

TOXICOLOGICAL PROFILE FOR
NITROPHENOLS:
2-NITROPHENOL
4-NITROPHENOL

Agency for Toxic Substances and Disease Registry
U.S. Public Health Service

July 1992

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.

FOREWORD

The Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the 250 most significant hazardous substances were published in the Federal Register on April 17, 1987; on October 20, 1988; on October 26, 1989; and on October 17, 1990. A revised list of 275 substances was published on October 17, 1991.

Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the lists. Each profile must include the following content:

- (A) An examination, summary, and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order 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 which present a significant risk to human health of acute, subacute, and chronic health effects.
- (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and 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 is intended to characterize succinctly the toxicological and adverse health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature (that has been peer-reviewed) that describes a hazardous substance's toxicological properties. Other pertinent literature is also presented but 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.

Foreword

Each toxicological profile begins with a public health statement, which 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 will be identified by ATSDR, the National Toxicology Program (NTP) of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the beginning of the document.

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 our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, the Centers for Disease Control, the NTP, and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



William L. Roper, M.D., M.P.H.
Administrator
Agency for Toxic Substances and
Disease Registry

CONTENTS

FOREWORD	iii
LIST OF FIGURES	ix
LIST OF TABLES	xi
1. PUBLIC HEALTH STATEMENT	1
1.1 WHAT ARE 2-NITROPHENOL AND 4-NITROPHENOL?	1
1.2 HOW MIGHT I BE EXPOSED TO 2-NITROPHENOL AND 4-NITROPHENOL?	2
1.3 HOW CAN 2-NITROPHENOL AND 4-NITROPHENOL ENTER AND LEAVE MY BODY?	2
1.4 HOW CAN 2-NITROPHENOL AND 4-NITROPHENOL AFFECT MY HEALTH?	3
1.5 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO 2-NITROPHENOL AND 4-NITROPHENOL?	4
1.6 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?	4
1.7 WHERE CAN I GET MORE INFORMATION?	4
2. HEALTH EFFECTS	5
2.1 INTRODUCTION	5
2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE	5
2.2.1 Inhalation Exposure	6
2.2.1.1 Death	6
2.2.1.2 Systemic Effects	6
2.2.1.3 Immunological Effects	11
2.2.1.4 Neurological Effects	11
2.2.1.5 Developmental Effects	11
2.2.1.6 Reproductive Effects	11
2.2.1.7 Genotoxic Effects	12
2.2.1.8 Cancer	12
2.2.2 Oral Exposure	12
2.2.2.1 Death	12
2.2.2.2 Systemic Effects	12
2.2.2.3 Immunological Effects	17
2.2.2.4 Neurological Effects	17
2.2.2.5 Developmental Effects	17
2.2.2.6 Reproductive Effects	18
2.2.2.7 Genotoxic Effects	18
2.2.2.8 Cancer	18
2.2.3 Dermal Exposure	18
2.2.3.1 Death	18
2.2.3.2 Systemic Effects	18
2.2.3.3 Immunological Effects	22
2.2.3.4 Neurological Effects	22
2.2.3.5 Developmental Effects	22
2.2.3.6 Reproductive Effects	22
2.2.3.7 Genotoxic Effects	23

2.2.3.8	Cancer	23
2.3	TOXICOKINETICS	23
2.3.1	Absorption	23
2.3.1.1	Inhalation Exposure	23
2.3.1.2	Oral Exposure	23
2.3.1.3	Dermal Exposure	24
2.3.2	Distribution	24
2.3.2.1	Inhalation Exposure	24
2.3.2.2	Oral Exposure	24
2.3.2.3	Dermal Exposure	24
2.3.2.4	Other Routes of Exposure	24
2.3.3	Metabolism	25
2.3.4	Excretion	26
2.3.4.1	Inhalation Exposure	26
2.3.4.2	Oral Exposure	26
2.3.4.3	Dermal Exposure	29
2.3.4.4	Other Routes of Exposure	29
2.4	RELEVANCE TO PUBLIC HEALTH	29
2.5	BIOMARKERS OF EXPOSURE AND EFFECT	36
2.5.1	Biomarkers Used to Identify and/or Quantify Exposure to 2-Nitrophenol and 4-Nitrophenol	37
2.5.2	Biomarkers Used to Characterize Effects Caused by 2-Nitrophenol and 4-Nitrophenol	37
2.6	INTERACTIONS WITH OTHER CHEMICALS	37
2.7	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	38
2.8	MITIGATION OF EFFECTS	38
2.9	ADEQUACY OF THE DATABASE	39
2.9.1	Existing Information on Health Effects of 2-Nitrophenol and 4-Nitrophenol	39
2.9.2	Data Needs	40
2.9.3	On-going Studies	47
3.	CHEMICAL AND PHYSICAL INFORMATION	49
3.1	CHEMICAL IDENTITY	49
3.2	PHYSICAL AND CHEMICAL PROPERTIES	49
4.	PRODUCTION, IMPORT, USE, AND DISPOSAL	53
4.1	PRODUCTION	53
4.2	IMPORT/EXPORT	53
4.3	USE	53
4.4	DISPOSAL	55
5.	POTENTIAL FOR HUMAN EXPOSURE	57
5.1	OVERVIEW	57
5.2	RELEASES TO THE ENVIRONMENT	58
5.2.1	Air	58
5.2.2	Water	61
5.2.3	Soil	61

5.3	ENVIRONMENTAL FATE	62
5.3.1	Transport and Partitioning	62
5.3.2	Transformation and Degradation	64
5.3.2.1	Air	64
5.3.2.2	Water	65
5.3.2.3	Soil	66
5.4	LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT	67
5.4.1	Air	67
5.4.2	Water	68
5.4.3	Soil	68
5.4.4	Other Environmental Media	69
5.5	GENERAL POPULATION AND OCCUPATIONAL EXPOSURE	69
5.6	POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	70
5.7	ADEQUACY OF THE DATABASE	70
5.7.1	Data Needs	71
5.7.2	On-going Studies	73
6.	ANALYTICAL METHODS	75
6.1	BIOLOGICAL MATERIALS	75
6.2	ENVIRONMENTAL SAMPLES	77
6.3	ADEQUACY OF THE DATABASE	77
6.3.1	Data Needs	79
6.3.2	On-going Studies	80
7.	REGULATIONS AND ADVISORIES	81
8.	REFERENCES	83
9.	GLOSSARY	101
APPENDICES		
A.	USER'S GUIDE	A-1
B.	ACRONYMS, ABBREVIATIONS, AND SYMBOLS	B-1
C.	PEER REVIEW	C-1

LIST OF FIGURES

2-1	Levels of Significant Exposure to 4-Nitrophenol - Inhalation	8
2-2	Levels of Significant Exposure to 2- and 4-Nitrophenol - Oral	15
2-3	Proposed Metabolic Pathway for 2-Nitrophenol	27
2-4	Proposed Metabolic Pathway for 4-Nitrophenol	28
2-5	Existing Information on Health Effects of 2-Nitrophenol	41
2-6	Existing Information on Health Effects of 4-Nitrophenol	42
5-1	Frequency of NPL Sites with Nitrophenols Contamination	59

LIST OF TABLES

2-1	Levels of Significant Exposure to 4-Nitrophenol - Inhalation	7
2-2	Levels of Significant Exposure to Nitrophenols - Oral	13
2-3	Levels of Significant Exposure to Nitrophenols - Dermal	19
2-4	Genotoxicity of 2-Nitrophenol <u>In Vitro</u>	34
2-5	Genotoxicity of 4-Nitrophenol <u>In Vitro</u>	35
3-1	Chemical Identities of 2-Nitrophenol and 4-Nitrophenol	50
3-2	Physical and Chemical Properties of 2-Nitrophenol and 4-Nitrophenol	51
4-1	Facilities that Manufacture or Process Nitrophenols	54
5-1	Releases to the Environment from Facilities that Manufacture or Process Nitrophenols	60
6-1	Analytical Methods for Determining 2-Nitrophenol and 4-Nitrophenol in Biological Materials	76
6-2	Analytical Methods for Determining 2-Nitrophenol and 4-Nitrophenol in Environmental Samples	78
7-1	Regulations and Guidelines Applicable to 2-Nitrophenol and 4-Nitrophenol	82

