

CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR COPPER

1.	SUMMARY AND CONCLUSIONS	1
1.1	Identity, physical and chemical properties	1
1.2	Analytical methods	1
1.3	Sources of human and environmental exposure	2
1.4	Environmental transport, distribution and transformation	2
1.5	Environmental levels and human exposure	3
1.6	Kinetics and metabolism in laboratory animals and humans	4
1.7	Effects on laboratory animals and <i>in vitro</i> test systems	5
1.8	Effects on humans	7
1.9	Effects on other organisms in the laboratory and field	8
1.10	Conclusions	10
1.10.1	Human health	10
1.10.2	Environmental effects	11
2.	IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES AND ANALYTICAL METHODS	12
2.1	Identity	12
2.2	Physical and chemical properties	13
2.3	Analytical methods	13
2.3.1	Sampling and sample preparation	13
2.3.1.1	Sampling	15
2.3.1.2	Separation and concentration	15
2.3.1.3	Sample preparation	16
2.3.1.4	“Clean” techniques for measurement of ultratrace copper levels	17
2.3.2	Detection and measurement	18
2.3.2.1	Gravimetric and colorimetric methods	18
2.3.2.2	Atomic absorption, emission and mass spectrometry methods	19

2.3.2.3	Specialized methodologies	21
2.4	Speciation	21
2.4.1	Speciation in water and sediments	22
2.4.1.1	Detection and quantification	22
2.4.2	Speciation in biological matrices	24
3.	SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE	25
3.1	Natural sources	25
3.2	Anthropogenic sources	26
3.2.1	Production levels and processes	26
3.3	Copper use	27
4.	ENVIRONMENTAL TRANSPORT AND DISTRIBUTION	30
4.1	Transport and distribution between media	30
4.1.1	Air	30
4.1.2	Water and sediment	32
4.1.3	Soil	36
4.1.4	Sewage sludge inputs to land	39
4.1.5	Biodegradation and abiotic degradation	41
4.2	Bioaccumulation	41
4.2.1	Microorganisms	41
4.2.2	Aquatic plants	42
4.2.3	Aquatic invertebrates	43
4.2.4	Fish	47
4.2.5	Terrestrial plants	48
4.2.6	Terrestrial invertebrates	49
4.2.7	Terrestrial mammals	50
5.	ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE	51
5.1	Environmental levels	51
5.1.1	Air	51
5.1.2	Water and sediment	53
5.1.3	Soil	57

5.1.4	Biota	58
	5.1.4.1 Aquatic	58
	5.1.4.2 Terrestrial	60
5.2	General population exposure	64
5.2.1	Air	64
5.2.2	Food and beverages	64
5.2.3	Drinking-water	68
	5.2.3.1 Organoleptic characteristics	68
	5.2.3.2 Copper concentrations in drinking-water	69
5.2.4	Miscellaneous exposures	70
5.3	Occupational exposures	71
5.4	Total human intake of copper from all environmental pathways	72
6.	KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS	74
6.1	Essentiality	74
6.2	Homoeostasis	77
	6.2.1 Cellular basis of homoeostasis	77
	6.2.2 Absorption in animals and humans	79
	6.2.3 Transport, distribution and storage	81
	6.2.4 Excretion	85
6.3	Methods of studying homoeostasis	87
	6.3.1 Analytical methods	87
	6.3.2 Intake	88
	6.3.3 Diet	88
	6.3.4 Balance studies	88
6.4	Biochemical basis of copper toxicity	94
6.5	Interactions with other dietary components	95
	6.5.1 Protein and amino acids	95
	6.5.2 Phytate and fibre	96
	6.5.3 Ascorbic acid	96
	6.5.4 Zinc	97
	6.5.5 Iron	98
	6.5.6 Carbohydrates	98
	6.5.7 Infant diets	98

6.5.8	Other interactions (molybdenum, manganese, selenium)	99
7.	EFFECTS ON LABORATORY MAMMALS AND IN VITRO TEST SYSTEMS	100
7.1	Single exposure	100
7.1.1	Oral	100
7.1.2	Dermal	100
7.1.3	Inhalation	102
7.2	Short-term exposure	102
7.2.1	Oral	103
7.2.2	Inhalation	104
	7.2.2.1 Copper(II) sulfate	104
	7.2.2.2 Copper chloride	104
7.3	Repeated exposure: subchronic toxicity	104
7.3.1	Oral	105
	7.3.1.1 Copper(II) sulfate	105
	7.3.1.2 Copper chloride	111
7.4	Long-term exposure chronic toxicity or carcinogenicity	111
7.5	Reproductive and developmental toxicity	111
7.6	Mutagenicity and related end-points	125
7.6.1	Copper sulfate	125
	7.6.1.1 <i>In vitro</i>	125
	7.6.1.2 <i>In vivo</i>	126
7.6.2	Other copper compounds	126
	7.6.2.1 <i>In vitro</i>	126
7.7	Other studies	127
7.7.1	Neurotoxicity	127
	7.7.1.1 Copper sulfate	127
	7.7.1.2 Copper chloride	128
7.7.2	Immunotoxicity	128
	7.7.2.1 Copper(II) sulfate	128
7.8	Biochemical mechanisms of toxicity	129
8.	EFFECTS ON HUMANS	130
8.1	General population: copper deficiency and toxicity	130

8.2	Copper deficiency	130
8.2.1	Clinical manifestations of copper deficiency	130
8.2.2	Biological indicators of copper deficiency: balance studies	136
8.3	Toxicity of copper in humans	136
8.3.1	Single exposure	136
8.3.2	Repeated oral exposures	137
8.3.2.1	Gastrointestinal and hepatic effects	137
8.3.2.2	Reproduction and development	140
8.3.2.3	Cancer	140
8.3.3	Dermal exposure	148
8.4	Disorders of copper homoeostasis: populations at risk	149
8.4.1	Menkes disease	149
8.4.2	Wilson disease	152
8.4.3	Hereditary aceruloplasminaemia	159
8.4.4	Indian childhood cirrhosis	160
8.4.5	Idiopathic copper toxicosis, or non-Indian childhood cirrhosis	163
8.4.6	Chronic liver diseases	165
8.4.7	Copper in infancy	165
8.4.8	Malabsorption syndromes	166
8.4.9	Parenteral nutrition	167
8.4.10	Haemodialysis patients	168
8.4.11	Cardiovascular diseases	168
8.5	Occupational exposure	170
9.	EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD	173
9.1	Bioavailability	173
9.1.1	Bioavailability in water	173
9.1.1.1	Predicting effects of copper on fish gill function	175
9.1.2	Bioavailability of metals in sediments	176
9.2	Essentiality	178
9.2.1	Animals	178

	10.3.2.2 Occupational risks	258
10.4	Evaluation of effects on the environment	258
	10.4.1 Concept of environmental risk assessment	258
	10.4.2 Components of risk assessment process for copper	259
10.5	Environmental risk assessment for copper	261
	10.5.1 Aquatic biota	261
	10.5.1.1 Overview of exposure data	261
	10.5.1.2 Overview of toxicity data	262
	10.5.2 Terrestrial biota	263
	10.5.2.1 Overview of exposure data	263
	10.5.2.2 Plant foliar levels	264
	10.5.2.3 Assessment of toxicity of copper in soil	264
11.	CONCLUSIONS AND RECOMMENDATIONS FOR PROTECTION OF HUMAN HEALTH AND THE ENVIRONMENT	266
	11.1 Human health	266
	11.2 Environmental protection	267
12.	FURTHER RESEARCH	268
	12.1 Health protection	268
	12.2 Environmental protection	268
13.	PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES	270
	REFERENCES	271
	RESUME ET CONCLUSIONS	335
	RESUMEN Y CONCLUSIONES	348