



Fifth Edition

Introduction to Environmental Toxicology

Molecular Substructures to Ecological Landscapes

Wayne G. Landis • Ruth M. Sofield • Ming-Ho Yu

Introduction to Environmental Toxicology



Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

Introduction to Environmental Toxicology

Molecular Substructures to Ecological Landscapes

Fifth Edition

by

Wayne G. Landis

Ruth M. Sofield

Ming-Ho Yu



CRC Press

Taylor & Francis Group

Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

© 2018 by Taylor & Francis Group, LLC
CRC Press is an imprint of Taylor & Francis Group, an Informa business

No claim to original U.S. Government works

Printed on acid-free paper

International Standard Book Number-13: 978-1-4987-5042-4 (Hardback)

This book contains information obtained from authentic and highly regarded sources. Reasonable efforts have been made to publish reliable data and information, but the author and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, please access www.copyright.com (<http://www.copyright.com/>) or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. CCC is a not-for-profit organization that provides licenses and registration for a variety of users. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

Trademark Notice: Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation without intent to infringe.

Library of Congress Cataloging-in-Publication Data

Names: Landis, Wayne G., author. | Sofield, Ruth M., author. | Yu, Ming-Ho, 1928- author.
Title: Introduction to environmental toxicology : molecular substructures to ecological landscapes / by Wayne Landis, Ruth Sofield and Ming-Ho Yu.
Description: Fifth edition. | Boca Raton : CRC Press, 2017. | Includes bibliographical references and index.
Identifiers: LCCN 2017008200 | ISBN 9781498750424 (hardback : alk. paper) | ISBN 9781498750448 (ebook : alk. paper)
Subjects: LCSH: Pollution. | Environmental toxicology.
Classification: LCC QH545.A1 L35 2017 | DDC 615.9/02--dc23
LC record available at <https://lccn.loc.gov/2017008200>

Visit the Taylor & Francis Web site at
<http://www.taylorandfrancis.com>

and the CRC Press Web site at
<http://www.crcpress.com>

Contents

Acknowledgments.....	xvii
About the Authors.....	xix
Chapter 1	
Introduction to Environmental Toxicology.....	1
1.1 Environmental Toxicology as an Interdisciplinary Science	1
1.2 A Brief History and Organizations in Environmental Toxicology	2
1.3 Interactions and Connections of Environmental Toxicology to the Management of Ecological Systems	3
1.3.1 Research Programs.....	3
1.3.2 Scientific Community.....	3
1.3.3 Risk Assessment.....	5
1.3.4 Governmental and Regulatory Agencies	5
1.3.5 Industry	6
1.3.6 General Public and Nongovernmental Organizations.....	6
1.4 Legislation.....	7
1.5 Introduction to this Textbook	8
Study Questions	10
Chapter 2	
Frameworks and Paradigms for Environmental Toxicology	11
2.1 The Fundamentals.....	11
2.2 Models.....	12
2.3 Fundamental Models for Environmental Toxicology	18
2.3.1 The Classical Viewpoint for Classifying Toxicological Effects	19
2.3.2 Chemical Physical–Chemical Characteristics	20
2.3.3 Bioaccumulation/Biotransformation/Biodegradation	20
2.3.4 Receptor and the Mode of Action	20
2.3.5 Biochemical and Molecular Effects	20
2.3.6 Physiological and Behavioral Effects.....	21
2.3.7 Population Parameters.....	21
2.3.8 Community Effects	22
2.3.9 Ecosystem Effects	23
2.3.10 The Adverse Outcome Pathway	23
2.4 An Alternative Framework Incorporating Complexity Theory.....	24
2.5 Spatial and Temporal Scales	25
2.6 Combining Scale and Ecological Dynamics: The Hierarchical Patch Dynamic Paradigm.....	26
2.7 Language as a Model	29
2.7.1 The Importance of Terminology and Language	29
2.7.2 The Language of Normative Science	29
2.7.3 Bending Science	31
Study Questions	32
References and Suggested Readings.....	33

Chapter 3	
Overview of Toxicity-Testing Methods.....	35
3.1 Introduction.....	35
3.1.1 Animal Care and Use Considerations.....	35
3.2 Standard Methods	37
3.2.1 Advantages of Standard Methods.....	37
3.2.2 Disadvantages of Standard Methods	38
3.3 Classification of Toxicity Tests	38
3.3.1 The Design of Toxicity Tests	40
3.3.1.1 Design Parameters for Single-Species Toxicity Tests	40
3.3.1.2 Exposure Scenarios	40
3.3.1.3 Test Organisms	42
3.3.1.4 Comparison of Test Species	43
3.4 Multispecies Toxicity Tests	44
3.4.1 The Design of Multispecies Toxicity Tests	44
3.4.2 The Nature of Multispecies Toxicity Tests	45
3.4.3 Summary of Design Guidelines for Multispecies Toxicity Tests	46
3.5 Overview of Specific Toxicity Tests.....	46
3.5.1 <i>Daphnia</i> 48 h Acute Toxicity Test	46
3.5.2 Algal 96 h Growth Toxicity Test.....	48
3.5.3 Acute Toxicity Tests with Aquatic Vertebrates and Macroinvertebrates.....	50
3.5.4 Terrestrial Vertebrate Toxicity Tests.....	53
3.5.5 Frog Embryo Teratogenesis Assay.....	58
3.6 Multispecies Toxicity Tests	59
3.6.1 Standardized Aquatic Microcosm	61
3.6.2 Mixed-Flask Culture.....	63
3.6.3 FIFRA Microcosm	65
3.6.4 Soil-Core Microcosm.....	68
3.7 Summary.....	68
Study Questions	69
Appendix: The Natural History and Utilization of Selected Test Species	70
Aquatic Vertebrates	70
Coho Salmon (<i>Oncorhynchus kisutch</i>)	70
Rainbow Trout (<i>Oncorhynchus mykiss</i>).....	70
Brook Trout (<i>Salvelinus fontinalis</i>).....	70
Goldfish (<i>Carassius auratus</i>).....	71
Fathead Minnow (<i>Pimephales promelas</i>)	71
Channel Catfish (<i>Ictalurus punctatus</i>)	71
Bluegill (<i>Lepomis macrochirus</i>).....	71
Green Sunfish (<i>Lepomis cyanellus</i>)	71
Invertebrates-Freshwater	72
Daphnids (<i>Daphnia magna</i> , <i>D. pulex</i> , <i>D. pulicaria</i> , <i>Ceriodaphnia dubia</i>)	72
Amphipods (<i>Gammarus lacustris</i> , <i>G. fasciatus</i> , <i>G. pseudolimnaeus</i> , <i>Hyalella azteca</i>)	72
Crayfish (<i>Orconectes</i> sp., <i>Combarus</i> sp., <i>Procambarus</i> sp., <i>Pacifastacus leniusculus</i>)	72
Stoneflies (<i>Pteronarcys</i> sp.)	73
Mayflies (<i>Baetis</i> sp., <i>Ephemerella</i> sp., <i>Hexagenia limbata</i> , <i>H. bilineata</i>)	73
Midges (<i>Chironomus</i> sp.).....	73

Snails (<i>Physa integra</i> , <i>P. heterostropha</i> , <i>Amnicola limosa</i>):	74
(Mollusca, Gastropoda).....	74
Planaria (<i>Dugesia tigrina</i>): (Platyhelminthes, Turbellaria)	74
Invertebrates: Saltwater.....	74
Copepods (<i>Acartia clausi</i> , <i>A. tonsa</i>)	74
Algae	75
<i>Chlamydomonas reinhardi</i>	75
<i>Ulothrix</i> sp.	75
<i>Microcystis aeruginosa</i>	75
<i>Anabaena flos-aquae</i>	75
Avian Species	75
Mallard (<i>Anas platyrhynchos</i>).....	75
Northern Bobwhite (<i>Colinus virginianus</i>)	75
Ring-Necked Pheasant (<i>Phasianus colchicus</i>).....	75
References.....	76
Chapter 4	
Analysis of Exposure-Response	79
4.1 Introduction	79
4.2 The Exposure-Response Curve.....	80
4.3 Thresholds and Hormesis.....	89
4.4 Terminologies from Hypothesis Testing	90
4.5 Overview of the Tools for the Analysis of Exposure-Response Relationships.....	91
4.5.1 Limitations and Alternatives to Hypothesis Testing.....	91
4.5.2 Comparison of Calculations of Several Programs for Calculating Probit Analysis	93
4.5.3 Modeling Using R and the DRC Package.....	94
4.5.4 Hypothesis Testing.....	95
4.6 Curve Fitting and Regression Modeling versus Hypothesis Testing	96
4.7 The Debate: Regression Model versus the Hypothesis-Testing Debate.....	99
4.8 Data Analysis and Interpretation of Multispecies Toxicity Tests	101
4.8.1 Univariate Methods.....	101
4.8.2 Multivariate Methods.....	102
4.8.3 Visualization	103
4.9 Summary of Design Guidelines for Multispecies Toxicity Tests.....	104
Study Questions	104
References and Suggested Readings.....	105
Chapter 5	
The Fate and Transport of Contaminants	109
5.1 Introduction to the Fate and Transport of Contaminants.....	109
5.2 Transport Mechanisms.....	128
5.2.1 Advection, Diffusion, and Dispersion	128
5.2.2 Long-Range Atmospheric Transport	129
5.3 Persistence.....	131
5.4 Biotransport.....	133
5.5 Abiotic Degradation/Transformation	133
5.6 Multimedia Box Models	135

5.7	Equilibrium	139
5.8	The Fugacity Approach	143
5.9	Bioconcentration versus Biomagnification	143
5.10	Bioavailability	145
5.10.1	Measures of Bioavailability	145
5.10.2	Metal Speciation and the Biotic Ligand Model.....	147
5.10.3	Acid Volatile Sulfide/Simultaneously Extracted Metals in Anoxic Sediment.....	148
5.11	Summary.....	149
	Study Questions	149
	References and Suggested Readings.....	150
 Chapter 6		
	Uptake and Modes of Action	157
6.1	Introduction.....	157
6.2	The Damage Process	157
6.2.1	Atmospheric Pollutants and Plants	157
6.2.2	Plant Injury	158
6.2.3	Vertebrates.....	159
6.2.3.1	Exposure	160
6.2.3.2	Uptake	160
6.2.3.3	Transport.....	160
6.2.3.4	Storage	160
6.2.3.5	Metabolism	160
6.2.3.6	Excretion	161
6.3	Mechanisms of Action	161
6.3.1	Disruption or Destruction of Cellular Structure	161
6.3.2	Direct Chemical Combination with a Cellular Constituent.....	161
6.3.3	Effect on Enzymes.....	162
6.3.4	Secondary Action as a Result of the Presence of a Pollutant	164
6.3.5	Metal Shift.....	166
6.4	Details of Specific Modes of Action.....	166
6.4.1	Narcosis	166
6.4.2	Organophosphates	167
6.4.3	Modes of Action of Chemical Warfare Agents	169
6.4.4	Monohaloacetic Acids	173
6.5	Receptor-Mediated Toxicity and Endocrine Disruption.....	175
6.5.1	Specificity of the Hormone-Receptor Interaction	178
6.5.2	The Receptor Pathway for TCDD	180
6.5.3	The Structure-Activity Relationships of PCB and Related Compounds	182
6.5.4	Polybrominated Diphenylethers	187
6.6	The Multiple Modes of Action of Atrazine	188
6.7	Adverse Outcome Pathway Models	191
6.8	Introduction to Quantitative Structure-Activity Relationships.....	193
6.8.1	Construction of Quantitative Structure-Activity Relationships Models.....	195
6.8.2	Typical Quantitative Structure-Activity Relationships Model Development	196
6.8.3	Estimation of Toxicity Using Quantitative Structure-Activity Relationships....	198
	Study Questions	199
	References and Suggested Readings.....	200

Chapter 7	
Modification in Toxic Responses, Mixtures, and Climate Change	203
7.1 Introduction	203
7.2 Physicochemical Properties of Pollutants	203
7.3 Time and Mode of Exposure.....	203
7.4 Environmental Factors	204
7.4.1 Temperature.....	204
7.4.2 Humidity.....	204
7.4.3 Light Intensity	204
7.5 Biological Factors Affecting Toxicity	205
7.5.1 Diseases.....	205
7.5.2 Behavioral Factors.....	206
7.5.3 Sex Variation	206
7.5.4 Nutritional Factors.....	206
7.5.5 Fasting or Starvation	207
7.5.6 Proteins.....	207
7.5.7 Carbohydrates.....	208
7.5.8 Lipids.....	208
7.5.9 Vitamin A.....	209
7.5.10 Vitamin D.....	209
7.5.11 Vitamin E	209
7.5.12 Vitamin C	210
7.5.13 Minerals.....	211
7.6 Mixtures and the Effects on Toxicity.....	211
7.6.1 Synergism and Potentiation.....	212
7.6.2 Antagonism	212
7.6.3 Estimating the Toxicity of Mixtures	213
7.6.4 Simple Models of Mixture Toxicity	213
7.6.5 Mixture Estimation System.....	215
7.6.6 Estimating the Toxicity of Mixtures of Polynuclear Aromatic Hydrocarbons ..	216
7.7 Carbamate and Organophosphate Synergistic Toxicity	218
7.8 Climate Change and Toxicology	220
Study Questions	223
References and Suggested Readings.....	224
Chapter 8	
Inorganic Gaseous Pollutants	227
8.1 Sulfur Oxides	227
8.1.1 Sources of SO ₂	227
8.1.2 Characteristics of SO ₂	228
8.1.3 Effects on Plants.....	228
8.1.4 Effect on Animals	230
8.1.5 Effect on Humans.....	230
8.2 Nitrogen Oxides	231
8.2.1 Forms and Formation of Nitrogen Oxides	231
8.2.2 Major Reactive N Species in the Troposphere	231
8.2.3 Effects on Plants.....	232
8.2.4 Effects on Humans and Animals	233

8.2.5	Physiological Effects	233
8.2.6	Biochemical Effects.....	233
8.3	Ozone	233
8.3.1	Sources	233
8.3.2	Photochemical Smog	234
8.3.3	Effects on Plants	235
8.3.4	Effects on Humans and Animals.....	235
8.3.5	Biochemical Effects.....	236
8.4	Carbon Monoxide	238
8.4.1	Formation of CO.....	238
8.4.2	Human Exposure to CO	238
8.4.3	Toxicological Effects	239
8.4.4	Mechanism of Action	240
	Study Questions	240
	References and Suggested Readings	240

Chapter 9

	Fluoride as a Contaminant of Developing Economies	243
9.1	Environmental Sources and Forms of Fluoride.....	243
9.1.1	Minerals and Soils.....	243
9.1.2	Natural Waters.....	243
9.1.3	Foods	243
9.1.4	Air.....	244
9.2	Industrial Sources of Fluoride Pollution	244
9.3	Effects on Plants	246
9.3.1	Injuries to Leaf Tissues	246
9.3.2	Effect on Germination.....	247
9.3.3	Biochemical Effect	248
9.4	Effects on Animals	248
9.4.1	Acute Effects	248
9.4.2	Chronic Effects.....	248
9.5	Effects on Human Health	250
9.5.1	Daily Intake	250
9.5.2	Absorption	250
9.5.3	Acute Toxicity.....	250
9.5.4	Chronic Toxicity	251
9.6	Biochemical Effect	251
	Study Questions	253
	References and Suggested Readings	253

Chapter 10

	Metals.....	255
10.1	Introduction.....	255
10.2	Lead	256
10.2.1	Properties and Uses	256
10.2.2	Exposure	256
	10.2.2.1 Atmospheric Lead.....	256

10.2.2.2	Waterborne Lead	256
10.2.2.3	Lead in Food and Edible Nonfood Items	257
10.2.2.4	Lead in Soils	257
10.2.3	Lead Toxicity	258
10.2.3.1	Effect on Plants.....	258
10.2.3.2	Effect on Animals	258
10.2.3.3	Effect on Humans	258
10.2.3.4	Biochemical Effect	259
10.3	Cadmium	260
10.3.1	Properties and Uses	260
10.3.2	Exposure.....	261
10.3.3	Cadmium Toxicity	261
10.3.3.1	Effect on Plants.....	261
10.3.3.2	Effects on Animals/Humans	262
10.3.3.3	Biochemical Effect	262
10.4	Mercury	263
10.4.1	Properties and Uses	263
10.4.2	Sources of Mercury Pollution.....	263
10.4.3	Toxicity	264
10.4.3.1	Effect on Plants.....	264
10.4.3.2	Effect on Animals	264
10.4.3.3	Terrestrial Animals.....	264
10.4.3.4	Effect on Human Health	264
10.4.3.5	Biochemical Effect	265
	Study Questions	266
	References and Suggested Readings.....	266

Chapter 11

	Emerging Contaminants	269
11.1	Contaminant Classification	269
11.2	Microplastics.....	270
11.2.1	Properties and Uses	271
11.2.2	Extent of Contamination and Sources	271
11.2.3	Exposure and Toxicity	272
11.2.4	Exposure and Toxicity to Aquatic Life.....	272
11.3	Engineered Nanomaterials	273
11.3.1	Terminology and Types of Engineered Nanomaterials (ENMs).....	273
11.3.2	Properties and Uses	274
11.3.3	Extent of Contamination and Sources	275
11.3.4	Exposure and Toxicity	276
11.4	Neonicotinoid Insecticides.....	276
11.4.1	Properties and Uses	277
11.4.2	Sources and Extent of Contamination.....	278
11.4.3	Mode of Action.....	278
11.4.4	Exposure and Toxicity to Nontarget Organisms: Vertebrates	279
11.4.5	Exposure and Toxicity to Nontarget Organisms: Invertebrates	279
	Study Questions	281
	References and Suggested Readings.....	281

Chapter 12	
Biotransformation, Detoxification, and Biodegradation	285
12.1 Introduction.....	285
12.2 Metabolism of Environmental Chemicals: Biotransformation.....	285
12.3 Types of Biotransformation	286
12.4 Mechanisms of Biotransformation	286
12.5 Consequence of Biotransformation	290
12.6 Microbial Degradation.....	291
12.7 Bioremediation	298
12.7.1 Isolation and Engineering of Degradative Organisms	300
12.7.2 The Genetics of Degradative Elements	301
12.8 An Example of a Detoxification Enzyme: The Organophosphorous Acid Anhydrolases.....	302
12.8.1 Characteristics of the <i>opd</i> Gene Product and Other Bacterial Organophosphorous Acid Anhydrolases	304
12.8.2 Eukaryotic Organophosphorous Acid Anhydrolases	306
12.8.3 Characteristics of Other Invertebrate Metazoan Activities.....	307
12.8.4 Characteristics of the Fish Activities.....	308
12.8.5 Comparison of the Organophosphorous Acid Anhydrases	308
12.8.6 Natural Role of the Organophosphorous Acid Anhydrases	309
Study Questions	311
References and Suggested Readings.....	311
Chapter 13	
Ecological Effects from Biomarkers to Populations.....	317
13.1 Introduction.....	317
13.2 Terminology and Context	317
13.3 The Key to Context, the Hierarchical Patch Dynamics Paradigm	319
13.4 Measurement of Ecological Effects at Various Scales of Biological Organization	322
13.5 Bioaccumulation/Biotransformation/Biodegradation	324
13.6 Molecular and Physiological Indicators of Chemical Stress-Biomarkers	325
13.7 Enzymatic and Biochemical Processes.....	325
13.8 Physiological and Histological Indicators	326
13.9 Toxicity Tests and Population-Level Measures	328
13.9.1 Sentinel Organisms and In Situ Biomonitoring	329
13.9.2 Population Parameters	330
13.10 Assemblage and Community Parameters	331
13.11 Effects at the Population Scale	334
13.11.1 Populations	334
13.11.2 Modeling of Populations Using Age Structure and Survivorship Models	334
13.11.2.1 Population Biology, Nonlinear Systems, and Chaos	334
13.11.3 Age-Structured Populations	339
13.12 Measurement of Effects on Populations	342
13.12.1 Point Estimates, TRVs, NOECs, and LD50s.....	342
13.12.2 Intrinsic Rate of Growth and Age Structure	343
13.12.3 Variability in λ	344
13.12.4 Biomass, Percent Cover, Productivity	345

13.12.5	Change in the Pattern of the Age Structure	346
13.12.5.1	Normalized Effects Vector.....	346
13.12.5.2	So What Measure to Use?	349
13.13	Observed Changes in Age Structure Experimental and Field Populations.....	350
13.14	Contaminants in Spatially Structured Populations	352
13.14.1	The Spatial Structure of Populations.....	352
13.14.2	The Use of Metapopulation Models to Investigate Toxicant Effects	353
13.14.3	Patch Dynamic Models Based on Sromberg et al. (1998).....	354
13.14.4	Interacting Populations in a Patchy Environment	357
13.14.5	The Importance of Patch Dynamics.....	362
13.15	Implications	363
	Appendix: Age-Structured Population Modeling in Detail.....	364
	Study Questions	366
	References and Suggested Readings.....	367
Chapter 14		
	Ecological Effects: Community to Landscape Scales of Toxicological Impacts	373
14.1	Introduction.....	373
14.2	Community Effects.....	373
14.2.1	Competition and Indirect Effects	373
14.2.2	Resource Competition as a Model of the Direct and Indirect Effects of Pollutants	373
14.2.2.1	Case 1	376
14.2.2.2	Case 2	377
14.2.3	Effects on Ecosystems or Ecological Structures	381
14.2.3.1	Similarity Measures.....	381
14.2.3.2	Classification	382
14.2.3.3	Clustering	382
14.3	Application of Multivariate Techniques	383
14.4	Normalized Ecosystem Strain.....	383
14.5	State Space of Ecosystems.....	384
14.6	Nonmetric Clustering and Association Analysis	386
14.7	Projections for Visualizing Ecosystem Dynamics	387
14.8	Examples of the Use of Multivariate Methods in Multispecies Toxicity Tests and Field Studies.....	389
14.8.1	SiZer and the Detection of Thresholds.....	392
14.8.2	Pollution-Induced Community Tolerance	393
14.9	Interpretation of Ecosystem Level Impacts	394
14.10	An Alternative Model, the Community Conditioning Hypothesis.....	397
	Study Questions	398
	References and Suggested Readings.....	399
Chapter 15		
	Ecological Risk Assessment	403
15.1	Introduction.....	403
15.2	The Fundamentals of Risk Assessment	403
15.3	Ecological Risk Assessment	404

15.4	Ecological Risk-Assessment Framework.....	405
15.4.1	Problem Formulation.....	406
15.4.2	Conceptual Models.....	410
15.4.3	Analysis	411
15.4.4	Exposure Analysis	411
15.4.5	Characterization of Ecological Effects.....	412
15.4.5.1	Ecological Response Analyses	413
15.4.5.2	Stressor-Response Profile	414
15.4.5.3	Data Acquisition, Verification, and Monitoring	414
15.5	Risk Characterization	414
15.5.1	Integration.....	415
15.5.2	Risk Description	416
15.5.3	Interpretation of Ecological Significance	417
15.5.4	Discussion between the Risk Assessor and Risk Manager.....	417
15.5.5	Data Acquisition, Verification, and Monitoring	417
15.6	Techniques in Ecological Risk Assessment.....	418
15.6.1	Calculating Ecological Risk	418
15.6.2	The Curve Model.....	418
15.6.3	Spatially Distinct Risk Quotients	419
15.6.4	Monte Carlo Simulation and Analysis	420
15.7	A Ranking Approach to Multiple Stressors and Wide Area Ecological Risk Assessment	422
15.7.1	A Simple Example.....	426
15.7.2	Advantages and Dangers of the Ranking Approach	427
15.8	Establishing Causation and the Weight of Evidence Approach.....	428
15.8.1	Criteria for Causation	428
15.8.2	Weight of Evidence	429
15.8.3	A General Model for Regional Risk Assessment: The 10 Steps	430
15.8.4	The Cherry Point Case Study	433
15.8.4.1	Step 1. List the Important Management Goals for the Region. What Do You Care about and Where?	434
15.8.4.2	Step 2. Make a Map. Include Potential Sources and Habitats Relevant to the Management Goals	435
15.8.4.3	Step 3. Break the Map into Regions Based on a Combination of Management Goals, Sources, and Habitats	435
15.8.4.4	Step 4. Make a Conceptual Model That Ties the Stressors to the Receptors and to the Assessment Endpoints.....	437
15.8.4.5	Step 5. Decide on an Evaluation Scheme for Each Source, Stressor, and Habitat to Allow the Calculation of Risk to the Assessment Endpoints	439
15.8.4.6	Step 6. Calculate the Risks	441
15.8.4.7	Step 7. Evaluate Uncertainty and Sensitivity Analysis of the Relative Rankings.....	443