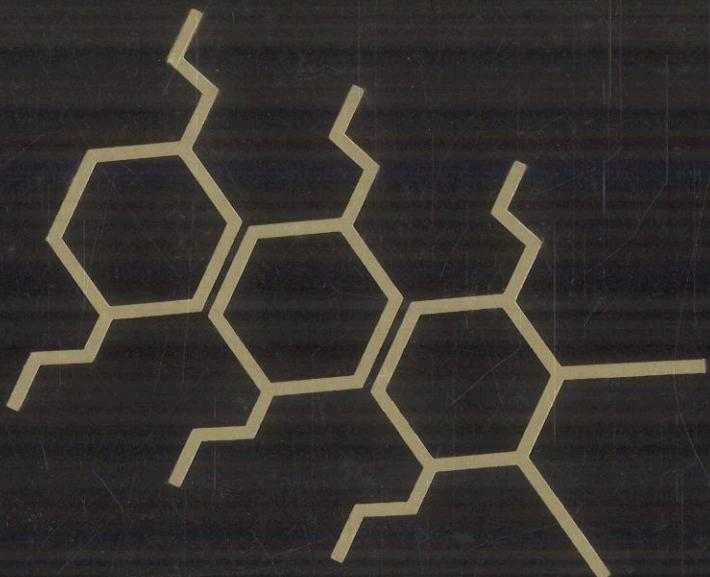


THIRD EDITION

HAYES'

HANDBOOK OF
PESTICIDE
TOXICOLOGY

VOLUME 2



EDITED BY
ROBERT KRIEGER

ASSOCIATE EDITORS

JOHN DOULL, ERNEST HODGSON, HOWARD MAIBACH,
LAWRENCE REITER, LEONARD RITTER, JOHN ROSS,
WILLIAM SLIKKER, JR., JOOP VAN HEMMEN



Contents of Volume 2

Contributors

Section VIII Regional and Global Environmental Exposure Assessments

56. Ecotoxicological Risk Assessment of Pesticides in the Environment	1191
56.1 Introduction	1191
56.1.1 Risk Assessment of Pesticides	1191
56.1.2 Assessing Risks from Pesticides in Relation to Other Substances	1193
56.1.3 Protection Goals, Assessment Endpoints, and Measures of Effects	1195
56.2 The Risk Assessment Analysis	1199
56.2.1 Characterizing Effects	1200
56.2.2 Characterizing Exposure	1203
56.3 Risk Assessment of Pesticides	1206
56.3.1 Scoring Systems and Setting of Criteria	1206
56.3.2 The Hazard Quotient	1207
56.3.3 Probabilistic Risk Assessment	1207
56.4 Risk Communication	1212
Conclusion	1213
57. Environmental Transport and Fate	1219
57.1 Introduction	1219
57.2 Principles	1221
57.2.1 The Dissipation Process	1221
57.2.2 Environmental Compartments	1221
57.2.3 Structure	1222
57.2.4 Activation–Deactivation	1224
57.3 Environmental Transport and Fate Modeling	1224
57.3.1 Physical Models	1224
57.3.2 Mathematical or Computer Models	1225
Conclusion	1225

58. Hydrophobicity as a Key Physicochemical Parameter of Environmental Toxicology of Pesticides	1229
58.1 Introduction	1229
58.2 Measurements and Experimental Estimations of Log <i>P</i>	1229
58.2.1 Direct Partitioning (Shake-Flask and Slow-Stirring) Method	1229
58.2.2 Potentiometric Titration Method for Ionizable Pesticides	1231
58.2.3 High-Performance Liquid Chromatographic Method	1231
58.3 Nonexperimental Estimations of Log <i>P</i>	1232
58.3.1 Scope and Limitation of the Additive Nature of Log <i>P</i> Values	1232
58.3.2 Empirical (Manual) Procedure	1233
58.3.3 Empirical Procedure Using Relationships with Log <i>P</i> Values of Simpler Compounds	1234
58.3.4 Empirical Procedure Using Free-Energy Related Substituent Parameters	1235
58.3.5 Computer-Aided Procedures	1237
58.4 Physicochemical Significance of Log <i>P</i> in Environmental Quantitative Structure–Activity Relationships	1239
58.4.1 Behavior in Soil	1239
58.4.2 Bioaccumulation	1243
58.4.3 Aquatic Toxicity	1245
Acknowledgments	1248

Section IX Public Health Regulation and Epidemiology

59. Studies in Humans	1255
59.1 Cases	1255
59.2 Medical Use	1256
59.3 Use Experience	1256
59.4 Volunteers	1256
59.4.1 Introduction	1256
59.4.2 Legal and Ethical Considerations	1258

59.4.3	Design of Studies	1264	60.4.2	Symptoms and Signs	1299
59.4.4	Motivation of Volunteers	1271	60.4.3	Treatment	1302
59.4.5	Studies of Pesticides in Volunteers	1271	60.5	Chronic Poisoning by Pesticides	1302
59.4.6	Conclusion	1274	60.5.1	Types of Chronic Pesticide Toxicity	1303
59.5	Measurement of Exposure and Dose Under Practical Conditions	1275	60.5.2	Background Accumulation	1304
59.5.1	Measurement of Respiratory Exposure	1275	60.5.3	Symptoms and Signs	1305
59.5.2	Measurement of Dermal Exposure	1278	60.5.4	Assessment of Exposure History	1305
59.5.3	Measurement of Oral Exposure	1280	60.5.5	Assessment of Symptoms	1306
59.5.4	Problems of Measuring Separate Contributions from Different Routes of Exposure	1281	60.5.6	Assessment of Signs	1306
59.5.5	Measurement of Absorbed Dose	1282	60.5.7	Workup of Neurotoxicity	1308
59.6	Regulation of Pesticides and Other Chemicals by the EPA	1285	60.5.8	Risks of Pesticide-Induced Cancer	1308
59.6.1	EPA's Risk Assessment Approach	1286	60.5.9	Treatment	1309
59.6.2	Utility of Human Data in Risk Assessment	1286	Conclusion		1309
59.6.3	Attributes and Limitations of Laboratory Animal Data	1287			
59.6.4	Use of Toxicokinetic Data for Species-to-Species Extrapolations	1288			
59.6.5	Events Leading to NRC's Review of the EPA's Use of Data from Human Dosing Studies	1288			
59.6.6	EPA's Charge to the NAS	1289			
59.6.7	NRC Committee and its Major Recommendations	1289			
Conclusion		1290			
60.	Diagnosis and Treatment of Poisoning Due to Pesticides	1295			
60.1	Introduction	1295			
60.2	Types of Pesticides	1295			
60.3	General Management of Acute Poisoning	1296			
60.3.1	Skin Decontamination	1297			
60.3.2	Activated Charcoal	1297			
60.3.3	Gastric Lavage	1298			
60.3.4	Cathartics	1298			
60.3.5	Whole-bowel Irrigation	1299			
60.3.6	Eye Contamination	1299			
60.4	Acute Poisoning by Pesticides	1299			
60.4.1	Epidemiology	1299			
61.	Surveillance of Pesticide- Related Illness and Injury in Humans	1313			
61.1	Introduction	1313			
61.2	Surveillance Systems	1314			
61.2.1	American Association of Poison Control Centers' National Poison Data System	1314			
61.2.2	State-based Surveillance Systems	1325			
61.2.3	California Department of Pesticide Regulation	1332			
61.2.4	Bureau of Labor Statistics	1339			
61.2.5	Vital Status Statistics: Multiple Causes of Death	1342			
61.2.6	National Hospital Discharge Studies: Colorado State University	1343			
61.2.7	National Hospital Discharge Survey: National Center for Health Statistics	1344			
61.2.8	South Carolina Hospital Discharge Surveys	1345			
61.2.9	National Agricultural Workers Survey	1346			
61.2.10	Surveillance Efforts of International Organizations	1347			
61.3	U.S. Environmental Protection Agency Regulations	1349			
61.3.1	The Federal Insecticide, Fungicide, and Rodenticide Act	1349			
61.3.2	Federal Reporting Requirements for Risk Information	1350			

61.3.3	National Peptide Information Center	1350	63.2	Risk-Perception Studies	1381
61.3.4	Worker Protection Standard	1350	63.2.1	Social, Cultural, and Political Influences on Risk Perception	1384
61.4	Evaluating Surveillance Systems	1351	63.3	Intuitive Toxicology: Expert and Lay Judgments of Chemical Risks Conclusion	1388
61.5	Case Definition for Acute Pesticide-Related Illness and Injury	1352			1390
61.5.1	The National Public Health Surveillance System Case Definition	1353			
61.6	Limitations of Pesticide Poisoning Surveillance Data	1354	Section X		
61.6.1	Denominators	1354	Organophosphorous and N-Methyl Carbamate Insecticides		
61.6.2	Limitations Related to Definitions	1356			
61.6.3	Limitations Related to Sensitivity	1357	64.	Chemistry of Organophosphorus Insecticides	1395
61.6.4	Legitimate uses for Surveillance Data	1357	64.1	Introduction	1395
61.6.5	Mechanisms to Strengthen the Surveillance of Acute Pesticide-Related Illness	1358	64.1.1	History	1395
61.7	Fundamentals of Epidemiology	1360	64.1.2	Classification and Nomenclature	1395
61.7.1	Principles of Epidemiology	1360	64.1.3	Synthesis	1396
61.7.2	Epidemiologic Study Designs	1360	64.1.4	Reactions	1398
61.7.3	Evaluating Pesticide Health Information	1363	65.	The Metabolism of Organophosphorus Insecticides	1399
61.8	Internet and Telephone Resources for Pesticide Information Conclusion	1364	65.1	Introduction	1399
		1365	65.2	Oxidations	1400
62.	Risk Assessment and Risk Management: The Regulatory Process	1371	65.2.1	Cytochromes P450	1400
62.1	Introduction	1371	65.2.2	Flavin Monooxygenases	1401
62.2	Historical Background of Pesticide Regulation in the United States	1371	65.3	Reductions	1402
62.3	Current State of Pesticide Regulation in the United States	1372	65.4	Hydrolysis	1402
62.3.1	FIFRA—Key Changes and Additions	1373	65.5	Conjugations	1404
62.3.2	FFDCA—Key Changes and Additions	1374	65.6	Summary	1404
62.4	Current Regulatory Process	1377	66.	Organophosphorus Insecticide Pharmacokinetics	1409
62.4.1	Registration	1377	66.1	Background	1409
62.4.2	Reregistration and Registration Renewal	1378	66.2	Pharmacokinetic Principles of Importance to Organophosphorus Insecticides	1411
62.4.3	Special Review	1379	66.2.1	Compartmental Pharmacokinetic Models	1411
62.5	Web Sites	1380	66.2.2	Physiologically-Based Pharmacokinetic Models	1412
63.	Perceptions of Pesticides as Risks to Human Health	1381	66.3	Pharmacokinetic Approaches Applied to Organophosphorus Insecticides	1415
63.1	Introduction	1381	66.3.1	Application of Pharmacokinetics to Understand the Overall	

	Disposition and Clearance of Organophosphorus Insecticides	1415	67.4.3 Isolation and Localization	1444
66.3.2	Development of Pharmacokinetic Models for Quantitative Biological Monitoring to Assess Organophosphorus Insecticide Exposure in Humans	1417	67.4.4 Molecular Biology	1445
66.3.3	The Application of Pharmacokinetics for Quantifying Exposure to Organophosphorus Insecticides	1421	67.4.5 Structure of the Catalytic Domain	1445
66.3.4	Studies that Facilitate Extrapolation of Dosimetry and Biological Response from Animals to Humans and the Assessment of Human Health Risk	1423	67.5 Role of Neuropathy Target Esterase in Organophosphorus Ester-Induced Delayed Neuropathy: A Toxic Gain of Function?	1447
	Conclusion	1429	67.6 Role of Neuropathy Target Esterase in Organophosphorus Ester-Induced Delayed Neuropathy: A Relative Loss of Function in Phospholipid Metabolism?	1448
	Acknowledgments	1430	Conclusion	1451
67. Neuropathy Target Esterase		1435	68. Cholinesterases	1457
67.1	Introduction	1435	68.1 Introduction	1457
67.2	Identification of Neuropathy Target Esterase	1435	68.2 Distribution	1457
67.2.1	Organophosphorus Ester Insecticides: General Reactions with Serine Esterases	1435	68.3 Substrate Preferences and Selective Inhibitors	1459
67.2.2	Neuropathy Target Esterase as the Target for Initiation of Organophosphorus Ester-Induced Delayed Neuropathy	1437	68.4 Multiple Molecular Forms and Life History	1459
67.2.3	Possible Involvement of other Esterases in Organophosphorus Ester-Induced Delayed Neuropathy	1438	68.5 Mechanism of Hydrolysis	1461
67.3	Toxicological Applications	1439	68.6 Toxicities of Anticholinesterases	1463
67.3.1	Hen Test	1439	68.7 Assay Techniques	1465
67.3.2	Structure-Activity Relationships and Prediction of Organophosphorus Ester-Induced Delayed Neuropathy Potential in Hens	1439	68.7.1 Radiometric	1465
67.3.3	Application of Neuropathy Target Esterase Studies to Human Risk Assessment	1440	68.7.2 pH	1465
67.3.4	Biomarkers and Biosensors	1442	68.7.3 Thiol Substrates and the Ellman Assay	1466
67.4	Nature and Properties of Neuropathy Target Esterase	1443	68.7.4 Variability	1468
67.4.1	Biochemical Studies	1443	68.8 Standards	1469
67.4.2	Enzymology	1443	68.9 Field Kits	1469
			68.10 Regulatory Matters: Are ChE Inhibitions Adverse Effects?	1471
			68.11 Blood ChEs and Detection of Exposure	1471
			68.12 Reactivation of Inhibited AChE	1471
			68.13 Significance of Blood ChEs	1471
			68.14 Direct Effects	1472
			68.15 Antidotes	1472
			68.16 Risk Assessment and ChEs Conclusion	1473
			Acknowledgment	1474
			69. Organophosphorus-Induced Delayed Neuropathy	1479
			69.1 History	1479
			69.2 Chemistry of Organophosphorus Compounds	1480
			69.3 Clinical Manifestations	1481
			69.3.1 Human	1481
			69.3.2 Animal	1481
			69.4 Neuropathology	1482

69.5	Neuropathology of Mammalian Animal Models	1486	71.7.7	Reproductive and Developmental Effects	1536
69.6	Pathogenesis	1490	71.7.8	Neurotoxicity	1537
69.7	Factors Influencing the Development of Organophosphorus-Induced Delayed Neuropathy	1493	71.7.9	Human Volunteer Study	1538
69.8	Testing for Organophosphorus-Induced Delayed Neuropathy Conclusion	1495 1497	71.7.10	Toxicology Studies on Malaoxon	1540
			Conclusions	Acknowledgments	1541 1542
70.	Chlorpyrifos	1505	72.	Clinical Toxicology of Anticholinesterase Agents in Humans	1543
70.1	Introduction and Regulatory Aspects	1505	72.1	The Cholinergic Syndrome	1543
70.2	Physicochemical Properties	1505	72.1.1	Etiology	1543
70.3	Toxicokinetic Properties	1506	72.1.2	Pathogenesis	1545
	70.3.1 Absorption	1506	72.1.3	Clinical Manifestations	1547
	70.3.2 Distribution	1507	72.2	The Intermediate Syndrome	1564
	70.3.3 Metabolism	1507	72.2.1	Etiology	1564
	70.3.4 Excretion	1510	72.2.2	Pathogenesis	1564
70.4	Exposure	1510	72.2.3	Clinical Manifestations	1565
70.5	Toxicological Profile	1511	72.3	Delayed Polyneuropathy	1565
	70.5.1 Mechanism of Action	1511	72.3.1	Etiology	1566
	70.5.2 Acute and Subchronic Toxicity	1512	72.3.2	Pathogenesis	1567
	70.5.3 Chronic Toxic Effects	1514	72.3.3	Clinical Manifestations	1567
	70.5.4 Genotoxicity and Carcinogenicity	1515	72.4	Long-Term Exposures	1569
	70.5.5 Reproductive and Developmental Toxicity	1516	72.4.1	Neurological, Psychiatric, and Behavioral Effects	1569
70.6	Toxic Interactions Conclusion	1518 1519	72.4.2	Other Effects	1574
			72.4.3	Biomonitoring Occupational Exposures	1575
71.	Malathion: A Review of Toxicology	1527	73.	Application of Physiologically Based Pharmacokinetic/Pharmacodynamic Modeling in Cumulative Risk Assessment for <i>N</i>-Methyl Carbamate Insecticides	1591
71.1	Introduction	1527	73.1	Need for Cumulative Risk Assessments for <i>N</i> -Methyl Carbamate Insecticides	1591
71.2	Mode of Action	1528	73.2	Methodologies for Performing Cumulative Risk Assessments for <i>N</i> -Methyl Carbamates	1593
71.3	Basic Physical and Chemical Properties	1528	73.2.1	Relative Potency Factor Approach Using an Index Chemical	1593
71.4	Impurities	1528	73.2.2	Advances in the PBPK/PD Modeling Approach	1594
71.5	Metabolism of Malathion	1529	73.3	Application of the Constructed PBPK/PD Model	1598
71.6	Human Exposure to Malathion	1531	73.3.1	Toxicity Study of Carbofuran	1598
71.7	Effects seen in Animal Toxicology Studies	1531	73.3.2	Construction and Application of a Cumulative PBPK/PD Model of Three NMCS	1599
	71.7.1 Absorption, Distribution, Metabolism, and Excretion	1531			
	71.7.2 Review of Toxicology Studies	1532			
	71.7.3 Acute Toxicity	1532			
	71.7.4 Short-Term and Subchronic Toxicity	1533			
	71.7.5 Genotoxicity	1534			
	71.7.6 Long-Term Studies	1535			

77. Toxicology and Mode of Action of Pyrethroid Insecticides	1665	Section XII	Herbicides
77.1 Introduction	1665		
77.2 Chemistry and Insecticidal Action	1666		
77.2.1 Development of Synthetic Pyrethrroids	1666	78.1 Chemistry and Formulations	1689
77.2.2 Structure–Activity Relationships	1666	78.2 Uses	1689
77.2.3 Mechanism of Insecticidal Activity	1667	78.3 Hazard Identification	1689
77.3 Acute Neurotoxic Actions in Mammals	1668	78.3.1 Pharmacokinetics and Metabolism	1690
77.3.1 Acute Toxicity	1668	78.3.2 Acute Toxicity	1691
77.3.2 Structure–Toxicity Relationships	1669	78.3.3 Short- and Long-Term Toxicity and Oncogenic Potential	1691
77.3.3 Two Syndromes of Pyrethroid Intoxication	1669	78.3.4 Reproductive and Developmental Toxicity	1699
77.3.4 Neurochemical Consequences of Pyrethroid Intoxication	1670	78.3.5 Neurotoxicity	1700
77.3.5 Age-Related Differences in Pyrethroid Sensitivity	1670	78.3.6 Metabolites other than ETU	1700
77.3.6 Reports of Neurotoxic Effects in Humans	1670	78.3.7 Hazard Characterization	1700
77.4 Behavioral Neurotoxicity	1671	78.4 Dose–Response	1700
77.4.1 Effects on Motor Activity	1671	78.4.1 NOAEL and Acceptable Daily Intake—ETU	1700
77.4.2 Effects on Acoustic Startle Response	1671	78.4.2 NOAEL and Acceptable Daily Intake—EBDCS	1701
77.4.3 Effects on Conditioned Behavior	1672	78.4.3 Acute Reference Dose	1702
77.4.4 Results of Regulatory Neurotoxicity Studies	1672	78.4.4 Endpoints for Assessment of Dermal and Respiratory Exposure	1702
77.5 Neurotoxic Effects Following Dermal Exposure	1672	78.4.5 Carcinogenicity Classification and Low Dose Risk Assessment	1702
77.6 Developmental Neurotoxicity	1673	78.5 Toxicology in Humans	1703
77.7 Actions on Voltage-Gated Sodium Channels	1673	78.6 Risk Characterization	1703
77.7.1 Electrophysiological Studies	1673	78.6.1 Dietary Exposure and Risks	1703
77.7.2 Differential Sensitivity of Sodium Channel Isoforms	1674	78.6.2 Worker Exposure and Risks	1704
77.7.3 State-Dependent Actions of Pyrethrroids	1675	Conclusion	1704
77.7.4 The Pyrethroid Receptor on Sodium Channels	1675		
77.7.5 Correlation of Sodium Channel Effects with Toxicity	1677		
77.8 Actions of Pyrethrroids on Other Neuronal Targets	1677	79. Symmetrical Triazine Herbicides: A Review of Regulatory Toxicity Endpoints	1711
77.8.1 Actions of Pyrethrroids on Voltage-Gated Calcium Channels	1677	79.1 Introduction	1711
77.8.2 Actions of Pyrethrroids on Voltage-Gated Chloride Channels	1679	79.1.1 Chemistry	1711
77.8.3 Actions of Pyrethrroids on GABA _A Receptors	1680	79.1.2 Uses	1711
Conclusion	1682	79.2 Hazard Identification	1711
		79.2.1 Acute Studies	1713
		79.2.2 Toxicity after Repeat Exposure	1713
		79.2.3 Developmental and Reproductive Toxicity	1714
		79.2.4 Mutagenicity	1716
		79.2.5 Oncogenicity Assessment	1716
		79.3 Mode of Action for Mammary Tumor Formation in the Sprague-Dawley Rat at High Doses	1717
		79.4 Epidemiology	1719

79.5	Chlorotriazine Cancer Classification	1720	82.4	Butachlor	1760	
79.6	Overall Hazard Assessment	1721	82.4.1	Identity, Properties, and Uses	1760	
80.	Phenylurea Herbicides	1725	82.4.2	Toxicity to Laboratory Animals	1760	
80.1	Introduction	1725	82.5	Metolachlor	1762	
80.2	Diuron	1725	82.5.1	Identity, Properties, and Uses	1762	
80.3	Fluometuron	1727	82.5.2	Toxicity to Laboratory Animals	1762	
80.4	Isoproturon	1728	82.6	Propachlor	1763	
	Conclusion	1730	82.6.1	Identity, Properties, and Uses	1763	
			82.6.2	Toxicity to Laboratory Animals	1763	
			82.6.3	Human Experience	1765	
81.	Protoporphyrinogen Oxidase-Inhibiting Herbicides	1733	82.7	Mode-of-Action Evaluations:		
81.1	Introduction	1733		Oncogenicity	1765	
81.2	Commercially Available Protox Inhibitors	1733		82.7.1	Rat Nasal Tumors	1765
81.2.1	Diphenyl Ether Protoporphyrinogen Oxidase Inhibitors	1733		82.7.2	Rat Stomach Tumors	1767
81.2.2	Non-Diphenyl Ether Protoporphyrinogen Oxidase Inhibitors	1733		82.7.3	Rat Thyroid Tumors	1767
81.3	Agricultural Use	1734		82.8	Common Mechanism of Toxicity	1768
81.3.1	Crops and Weeds	1734	83.	Paraquat	1771	
81.3.2	Mode of Application	1736	83.1	Identity, Properties, and Use	1771	
81.4	Behavior in Plants	1737	83.1.1	Chemical Name	1771	
81.4.1	Absorption, Translocation, and Metabolism	1737	83.1.2	Structure	1771	
81.4.2	Mode of Action	1738	83.1.3	Synonyms	1771	
81.4.3	Mode of Resistance	1740	83.1.4	Physical and Chemical Properties	1771	
81.4.4	Genetically Engineered Resistance	1742	83.1.5	History, Formulations, and Uses	1771	
81.5	Environmental Impact	1742	83.2	Toxicity to Laboratory Animals	1772	
81.5.1	Interaction with Soil	1742	83.2.1	Signs of Toxicity	1772	
81.5.2	Degradation in the Environment	1742	83.2.2	Acute Toxicity	1772	
81.5.3	Ecotoxicology	1742	83.2.3	Irritation and Sensitization	1774	
81.6	Mammalian Toxicology	1743	83.2.4	Subchronic Toxicity	1774	
81.6.1	Skin and Oral	1743	83.2.5	<i>Mutagenic and Carcinogenic</i> Potential	1775	
81.6.2	Teratogenicity and Mutagenicity	1745	83.2.6	Effects on Reproduction, Embryotoxicity and Teratogenicity	1776	
81.6.3	Effects on Mammalian Porphyrin Metabolism	1745	83.2.7	Pathology of the Lung	1776	
81.6.4	Metabolic Degradation in Animals	1746	83.2.8	Absorption	1777	
	Conclusion	1747	83.2.9	Distribution	1778	
82.	Chloracetanilides	1753	83.2.10	Metabolism	1779	
82.1	Introduction	1753	83.2.11	Excretion	1780	
82.2	Alachlor	1753	83.2.12	Accumulation of Paraquat into the Lung	1781	
82.2.1	Identity, Properties, and Uses	1753	83.2.13	Eflux of Paraquat from the Lung	1782	
82.2.2	Toxicity to Laboratory Animals	1753	83.2.14	Biochemical Mechanisms of Paraquat Toxicity	1783	
82.2.3	Human Experience	1757	83.2.15	Lipid Peroxidation Hypothesis	1785	
82.3	Acetochlor	1757	83.2.16	Oxidation of NADPH Hypothesis	1786	
82.3.1	Identity, Properties, and Uses	1757	83.2.17	The Role of Mitochondria in the Toxicity	1786	
82.3.2	Toxicity to Laboratory Animals	1758	83.2.18	The Involvement of Oxygen	1787	
			83.2.19	Effects on the Kidney	1787	
			83.2.20	Effects on the Central Nervous System	1788	
			83.2.21	Effects on Other Organs	1791	

83.2.22 Treatment of Poisoning in Animals	1791	85.4 Toxicokinetics	1849
83.2.23 Adsorption from the Gastrointestinal Tract	1791	85.5 Toxicity to Laboratory Animals	1850
83.2.24 Removal from the Bloodstream	1792	85.6 Toxicity to Humans	1850
83.2.25 Prevention of Accumulation into the Lung	1792	85.7 Reproductive Effects	1850
83.2.26 Free Radical Scavenging	1792	85.8 Genotoxic Effects	1850
83.2.27 Prevention of Lung Fibrosis	1793	85.9 Treatment of Poisoning Conclusion	1851
83.3 Toxicity to Humans	1793	86. Imidazolinones	1853
83.3.1 Experimental Exposure	1793	86.1 Identity, Properties, and Uses	1853
83.3.2 Accidental and Intentional Poisoning	1794	86.1.1 Chemical Names	1853
83.3.3 Use Experience	1795	86.1.2 Physical and Chemical Properties	1853
83.3.4 Atypical Cases of Various Origins	1798	86.1.3 Structure	1853
83.3.5 Clinical Findings and Dosage Response	1800	86.1.4 History and Uses	1854
83.3.6 Laboratory Findings	1804	86.2 Toxicity to Laboratory Animals	1854
83.3.7 Absorption	1805	86.2.1 Basic Findings	1854
83.3.8 Distribution	1805	86.2.2 Absorption, Distribution, Metabolism, and Excretion	1861
83.3.9 Metabolism	1806	86.2.3 Effects on Organs and Tissues	1862
83.3.10 Excretion	1806	86.2.4 Effects on Reproduction	1862
83.3.11 Pathology	1806	86.2.5 Pathology	1862
83.3.12 Treatment of Poisoning	1807	86.2.6 Genotoxicity Studies	1863
84. Phenoxy Herbicides (2,4-D)	1829	86.3 Toxicity to Humans	1863
84.1 Introduction	1829	86.3.1 Use Experience	1863
84.2 Physical and Chemical Properties	1829	86.3.2 Treatment of Poisoning	1863
84.2.1 2,4-D Acid, Salts, and Esters	1829		
84.2.2 2,4,5-T	1830		
84.2.3 2,4-DB	1830		
84.2.4 Dichlorprop (2,4-DP)	1831		
84.2.5 Mecoprop (MCPP)	1831		
84.2.6 MCPA	1831		
84.2.7 Silvex	1831		
84.3 History of Use	1831		
84.4 Formulations	1832		
84.5 Human Exposure to 2,4-D	1832		
84.6 Toxicological Studies	1832		
84.6.1 Absorption	1832		
84.6.2 Distribution	1833		
84.6.3 Pharmacokinetics	1833		
84.6.4 Metabolism	1833		
84.6.5 Excretion	1833		
84.6.6 Animal Studies	1834		
84.6.7 Genotoxicity	1840		
84.7 Studies in Humans	1840		
84.8 Summary	1841		
85. Dicamba	1849	87. Toxicology of Triazolopyrimidine Herbicides	1865
85.1 Synonyms	1849	87.1 Introduction	1865
85.2 Physical and Chemical Properties	1849	87.2 Cloransulam-Methyl	1866
85.3 Formulations and Uses	1849	87.2.1 Identity, Properties, and Uses	1866
		87.2.2 Toxicity to Laboratory Animals	1866
		87.2.3 Toxicity to Humans	1868
		87.3 Diclosulam	1868
		87.3.1 Identity, Properties, and Uses	1868
		87.3.2 Toxicity to Laboratory Animals	1869
		87.3.3 Toxicity to Humans	1870
		87.4 Florasulam	1870
		87.4.1 Identity, Properties, and Uses	1870
		87.4.2 Toxicity to Laboratory Animals	1871
		87.4.3 Toxicity to Humans	1873
		87.5 Flumetsulam	1873
		87.5.1 Identity, Properties, and Uses	1873
		87.5.2 Toxicity to Laboratory Animals	1873
		87.5.3 Toxicity to Humans	1875
		87.6 Metosulam	1875
		87.6.1 Identity, Properties, and Uses	1875
		87.6.2 Toxicity to Laboratory Animals	1875
		87.6.3 Toxicity to Humans	1877
		87.7 Penoxsulam	1877

87.7.1	Identity, Properties, and Uses	1877	89.4.4	Toxicokinetics and Metabolism in Laying Hens	1905
87.7.2	Toxicity to Laboratory Animals	1878	89.5	Toxicity to Laboratory Animals	1906
87.7.3	Toxicity to Humans	1879	89.5.1	Acute Toxicity	1906
87.8	<i>Pyroxsulam</i>	1879	89.5.2	Subchronic Toxicity	1906
87.8.1	Identity, Properties, and Uses	1879	89.5.3	Chronic Toxicity and Oncogenicity	1907
87.8.2	Toxicity to Laboratory Animals	1880	89.5.4	Effects on Liver Xenobiotic Metabolizing Enzymes in the Rat	1907
87.8.3	Toxicity to Humans	1881	89.5.5	Effects on Liver and Plasma Lipids in the Rat	1908
	Conclusion	1881	89.5.6	Effects on Reproduction and Development	1909
			89.5.7	Neurotoxic Effects	1910
			89.5.8	Pharmacological Effects	1911
Section XIII			89.6	Mutagenicity	1911
Fungicides			89.7	Toxicity to Humans	1911
88.	A Toxicological Assessment of Sulfur as a Pesticide	1889	89.7.1	Direct Observations and Health Records	1911
88.1	Introduction	1889	89.7.2	Diagnosis of Poisoning	1911
88.1.1	Usage	1889	89.7.3	Sensitization Observations	1912
88.1.2	Environmental Fate	1889	89.7.4	Proposed Treatment	1912
88.2	Toxicology Profile of Elemental Sulfur	1890	Conclusion		1912
88.2.1	Acute Exposure Oral Toxicity: 81-1	1890			
88.2.2	Acute Exposure Dermal Toxicity: 81-2	1890			
88.2.3	Acute Exposure Inhalation Toxicity: 81-3	1891			
88.2.4	Primary Eye Irritation: 81-4	1891	90.	Captan and Folpet	1915
88.2.5	Primary Dermal Irritation: 81-5	1892	90.1	Introduction	1915
88.2.6	Primary Dermal Sensitization: 81-6	1892	90.1.1	Overview	1915
88.3	Toxicology of Sulfur Dioxide	1892	90.1.2	History and Use	1916
88.4	Veterinary Effects of Sulfur	1893	90.1.3	Toxicological Overview	1916
88.5	Human Health Effects of Sulfur	1894	90.2	Physical Properties and Chemical Reactions	1917
88.5.1	Occupational exposure	1895	90.2.1	Overview	1917
88.6	Discussion	1899	90.2.2	Physical Properties	1918
	Conclusion	1900	90.2.3	Chemical Reactions	1918
	Acknowledgments	1900	90.2.4	Metabolism	1920
			90.2.5	Summary	1921
89.	Cyprodinil: A Fungicide of the Anilinopyrimidine Class	1903	90.3	Toxicology	1922
89.1	Introduction	1903	90.3.1	Acute Toxicology	1922
89.2	Identity, Properties, and Uses	1903	90.3.2	Subchronic Toxicity	1924
89.2.1	Chemical Name	1903	90.3.3	Chronic Toxicity	1926
89.2.2	Synonyms	1903	90.3.4	Developmental and Reproductive Toxicity	1927
89.2.3	Physical and Chemical Properties	1904	90.3.5	Mutagenicity	1928
89.2.4	History, Formulations, and Uses	1904	90.3.6	Carcinogenicity	1933
89.3	Biological Mode of Action	1904	90.4	Common Mechanism of Toxicity	1937
89.4	Absorption, Distribution, metabolism, and Excretion	1904	90.4.1	Captan and Folpet	1937
89.4.1	Toxicokinetics in Rats	1904	90.4.2	Captafol	1938
89.4.2	Metabolic Pathways in Rats	1904	90.4.3	Dichlofluanid and Tolyfluanid	1938
89.4.3	Toxicokinetics and Metabolism in Lactating Goats	1905	90.5	Human Risk Assessment	1939
			90.5.1	Cancer	1939
			90.5.2	Noncancer	1939
			Conclusion		1940
			Acknowledgments		1941

91. Mammalian Toxicokinetics and Toxicity of Chlorothalonil	1951	Section XIV	
91.1 Identity and Uses of Chlorothalonil	1951	Other Selected Pesticides	
91.1.1 Physical and Chemical Properties	1951		
91.2 Mammalian Toxicokinetics	1951	93. Toxicology of DDT and Some Analogues	
91.2.1 Oral Administration	1951	1975	
91.2.2 Dermal Administration	1953	93.1 Introduction	1975
91.3 Acute Toxicity	1953	93.2 DDT	1975
91.3.1 Oral	1953	93.2.1 Identity, Properties, and Uses	1976
91.3.2 Dermal	1954	93.2.2 Formulations and Production	1976
91.3.3 Intraperitoneal	1954	93.2.3 Toxicity to Laboratory Animals	1977
91.3.4 Inhalation	1954	93.2.4 Toxicity to Humans	1993
91.3.5 Skin Irritation	1954	93.3 TDE	2004
91.3.6 Eye Irritation	1954	93.3.1 Identity, Properties, and Uses	2004
91.3.7 Summary of Acute Toxicity	1955	93.3.2 Toxicity to Laboratory Animals	2004
91.4 Sensitization	1955	93.3.3 Toxicity to Humans	2007
91.4.1 Skin Sensitization	1955	93.4 Ethylan	2008
91.4.2 Respiratory Sensitization	1955	93.4.1 Identity, Properties, and Uses	2008
91.5 Subchronic Toxicity	1955	93.4.2 Toxicity to Laboratory Animals	2008
91.5.1 Oral	1955	93.4.3 Toxicity to Humans	2009
91.5.2 Dermal	1956	93.5 Methoxychlor	2010
91.5.3 Inhalation	1957	93.5.1 Identity, Properties, and Uses	2010
91.6 Chronic Toxicity	1957	93.5.2 Toxicity to Laboratory Animals	2010
91.7 Genotoxicity	1958	93.5.3 Toxicity to Humans	2014
91.7.1 <i>In Vitro</i> Genotoxicity Studies	1958	93.6 Chlorobenzilate	2014
91.7.2 <i>In Vivo</i> Genotoxicity Studies	1958	93.6.1 Identity, Properties, and Uses	2014
91.8 Carcinogenicity	1958	93.6.2 Toxicity to Laboratory Animals	2015
91.8.1 Mode of Carcinogenic Action	1959	93.6.3 Toxicity to Humans	2015
91.9 Reproductive Toxicity	1960	93.7 Dicofol	2015
91.9.1 Developmental Toxicity	1960	93.7.1 Identity, Properties, and Uses	2015
91.9.2 Fertility	1961	93.7.2 Toxicity to Laboratory Animals	2015
91.10 Investigative Toxicity Studies	1961	93.7.3 Toxicity to Humans	2016
91.10.1 Acute Effects on Hepatic and Renal Glutathione Content	1961	93.8. Acetofenate	2016
91.10.2 Effect of Dietary vs Gavage Dosing on Renal Toxicity in the Rat	1961	93.8.1 Identity, Properties and Uses	2016
91.11 Human Data	1962	93.8.2 Toxicity	2016
91.11.1 Dermal Effects	1962	Conclusion	2016
91.11.2 Ocular Effects	1962		
91.11.3 Respiratory Effects	1962		
91.11.4 Clinical Cases and Poisoning Incidents	1963		
92. Inhibitors of Aromatic Acid Biosynthesis	1967	94. Boric Acid and Inorganic Borate Pesticides	2033
92.1 Introduction	1967	94.1 Introduction	2033
92.2 Glyphosate	1967	94.1.1 Background	2033
92.2.1 Identity, Properties, and Uses	1967	94.1.2 Chapter Coverage	2033
92.2.2 Toxicity to Laboratory Animals	1968	94.1.3 Product Uses	2034
92.2.3 Human Experience	1970	94.2 Names and Chemical/Physical properties	2035
		94.2.1 Boric Acid	2035
		94.2.2 Sodium Borate Salts	2035
		94.3 Exposure	2035
		94.3.1 Dietary Exposure	2035
		94.3.2 Occupational Exposure	2035
		94.3.3 Residential Exposure	2035

94.4	94.3.4 Environmental Exposure Biological Importance 94.4.1 Essentiality in Plants 94.4.2 Biological Importance in Animals (Vertebrates) 94.4.3 Biological Importance in Humans	2036 2036 2036 2037 2037	96.	Interactions with the Gamma-Aminobutyric Acid A-Receptor: Polychlorocycloalkanes and Recent Congeners and Other Ligands	2065
94.5	Toxicokinetics 94.5.1 Absorption 94.5.2 Distribution 94.5.3 Metabolism 94.5.4 Excretion	2038 2038 2038 2039 2039	96.1	Introduction	2065
94.6	Toxicology 94.6.1 Efficacy (Invertebrate and Fungi) 94.6.2 Laboratory Studies	2040 2040	96.2	Discovery of Polychlorocycloalkane Metabolism as a Factor in Toxicity 96.2.1 Background 96.2.2 Lindane, Aldrin, Dieldrin, Isodrin, and Endrin and Analogues 96.2.3 Heptachlor, Chlordene, Dihydroheptachlor, Chlordane, and Isobenzan	2065 2066 2071
94.7	Accidental Poisonings 94.7.1 Animals 94.7.2 Humans	2042 2042	96.2.4	Endosulfan (Thiodan)	2073
94.8	Findings from Studies with Humans 94.8.1 Occupational Studies 94.8.2 Epidemiological Studies	2043 2043 2044	96.2.5	Toxaphene, Mirex, Chlordcone (Kepone)	2075
95.	Imidacloprid: A Neonicotinoid Insecticide	2055	96.3	Structure-Toxicity Relationship and Mode of Action 96.3.1 Fully Chlorinated Cyclodienes: Substituted Hexachloronorbornenes (HCNB) 96.3.2 Compounds with Fewer, or no Chlorine Atoms	2076 2076 2078
95.1	Introduction	2055	96.3.3	Links between Polychlorocycloalkane and Recent Heterocyclics Apparently Acting at the Chloride Ionophore	2081
95.2	Historical Overview 95.2.1 Chemistry 95.2.2 Nicotinic Activity	2055 2055 2056	96.4	Molecular Mechanism of Action 96.4.1 Topography of The Gamma-Aminobutyric Acid A-Receptor 96.4.2 Molecular Biology of Cyclodiene Resistance 96.4.3 Molecular Toxicology of Noncompetitive Chloride Ionophore Blockers	2082 2082 2083
95.3	Metabolism and Toxicokinetics	2057	96.4.3	Conclusion	2083
95.4	Mammalian Toxicology	2057	97.	The Role of P-glycoprotein in Preventing Developmental and Neurotoxicity: Avermectins – A Case Study	2093
95.5	Acute Toxicity	2057	97.1	Introduction	2093
95.6	Subchronic Toxicity 95.6.1 Rat 95.6.2 Dog	2058 2058 2059	97.2	Chemistry and Formulations	2093
95.7	Chronic Toxicity and Carcinogenicity 95.7.1 Rat 95.7.2 Mouse 95.7.3 Classification for Carcinogenicity 95.7.4 Dog	2059 2059 2059 2060 2060	97.3	Uses	2095
95.8	Mutagenicity	2060	97.4	Mode of Action of the Avermectins	2096
95.9	Developmental Toxicity 95.9.1 Rat 95.9.2 Rabbit	2060 2060	97.5	Hazard Identification and Dose Response	2096
95.10	Reproductive Toxicity	2061	97.6	Humans: Experience with Ivermectin	2101
95.11	Neurotoxicity 95.11.1 General 95.11.2 Acute Neurotoxicity 95.11.3 Subchronic Neurotoxicity 95.11.4 Comparison with other Neonicotinoids 95.11.5 Developmental Neurotoxicity Conclusion	2061 2061 2061 2062 2062 2063	97.7	Risk Characterization	2102

97.8	Importance of the P-Glycoprotein Blood-Brain Barrier	2104	99.5.2 Non-Dietary Exposure	2145	
	Conclusion	2107	Risk characterization	2146	
			99.6.1 Cancer	2146	
			99.6.2 Non-Cancer Effects	2146	
98.	DEET	2111	100.	Rodenticides	2153
98.1	Introduction	2111	100.1	Introduction	2153
98.2	Chemistry	2111	100.2	Fluoroacetic Acid and its Derivatives	2154
98.3	Overview of Toxicology Studies	2111	100.2.1	Sodium Fluoroacetate	2154
98.3.1	Acute Toxicity Studies	2112	100.2.2	Fluoroacetamide	2160
98.3.2	Subchronic Toxicity Studies	2113	100.2.3	Fluoroethanol	2163
98.3.3	Developmental Toxicity	2114	100.3	Substituted Ureas	2163
98.3.4	Reproductive Toxicity	2115	100.3.1	Pyriminil	2164
98.3.5	Chronic Toxicity and Oncogenicity	2115	100.4	Thioureas	2167
98.3.6	Neurotoxicity	2116	100.4.1	ANTU	2168
98.3.7	Genotoxicity Studies	2117	100.5	Anti-Vitamin K Compounds	2171
98.4	Pharmacokinetic Studies: Animals and Humans	2117	100.5.1	Overview	2171
98.4.1	Absorption, Distribution, Metabolism, and Excretion in Rats	2117	100.5.2	Resistance to Anticoagulant Rodenticides	2173
98.4.2	Absorption, Metabolism, and Excretion in Humans	2118	100.5.3	Warfarin	2174
98.4.3	DEET and Interactions with Other Environmental Chemicals (Ethanol and Sunscreens)	2119	100.5.4	Coumafuryl	2182
98.4.4	DEET and Interactions with Other Environmental Chemicals	2120	100.5.5	Diphacinone	2182
98.4.5	Human Aspects: Clinical Case Reports (Dermal Reactions)	2121	100.5.6	Brodifacoum	2184
98.4.6	Clinical Case Reports: Adverse Neurological Effects	2121	100.5.7	Chlorophacinone	2188
98.4.7	Regulatory Risk Assessment	2122	100.5.8	Difenacoum	2190
			100.5.9	Bromadiolone	2192
			100.5.10	Difethialone	2193
99.	The Safety Assessment of Piperonyl Butoxide	2127	100.6	Vitamin D-Related Compounds	2194
99.1	Chemistry and Formulations	2127	100.6.1	Ergocalciferol	2194
99.2	Uses	2127	100.6.2	Cholecalciferol	2197
99.3	Hazard Identification	2128	100.7	Miscellaneous Synthetic Organic Rodenticides	2200
99.3.1	Acute Toxicity	2128	100.7.1	Chloralose	2200
99.3.2	Subchronic Toxicity	2128	100.7.2	Norbormide	2202
99.3.3	Reproductive Toxicity	2131	100.7.3	Bromethalin	2204
99.3.4	Developmental Toxicity	2134	100.7.4	Banned Compounds	2205
99.3.5	Chronic Toxicity/Oncogenicity	2136	100.7.5	On-going Research for New Chemical Families with Rodenticidal Properties	2205
99.3.6	Genotoxicity	2140		Conclusion	2206
99.3.7	Mode of Action Considerations for Oncogenicity	2140			
99.3.8	Human Studies	2143			
99.3.9	Human Experience	2144			
99.4	Pharmacodynamics	2144	101.	Toxicology and Safety Evaluation of the New Insect Repellent Picaridin (Saltidin)	2219
99.5	Exposure Assessment	2145	101.1	Introduction	2219
	99.5.1 Dietary Exposure	2145	101.2	General Overview	2219
			101.2.1	Chemistry	2219
			101.2.2	Mode of Action	2219
			101.2.3	Effectiveness Against Disease Vectors	2220
			101.3	Metabolism and Toxicokinetics	2221

101.4 Mammalian Toxicology	2223	102.7.2 Diagnosis of Poisoning	2240
101.4.1 Acute Toxicity	2223	102.7.3 Sensitization Observations	2241
101.4.2 Subchronic toxicity	2224	102.7.4 Proposed Treatment	2241
101.4.3 Chronic Toxicity and Oncogenicity	2224	102.8 Reference Values and Conclusions	2241
101.4.4 Genotoxicity	2225	Acknowledgments	2242
101.5 Developmental Toxicity	2225		
101.5.1 Rat	2225		
101.5.2 Rabbit	2225		
101.6 Reproductive Toxicity	2225		
101.7 Neurotoxicity	2226		
101.7.1 Acute	2226		
101.7.2 Subchronic	2226		
101.8 Dermal Absorption	2226		
101.8.1 Rat	2226	103.1 Chemistry and Formulations	2245
101.8.2 Human Volunteers	2226	103.2 Uses	2245
101.8.3 Human Skin	2226	103.3 Hazard Identification: Toxicity to Laboratory Animals (Pre-1980)	2246
101.9 Exposure and Safety Evaluation	2227	103.3.1 Acute Toxicity	2246
Conclusion	2227	103.3.2 Subchronic Toxicity	2246
		103.4 Toxicity to Laboratory Animals (Post-1980)	2246
		103.4.1 Acute Toxicity	2246
		103.4.2 Acute Neurotoxicity	2247
		103.4.3 Time to Incapacitation	2247
		103.4.4 Therapeutic/Amelioration of Toxicity	2247
		103.4.5 Repeated Exposures	2248
		103.4.6 Subchronic Toxicity	2248
		103.4.7 Chronic Toxicity	2252
		103.4.8 Teratology Studies	2254
		103.4.9 Reproduction Toxicity	2254
		103.4.10 Genetic Toxicity	2255
		103.4.11 Uptake and Metabolism	2255
		103.5 Toxicology in Humans	2256
		103.6 Conclusion	2256
		103.6.1 Risk Characterization	2256
102. Chlorantraniliprole: An Insecticide of the Anthranilic Diamide Class	2231	104. Phosphine	2259
102.1 Introduction	2231	104.1 Identity, Properties, and Uses	2259
102.2 Identity, Properties, and Uses	2231	104.1.1 Physical Properties	2259
102.2.1 Chemical Name	2231	104.1.2 Chemistry	2259
102.2.2 Synonyms	2231	104.2 Sources, Uses, and Formulations	2260
102.2.3 Physical and Chemical Properties	2231	104.2.1 Natural Sources	2260
102.2.4 History, Formulations, and Uses	2232	104.2.2 Commercial Sources	2260
102.3 Biological Mode of Action	2232	104.3 Toxicology	2260
102.4 Absorption, Distribution, Metabolism, and Excretion	2232	104.3.1 Overview	2260
102.4.1 Toxicokinetics in Rats	2232	104.4 Toxicity and Mode of Action	2260
102.4.2 Metabolic Pathways in Rats	2233	104.4.1 Acute Toxicity	2260
102.4.3 Plasma Concentrations of Parent and Metabolites in Feeding Studies	2233	104.5 Animal Dose/Response	2261
102.5 Toxicity to Laboratory Animals	2233	104.5.1 Threshold for Lethality	2261
102.5.1 Acute Toxicity	2233	104.5.2 Acute and Subacute Dose/Response	2261
102.5.2 Subchronic Toxicity	2235	104.6 Absorption, Distribution, Metabolism, and Excretion	2261
102.5.3 Chronic Toxicity and Oncogenicity	2237	104.6.1 Direct Observations and Health Records	2261
102.5.4 Effects on Adrenal Function	2237	104.7 Cellular and Molecular Studies	2261
102.5.5 Effects on Reproduction and Development	2238		
102.5.6 Neurotoxic Effects	2239		
102.5.7 Immunotoxic Effects	2240		
102.6 Genotoxicity	2240		
102.7 Toxicity to Humans	2240		
102.7.1 Direct Observations and Health Records	2240		

104.7.1 General	2261	106.1.5 Formulations	2281
104.7.2 Cytochromes and Cytochrome Oxidase	2262	106.2 Uses	2281
104.7.3 Hemoglobin	2262	106.3 Hazard Identification	2282
104.8 Peroxidases, Lipid Peroxidation, Catalase, and Cholinesterase	2262	106.3.1 Acute Toxicity	2282
104.9 Genotoxicity, Cancer and Reproductive Effects	2263	106.3.2 Repeated Dose Toxicity	2282
104.10 Treatment of Poisoning	2263	106.3.3 Effects on Reproduction	2283
104.11 Regulatory Notes (Exposure Guidelines)	2264	106.3.4 Absorption, Distribution, Metabolism, and Excretion	2283
104.12 Summary and Comments	2264	106.3.5 Short-Term Assays	2285
105. Methyl Bromide	2267	106.3.6 Chronic Toxicity and Oncogenicity Assays	2285
105.1 Introduction	2267	106.4 Dose Response	2286
105.2 Chemical Properties and Pesticidal Uses of Methyl Bromide	2267	106.5 Toxicology in Humans	2288
105.3 Toxicology of Methyl Bromide	2268	106.5.1 Experimental Exposure	2288
105.3.1 Acute Toxicity	2268	106.5.2 Accidental Poisoning	2288
105.3.2 Subchronic Toxicity	2269	106.5.3 Use Experience	2288
105.3.3 Genetic Toxicity	2270	106.6 Summary Risk Characterization	2289
105.3.4 Developmental and Reproductive Toxicity	2272	107. Metam-Sodium	2293
105.3.5 Chronic Toxicity and Oncogenicity: Inhalation	2273	107.1 Introduction	2293
105.3.6 Chronic Toxicity and Oncogenicity: Dietary	2273	107.2 Acute toxicity	2294
105.3.7 Neurotoxicity	2274	107.3 Subchronic Toxicity	2294
105.3.8 Specific Target Organ Effects	2275	107.4 Genetic Toxicity	2295
105.4 Metabolism	2275	107.5 Developmental and Reproductive Toxicity	2297
105.4.1 Absorption	2275	107.6 Chronic/Oncogenicity Toxicity	2298
105.4.2 Distribution	2276	107.7 Nurotoxicity	2302
105.4.3 Identification and Quantitation of Metabolites	2276	107.8 Other Studies (Mammalian)	2303
105.4.4 Excretion	2277	107.9 Metabolism	2304
105.5 Human Exposure Conclusion	2277	108. Methyl Iodide	2307
106. 1,3-Dichloropropene	2281	108.1 Background	2307
106.1 Chemistry and Formulations	2281	108.2 Methyl Iodide Properties	2307
106.1.1 Chemical Name	2281	108.3 Registration Issues	2308
106.1.2 Structure	2281	108.4 Exposure Issues	2309
106.1.3 Synonyms	2281	108.4.1 Quantifying Exposure of Plant Pests to Mel	2309
106.1.4 Physical and Chemical Properties	2281	108.5 Crop Production	2311
		108.6 Environmental Fate of Methyl Iodide as a Soil Fumigant	2311
		108.6.1 Transformation in Aqueous Solution	2311
		108.6.2 Transformation in Soil	2312
		Conclusion	2316
		Index	2319