

RISK ASSESSMENT OF CHEMICALS

An Introduction

2nd edition

Edited by


C.J. van Leeuwen

*European Commission, Joint Research Centre, Ispra, Italy
Netherlands Organization for Applied Scientific Research TNO,
Zeist, The Netherlands*

and

T.G. Vermeire

National Institute for Public Health and the Environment, Bilthoven, The Netherlands

 Springer

CONTENTS

PREFACE	vii
EDITORS	ix
CONTRIBUTORS AND REVIEWERS	xi
ACKNOWLEDGEMENTS	xv
EXPLANATORY NOTES	xvii

PART I. INTRODUCTION

1	GENERAL INTRODUCTION	1
1.1	Introduction	1
1.2	The risk management process	2
1.2.1	Hazard identification (step 1)	3
1.2.2	Exposure assessment (step 2)	4
1.2.3	Effects assessment (step 3)	4
1.2.4	Risk characterization (step 4)	5
1.2.5	Risk classification (step 5)	6
1.2.6	Identification and risk-benefit analysis of risk reduction options (step 6)	6
1.2.7	Risk reduction (step 7)	8
1.2.8	Monitoring and review (step 8)	10
1.3	Further developments in the risk management process	11
1.3.1	Focus on risk reduction and responsible care	12
1.3.2	Risk communication and stakeholder participation	12
1.3.3	Risk assessment policy and the role of science	14
1.3.4	Integration in risk assessment	17
1.4	Disciplines, roles and responsibilities in risk management	18
1.5	How risks are expressed	19
1.6	Perception of risks	20
1.7	Uncertainty, variability and precaution	21
1.7.1	Uncertainty and variability	21
1.7.2	Quantifying uncertainty and validation	23
1.7.3	Precaution	25
1.8	Concluding remarks	27
1.9	Contents of the book	29

PART II. EXPOSURE ASSESSMENT

2.	EMISSIONS OF CHEMICALS TO THE ENVIRONMENT	37
2.1	Introduction	37
2.2	Chemical substances	37
2.2.1	Origin of chemical substances	37
2.2.2	Desirable and undesirable substances	38

2.3	Emissions and sources	38
2.3.1	Entry into the environment	38
2.3.2	Types of emissions and sources	43
2.3.3	Emissions in relation to risk assessment	44
2.3.4	Prevention and risk reduction measures	46
2.4	Data availability and generation	46
2.4.1	Measurements	46
2.4.2	Specific calculations	48
2.4.3	The application of emission factors	49
2.4.4	Generic approach to emission estimation	50
2.4.5	Three examples of estimating of emissions	55
2.5	Development of emission estimation and risk assessment tools	59
2.6	Emission estimation and REACH	61
2.6.1	Development of exposure scenarios	61
2.6.2	Challenges ahead	67
2.7	Further reading	68
3.	TRANSPORT, ACCUMULATION AND TRANSFORMATION PROCESSES	73
3.1	Introduction	73
3.2	Transport processes	73
3.2.1	Transport mechanisms	73
3.2.2	Equilibrium partitioning between phases	74
3.2.3	Intramedia transport in air	80
3.2.4	Intramedia transport in water	80
3.2.5	Intermedia transport	82
3.3	Bioaccumulation	90
3.3.1	Introduction	90
3.3.2	Aquatic bioaccumulation processes	90
3.3.3	Factors affecting bioconcentration	97
3.3.4	Biomagnification	101
3.3.5	Accumulation in terrestrial plants	106
3.3.6	Accumulation in terrestrial invertebrates	111
3.3.7	Accumulation in mammals and birds	113
3.3.8	Methods for measuring terrestrial bioaccumulation	114
3.4	Abiotic transformation processes	114
3.4.1	Introduction	114
3.4.2	Hydrolysis	115
3.4.3	Oxidation	117
3.4.4	Reduction	118
3.4.5	Photochemical degradation	119
3.4.6	Methods for measuring abiotic degradation	121
3.5	Biodegradation	121
3.5.1	Introduction	121
3.5.2	Aerobic biodegradation and metabolic pathways	122
3.5.3	Anaerobic biodegradation	124
3.5.4	Reasons for the environmental persistence of chemicals	126
3.5.5	Kinetics of biodegradation	127
3.5.6	Assessing biodegradability and biodegradation rates	129

3.6	Biotransformation	133
3.6.1	Introduction	133
3.6.2	Effects of biotransformation on xenobiotics	133
3.6.3	Types of biotransformation reactions	136
3.6.4	Factors influencing enzyme activity	139
3.6.5	Methods to measure biotransformation	141
3.6.6	Biotransformation of some specific groups of compounds	143
3.6.7	Enzyme inhibition and induction	145
3.6.8	Effect of enzyme induction on toxicity	146
3.7	Bioavailability	147
3.7.1	Introduction	147
3.7.2	Underlying concepts of bioavailability	150
3.7.3	Inclusion of bioavailability in risk assessment	151
3.8	Further reading	152
4.	ENVIRONMENTAL EXPOSURE ASSESSMENT	159
4.1	Introduction	159
4.1.1	Use of models in the assessment of exposure concentrations	159
4.1.2	Mass balance modelling	160
4.1.3	Model types	164
4.1.4	Models versus measurements	165
4.2	Air models	166
4.2.1	Introduction	166
4.2.2	Model types	166
4.2.3	Some examples of operational models	167
4.2.4	Application of a local air model in the risk assessment of industrial chemicals	168
4.2.5	Input requirements for air models	170
4.3	Water models	171
4.3.1	Introduction	171
4.3.2	Simple dilution models	171
4.3.3	Dispersion models	172
4.3.4	Compartment models	173
4.3.5	Estimation of the elimination of a chemical in a waste water treatment plant	175
4.3.6	Data requirements for water models	176
4.4.	Soil models	177
4.4.1	Introduction	177
4.4.2	Fate processes in soil modelling	177
4.4.3	Model types	178
4.4.4	Use of soil models in the risk assessment of industrial chemicals	178
4.4.5	Data requirements for soil models	180
4.5	Multimedia models	181
4.5.1	Introduction	181
4.5.2	Characteristics and assumptions	181
4.5.3	Data requirements for multimedia models	182
4.5.4	Applications and limitations	182
4.5.5	Application of multimedia models	184
4.6	Further reading	189

5.	HUMAN EXPOSURE ASSESSMENT	195
5.1	General introduction	195
5.2	Human exposure through the environment	196
5.2.1	Introduction	196
5.2.2	Choice of exposure scenario	196
5.2.3	Exposure through food products	197
5.2.4	Direct exposure through the environment	200
5.2.5	Derivation of the total daily uptake and sample calculations	200
5.3	Consumer exposure assessment	202
5.3.1	Introduction	202
5.3.2	Consumer exposure scenarios	203
5.3.3	Primary and secondary exposures associated with consumer products	206
5.3.4	Assessing exposure factors and data	207
5.3.5	Issues to be considered when performing an exposure assessment	208
5.3.6	Risk management measures for consumers	208
5.3.7	Presenting and reviewing the results in relation to uncertainty	211
5.4	Occupational exposure	212
5.4.1	Introduction	212
5.4.2	The workplace exposure scenario	214
5.4.3	The process for exposure assessment	217
5.4.4	Exposure and risk management measures	218
5.4.5	Discussion	221
5.5	Further reading	221

PART III. EFFECTS ASSESSMENT AND RISK CHARACTERIZATION

6.	TOXICITY TESTING FOR HUMAN HEALTH RISK ASSESSMENT	227
6.1	Introduction	227
6.2	General aspects of toxicity	228
6.3	Internal human exposure	229
6.3.1	Experimental biokinetics	229
6.3.2	(B)iokinetic modelling	234
6.4	Toxicity studies	235
6.4.1	General aspects	235
6.4.2	Acute effects: acute toxicity	240
6.4.3	Acute local effects: irritation and corrosivity	241
6.4.4	Sensitization	242
6.4.5	Repeated-dose toxicity	244
6.4.6	Genotoxicity	245
6.4.7	Carcinogenicity	248
6.4.8	Reproductive and developmental toxicity	251
6.4.9	Specific studies and toxicogenomics	254
6.4.10	<i>In vitro</i> tests for toxicity	256
6.5	Human health hazard assessment	258
6.5.1	Introduction	258
6.5.2	Classification and labelling	258
6.5.3	Dose-response assessment	260
6.5.4	Default assessment factors	266
6.5.5	Exposure to mixtures of chemicals	270
6.5.6	Concluding remarks	272

6.6	Risk characterization for human health	272
6.6.1	General aspects	272
6.6.2	Humans exposed via the environment	272
6.6.3	Workers	273
6.6.4	Consumers	273
6.6.5	Physicochemical properties	274
6.7	Further reading	274
7.	ECOTOXICOLOGICAL EFFECTS	281
7.1	Introduction	281
7.2	Fundamental aspects of ERA	282
7.2.1	Taxonomic diversity	282
7.2.2	Toxicological endpoints	283
7.2.3	Spatial scales	284
7.2.4	Temporal scales	284
7.2.5	Complexity of exposure	285
7.3	Aquatic toxicity	290
7.3.1	Exposure systems	290
7.3.2	Analysis of toxicity tests	293
7.3.3	Short-term toxicity	295
7.3.4	Long-term toxicity	300
7.3.5	Population dynamics	304
7.3.6	Multi-species studies	308
7.4	Sediment toxicity	313
7.4.1	Introduction	313
7.4.2	Exposure systems	314
7.4.3	Effects assessment	314
7.4.4	Sediment toxicity testing	318
7.5	Terrestrial toxicity	319
7.5.1	Introduction	319
7.5.2	Exposure systems	319
7.5.3	Effects assessment	322
7.5.4	Soil toxicity testing	322
7.6	Factors modifying toxicity	328
7.6.1	Introduction	328
7.6.2	Abiotic factors	328
7.6.3	Biotic factors	331
7.6.3	Biotic ligand models to predict toxicity of metals	331
7.7	Mixture toxicity	332
7.7.1	Mixture toxicity scales	332
7.7.2	Mixture toxicity studies	334
7.8	Ecotoxicogenomics	335
7.9	Endocrine disruption	336
7.10	Derivation of PNECs	337
7.10.1	Preliminary effects assessment using assessment factors	338
7.10.2	Refined effects assessment using species sensitivity distributions	338
7.10.3	Effects of secondary poisoning	341
7.10.4	Comprehensive assessment	343
7.11	Assessment of PBTs and vPvBs	345
7.12	Concluding remarks	346
7.13	Further reading	347

PART IV. DATA

8.	DATA: NEEDS, AVAILABILITY, SOURCES AND EVALUATION	357
8.1	Introduction	357
8.2	Data requirements in EU regulatory frameworks	357
8.2.1	Introduction	357
8.2.2	Industrial chemicals	357
8.2.3	Pesticides and biocides	360
8.2.4	Veterinary medicines and feed additives	361
8.2.5	Cosmetics	361
8.2.6	Food additives	362
8.2.7	Food contact materials	362
8.3	Data availability	362
8.4	Data sources	364
8.5	Data evaluation: quality and selection	364
8.5.1	Introduction and definitions	364
8.5.2	Scoring system for reliability	368
8.5.3	Determination of relevance and adequacy	370
8.5.4	Quality of modelled data	370
8.6	Concluding remarks	371
8.7	Further reading	371
9.	PREDICTING FATE-RELATED PHYSICOCHEMICAL PROPERTIES	375
9.1	Introduction	375
9.2	Types of molecular properties used in estimation methods	376
9.3	Thermodynamic partitioning between environmental phases	378
9.3.1	Octanol-water partition coefficient	378
9.3.2	Henry's law constant	382
9.3.3	Sorption constant	385
9.3.4	Vapour pressure	388
9.3.5	Bioconcentration	391
9.3.6	Water solubility	397
9.4	Degradation	403
9.4.1	Indirect photolysis in the air	403
9.4.2	Hydrolysis in the water phase	404
9.4.3	Biodegradation	408
9.4.4	Compartmental half-lives	412
9.5	Handbooks, software and web resources	414
9.6	Further reading	415
10.	PREDICTING TOXICOLOGICAL AND ECOTOXICOLOGICAL ENDPOINTS	427
10.1	Introduction	427
10.2	Development and validation of SARs and QSARs	427
10.2.1	Development of (Q)SAR models	427
10.2.2	OECD principles for (Q)SAR validation	428
10.3	Prediction of human health endpoints	430
10.3.1	Acute toxicity	430
10.3.2	Skin sensitization	432
10.3.3	Chronic toxicity	434
10.3.4	Mutagenicity and carcinogenicity	435
10.3.5	Reproductive toxicity	438

10.3.6	Biokinetic parameters	438
10.3.7	Chemical metabolism and biotransformation	440
10.4	Prediction of ecotoxicity endpoints	442
10.4.1	Classification of chemicals by modes of toxic action	442
10.4.2	QSARs for narcotic chemicals	443
10.4.3	QSARs for other modes of action	445
10.5	Computer programs and databases	447
10.5.1	Computer programs	447
10.5.2	Databases	449
10.6	Regulatory applications	452
10.6.1	Introduction	452
10.6.2	Priority setting	452
10.6.3	Classification and labelling	453
10.6.4	Risk assessment	453
10.6.5	PBT and vPvB assessment	454
10.7	Concluding remarks	455
10.8	Further reading	455
11.	INTELLIGENT TESTING STRATEGIES	467
11.1	Introduction	467
11.1.1	Streamlining the hazard and risk assessment process	468
11.1.2	Animal testing and testing costs	468
11.1.3	The need for integrated testing approaches	470
11.2	Components of ITS	470
11.2.1	Chemical categories and read-across	471
11.2.2	SARs and QSARs	475
11.2.3	Thresholds of toxicological concern (TTCs)	476
11.2.4	Exposure-based waiving	480
11.2.5	<i>In vitro</i> methods	480
11.2.6	Optimized <i>in vivo</i> tests	482
11.2.7	Concluding remarks	483
11.3	Examples of ITS	485
11.3.1	Degradation	485
11.3.2	Bioconcentration	485
11.3.3	Aquatic toxicity	486
11.3.4	Irritation and corrosivity	493
11.3.5	Skin sensitization	497
11.3.6	Reproductive and developmental toxicity	498
11.4	Summary and concluding remarks	500
11.5	Further reading	504

PART V. RISK ASSESSMENT AND MANAGEMENT OF INDUSTRIAL CHEMICALS

12.	THE MANAGEMENT OF INDUSTRIAL CHEMICALS IN THE EU	511
12.1	Introduction	511
12.1.1	Background	512
12.1.2	Towards solutions	514
12.1.3	The further development of REACH	515
12.1.4	Aim of the REACH legislation	515
12.1.5	Costs and benefits	516

12.2	A brief overview of REACH	516
12.2.1	Introduction	516
12.2.2	Registration (Title II)	517
12.2.3	Data sharing and avoidance of unnecessary testing (Title III)	524
12.2.4	Information in the supply chain (Title IV)	524
12.2.5	Downstream users (Title V)	525
12.2.6	Evaluation (Title VI)	525
12.2.7	Authorization (Title VII)	526
12.2.8	Restrictions (Title VIII)	527
12.2.9	Fees and charges (Title IX)	528
12.2.10	Agency (Title X)	529
12.2.11	Classification and labelling inventory (Title XI)	529
12.2.12	Information (Title XII)	530
12.2.13	Competent authorities (Title XIII)	530
12.2.14	Enforcement (Title XIV)	530
12.2.15	Transitional and final provisions (Title XV)	531
12.3	Elements of the chemical safety report	531
12.3.1	General introduction	531
12.3.2	Environmental hazard assessment	533
12.3.3	Human health hazard assessment	534
12.3.4	Physicochemical hazard assessment	534
12.3.5	PBT and vPvB assessment	534
12.3.6	Exposure assessment	535
12.3.7	Risk characterization for human health and the environment	536
12.3.8	Potential iterations of the CSA	537
12.3.9	Risk management measures	537
12.3.10	Communicating uncertainty in the CSA	540
12.3.11	Format of the CSR	540
12.3.12	Concluding remarks	541
12.4	Safety Data Sheets	541
12.4.1	Safety data sheets for dangerous substances	542
12.4.2	Information required in the SDS	542
12.4.3	Information down the supply chain	542
12.4.4	Information up the supply chain	543
12.4.5	Information for workers and obligation to keep and make information available	543
12.5	Concluding remarks	543
12.6	Further reading	543
13.	THE MANAGEMENT OF INDUSTRIAL CHEMICALS IN THE USA	553
13.1	Introduction	553
13.2	EPA risk assessment and risk management under TSCA	553
13.2.1	TSCA risk assessment and risk thresholds for taking action	554
13.2.2	Risk assessment mechanisms	554
13.2.3	Exposure assessment can modulate need for risk assessment	557
13.3	Command and control mechanisms	557
13.3.1	TSCA inventory (TSCA §8)	557
13.3.2	Testing of chemicals (TSCA §4)	557
13.3.3	Control of new chemicals (TSCA §5)	557
13.3.4	Control of existing chemical substances (TSCA §6)	558
13.3.5	PCBs, asbestos, and lead	558

13.4	Examples of EPA's gatekeeper/guardian role	558
13.4.1	High production challenge program	559
13.4.2	Perfluorinated acids	561
13.4.3	Polybrominated diphenyl ethers	562
13.4.4	Lead	563
13.5	EPA's role as facilitator of stewardship	564
13.5.1	Pollution prevention and voluntary partnerships	564
13.5.2	Examples of EPA as facilitator of voluntary partnerships	564
13.5.3	Design for the environment	565
13.5.4	Sustainable futures	567
13.5.5	Hospitals for a healthy environment	568
13.5.6	Partnership results	568
13.6	Conclusions	569
13.6.1	Statutory risk reduction	569
13.6.2	Statutory/voluntary approaches	569
13.6.3	Voluntary environmental stewardship	569
13.7	Further reading	570
14.	THE MANAGEMENT OF INDUSTRIAL CHEMICALS IN JAPAN	575
14.1	Introduction	575
14.2	Chemical Substances Control Act	575
14.2.1	History of enactment and amendments to the CSCL	576
14.2.2	Types of chemicals regulated under the CSCL	578
14.2.3	Notification and evaluation of new chemicals	581
14.2.4	Data requirements and assessment criteria	582
14.2.5	Procedures for the evaluation of new and existing chemicals	583
14.3	Examination of existing chemicals	584
14.3.1	Collection of hazard information – Japan Challenge Program	584
14.3.2	GHS classification	585
14.3.3	Environmental monitoring	585
14.3.4	Initial risk assessments	586
14.3.5	Other risk assessments	587
14.4	Future of chemical management in Japan	587
14.5	Further reading	589
15.	THE MANAGEMENT OF INDUSTRIAL CHEMICALS IN CANADA	591
15.1	Introduction	591
15.2	Legislative background	591
15.2.1	Federal-provincial regulatory structure	591
15.2.2	Evolution of the Canadian Environmental Protection Act	592
15.2.3	The current Canadian Environmental Protection Act (CEPA-1999)	592
15.2.4	Administration of the CEPA	593
15.2.5	The CEPA definition of "environment"	593

15.3	CEPA's provisions for toxic substances	594
15.3.1	CEPA definitions of substance and toxic	594
15.3.2	Provisions for new substances	594
15.3.3	Provisions for existing substances	596
15.3.4	Categorization of the Domestic Substances List	597
15.3.5	Options for controlling existing substances	598
15.3.6	Virtual elimination	599
15.3.7	Significant new activities	599
15.3.8	Information gathering	599
15.3.9	Consultation and communication	601
15.4	Health assessments under CEPA	601
15.4.1	Comprehensive framework for health risk assessments under CEPA-1999	601
15.4.2	PSL assessments	606
15.4.3	Mixtures of substances	608
15.4.4	Data requirements, information gathering and peer involvement	608
15.5	Environmental assessment of existing substances	610
15.5.1	Categorization	610
15.5.2	Ecological screening assessments	610
15.5.3	PSL assessments	611
15.6	Management of toxic substances	612
15.6.1	Priority substances	612
15.6.2	The chemicals management plan	612
15.7	Concluding remarks	613
15.8	Further reading	615
16.	THE OECD CHEMICALS PROGRAMME	623
16.1	Introduction	623
16.2	The basis: mutual acceptance of data	624
16.2.1	The OECD test guidelines programme	624
16.2.2	The OECD principles of GLP	630
16.3	The OECD existing chemicals programme	630
16.3.1	The OECD high production volume chemicals programme	630
16.3.2	Collaboration with national/regional programmes	632
16.3.3	The OECD project on (quantitative) structure-activity relationships	633
16.4	The new chemicals programme	636
16.5	The risk assessment programme	636
16.6	The risk management programme	636
16.7	Other activities related to environment, health and safety	637
16.8	Further reading	637
GLOSSARY		639
INDEX		673