

CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR CARBON TETRACHLORIDE

PREAMBLE	ix
ABBREVIATIONS	xviii
1. SUMMARY	1
2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, AND ANALYTICAL METHODS	6
2.1 Identity	6
2.2 Physical and chemical properties	7
2.3 Conversion factors	8
2.4 Analytical methods	8
2.4.1 Sampling and analysis in air	13
2.4.2 Sampling and analysis in water	13
2.4.3 Sampling and analysis in biological samples	14
2.4.3.1 Blood and tissues	14
2.4.3.2 Urine	14
2.4.3.3 Fish	14
2.4.4 Sampling and analysis in foodstuffs	14
3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE	16
3.1 Natural occurrence	16
3.2 Anthropogenic sources	16
3.2.1 Production	16
3.2.1.1 Direct production and procedures	16
3.2.1.2 Indirect production	17
3.2.1.3 Emissions	18
3.2.2 Uses	18

4.	ENVIRONMENTAL TRANSPORT, DISTRIBUTION AND TRANSFORMATION	19
4.1	Transport and distribution between media	19
4.1.1	Transport	19
4.1.2	Distribution	19
4.1.3	Removal from the atmosphere; global warming potential	21
4.1.4	Removal from water	22
4.1.5	Removal from soil	22
4.2	Abiotic degradation	22
4.2.1	Degradation in atmosphere	22
4.2.1.1	Photodegradation	22
4.2.1.2	Photolysis	23
4.2.1.3	Ozone-depletion potential	23
4.2.2	Degradation in water	24
4.2.3	Other degradation processes	24
4.3	Biotic degradation	24
4.3.1	Aerobic	24
4.3.2	Anaerobic	25
4.4	Bioaccumulation	26
5.	CONCENTRATIONS IN THE ENVIRONMENT AND EXPOSURE	28
5.1	Environmental levels	28
5.1.1	Air	28
5.1.2	Water	28
5.1.3	Soil and sediment	30
5.1.4	Biota	30
5.2	General population exposure	30
5.2.1	Outdoor air	30
5.2.2	Indoor air	30
5.2.3	Drinking-water	32
5.2.4	Foodstuffs	33
5.2.5	Intake averages	34
5.3	Occupational exposure	34

6.	KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS	36
6.1	Pharmacokinetics	36
6.1.1	Absorption	36
6.1.1.1	Oral	36
6.1.1.2	Dermal	37
6.1.1.3	Inhalation	37
6.1.2	Distribution	38
6.1.3	Elimination and fate	40
6.1.4	Physiologically based pharmacokinetic modelling	42
6.2	Biotransformation and covalent binding of metabolites	43
6.3	Human studies	48
6.3.1	Uptake	48
6.3.1.1	Dermal	48
6.3.1.2	Inhalation	49
6.3.2	Elimination	49
7.	EFFECTS ON LABORATORY MAMMALS AND <i>IN VITRO</i> TEST SYSTEMS	50
7.1	Single exposure	50
7.1.1	Lethality	50
7.1.2	Non-lethal effects	50
7.1.2.1	Oral exposure	50
7.1.2.2	Inhalation exposure	55
7.1.2.3	Subcutaneous and intraperitoneal exposure	57
7.1.2.4	Dermal exposure	59
7.2	Short-term exposure	59
7.2.1	Oral exposure	59
7.2.2	Inhalation exposure	62
7.2.3	Intraperitoneal exposure	66
7.3	Long-term exposure	68
7.4	Irritation	70
7.4.1	Skin irritation	70
7.4.2	Eye irritation	70

7.5	Toxicity to the reproductive system, embryotoxicity, teratogenicity	71
7.5.1	Reproduction	71
7.5.2	Embryotoxicity and teratogenicity	71
7.5.2.1	Oral exposure	72
7.5.2.2	Inhalation exposure	72
7.6	Mutagenicity	73
7.7	Carcinogenicity	83
7.7.1	Mice	83
7.7.2	Rats	85
7.8	Special studies	86
7.8.1	Immunotoxicity	86
7.8.2	Influence of oxygen levels	87
7.9	Factors modifying toxicity	88
7.9.1	Dosing vehicles	88
7.9.2	Diet	89
7.9.3	Alcohol	90
7.9.4	Enhancement of carbon tetrachloride-induced hepatotoxicity by various compounds	93
7.9.5	Reduction of carbon tetrachloride-induced hepatotoxicity by various compounds	97
7.10	Mode of action	100
8.	EFFECTS ON HUMANS	105
8.1	Controlled studies	105
8.1.1	Inhalation	105
8.1.2	Dermal	105
8.2	Case reports	106
8.3	Epidemiology	108
8.3.1	Non-cancer epidemiology	108
8.3.2	Cancer epidemiology	109
9.	EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD	113
9.1	Toxicity to microorganisms	113
9.2	Aquatic toxicity	113
9.2.1	Algae	113

9.2.2	Invertebrates	113
9.2.3	Vertebrates	118
9.3	Terrestrial toxicity	118
9.3.1	Earthworms	118
10.	EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT	120
10.1	Evaluation of human health risks	120
10.1.1	Exposure	120
10.1.2	Health effects	121
10.1.3	Approaches to health risk assessment	122
10.1.3.1	Calculation of a TDI based on oral data	122
10.1.3.2	Calculation of a TC based on inhalation data	123
10.1.3.3	Summary of the results of risk assessment	124
10.1.3.4	Conclusions based on exposure and health risk assessment	124
10.2	Evaluation of effects on the environment	125
11.	FURTHER RESEARCH	128
12.	PREVIOUS EVALUATION BY INTERNATIONAL BODIES	129
	REFERENCES	130
	RÉSUMÉ	166
	RESUMEN	172