

CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR GUIDANCE VALUES FOR HUMAN EXPOSURE LIMITS

SUMMARY	13
1. INTRODUCTION	15
1.1 Scope and purpose	15
1.2 Guidance value	16
1.3 Quality of data	16
1.4 Clarity and transparency of presentations	17
2. GUIDANCE VALUES	18
2.1 General considerations	18
2.1.1 Precision of a guidance value	18
2.2 Derivation of guidance values	18
2.3 Interpretation and use of guidance values	19
2.4 Terminology	20
3. APPLICATION OF THE TOXICITY DATA BASE TO DETERMINE TOLERABLE INTAKES	23
3.1 Approaches to risk assessment	23
3.1.1 Non-threshold effects	23
3.1.2 Threshold effects	25
3.1.2.1 Uncertainty factors	27
3.1.2.2 Relevant toxicokinetic and toxicodynamic data	29
3.1.2.3 Uncertainty factors for occupational exposure	30
4. PROCEDURE FOR EXTRAPOLATION FROM A TOXICITY DATA BASE TO A TOLERABLE INTAKE	32
4.1 Overall procedure	32
4.2 Selection of pivotal study and critical effect(s)	32
4.3 Adequacy of the pivotal study	34
4.4 Interspecies extrapolation	34
4.5 Inter-individual variability in humans	35
4.6 Other considerations	36
4.6.1 Adequacy of the overall data base	36
4.6.2 Nature of toxicity	36
4.7 Final review of the total uncertainty factor	37

4.8	Precision of the tolerable intake	37
4.9	Alternative approaches	38
5.	ALLOCATION OF TOLERABLE INTAKES TO DERIVE GUIDANCE VALUES	39
5.1	General considerations	39
5.2	General approach	40
5.3	Detailed approach	41
5.3.1	Biomarkers of exposure	41
5.3.2	Critical effects which are not route specific	41
5.3.3	Difference in magnitude of effect by route of exposure	42
5.3.4	Route-specific effect variation at portals of entry (due to local bioactivation or local effects)	42
5.3.5	Limited data base	43
6.	EXAMPLES OF THE DERIVATION OF GUIDANCE VALUES	44
	REFERENCES	48
	APPENDIX 1: EXAMPLES - DEVELOPMENT OF GUIDANCE VALUES	52
	APPENDIX 2: GRAPHICAL APPROACHES	63
	APPENDIX 3: ALTERNATIVE APPROACHES	65
	APPENDIX 4: BODY WEIGHT AND VOLUMES OF INTAKE FOR REFERENCE MAN	68
	RESUME	70
	RESUMEN	72