CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR CHLOROFORM

1. SUMMARY 13

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, AND ANALYTICAL METHODS 19

2.1 Identity 19
2.2 Physical and chemical properties 19
2.3 Conversion factors 21
2.4 Analytical methods 21
2.4.1 Sampling and analysis in air 28
2.4.1.1 Direct measurement 28
2.4.1.2 Adsorption-liquid desorption 28
2.4.1.3 Adsorption-thermal desorption 28
2.4.1.4 Cold trap-heating 28
2.4.2 Sampling and analysis in water 28
2.4.3 Sampling and analysis in biological samples 29
2.4.3.1 Blood and tissues 29
2.4.3.2 Urine 29
2.4.3.3 Fish 29
2.4.4 Sampling and analysis in soil gas 30

3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE 31

3.1 Natural occurrence 31
3.2 Anthropogenic sources 31
3.2.1 Production 31
3.2.1.1 Direct production levels and processes 31
3.2.1.2 Indirect production 31
3.2.1.3 Emissions from direct production and use 33
3.2.1.4 Emissions from indirect production 34
3.2.2 Uses 34

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION AND TRANSFORMATION 35

4.1 Transport and distribution between media 35
4.1.1 Transport 35
4.1.2 Distribution 35

4.1.3 Removal from the atmosphere 35
4.2 Biotic degradation 36
4.3 Bioaccumulation 38

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE 39

5.1 Environmental levels 39
5.1.1 Ambient air 39
5.1.2 Indoor air 40
5.1.3 Water 41
5.1.3.1 Sea water 41
5.1.3.2 Rivers and lakes 41
5.1.3.3 Rain water 41
5.1.3.4 Waste water 41
5.1.3.5 Ground water 42
5.1.3.6 Drinking-water 42
5.1.4 Soil 43
5.1.5 Foodstuffs 43
5.2 General population exposure 44
5.2.1 Outdoor air 44
5.2.2 Indoor air 45
5.2.3 Drinking-water 46
5.2.4 Foodstuffs 46
5.3 Occupational exposure during manufacture, formulation or use 46

6. KINETICS IN LABORATORY ANIMALS AND HUMANS 48

6.1 Pharmacokinetics 48
6.1.1 Absorption 48
6.1.1.1 Oral 48
6.1.1.2 Dermal 48
6.1.1.3 Inhalation 49
6.1.2 Distribution 49
6.1.3 Elimination and fate 51
6.1.4 Physiologically based pharmacokinetic modelling for chloroform 53
6.2 Biotransformation and covalent binding of metabolites 54
6.3 Human studies 60
6.3.1 Uptake 60
6.3.1.1 Oral 60
6.3.1.2 Dermal 60
6.3.1.3 Inhalation 61

6.3.2 Distribution 61
6.3.3 Elimination 62
6.3.4 Biotransformation 62

7. EFFECTS ON LABORATORY MAMMALS AND *IN VITRO* TEST SYSTEMS 63

7.1 Single exposure 63
7.1.1 Lethality 63
7.1.2 Non-lethal effects 63
7.1.2.1 Oral exposure 63
7.1.2.2 Subcutaneous and intraperitoneal exposure 68
7.1.2.3 Inhalation exposure 70
7.1.2.4 Dermal exposure 71
7.2 Short-term exposure 71
7.2.1 Oral exposure 71
7.2.1.1 Mice 71
7.2.1.2 Rats 74
7.2.2 Inhalation exposure 75
7.3 Long-term exposure 77
7.4 Skin and eye irritation 78
7.5 Reproductive toxicity, embryotoxicity and teratogenicity 78
7.5.1 Reproduction 78
7.5.2 Embryotoxicity and teratogenicity 79
7.5.2.1 Oral exposure 79
7.5.2.2 Inhalation exposure 80
7.6 Mutagenicity and related end-points 81
7.7 Carcinogenicity 100
7.7.1 Mice 100
7.7.2 Rats 102
7.7.3 Dogs 104
7.7.4 Studies on initiating-promoting activity 104
7.7.4.1 Mice 104
7.7.4.2 Rats 105
7.8 *In vitro* studies 107
7.9 Factors modifying toxicity; toxicity of metabolites 109

8. EFFECTS ON HUMANS 113

8.1 Acute non-lethal effects 113
8.2 Epidemiology 115
8.2.1 Occupational exposure 115
8.2.2 General exposure 116

8.3 Abuse and addiction 117

9. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD 118

9.1 Freshwater organisms 118
9.1.1 Short-term toxicity 118
9.1.2 Long-term toxicity 125
9.2 Marine organisms 125

10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT 126

10.1 Evaluation of human health risks 126
10.1.1 Exposure 126
10.1.2 Health effects 126
10.1.3 Approaches to risk assessment 128
10.1.3.1 Non-neoplastic effects 129
10.1.3.2 Neoplastic effects 129
10.2 Evaluation of effects in the environment 131

11. FURTHER RESEARCH 132

12. PREVIOUS EVALUATION BY INTERNATIONAL BODIES 133

REFERENCES 134

RESUME 162

RESUMEN 169