

---

## CONTENTS

### ENVIRONMENTAL HEALTH CRITERIA FOR ELEMENTAL SPECIATION IN HUMAN HEALTH RISK ASSESSMENT

PREAMBLE	ix
ACRONYMS AND ABBREVIATIONS	xvii
1. SUMMARY	1
1.1 Scope and purpose of the document	1
1.2 Definitions	1
1.3 Structural aspects of speciation	1
1.4 Analytical techniques and methodology	2
1.5 Bioaccessibility and bioavailability	3
1.6 Toxicokinetics and biomonitoring	4
1.6.1 Toxicokinetics	4
1.6.2 Biomonitoring	5
1.7 Molecular and cellular mechanisms of metal toxicity	6
1.8 Health effects	7
2. DEFINITIONS OF SPECIES AND SPECIATION	8
3. STRUCTURAL ASPECTS OF SPECIATION	11
3.1 Isotopic composition	11
3.2 Electronic and oxidation states	12
3.3 Inorganic and organic compounds and complexes	15
3.4 Organometallic species	18
3.5 Macromolecular compounds and complexes	21
4. ANALYTICAL TECHNIQUES AND METHODOLOGY	22
4.1 Introduction	22
4.2 Sample collection and storage	24
4.3 Sample preparation	28
4.3.1 Preliminary treatment of biological fluids	28

4.3.2	Preliminary treatment of tissues and plants	30
4.3.3	Choice between low molecular mass and high molecular mass compounds	32
4.3.4	Desalting	32
4.3.5	Sample cleanup	33
4.3.6	Extraction procedures	33
4.3.7	Preconcentration of the species	34
4.3.8	Derivatization	34
4.4	Separation techniques	35
4.4.1	Liquid chromatography	35
4.4.2	Gas chromatography	36
4.4.3	Capillary electrophoresis	37
4.4.4	Gel electrophoresis	37
4.5	Sequential extraction schemes for the fractionation of sediments, soils, aerosols, and fly ash	38
4.6	Detection: elemental and molecular	39
4.6.1	Atomic absorption spectrometry	39
4.6.2	Atomic fluorescence spectrometry	41
4.6.3	Atomic emission spectrometry	41
4.6.4	Inductively coupled plasma mass spectrometry	41
4.6.5	Plasma source time-of-flight mass spectrometry	42
4.6.6	Glow discharge plasmas as tunable sources for elemental speciation	42
4.6.7	Electrospray mass spectrometry	43
4.6.8	Electrochemical methods	43
4.7	Calibration in elemental speciation analysis	44
4.8	Reference materials	45
4.9	Direct speciation analysis of elements and particles	45
4.10	State of the art	46
5.	BIOACCESSIBILITY AND BIOAVAILABILITY	48
5.1	Introduction	48
5.2	Bioaccessibility of elements in soils and sediments	48
5.2.1	Factors affecting the mobility and accessibility of elements in terrestrial (soil) environments	48
5.2.2	Factors affecting the mobility and accessibility of elements in sediment	

	environments	50
5.3	Determinants of bioavailability	52
5.3.1	Uptake by carriers	55
5.3.2	Uptake and physical form	59
5.3.3	Uptake and complexation	60
5.3.4	Selective uptake according to charge and size	62
5.3.5	Selective uptake according to binding affinity for different cationic centres	63
5.3.6	Selective uptake involving kinetic binding traps, with or without accompanying redox reactions	63
5.3.7	Uptake of organometallic compounds	65
5.3.8	Exposure concentration and uptake	65
5.3.9	Competition in the uptake and toxicity of non-nutrient elements	66
5.4	Incorporation of bioaccessibility and bioavailability considerations in risk assessment	67
5.4.1	Bioaccessibility and bioavailability in current approaches to environmental and human risk assessment	68
5.4.2	The biotic ligand model	68
6.	TOXICOKINETICS AND BIOLOGICAL MONITORING	70
6.1	Introduction	70
6.2	Absorption	72
6.2.1	Chromium	73
6.2.2	Manganese	74
6.2.3	Iron	76
6.2.4	Cobalt	76
6.2.5	Nickel	77
6.2.6	Copper	78
6.2.7	Arsenic	78
6.2.8	Selenium	80
6.2.9	Cadmium	81
6.2.10	Mercury	81
6.2.11	Lead	83
6.3	Disposition, excretion, and protein binding	85
6.3.1	Chromium	86

6.3.2	Manganese	88
6.3.3	Copper	89
6.3.4	Zinc	90
6.3.5	Arsenic	90
6.3.6	Selenium	91
6.3.7	Silver	91
6.3.8	Cadmium	92
6.3.9	Mercury	93
6.3.10	Lead	96
6.4	Biotransformation	97
6.4.1	Chromium	98
6.4.2	Manganese	98
6.4.3	Arsenic	98
6.4.4	Selenium	102
6.4.5	Mercury	102
6.5	Exposure assessment and biological monitoring	104
6.5.1	Exposure assessment	104
6.5.2	Speciation in biological monitoring	105
7.	MOLECULAR AND CELLULAR MECHANISMS OF METAL TOXICITY	111
7.1	Introduction	111
7.2	Mechanisms of DNA damage and repair	111
7.3	Metal-protein interactions	114
7.4	Generation of reactive oxygen species	119
7.5	Effects on the immune system	120
7.5.1	Mechanisms of sensitization	120
7.5.2	Immunosuppression	121
8.	HEALTH EFFECTS	122
8.1	Introduction	122
8.2	Acute toxicity	122
8.2.1	Chromium	122
8.2.2	Nickel	123
8.2.3	Arsenic	124
8.2.4	Tin	126
8.2.5	Barium	127
8.2.6	Mercury	128
8.2.7	Lead	129
8.3	Sensitization and irritation	130

8.3.1	Chromium	131
8.3.2	Nickel	132
8.3.3	Palladium	132
8.3.4	Platinum	133
8.4	Lung toxicity	134
8.4.1	Cobalt	134
8.5	Neurotoxicity	136
8.5.1	Manganese	136
8.5.2	Tin	137
8.5.3	Mercury	138
8.5.4	Thallium	141
8.5.5	Lead	142
8.6	Nephrotoxicity	144
8.6.1	Cadmium	144
8.7	Reproductive toxicity	145
8.7.1	Nickel	145
8.7.2	Mercury	146
8.8	Genotoxicity	148
8.8.1	Chromium	148
8.8.2	Cobalt	150
8.9	Carcinogenicity	153
8.9.1	Chromium	153
8.9.2	Cobalt	154
8.9.3	Nickel	156
8.9.4	Arsenic	158
9.	CONCLUSIONS AND RECOMMENDATIONS	162
	REFERENCES	164
	RESUME	220
	RESUMEN	228
	INDEX OF ELEMENTS	236