

# CONTENTS

## ENVIRONMENTAL HEALTH CRITERIA FOR FLUORIDES

PREAMBLE	ix
ACRONYMS AND ABBREVIATIONS	xxi
1. SUMMARY AND CONCLUSIONS	1
1.1 Identity, physical and chemical properties and analytical methods	1
1.2 Sources of human and environmental exposure	1
1.3 Environmental transport, distribution and transformation	2
1.4 Environmental levels and human exposure	3
1.5 Kinetics and metabolism in humans and laboratory animals	7
1.6 Effects on laboratory mammals and <i>in vitro</i> test systems	8
1.7 Effects on humans	10
1.8 Effects on other organisms in the laboratory and field	11
1.9 Evaluation of human health risks and effects on the environment	14
1.10 Conclusions	15
2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES AND ANALYTICAL METHODS	17
2.1 Identity and physical and chemical properties	17
2.2 Analytical methods	18
3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE	20
3.1 Natural occurrence	20
3.2 Anthropogenic sources	20
3.2.1 Production and use	20

3.2.1.1	Hydrogen fluoride	20
3.2.1.2	Calcium fluoride	21
3.2.1.3	Sodium fluoride	21
3.2.1.4	Fluorosilicic acid	21
3.2.1.5	Sodium hexafluorosilicate	22
3.2.1.6	Sulfur hexafluoride	22
3.2.1.7	Fluorapatite	22
3.2.1.8	Phosphate fertilizers	22
3.2.2	Emissions	23
4.	ENVIRONMENTAL TRANSPORT, DISTRIBUTION AND TRANSFORMATION	24
4.1	Transport and distribution between media	24
4.1.1	Atmosphere	24
4.1.2	Water and sediment	28
4.1.3	Soil	30
4.2	Speciation and complexation	34
4.2.1	Atmosphere	34
4.2.2	Water	34
4.3	Bioaccumulation	34
5.	ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE	38
5.1	Environmental levels	38
5.1.1	Surface water	38
5.1.2	Air	41
5.1.3	Soil	41
5.1.4	Biota	43
	5.1.4.1 Aquatic organisms	43
	5.1.4.2 Terrestrial organisms	48
5.2	General population exposure	53
5.2.1	Drinking-water	53
5.2.2	Food	56
5.2.3	Indoor air	61
5.2.4	Consumer products	63
5.2.5	Intake estimates	63
5.3	Occupational exposure	70

6.	KINETICS AND METABOLISM IN HUMANS AND LABORATORY ANIMALS	71
6.1	Absorption	71
6.1.1	Absorption in humans	71
6.1.2	Absorption in laboratory animals	73
6.2	Distribution and retention	74
6.2.1	Fluoride in blood	74
6.2.2	Distribution in soft tissues	76
6.2.3	Distribution to calcified tissues	76
6.2.4	Transplacental transfer	78
6.2.5	Fluoride levels in human tissues and organs	78
6.3	Elimination	80
6.3.1	Renal handling of fluoride	80
6.3.2	Excretion via breast milk	80
6.3.3	Excretion via faeces, sweat and saliva	81
7.	EFFECTS ON LABORATORY MAMMALS AND <i>IN VITRO</i> TEST SYSTEMS	83
7.1	Single exposure	83
7.2	Short- and medium-term exposure	84
7.3	Long-term exposure and carcinogenicity	86
7.4	Mutagenicity and related end-points	92
7.4.1	<i>In vitro</i> genotoxicity	92
7.4.2	<i>In vivo</i> genotoxicity	94
7.5	Reproductive toxicity	95
7.6	Immunotoxicity	97
7.7	Mechanisms of action	97
7.8	Interaction with other substances	97
8.	EFFECTS ON HUMANS	100
8.1	General population	100
8.1.1	Acute toxicity	100
8.1.2	Clinical studies	101
8.1.2.1	Skeletal effects	101
8.1.2.2	Haematological, hepatic or renal effects	102
8.1.3	Epidemiological studies	102

	8.1.3.1 Cancer	102
	8.1.3.2 Skeletal fluorosis	104
	8.1.3.3 Skeletal fracture	111
	8.1.3.4 Reproductive effects	116
	8.1.3.5 Respiratory effects	116
	8.1.3.6 Neurobehavioural effects	117
	8.1.3.7 Genotoxic effects	118
	8.1.3.8 Dental effects	119
	8.1.4 Interactions with other substances	125
8.2	Occupationally exposed workers	126
	8.2.1 Case reports	126
	8.2.2 Epidemiological studies	126
	8.2.2.1 Cancer	126
	8.2.2.2 Skeletal effects	127
	8.2.2.3 Respiratory effects	128
	8.2.2.4 Haematological, hepatic or renal effects	128
	8.2.2.5 Genotoxic effects	128
9.	EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD	130
9.1	Laboratory experiments	130
	9.1.1 Microorganisms	130
	9.1.1.1 Water	130
	9.1.1.2 Soil	132
	9.1.2 Aquatic organisms	132
	9.1.2.1 Plants	132
	9.1.2.2 Invertebrates	133
	9.1.2.3 Vertebrates	138
	9.1.3 Terrestrial organisms	142
	9.1.3.1 Plants	142
	9.1.3.2 Invertebrates	148
	9.1.3.3 Vertebrates	149
9.2	Field observations	153
	9.2.1 Microorganisms	153
	9.2.2 Aquatic organisms	153
	9.2.3 Terrestrial organisms	154
	9.2.3.1 Plants	154
	9.2.3.2 Invertebrates	158
	9.2.3.3 Vertebrates	158

<b>10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT</b>	<b>163</b>
10.1 Evaluation of human health risks	163
10.1.1 Exposure	163
10.1.2 Hazard identification	164
10.1.3 Exposure-response analysis for adverse effects in bone	170
10.2 Evaluation of effects on the environment	172
10.2.1 Exposure	172
10.2.2 Effects	175
10.2.3 Evaluation	176
<b>11. CONCLUSIONS AND RECOMMENDATIONS FOR PROTECTION OF HUMAN HEALTH AND THE ENVIRONMENT</b>	<b>179</b>
11.1 Conclusions	179
11.2 Recommendations	180
<b>12. FURTHER RESEARCH</b>	<b>181</b>
12.1 Health effects research	181
12.2 Environmental effects research	182
<b>13. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES</b>	<b>184</b>
<b>REFERENCES</b>	<b>185</b>
<b>RESUME ET CONCLUSIONS</b>	<b>232</b>
<b>RESUMEN Y CONCLUSIONES</b>	<b>251</b>