

CONTENTS

PREFACE TO THE FOURTH EDITION	xxi
CONTRIBUTORS	xxiii
PART I INTRODUCTION	1
1. Introduction to Toxicology	3
<i>Ernest Hodgson</i>	
1.1 Definition and Scope	3
1.2 Relationship to Other Sciences	9
1.3 A Brief History of Toxicology	10
1.4 Dose–Response Relationships	11
1.5 Sources of Toxic Compounds	12
1.6 Movement of Toxicants in the Environment	12
Bibliography and Suggested Reading	13
Sample Questions	14
2. Introduction to Biochemical and Molecular Methods in Toxicology	15
<i>Ernest Hodgson, Gerald A. Leblanc, Sharon A. Meyer, and Robert C. Smart</i>	
2.1 Introduction	15
2.2 Cell Culture Techniques	15
2.2.1 Suspension Cell Culture	16
2.2.2 Monolayer Cell Culture	16
2.2.3 Indicators of Toxicity in Cultured Cells	16
2.2.4 Use of Stem Cells	17
2.2.5 Cell Culture Models as “Alternative” Toxicity Tests	19
2.3 Molecular Techniques	19
2.3.1 Molecular Cloning	20
2.3.2 cDNA and Genomic Libraries	20
2.3.3 Northern and Southern Blot Analysis	21
2.3.4 PCR	22
2.3.5 Evaluation of Gene Expression, Regulation, and Function	22
2.4 Immunochemical Techniques	23
2.5 Proteomics	26
2.6 Metabolomics	26
2.7 Bioinformatics	26
2.8 Summary and Conclusions	27

Bibliography and Suggested Reading	27
Sample Questions	27
PART II CLASSES OF TOXICANTS	29
3. Exposure Classes, Toxicants in Air, Water, Soil, Domestic, and Occupational Settings	31
<i>W. Gregory Cope</i>	
3.1 Air Pollutants	31
3.1.1 History	31
3.1.2 Types of Air Pollutants	32
3.1.3 Sources of Air Pollutants	33
3.1.4 Examples of Air Pollutants	34
3.1.5 Environmental Effects	37
3.2 Water and Soil Pollutants	38
3.2.1 Sources of Water and Soil Pollutants	38
3.2.2 Examples of Pollutants	39
3.3 Occupational Toxicants	42
3.3.1 Regulation of Exposure Levels	43
3.3.2 Routes of Exposure	44
3.3.3 Examples of Industrial Toxicants	44
Bibliography and Suggested Reading	46
Air Pollutants	46
Water and Soil Pollutants	47
Occupational Toxicants	47
Sample Questions	47
4. Classes of Toxicants: Use Classes	49
<i>W. Gregory Cope and Ernest Hodgson</i>	
4.1 Introduction	49
4.2 Metals	49
4.2.1 History	49
4.2.2 Common Toxic Mechanisms and Sites of Action	50
4.2.3 Lead	51
4.2.4 Mercury	52
4.2.5 Cadmium	53
4.2.6 Chromium	53
4.2.7 Arsenic	54
4.2.8 Treatment of Metal Poisoning	54
4.3 Agricultural Chemicals (Pesticides)	55
4.3.1 Introduction	55
4.3.2 Definitions and Terms	56
4.3.3 Organochlorine Insecticides	59

4.3.4	Organophosphorus (OP) Insecticides	60
4.3.5	Carbamate Insecticides	61
4.3.6	Botanical Insecticides	61
4.3.7	Pyrethroid Insecticides	62
4.3.8	New Insecticide Classes	62
4.3.9	Herbicides	62
4.3.10	Fungicides	64
4.3.11	Rodenticides	64
4.3.12	Fumigants	65
4.3.13	Conclusions	65
4.4	Food Additives and Contaminants	65
4.5	Toxins	66
4.5.1	History	66
4.5.2	Microbial Toxins	67
4.5.3	Mycotoxins	67
4.5.4	Algal Toxins	68
4.5.5	Plant Toxins	69
4.5.6	Animal Toxins	70
4.6	Solvents	71
4.7	Therapeutic Drugs	71
4.8	Drugs of Abuse	72
4.9	Combustion Products	72
4.10	Cosmetics	74
	Bibliography and Suggested Reading	74
	General	74
	Metals	74
	Pesticides	75
	Toxins	75
	Solvents	75
	Therapeutic Drugs	75
	Sample Questions	75

PART III TOXICANT PROCESSING *IN VIVO* **77**

5. Absorption and Distribution of Toxicants **79**

Ronald E. Baynes and Ernest Hodgson

5.1	Introduction	79
5.2	Cell Membranes	80
5.3	Mechanisms of Transport	82
5.3.1	Passive Diffusion	83
5.3.2	Carrier-Mediated Membrane Transport	86
5.4	Physicochemical Properties Relevant to Diffusion	87
5.4.1	Ionization	88
5.4.2	Partition Coefficients	89

5.5	Routes of Absorption	90
5.5.1	Extent of Absorption	91
5.5.2	Gastrointestinal Absorption	92
5.5.3	Dermal Absorption	94
5.5.4	Respiratory Penetration	97
5.6	Toxicant Distribution	99
5.6.1	Physicochemical Properties and Protein Binding	99
5.6.2	V_d	106
5.7	Toxicokinetics	108
	Bibliography and Suggested Reading	112
	Sample Questions	113
6.	Metabolism of Toxicants	115
	<i>Ernest Hodgson and Randy L. Rose</i>	
6.1	Introduction	115
6.2	Phase I Reactions	116
6.2.1	The Endoplasmic Reticulum, Microsomes, and Monooxygenations	116
6.2.2	The CYP-Dependent Monooxygenase System	118
6.2.3	The FMO	132
6.2.4	Nonmicrosomal Oxidations	135
6.2.5	Co-oxidation by Cyclooxygenase (COX)	137
6.2.6	Reduction Reactions	138
6.2.7	Hydrolysis	140
6.2.8	Epoxide Hydration	142
6.2.9	DDT Dehydrochlorinase	143
6.3	Phase II Reactions	143
6.3.1	Glucuronide Conjugation	143
6.3.2	Glucoside Conjugation	145
6.3.3	Sulfate Conjugation	145
6.3.4	Methyltransferases	147
6.3.5	GSTs and Mercapturic Acid Formation	149
6.3.6	Cysteine Conjugate β -Lyase	151
6.3.7	Acylation	152
6.3.8	Phosphate Conjugation	154
	Bibliography and Suggested Reading	154
	Sample Questions	155
7.	Reactive Metabolites	157
	<i>Ernest Hodgson and Randy L. Rose</i>	
7.1	Introduction	157
7.2	Activation Enzymes	158
7.3	Nature and Stability of Reactive Metabolites	160
7.4	Fate of Reactive Metabolites	161
7.4.1	Binding to Cellular Macromolecules	161
7.4.2	Lipid Peroxidation	161

7.4.3	Trapping and Removal: Role of Glutathione	162
7.4.4	Trapping and Removal: Role of Epoxide Hydration	162
7.5	Factors Affecting Toxicity of Reactive Metabolites	162
7.5.1	Levels of Activating Enzymes	163
7.5.2	Levels of Conjugating Enzymes	163
7.5.3	Levels of Cofactors or Conjugating Chemicals	163
7.6	Reactive Oxygen Species	163
7.7	Examples of Activating Reactions	164
7.7.1	Piperonyl Butoxide	164
7.7.2	Chlorpyrifos	164
7.7.3	Vinyl Chloride	165
7.7.4	Methanol	165
7.7.5	Aflatoxin B ₁	165
7.7.6	Carbon Tetrachloride (Tetrachloromethane)	166
7.7.7	Acetylaminofluorene	166
7.7.8	Benzo(a)pyrene	167
7.7.9	Acetaminophen	168
7.7.10	Cycasin	169
7.8	Summary and Conclusions	170
	Bibliography and Suggested Reading	171
	Sample Questions	171

8. Chemical and Physiological Effects on Xenobiotic Metabolism 173

Andrew D. Wallace and Ernest Hodgson

8.1	Introduction	173
8.2	Nutritional Effects	173
8.2.1	Protein	173
8.2.2	Carbohydrates	174
8.2.3	Lipids	174
8.2.4	Micronutrients	175
8.2.5	Starvation and Dehydration	175
8.2.6	Nutritional Requirements in Xenobiotic Metabolism	175
8.3	Physiological Effects	176
8.3.1	Development	176
8.3.2	Gender Differences	178
8.3.3	Hormones	180
8.3.4	Pregnancy	182
8.3.5	Disease	182
8.3.6	Diurnal Rhythms	182
8.4	Comparative and Genetic Effects	182
8.4.1	Variations among Taxonomic Groups	183
8.4.2	Selectivity	188
8.4.3	Genetic Differences	189
8.5	Chemical Effects	191
8.5.1	Inhibition	192

x CONTENTS

8.5.2	Induction	199
8.5.3	Biphasic Effects: Inhibition and Induction	207
8.6	Environmental Effects	207
8.6.1	Temperature	207
8.6.2	Ionizing Radiation	208
8.6.3	Light	208
8.6.4	Moisture	208
8.6.5	Altitude	208
8.6.6	Other Stress Factors	209
8.7	Summary and Conclusions	209
	Bibliography and Suggested Reading	210
	Sample Questions	211
9.	Elimination of Toxicants	213
	<i>Gerald A. Leblanc</i>	
9.1	Introduction	213
9.1.1	Size	213
9.1.2	Surface Area to Body Mass Ratio	214
9.1.3	Compartmentalization	214
9.1.4	Lipid Content	214
9.1.5	Barriers to the Environment	214
9.2	Transport	215
9.3	Renal Elimination	216
9.3.1	Size	216
9.3.2	Water Solubility	216
9.4	Hepatic Elimination	217
9.4.1	Entero-Hepatic Circulation	219
9.4.2	Active Transporters of the Bile Canaliculus	220
9.5	Respiratory Elimination	220
9.6	Conclusion	221
	Bibliography and Suggested Reading	221
	Sample Questions	222
PART IV	TOXIC ACTION	223
10.	Acute Toxicity	225
	<i>Gerald A. Leblanc</i>	
10.1	Introduction	225
10.2	Acute Exposure and Effect	225
10.3	Dose–Response Relationships	227
10.4	Nonconventional Dose–Response Relationships	229
10.5	Alternative Methods	230
10.5.1	Up-Down Method	231
10.5.2	Fixed-Dose Method	231
10.5.3	<i>In Vitro</i> Methods	231

10.6	Mechanisms of Acute Toxicity	231
10.6.1	Narcosis	231
10.6.2	Acetylcholinesterase Inhibition	232
10.6.3	Ion Channel Modulators	232
10.6.4	Inhibitors of Cellular Respiration	234
	Bibliography and Suggested Reading	236
	Sample Questions	236
11.	Chemical Carcinogenesis and Mutagenesis	237
	<i>Robert C. Smart</i>	
11.1	DNA Damage and Mutagenesis	237
11.2	General Aspects of Cancer	239
11.3	Human Cancer	242
11.3.1	Causes, Incidence, and Mortality Rates of Human Cancer	242
11.3.2	Known Human Carcinogens	246
11.3.3	Classification of Human Carcinogens	248
11.3.4	Usefulness and Limitations of Mutagenicity Assays for the Identification of Carcinogens	250
11.4	Classes of Agents That Are Associated with Carcinogenesis	251
11.4.1	DNA Damaging Agents	252
11.4.2	Epigenetic Agents	252
11.5	General Aspects of Chemical Carcinogenesis	254
11.5.1	Initiation-Promotion Model	256
11.5.2	Metabolic Activation of Chemical Carcinogens and DNA Adduct Formation	257
11.6	Oncogenes	259
11.6.1	Ras Oncogene	261
11.7	Tumor Suppressor Genes	262
11.7.1	p53 Tumor Suppressor Gene	262
	Bibliography and Suggested Reading	264
	Sample Questions	264
12.	Teratogenesis	265
	<i>Jill A. Barnes and Ida M. Washington</i>	
12.1	Introduction	265
12.2	Overview of Embryonic Development	266
12.2.1	Fertilization	266
12.2.2	Cleavage Stages	266
12.2.3	Determination	266
12.2.4	Gastrulation	267
12.2.5	Differentiation	267
12.2.6	Organogenesis	267
12.2.7	Fetal Period	268

12.3	Principles of Teratogenesis	268
12.3.1	Wilson's Principles	268
12.3.2	Critical Period	268
12.4	Mechanisms of Teratogenesis	268
12.4.1	Genetic Factors	269
12.4.2	Teratogens	270
12.5	Future Considerations	272
	Bibliography and Suggested Reading	272
	Sample Questions	272
 PART V ORGAN TOXICITY		275
13.	Hepatotoxicity	277
	<i>Andrew D. Wallace and Sharon A. Meyer</i>	
13.1	Introduction	277
13.1.1	Liver Structure	277
13.1.2	Liver Function	278
13.2	Susceptibility of the Liver	279
13.3	Types of Liver Injury	279
13.3.1	Fatty Liver	280
13.3.2	Cholestasis	281
13.3.3	Fibrosis and Cirrhosis	282
13.3.4	Necrosis	282
13.3.5	Apoptosis	282
13.3.6	Hepatitis	283
13.3.7	Carcinogenesis	283
13.4	Mechanisms of Hepatotoxicity	283
13.5	Examples of Hepatotoxicants	285
13.5.1	Carbon Tetrachloride	285
13.5.2	Ethanol	286
13.5.3	Bromobenzene	287
13.5.4	Acetaminophen	287
13.5.5	Troglitazone	288
13.6	Metabolic Activation of Hepatotoxicants	288
	Bibliography and Suggested Reading	289
	Sample Questions	289
14.	Nephrotoxicity	291
	<i>Joan B. Tarloff and Andrew D. Wallace</i>	
14.1	Introduction	291
14.1.1	Structural Organization of the Kidney	291
14.1.2	Function of the Renal System	292
14.2	Factors Contributing to Nephrotoxicity	292

14.3	Examples of Nephrotoxicants	293
14.3.1	Metals	295
14.3.2	Antimicrobial Agents	295
14.3.3	Agents that Precipitate in Renal Tubules	298
14.3.4	Halogenated Hydrocarbons	299
14.3.5	Analgesics	301
14.4	Summary	301
	Bibliography and Suggested Reading	301
	Sample Questions	302
15.	Toxicology of the Nervous System	303
	<i>Bonita L. Blake</i>	
15.1	Introduction	303
15.2	The Nervous System	303
15.2.1	The Neuron	304
15.2.2	Neurotransmitters and Their Receptors	308
15.2.3	Glial Cells	309
15.2.4	The Blood–Brain Barrier	310
15.2.5	The Energy-Dependent Nervous System	311
15.3	Toxicant Effects on the Nervous System	312
15.3.1	Structural Effects of Toxicants on Neurons	312
15.3.2	Toxicant-Mediated Alterations in Synaptic Function	315
15.4	Neurotoxicity Testing	317
15.4.1	<i>In Vivo</i> Tests of Animal Exposure	317
15.4.2	<i>In Vivo</i> Tests of Human Exposure	318
15.4.3	<i>In Vitro</i> Neurochemical and Histopathological End points	320
15.5	Summary	321
	Bibliography and Suggested Reading	322
	Sample Questions	322
16.	Reproductive System	323
	<i>Heather Patisaul</i>	
16.1	Introduction	323
16.1.1	Defining Reproductive Toxicity	323
16.1.2	Defining Endocrine Disruption	324
16.2	The Hypothalamic-Pituitary-Gonadal Axis	324
16.3	Male Reproductive Physiology	326
16.4	Disruption of Male Reproduction By Toxicants	330
16.4.1	Pesticides	330
16.4.2	Metals	331
16.4.3	Plastics	332
16.5	Female Reproductive Physiology	332
16.5.1	The Ovulatory Cycle	333

16.6	Disruption of Female Reproduction by Toxicants	335
16.6.1	Cigarette Smoke	336
16.6.2	Diethylstilbestrol (DES)	336
16.6.3	Pesticides	337
16.6.4	Plastics	338
16.6.5	Phytoestrogens	338
16.6.6	Others	341
16.7	Summary	341
	Bibliography and Suggested Reading	341
	Sample Questions	343
17.	Endocrine Toxicology	345
	<i>Gerald A. Leblanc</i>	
17.1	Introduction	345
17.2	Endocrine System	345
17.2.1	Nuclear Receptors	349
17.2.2	Membrane-Bound Steroid Hormone Receptors	350
17.3	Endocrine Disruption	352
17.3.1	Hormone Receptor Agonists	352
17.3.2	Hormone Receptor Antagonists	355
17.3.3	Organizational Versus Activational Effects of Endocrine Toxicants	356
17.3.4	Inhibitors of Hormone Synthesis	356
17.3.5	Inducers of Hormone Clearance	357
17.3.6	Hormone Displacement from Binding Proteins	358
17.4	Incidents of Endocrine Toxicity	358
17.4.1	Organizational Toxicity	358
17.4.2	Activational Toxicity	359
17.4.3	Hypothyroidism	361
17.5	Conclusion	361
	Bibliography and Suggested Reading	362
	Sample Questions	362
18.	Respiratory Toxicology	363
	<i>James C. Bonner</i>	
18.1	Introduction	363
18.2	Anatomy and Function of the Respiratory Tract	363
18.2.1	Upper Respiratory Tract as a Site of Toxicity	365
18.2.2	Lower Respiratory Tract as a Site of Toxicity	366
18.2.3	Airways of the Lower Respiratory Tract	367
18.2.4	Parenchyma of the Lower Respiratory Tract	369
18.2.5	Circulatory, Lymphatic, and Nervous System of the Lung	371
18.3	Toxicant-Induced Lung Injury, Remodeling, and Repair	373
18.3.1	Oxidative Stress and Lung Injury	374

18.3.2	Antioxidant Mechanisms in the Lung	376
18.3.3	Respiratory Tract Injury from Inhaled Particles and Fibers	376
18.3.4	Particle and Fiber Deposition and Clearance	377
18.3.5	Respiratory Tract Injury from Gases and Vapors	379
18.4	Occupational and Environmental Lung Diseases	380
18.4.1	Pulmonary Fibrosis	381
18.4.2	Asthma	381
18.4.3	Hypersensitivity Pneumonitis (HP)	382
18.4.4	COPD	383
18.4.5	Lung Cancer	384
	Bibliography and Suggested Reading	385
	Sample Questions	385
19.	Immune System	387
	<i>MaryJane K. Selgrade</i>	
19.1	Introduction	387
19.2	The Immune System	388
19.3	Immune Suppression	391
19.4	Classification of Immune-Mediated Injury (Hypersensitivity)	396
19.5	Effects of Chemicals on Allergic Disease	398
19.5.1	ACD	398
19.5.2	Respiratory Allergens	400
19.5.3	Adjuvants	402
19.5.4	Systemic Hypersensitivity	402
19.6	Other Issues: Autoimmunity and the Developing Immune System	403
	Bibliography and Suggested Reading	404
	Sample Questions	404
PART VI	APPLIED TOXICOLOGY	407
20.	Toxicity Testing	409
	<i>Ernest Hodgson and Helen Cunny</i>	
20.1	Introduction	409
20.2	Experimental Administration of Toxicants	412
20.2.1	Introduction	412
20.2.2	Routes of Administration	412
20.3	Chemical and Physical Properties	414
20.4	Exposure and Environmental Fate	414
20.5	<i>In Vivo</i> Tests	415
20.5.1	Acute Toxicity	415
20.5.2	Subchronic Tests	421
20.5.3	Chronic Tests	427
20.5.4	Special Tests	435

20.6	<i>In Vitro</i> and Other Short-Term Tests	442
20.6.1	Introduction	442
20.6.2	Prokaryote Mutagenicity	442
20.6.3	Eukaryote Mutagenicity	444
20.6.4	DNA Damage and Repair	447
20.6.5	Chromosome Aberrations	448
20.6.6	Mammalian Cell Transformation	450
20.6.7	General Considerations and Testing Sequences	450
20.7	Ecological Effects	451
20.7.1	Laboratory Tests	451
20.7.2	Simulated Field Tests	452
20.7.3	Field Tests	452
20.8	Risk Analysis	453
20.9	The Future of Toxicity Testing	453
	Bibliography and Suggested Reading	454
	Sample Questions	455
21.	Forensic and Clinical Toxicology	457
	<i>Sharon A. Meyer and Bonita L. Blake</i>	
21.1	Introduction	457
21.2	Forensic Toxicology	457
21.2.1	Overview	457
21.2.2	Evidentiary Requirements	459
21.2.3	Sample Type and Chemical Classes Analyzed in Forensic Toxicology	460
21.3	Clinical Toxicology	462
21.3.1	Overview	462
21.3.2	Clinical Toxicology and Health Care	462
21.3.3	Training and Certification	463
21.3.4	Clinical Management of Toxicant Exposure	464
21.4	Analytical Methods in Forensic and Clinical Toxicology	469
	Bibliography and Suggested Reading	472
	Sample Questions	473
22.	Prevention of Toxicity	475
	<i>Ernest Hodgson</i>	
22.1	Introduction	475
22.2	Legislation and Regulation	475
22.2.1	Federal Government	476
22.2.2	State Governments	481
22.2.3	Legislation and Regulation in Other Countries	482
22.3	Prevention in Different Environments	482
22.3.1	Home	482
22.3.2	Workplace	483
22.3.3	Pollution of Air, Water, and Land	484

22.4 Education	485
Bibliography and Suggested Reading	486
Sample Questions	487
23. Human Health Risk Assessment	489
<i>Ronald E. Baynes</i>	
23.1 Introduction	489
23.2 Risk Assessment Methods	490
23.2.1 Hazard Identification	491
23.2.2 Exposure Assessment	492
23.2.3 Dose Response and Risk Characterization	492
23.3 Noncancer Risk Assessment	493
23.3.1 Default Uncertainty and Modifying Factors	494
23.3.2 Derivation of Developmental Toxicant RfD	496
23.3.3 Determination of RfD and RfC of Naphthalene using the NOAEL Approach	496
23.3.4 Benchmark Dose Approach	497
23.3.5 Determination of BMD and BMDL for ETU	498
23.3.6 Quantifying Risk for Noncarcinogenic Effects: Hazard Quotient	498
23.3.7 Chemical Mixtures	499
23.4 Cancer Risk Assessment	500
23.5 PBPK Modeling	503
Bibliography and Suggested Reading	504
Sample Questions	505
 PART VII ENVIRONMENTAL TOXICOLOGY	 507
24. Toxicant Analysis: Analytical Methods and Quality Assurance	509
<i>Chris Hofelt</i>	
24.1 Introduction	509
24.2 Environmental Sample Collection Methods	510
24.2.1 Sampling Schemes	510
24.2.2 Environmental Matrices	512
24.3 Analytical Techniques	514
24.3.1 Extraction Techniques	515
24.3.2 Sample Cleanup and Enrichment	516
24.3.3 Analysis	519
24.4 Quantification, QA, and QC	525
24.4.1 Quantification Approaches and Techniques	525
24.4.2 QA and QC	526
24.5 Summary	528
Bibliography and Suggested Reading	528
Sample Questions	529

25. Basics of Environmental Toxicology	531
<i>Gerald A. Leblanc and David B. Buchwalter</i>	
25.1 Introduction	531
25.2 Environmental Persistence	532
25.2.1 Abiotic Degradation	533
25.2.2 Biotic Degradation	533
25.2.3 Nondegradative Elimination Processes	534
25.3 Bioaccumulation	535
25.3.1 Factors That Influence Bioaccumulation	538
25.4 Toxicity	539
25.4.1 Acute Toxicity	539
25.4.2 Mechanisms of Acute Toxicity	540
25.4.3 Chronic Toxicity	541
25.4.4 Species-Specific Chronic Toxicity	543
25.4.5 Abiotic and Biotic Interactions	543
25.5 Conclusion	546
Bibliography and Suggested Reading	547
Sample Questions	547
26. Transport and Fate of Toxicants in the Environment	549
<i>Damian Shea</i>	
26.1 Introduction	549
26.2 Sources of Toxicants to the Environment	550
26.3 Transport Processes	553
26.3.1 Advection	553
26.3.2 Diffusion	555
26.4 Equilibrium Partitioning	557
26.4.1 Air–Water Partitioning	558
26.4.2 Octanol–Water Partitioning	558
26.4.3 Lipid–Water Partitioning	559
26.4.4 Particle–Water Partitioning	559
26.5 Transformation Processes	560
26.5.1 Reversible Reactions	561
26.5.2 Irreversible Reactions	563
26.6 Environmental Fate Models	567
Bibliography and Suggested Reading	569
Sample Questions	569
27. Environmental Risk Assessment	571
<i>Damian Shea</i>	
27.1 Introduction	571
27.2 Formulating The Problem	573
27.2.1 Selecting Assessment End Points	573
27.2.2 Developing Conceptual Models	576

27.2.3	Selecting Measures	576
27.3	Analyzing Exposure and Effects Information	578
27.3.1	Characterizing Exposure	579
27.3.2	Characterizing Ecological Effects	580
27.4	Characterizing Risk	582
27.4.1	Estimating Risk	583
27.4.2	Describing Risk	583
27.5	Managing Risk	587
	Bibliography and Suggested Reading	588
	Sample Questions	589
 PART VIII NEW APPROACHES IN TOXICOLOGY		 591
28.	Perspectives on Informatics in Toxicology	593
	<i>Seth W. Kullman, Carolyn J. Mattingly, Joel N. Meyer, and Andrew Whitehead</i>	
28.1	Introduction	593
28.2	Transcriptomics	594
28.3	Annotation Resources	595
28.3.1	Logistics	595
28.3.2	Statistics	595
28.3.3	Types of Annotation	596
28.4	Genome Sequencing, Resequencing and Genotyping	597
28.5	Epigenomic Profiling	598
28.6	Computational Toxicology	599
28.7	Informatics Tools in Toxicology	601
	Bibliography and Suggested Reading	602
	Sample Question	605
 29.	 Future Considerations	 607
	<i>Ernest Hodgson</i>	
29.1	Introduction	607
29.2	Risk Assessment	609
29.2.1	Hazard and Exposure Assessment	609
29.2.2	Toxicogenomics	610
29.2.3	Proteomics	610
29.2.4	Metabolomics	611
29.2.5	Systems Biology Approach to Risk Assessment	611
29.2.6	Endocrine Disruptors	612
29.2.7	Genetically Modified Plants (GMPs)	612
29.3	Risk Management	613
29.4	Risk Communication	613
29.5	<i>In Vivo</i> Toxicity	614
29.6	<i>In Vitro</i> Toxicity	614

xx CONTENTS

29.7	Molecular and Biochemical Toxicology	614
29.8	Development of Selective Toxicants	615
29.9	Summary and Conclusions	616
	Bibliography and Suggested Reading	616
	Sample Questions	617

	GLOSSARY	619
--	-----------------	------------

	INDEX	638
--	--------------	------------