

CONTENTS

PRINCIPLES FOR THE ASSESSMENT OF RISKS TO HUMAN HEALTH FROM EXPOSURE TO CHEMICALS

PREAMBLE	vii
ABBREVIATIONS	xx
1. SUMMARY	1
2. INTRODUCTION	5
3. HEALTH HAZARD IDENTIFICATION	7
3.1 Introduction	7
3.2 Human data	8
3.2.1 Criteria for establishing causality	10
3.3 Animal studies	13
3.4 <i>In vitro</i> studies	15
3.5 Structure–activity relationships	16
4. DOSE–RESPONSE	18
4.1 Introduction	18
4.2 Considerations in dose–response assessment	20
4.2.1 Introduction	20
4.2.2 Inter- and intra-species considerations	20
4.2.2.1 Introduction	20
4.2.2.2 Species differences	21
4.2.2.3 Human variability	22
4.3 Non-neoplastic (threshold) effects	22
4.3.1 Characterization of threshold	23
4.3.1.1 No-observed-adverse-effect level (NOAEL)	23
4.3.1.2 Benchmark dose/concentration	23
4.3.1.3 Lowest-observed-adverse-effect level	24

4.3.2	Uncertainty factors	24
4.4	Quantitative risk assessment for neoplastic (non-threshold) effects	28
4.4.1	Introduction	28
4.4.2	Linear extrapolation	29
4.4.3	Estimation of potency in the experimental range	31
4.4.4	Two-stage clonal expansion model	32
4.4.5	Proportional analyses – carcinogenic and non-neoplastic effects	33
5.	EXPOSURE ASSESSMENT	34
5.1	Definition of exposure and related terms	34
5.2	Exposure and dose	35
5.3	Approaches to quantification of exposure	40
5.3.1	Measurement at point of contact (personal monitoring)	41
5.3.2	Scenario evaluation method (time activity and monitoring/modelling)	41
5.3.3	Biomarkers of exposure/estimation of internal dose	47
5.4	Variability and uncertainty	49
5.4.1	Assessing uncertainty	51
5.5	Exposure settings	51
5.5.1	Exposure in the general environment	51
5.5.2	Occupational settings	52
5.5.3	Consumer products	53
6.	RISK CHARACTERIZATION AND IMPLICATIONS FOR RISK MANAGEMENT	58
6.1	General considerations	58
6.2	Considerations in risk characterization	59
6.3	Considerations in risk management	62
6.3.1	Societal factors	62
6.3.2	Individual and population risks	63
6.3.3	Comparative risk	65
6.3.4	Risk perception	65
6.3.5	Risk and hazard communication	66

6.3.6	Economic factors	71
	6.3.6.1 Cost-benefit analyses	71
6.3.7	Political factors	72
6.3.8	Regulatory limits	73
6.4	Risk management options	75
	6.4.1 Risk reduction	75
	6.4.1.1 Technology-based criteria	76
	REFERENCES	77
	APPENDIX	88
	RÉSUMÉ	101
	RESUMEN	106