD	v
QUICK REFERENCE FOR HEALTH CARE PROVIDERS.....	vii
CONTRIBUTORS	ix
PEER REVIEW	xi
CONTENTS.....	xiii
LIST OF FIGURES	xvii
LIST OF TABLES	xix
1. PUBLIC HEALTH STATEMENT.....	1
1.1 WHAT IS NICKEL?	1
1.2 WHAT HAPPENS TO NICKEL WHEN IT ENTERS THE ENVIRONMENT?.....	2
1.3 HOW MIGHT I BE EXPOSED TO NICKEL?	3
1.4 HOW CAN NICKEL ENTER AND LEAVE MY BODY?	5
1.5 HOW CAN NICKEL AFFECT MY HEALTH?.....	5
1.6 HOW CAN NICKEL AFFECT CHILDREN?.....	7
1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO NICKEL?.....	8
1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO NICKEL?	8
1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?	9
1.10 WHERE CAN I GET MORE INFORMATION?	10
2. RELEVANCE TO PUBLIC HEALTH	11
2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO NICKEL IN THE UNITED STATES.....	11
2.2 SUMMARY OF HEALTH EFFECTS	12
2.3 MINIMAL RISK LEVELS	17
3. HEALTH EFFECTS	25
3.1 INTRODUCTION	25
3.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	25
3.2.1 Inhalation Exposure	27
3.2.1.1 Death	27
3.2.1.2 Systemic Effects.....	28
3.2.1.3 Immunological and Lymphoreticular Effects	74
3.2.1.4 Neurological Effects	76
3.2.1.5 Reproductive Effects.....	77
3.2.1.6 Developmental Effects.....	78
3.2.1.7 Cancer	79
3.2.2 Oral Exposure.....	90
3.2.2.1 Death	90
3.2.2.2 Systemic Effects.....	91
3.2.2.3 Immunological and Lymphoreticular Effects	116
3.2.2.4 Neurological Effects	117

3.2.2.5	Reproductive Effects.....	118
3.2.2.6	Developmental Effects.....	120
3.2.2.7	Cancer.....	123
3.2.3	Dermal Exposure.....	123
3.2.3.1	Death.....	123
3.2.3.2	Systemic Effects.....	123
3.2.3.3	Immunological and Lymphoreticular Effects.....	128
3.2.3.4	Neurological Effects.....	129
3.2.3.5	Reproductive Effects.....	129
3.2.3.6	Developmental Effects.....	130
3.2.3.7	Cancer.....	130
3.3	GENOTOXICITY.....	130
3.4	TOXICOKINETICS.....	134
3.4.1	Absorption.....	135
3.4.1.1	Inhalation Exposure.....	135
3.4.1.2	Oral Exposure.....	136
3.4.1.3	Dermal Exposure.....	137
3.4.2	Distribution.....	138
3.4.2.1	Inhalation Exposure.....	138
3.4.2.2	Oral Exposure.....	140
3.4.2.3	Dermal Exposure.....	141
3.4.2.4	Other Routes of Exposure.....	141
3.4.3	Metabolism.....	142
3.4.4	Elimination and Excretion.....	142
3.4.4.1	Inhalation Exposure.....	142
3.4.4.2	Oral Exposure.....	143
3.4.4.3	Dermal Exposure.....	144
3.4.5	Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models.....	144
3.5	MECHANISMS OF ACTION.....	153
3.5.1	Pharmacokinetic Mechanisms.....	153
3.5.2	Mechanisms of Toxicity.....	154
3.5.3	Animal-to-Human Extrapolations.....	156
3.6	TOXICITIES MEDIATED THROUGH THE NEUROENDOCRINE AXIS.....	157
3.7	CHILDREN'S SUSCEPTIBILITY.....	158
3.8	BIOMARKERS OF EXPOSURE AND EFFECT.....	161
3.8.1	Biomarkers Used to Identify or Quantify Exposure to Nickel.....	162
3.8.2	Biomarkers Used to Characterize Effects Caused by Nickel.....	164
3.9	INTERACTIONS WITH OTHER CHEMICALS.....	164
3.10	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE.....	166
3.11	METHODS FOR REDUCING TOXIC EFFECTS.....	167
3.11.1	Reducing Peak Absorption Following Exposure.....	167
3.11.2	Reducing Body Burden.....	168
3.11.3	Interfering with the Mechanism of Action for Toxic Effects.....	169
3.12	ADEQUACY OF THE DATABASE.....	170
3.12.1	Existing Information on Health Effects of Nickel.....	170
3.12.2	Identification of Data Needs.....	172
3.12.3	Ongoing Studies.....	182
4.	CHEMICAL AND PHYSICAL INFORMATION.....	185
4.1	CHEMICAL IDENTITY.....	185
4.2	PHYSICAL AND CHEMICAL PROPERTIES.....	185

5. PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	195
5.1 PRODUCTION	195
5.2 IMPORT/EXPORT	197
5.3 USE.....	202
5.4 DISPOSAL	203
6. POTENTIAL FOR HUMAN EXPOSURE	205
6.1 OVERVIEW	205
6.2 RELEASES TO THE ENVIRONMENT	213
6.2.1 Air	213
6.2.2 Water.....	216
6.2.3 Soil	219
6.3 ENVIRONMENTAL FATE.....	220
6.3.1 Transport and Partitioning.....	220
6.3.2 Transformation and Degradation	229
6.3.2.1 Air	229
6.3.2.2 Water.....	230
6.3.2.3 Sediment and Soil	231
6.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	231
6.4.1 Air	231
6.4.2 Water.....	235
6.4.3 Sediment and Soil	238
6.4.4 Other Environmental Media.....	241
6.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	243
6.6 EXPOSURES OF CHILDREN	253
6.7 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	255
6.8 ADEQUACY OF THE DATABASE.....	256
6.8.1 Identification of Data Needs	257
6.8.2 Ongoing Studies	260
7. ANALYTICAL METHODS	265
7.1 BIOLOGICAL MATERIALS	265
7.2 ENVIRONMENTAL SAMPLES.....	268
7.3 ADEQUACY OF THE DATABASE.....	274
7.3.1 Identification of Data Needs	275
7.3.2 Ongoing Studies	276
8. REGULATIONS AND ADVISORIES	279
9. REFERENCES	285
10. GLOSSARY	345

APPENDICES

A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS A-1

B. USER’S GUIDE..... B-1

C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS..... C-1

D. INDEX D-1

LIST OF FIGURES

3-1. Levels of Significant Exposure to Nickel - Inhalation	59
3-2. Levels of Significant Exposure to Nickel - Oral.....	105
3-3. Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance	186
3-4. Diagram of the Compartmental Model of Nickel Metabolism.....	188
3-5. Existing Information on Health Effects of Nickel.....	214
6-1. Frequency of NPL Sites with Nickel Contamination	250

LIST OF TABLES

3-1. Levels of Significant Exposure to Nickel - Inhalation	29
3-2. Comparison of Risk of Dying of Lung Cancer at Different Levels of Cumulative Exposure to Sulfidic Nickel by Different Levels of Combined Cumulative Exposure to Oxidic and Soluble Nickel in the Mond/INCO (Clydach) Nickel Refinery	82
3-3. Comparison of Risk of Dying of Lung Cancer at Different Levels of Cumulative Exposure to Oxidic Nickel by Different Levels of Combined Cumulative Exposure to Sulfidic and Soluble Nickel in the Mond/INCO (Clydach) Nickel Refinery	83
3-4. Comparison of Risk of Dying of Lung Cancer at Different Levels of Cumulative Exposure to Soluble Nickel by Different Levels of Combined Cumulative Exposure to Sulfidic and Oxidic Nickel in the Mond/INCO (Clydach) Nickel Refinery	84
3-5. Comparison of Risk of Dying of Lung Cancer at Different Levels of Cumulative Exposure to Metallic Nickel by Different Levels of Combined Cumulative Exposure to Sulfidic, Oxidic, and Soluble Nickel in the Mond/INCO (Clydach) and Falconbridge (Kristainsand) Nickel Refineries	85
3-6. Alveolar/Bronchiolar Neoplasms and Adrenal Medulla Proliferative Lesions in Rats	88
3-7. Alveolar/Bronchiolar Neoplasms in Mice	94
3-8. Levels of Significant Exposure to Nickel - Oral.....	92
3-9. Levels of Significant Exposure to Nickel - Dermal.....	124
3-10. Genotoxicity of Nickel <i>In Vivo</i>	136
3-11. Genotoxicity of Nickel <i>In Vitro</i>	144
3-12. Kinetic Parameters of Nickel Sulfate Absorption, Distribution, and Elimination in Humans	189
3-13. Clearance Rate Coefficient Constants of Nickel Compounds	193
3-14. Ongoing Studies on Nickel Health Effects	226
4-1. Chemical Identity of Nickel and Compounds.....	228
4-2. Physical and Chemical Properties of Nickel and Compounds	234
5-1. Facilities that Produce, Process, or Use Nickel Metal.....	242
5-2. Facilities that Produce, Process, or Use Nickel Compounds	244
6-1. Releases to the Environment from Facilities that Produce, Process, or Use Nickel.....	251
6-2. Releases to the Environment from Facilities that Produce, Process, or Use Nickel Compounds	253

6-3. Total Dietary Exposure Estimates of Study Participants to Nickel Based on the Dietary Information Obtained from the NHEXAS Arizona Study	289
6-4. Dietary Exposure Estimates of U.S. Populations to Nickel Based on the Dietary Exposure Potential Model (DEPM)	292
6-5. Nickel Levels in Air and Distribution of Different Forms of Nickel as a Proportion (by Weight) of Total Nickel in Selected Departments and Time Periods at a Nickel Refinery in Norway	295
6-6. Ongoing Studies on Environmental Fate and the Potential for Human Exposure to Nickel	313
7-1. Analytical Methods for Determining Nickel in Biological Materials	331
7-2. Analytical Methods for Determining Nickel in Environmental Samples	334
7-3. Ongoing Studies Involving Sample Collection and the Characterization and Quantification of Nickel	341
8-1. Regulations and Guidelines Applicable to Nickel and Nickel Compounds	345