
CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR METHYLENE CHLORIDE

1. SUMMARY	21
1.1 Identity, physical and chemical properties, and analytical methods	21
1.2 Sources of human and environmental exposure	21
1.3 Environmental transport, distribution and transformation	21
1.4 Environmental levels and human exposure	22
1.5 Kinetics and metabolism	23
1.6 Effects on organisms in the environment	24
1.7 Effects on laboratory mammals and <i>in vitro</i> test systems	24
1.7.1 Single exposure	24
1.7.2 Short- and long-term exposure	25
1.7.3 Skin and eye irritation	25
1.7.4 Developmental and reproductive toxicity	25
1.7.5 Mutagenicity and related end-points	26
1.7.6 Chronic toxicity and carcinogenicity	26
1.8 Effects on humans	29
2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, AND ANALYTICAL METHODS	30
2.1 Identity	30
2.2 Physical and chemical properties	31
2.3 Conversion factors	31
2.4 Analytical methods	31
3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE	37
3.1 Natural occurrence	37
3.2 Anthropogenic sources	37
3.2.1 Production	37
3.2.2 Uses	37
3.2.3 Consumer applications	38
3.2.4 Sources in the environment	39

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION AND TRANSFORMATION	40
Appraisal	40
4.1 Transport and distribution between media	40
4.1.1 Water/air	40
4.1.2 Soil/air	42
4.1.3 Water/soil	42
4.1.4 Multicompartment distribution	42
4.2 Abiotic degradation	42
4.2.1 Atmosphere	42
4.2.2 Water	45
4.2.3 Soil	46
4.3 Biotransformation	46
4.3.1 Aerobic	46
4.3.2 Anaerobic	48
4.3.3 Bioaccumulation	51
4.4 Interaction with other physical, chemical or biological factors	51
5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE	52
Appraisal	52
5.1 Environmental levels	52
5.1.1 Atmosphere	52
5.1.1.1 Ambient air	52
5.1.1.2 Precipitation	52
5.1.2 Water	55
5.1.3 Aquatic organisms	59
5.1.4 Soil and sediment	59
5.2 Human exposure	60
5.2.1 General population	60
5.2.1.1 Indoor air	60
5.2.1.2 Drinking-water	60
5.2.1.3 Foodstuffs	61
5.2.1.4 Consumer exposure	63
5.2.2 Occupational exposure	65
5.2.2.1 Production	65
5.2.2.2 Paint stripping and related activities	65
5.2.2.3 Aerosol production and use	69
5.2.2.4 Use as a process solvent	69
5.2.2.5 Cleaning and degreasing	70
5.2.3 Occupational exposure limits	70

5.3	Human monitoring data	73
5.3.1	Body burden	73
5.3.2	Occupational exposure studies	73
5.3.3	Biological exposure indices	74
6.	KINETICS AND METABOLISM	76
6.1	Absorption	77
6.1.1	Inhalation exposure	77
6.1.1.1	Human studies	77
6.1.1.2	Animal studies	78
6.1.2	Oral exposure	79
6.1.3	Dermal exposure	79
6.2	Distribution	80
6.2.1	Inhalation exposure	80
6.2.1.1	Human studies	80
6.2.1.2	Animal studies	81
6.2.2	Oral exposure	82
6.2.3	Dermal exposure	82
6.3	Metabolism	82
6.3.1	<i>In vitro</i> studies	82
6.3.2	<i>In vivo</i> studies	85
6.4	Elimination and excretion	87
6.4.1	Inhalation exposure	87
6.4.1.1	Human studies	87
6.4.1.2	Animal studies	89
6.4.2	Oral exposure	89
6.4.3	Dermal exposure	90
7.	EFFECTS ON ORGANISMS IN THE ENVIRONMENT	91
7.1	Microorganisms	91
7.1.1	Bacteria	91
7.1.1.1	Aerobic bacteria	91
7.1.1.2	Anaerobic bacteria	92
7.1.2	Protozoa	93
7.1.3	Algae	93
7.2	Aquatic organisms	93
7.2.1	Plants	95
7.2.2	Invertebrates	95
7.2.2.1	Insects	95
7.2.2.2	Crustaceans	95
7.2.2.3	Molluscs	95

7.2.3	Fish	95
7.2.3.1	Acute toxicity	95
7.2.3.2	Chronic toxicity and reproduction	99
7.2.4	Amphibians	99
7.3	Terrestrial organisms	102
7.4	Population and ecosystem effects	102
7.4.1	Soil microorganisms	102
7.4.2	Sediment microorganisms	103
7.4.3	Microcosms and mesocosms	103
8.	EFFECTS ON LABORATORY MAMMALS AND <i>IN VITRO</i> TEST SYSTEMS	104
8.1	Single exposure	104
8.1.1	Acute toxicity data	104
8.1.2	Oral administration	104
8.1.3	Inhalation administration	107
8.1.3.1	Rat	107
8.1.3.2	Mouse	108
8.1.3.3	Other animals	109
8.1.4	Dermal administration	110
8.1.5	Intraperitoneal administration	110
8.1.6	Intravenous administration	111
8.1.7	Subcutaneous administration	111
8.1.8	Appraisal	112
8.2	Short-term exposure	112
8.2.1	Oral administration	112
8.2.2	Subcutaneous administration	112
8.2.3	Inhalation administration	112
8.2.3.1	Rat	112
8.2.3.2	Other animals	113
8.3	Long-term exposure	115
8.3.1	Rat	115
8.3.1.1	Inhalation exposure	115
8.3.1.2	Oral exposure	116
8.3.2	Mouse	116
8.3.2.1	Inhalation exposure	116
8.3.2.2	Oral exposure	117
8.3.3	Other animals	117
8.3.4	Appraisal	118
8.4	Skin and eye irritation; skin sensitization	119
8.4.1	Skin irritation	119
8.4.2	Eye irritation	119
8.4.3	Sensitization	119

8.4.4	Appraisal	119
8.5	Developmental and reproductive toxicity	119
8.5.1	Developmental toxicity	119
8.5.2	Reproductive toxicity	121
8.5.3	Appraisal	121
8.6	Mutagenicity and related end-points	122
8.6.1	<i>In vitro</i>	122
8.6.1.1	Bacteria	122
8.6.1.2	Fungi and yeasts	135
8.6.1.3	Mutation in mammalian cells	135
8.6.1.4	Chromosomal effects	135
8.6.1.5	DNA damage	136
8.6.1.6	DNA binding <i>in vitro</i>	136
8.6.1.7	Cell transformation	137
8.6.2	<i>In vivo</i>	137
8.6.2.1	Chromosome damage	137
8.6.2.2	Drosophila	141
8.6.2.3	DNA damage	142
8.6.2.4	DNA binding	142
8.6.2.5	Dominant lethal assay	143
8.6.2.6	Replicative DNA synthesis	143
8.6.3	Appraisal	144
8.7	Chronic toxicity and carcinogenicity	145
8.7.1	Inhalation exposure	145
8.7.1.1	Rat	145
8.7.1.2	Mouse	151
8.7.1.3	Hamster	152
8.7.2	Oral administration	154
8.7.2.1	Rat	154
8.7.2.2	Mouse	154
8.7.3	Appraisal	157
8.8	Mechanistic studies	158
8.8.1	<i>In vitro</i> metabolic studies	158
8.8.2	<i>In vivo</i> metabolic studies	160
8.8.3	Pulmonary effects	161
8.8.4	Studies on oncogene activation	162
8.8.5	The use of mechanistic studies in extrapolation	163
8.8.6	Mammary tumour promotion	165
8.8.7	Appraisal	166
8.9	Interspecies and dose extrapolations by kinetic modelling	167

9. EFFECTS ON HUMANS	169
9.1 General population exposure	169
9.1.1 Environmental exposure	169
9.1.2 Oral exposure	169
9.2 Occupational exposure	170
9.2.1 Short-term exposure	170
9.2.1.1 Case studies	170
9.2.1.2 Skin and eye effects	172
9.2.1.3 Laboratory studies	173
9.2.2 Long-term exposure	174
9.2.2.1 Case studies	174
9.3 Appraisal of human effects	181
10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT	183
10.1 Evaluation of human health risks	183
10.2 Evaluation of effects on the environment	186
REFERENCES	188
RESUME	222
RESUMEN	233