



Toxicological Profile for Acrylonitrile

April 2025



U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry

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.

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-duration 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 due to acute-, intermediate-, and chronic-duration exposures; 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.



Christopher M. Reh, Ph.D.

Associate Director

Agency for Toxic Substances and Disease Registry
Centers for Disease Control and Prevention

VERSION HISTORY

Date	Description
April 2025	Final toxicological profile released
August 2023	Draft for public comment toxicological profile released
December 1990	Final toxicological profile released

CONTRIBUTORS & REVIEWERS

CHEMICAL MANAGER TEAM

Mohammad Shoeb, Ph.D. (Lead)
Obaid Faroon, D.V.M., Ph.D. (Retired)
Custodio Muianga, M.P.H., Ph.D.
Breanna Alman, M.P.H.

Lisa Ingerman, Ph.D., D.A.B.T.
Savannah Sierco, M.S.

SRC, Inc., North Syracuse, NY

ATSDR, Office of Innovation and Analytics, Atlanta, GA

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 Hazard Assessment; ATSDR, Office of Capacity Development and Applied Prevention Science; ATSDR, Office of Science; NCEH, Division of Laboratory Sciences; NCEH, Division of Environmental Health Science and Practice; EPA, Office of Research and Development; EPA, Office of Water.

PEER REVIEWERS

1. Gary M. Marsh, Ph.D., F.A.C.E.; Professor Emeritus of Biostatistics and Epidemiology; Founding Director, Center for Occupational Biostatistics & Epidemiology; Department of Biostatistics; School of Public Health; University of Pittsburgh; Pittsburgh, Pennsylvania
2. Vernon E. Walker, D.V.M., Ph.D.; Genetic Toxicology Laboratory; Department of Pathology and Laboratory Medicine; Larner College of Medicine; University of Vermont; Jericho, Vermont
3. Stella Koutros, Ph.D., M.P.H.; Investigator; National Cancer Institute; Division of Cancer Epidemiology and Genetics; Occupational and Environmental Epidemiology Branch; Bethesda, Maryland
4. Deborah Cory-Slechta, Ph.D.; Department of Environmental Medicine; University of Rochester Medical Center; Rochester, New York
5. Ivan Rusyn, M.D., Ph.D.; Professor and Chair; Department of Veterinary Integrative Biosciences; College of Vet Medicine & Biomedical Sciences, Texas A&M University; College Station, Texas

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	ii
FOREWORD	iii
VERSION HISTORY	iv
CONTRIBUTORS & REVIEWERS	v
CONTENTS	vii
LIST OF FIGURES	ix
LIST OF TABLES	x
CHAPTER 1. RELEVANCE TO PUBLIC HEALTH	1
1.1 OVERVIEW AND U.S. EXPOSURES	1
1.2 SUMMARY OF HEALTH EFFECTS	1
1.3 MINIMAL RISK LEVELS (MRLs)	5
CHAPTER 2. HEALTH EFFECTS	8
2.1 INTRODUCTION	8
2.2 DEATH	52
2.3 BODY WEIGHT	53
2.4 RESPIRATORY	53
2.5 CARDIOVASCULAR	55
2.6 GASTROINTESTINAL	55
2.7 HEMATOLOGICAL	56
2.8 MUSCULOSKELETAL	57
2.9 HEPATIC	58
2.10 RENAL	59
2.11 DERMAL	59
2.12 OCULAR	60
2.13 ENDOCRINE	60
2.14 IMMUNOLOGICAL	60
2.15 NEUROLOGICAL	61
2.16 REPRODUCTIVE	63
2.17 DEVELOPMENTAL	64
2.18 OTHER NONCANCER	65
2.19 CANCER	65
2.20 GENOTOXICITY	73
CHAPTER 3. TOXICOKINETICS, SUSCEPTIBLE POPULATIONS, BIOMARKERS, CHEMICAL INTERACTIONS	78
3.1 TOXICOKINETICS	78
3.1.1 Absorption	78
3.1.2 Distribution	79
3.1.3 Metabolism	80
3.1.4 Excretion	83
3.1.5 Physiologically Based Pharmacokinetic (PBPK)/Pharmacodynamic (PD) Models	84
3.1.6 Animal-to-Human Extrapolations	87
3.2 CHILDREN AND OTHER POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	88
3.3 BIOMARKERS OF EXPOSURE AND EFFECT	89
3.3.1 Biomarkers of Exposure	90

3.3.2	Biomarkers of Effect	91
3.4	INTERACTIONS WITH OTHER CHEMICALS	91
CHAPTER 4. CHEMICAL AND PHYSICAL INFORMATION		93
4.1	CHEMICAL IDENTITY	93
4.2	PHYSICAL AND CHEMICAL PROPERTIES	93
CHAPTER 5. POTENTIAL FOR HUMAN EXPOSURE		95
5.1	OVERVIEW	95
5.2	PRODUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	97
5.2.1	Production	97
5.2.2	Import/Export	99
5.2.3	Use	99
5.2.4	Disposal	100
5.3	RELEASES TO THE ENVIRONMENT	100
5.3.1	Air	101
5.3.2	Water	103
5.3.3	Soil	104
5.4	ENVIRONMENTAL FATE	104
5.4.1	Transport and Partitioning	104
5.4.2	Transformation and Degradation	105
5.5	LEVELS IN THE ENVIRONMENT	107
5.5.1	Air	109
5.5.2	Water	110
5.5.3	Sediment and Soil	112
5.5.4	Other Media	112
5.6	GENERAL POPULATION EXPOSURE	113
5.7	POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	118
CHAPTER 6. ADEQUACY OF THE DATABASE		120
6.1	Information on Health Effects	120
6.2	Identification of Data Needs	120
6.3	Ongoing Studies	126
CHAPTER 7. REGULATIONS AND GUIDELINES		127
CHAPTER 8. REFERENCES		130
APPENDICES		
APPENDIX A.	ATSDR MINIMAL RISK LEVEL WORKSHEETS	A-1
APPENDIX B.	LITERATURE SEARCH FRAMEWORK FOR ACRYLONITRILE	B-1
APPENDIX C.	FRAMEWORK FOR ATSDR'S SYSTEMATIC REVIEW OF HEALTH EFFECTS DATA FOR ACRYLONITRILE	C-1
APPENDIX D.	USER'S GUIDE	D-1
APPENDIX E.	QUICK REFERENCE FOR HEALTH CARE PROVIDER	E-1
APPENDIX F.	GLOSSARY	F-1
APPENDIX G.	ACRONYMS, ABBREVIATIONS, AND SYMBOLS	G-1

LIST OF FIGURES

1-1. Health Effects Found in Animals Following Inhalation Exposure to Acrylonitrile	2
1-2. Health Effects Found in Animals Following Oral Exposure to Acrylonitrile	3
1-3. Summary of Sensitive Targets of Acrylonitrile – Inhalation.....	5
1-4. Summary of Sensitive Targets of Acrylonitrile – Oral.....	6
2-1. Overview of the Number of Studies Examining Acrylonitrile Health Effects	11
2-2. Levels of Significant Exposure to Acrylonitrile – Inhalation.....	18
2-3. Levels of Significant Exposure to Acrylonitrile – Oral.....	41
3-1. Proposed Metabolic Scheme for Acrylonitrile	81
5-1. Number of NPL Sites with Acrylonitrile Contamination	95
6-1. Summary of Existing Health Effects Studies on Acrylonitrile by Route and Endpoint.....	121

LIST OF TABLES

1-1. Minimal Risk Levels (MRLs) for Acrylonitrile	7
2-1. Levels of Significant Exposure to Acrylonitrile – Inhalation.....	12
2-2. Levels of Significant Exposure to Acrylonitrile – Oral.....	27
2-3. Levels of Significant Exposure to Acrylonitrile – Dermal.....	51
2-4. Cancer Outcomes in Humans Exposed to Acrylonitrile.....	67
2-5. Occupational Studies Included in Meta Analyses	70
2-6. Neoplastic Tumors Reported in Rats and Mice Chronically Exposed to Acrylonitrile.....	70
2-7. Genotoxicity of Acrylonitrile <i>In Vitro</i>	73
2-8. Genotoxicity of Acrylonitrile <i>In Vivo</i>	75
4-1. Chemical Identity of Acrylonitrile.....	93
4-2. Physical and Chemical Properties of Acrylonitrile.....	93
5-1. Facilities that Produce, Process, or Use Acrylonitrile	98
5-2. Industrial Uses of Acrylonitrile Reported Under the Chemical Data Reporting (CDR)	100
5-3. Releases to the Environment from Facilities that Produce, Process, or Use Acrylonitrile.....	101
5-4. Acrylonitrile Emissions Estimated by Sector	103
5-5. Lowest Limit of Detection Based on Standards	107
5-6. Summary of Environmental Levels of Acrylonitrile	108
5-7. Acrylonitrile Levels in Water, Soil, and Air of National Priorities List (NPL) Sites.....	108
5-8. Summary of Annual Concentration of Acrylonitrile (ppbv) Measured in Ambient Air at Locations Across the United States	109
5-9. Summary of Concentrations of Acrylonitrile (ppb) Measured in Surface Water and Groundwater Across the United States.....	110
5-10. Summary of Concentrations of Acrylonitrile (ppb) Measured in Surface and Groundwater at Superfund Sites.....	111
5-11. Summary of Concentrations of Acrylonitrile (ppb) Measured in Sediment at Superfund Sites	112
5-12. Estimated Levels of Human Exposure to Acrylonitrile for Nonoccupational and Occupational Exposure.....	114

5-13. Urinary N-Acetyl-S-(2-Cyanoethyl)-L-Cysteine (2CyEMA) Levels (Creatinine Adjusted) (µg/g Creatinine) in the U.S. General Population.....	115
5-14. Estimated Levels of Worker Exposure to Acrylonitrile (ppm) at Plants Across Three Decades.....	118
7-1. Regulations and Guidelines Applicable to Acrylonitrile.....	127