

CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR ACETALDEHYDE

Preamble	8
Introduction	17
1. SUMMARY	19
1.1 Identity, physical and chemical properties, and analytical methods	19
1.2 Sources of human and environmental exposure	19
1.3 Environmental transport, distribution, and transformation	19
1.4 Environmental levels and human exposure	20
1.5 Kinetics and metabolism	20
1.5.1 Absorption, distribution, and elimination	20
1.5.2 Metabolism	21
1.5.3 Reaction with other components	22
1.6 Effects on organisms in the environment	22
1.6.1 Aquatic organisms	22
1.6.2 Terrestrial organisms	22
1.7 Effects on experimental animals and <i>in vitro</i> test systems	23
1.7.1 Single exposure	23
1.7.2 Short- and long-term exposures	23
1.7.3 Reproduction, embryotoxicity, and teratogenicity	23
1.7.4 Mutagenicity and related end-points	24
1.7.5 Carcinogenicity	24
1.7.6 Special studies	24
1.8 Effects on humans	24
1.9 Evaluation of human health risks and effects on the environment	25
2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, AND ANALYTICAL METHODS	27
2.1 Identity	27
2.2 Physical and chemical properties	27
2.3 Conversion factors	28
2.4 Analytical methods	28

3.	SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE	37
3.1	Natural occurrence	37
3.2	Anthropogenic sources	37
3.2.1	Production	37
3.2.1.1	Production levels and processes	37
3.2.1.2	Emissions	37
3.2.2	Uses	38
3.2.3	Waste disposal	39
3.2.4	Other sources	39
4.	ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION	41
4.1	Transport and distribution between media	41
4.2	Abiotic degradation	41
4.3	Biodegradation	42
5.	ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE	44
5.1	Environmental levels	44
5.1.1	Air	44
5.1.2	Water	45
5.1.3	Soil	45
5.1.4	Food	45
5.1.5	Cigarette smoke	46
5.2	General population exposure	46
5.3	Occupational exposure	47
6.	KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS	48
6.1	Absorption	48
6.2	Distribution	48
6.2.1	Animal studies	48
6.2.1.1	Distribution after inhalation exposure	48
6.2.1.2	Distribution to the embryo and fetus	48
6.2.1.3	Distribution to the brain	49
6.2.2	Human studies	49
6.3	Metabolism	50
6.3.1	Animal studies	50
6.3.1.1	Liver	51

6.3.1.2	Respiratory tract	51
6.3.1.3	Kidneys	52
6.3.1.4	Testes and ovaries	52
6.3.1.5	Embryonic tissue	52
6.3.1.6	Metabolism during pregnancy	52
6.3.2	Human studies	52
6.4	Elimination	53
6.5	Reaction with cellular macromolecules	53
6.5.1	Proteins	53
6.5.2	Nucleic acids	55
7.	EFFECTS ON ORGANISMS IN THE ENVIRONMENT	57
7.1	Aquatic organisms	57
7.2	Terrestrial organisms	57
8.	EFFECTS ON EXPERIMENTAL ANIMALS AND <i>IN VITRO</i> TEST SYSTEMS	59
8.1	Single exposure	59
8.1.1	LD ₅₀ and LC ₅₀ values	59
8.2	Short-term exposure	60
8.2.1	Oral	60
8.2.2	Inhalation	60
8.2.3	Dermal	61
8.2.4	Parenteral	61
8.3	Skin and eye irritation; sensitization	62
8.4	Long-term exposure	62
8.4.1	Oral	62
8.4.2	Inhalation	62
8.5	Reproductive and developmental toxicity	63
8.6	Mutagenicity and related end-points	63
8.6.1	Bacteria	63
8.6.2	Non-mammalian eukaryotic systems	71
8.6.2.1	Gene mutation assays	71
8.6.2.2	Chromosome alterations	71
8.6.3	Cultured mammalian cells	71
8.6.3.1	Gene mutation assays	71
8.6.3.2	Chromosome alterations and sister chromatid exchange	71
8.6.4	<i>In vivo</i> assays	72
8.6.4.1	Somatic cells	72
8.6.4.2	Germ cells	73
8.6.5	Other assays	73

8.6.5.1	DNA single-strand breaks	73
8.6.5.2	DNA cross-linking	73
8.6.6	Cell transformation	75
8.7	Carcinogenicity bioassays	75
8.7.1	Inhalation exposure	75
8.7.2	Co-carcinogenicity and promotion studies	78
8.8	Neurological effects	79
8.9	Immunological effects	79
8.9.1	Direct effects on immune cells	79
8.9.2	Generation of antibodies reacting with acetaldehyde-modified proteins	80
8.9.3	Related immunological effects	81
8.10	Biochemical effects	81
9.	EFFECTS ON HUMANS	82
9.1	General population exposure	82
9.2	Occupational exposure	82
9.2.1	General observations	82
9.2.2	Clinical studies	82
9.2.3	Epidemiological studies	83
9.3	Effects of endogenous acetaldehyde	83
9.3.1	Effects of ethanol possibly attributable to acetaldehyde or acetaldehyde metabolism	83
10.	EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT	85
10.1	Evaluation of human health risks	85
10.1.1	Exposure	85
10.1.2	Health effects	85
10.1.3	Approaches to risk assessment	87
10.2	Evaluation of effects on the environment	89
11.	RECOMMENDATIONS FOR RESEARCH	91
	REFERENCES	92
	RESUME	113
	RESUMEN	122