

# TABLE OF CONTENTS

## Haschek and Rousseaux's Handbook of Toxicologic Pathology, Volume 1: Principles and Practice of Toxicologic Pathology 4th Edition

- Cover image
- Title page
- Table of Contents
- Copyright
- Dedication
- Contributors
- About the Editors
- Preface to the 4th Edition
- **Chapter 1. Toxicologic Pathology: An Introduction**
  - 1. An Overview of Toxicologic Pathology
  - 2. What Is Toxicologic Pathology?
  - 3. The Basis of Toxicologic Pathology
  - 4. Challenges in Toxicologic Pathology
  - 5. Training and Certification in Toxicologic Pathology
  - 6. The “Practitioner” of Toxicologic Pathology
  - 7. Summary
- **Part 1. Principles of Toxicologic Pathology**
- **Chapter 2. Biochemical and Molecular Basis of Toxicity**
  - 1. Introduction
  - 2. General Principles of Xenobiotic Disposition
  - 3. Interactions of Toxicants with Cellular and Molecular Targets
  - 4. Idiosyncratic Mechanisms of Toxicity
  - 5. Protective Mechanisms, Repair Mechanisms, and Adaptation or Failure

- 6. Summary and Conclusions
- **Chapter 3. ADME Principles in Small Molecule Drug Discovery and Development: An Industrial Perspective**
- 1. Introduction
- 2. General ADME Principles
- 3. Discovery Overview
- 4. Absorption, Bioavailability, and PK/TK Studies
- 5. Distribution
- 6. Metabolism
- 7. Excretion
- 8. Physiologically Based PK modeling
- 9. Development
- 10. Mass Balance Studies
- 11. Tissue Distribution Studies
- 12. Drug Metabolism Studies in Development
- 13. Excretion Studies
- 14. Specialized Excretion Studies
- 15. General Timing of Development ADME Studies
- 16. Conclusions
- **Chapter 4. Biotherapeutics ADME and PK/PD Principles**
- 1. Introduction
- 2. Pharmacokinetics of Biotherapeutics
- 3. Pharmacodynamics of Biotherapeutics
- 4. PK–PD Modeling and Interspecies Scaling
- 5. Summary
- **Chapter 5. Principles of Pharmacodynamics and Toxicodynamics**
- 1. Introduction: Definition of Pharmacodynamics and Toxicodynamics
- 2. Mechanism of Drug Action and Adverse Drug Reaction
- 3. Types of Adverse Drug Reaction: Intrinsic (Type A) Versus Idiosyncratic (Type B)
- 4. Types of Xenobiotic–Target Interaction

- 5. Exposure-Dependent Response
- 6. Response Following Chronic Dosing
- 7. Quantitative Modeling for Pharmacokinetic/Pharmacodynamic and Toxicodynamic Data Analysis
- **Chapter 6. Morphologic Manifestations of Toxic Cell Injury**
- 1. Introduction
- 2. Adaptation
- 3. Irreversible versus Reversible Cell Injury
- 4. Irreversible Cell Injury
- 5. Conclusion
- **Chapter 7. The Role of Pathology in Evaluation of Reproductive, Developmental, and Juvenile Toxicity**
- 1. Introduction
- 2. Reproductive Toxicity Assessment
- 3. Pregnancy and Developmental Toxicity
- 4. Juvenile Toxicity Assessment
- 5. Conclusions
- Abbreviations
- Chapter 8. Carcinogenesis: Mechanisms and Evaluation
- 1. Introduction
- 2. Mechanisms of Chemically Induced Carcinogenesis
- 3. Identification of Carcinogens—Testing Programs and Guidelines
- 4. Evolving and New Technologies
- 5. Conclusions
- **Part 2. Methods in Toxicologic Pathology**
- **Chapter 9. Basic Approaches in Anatomic Toxicologic Pathology**
- 1. Introduction
- 2. General Considerations in Study Protocol Development
- 3. In-Life Evaluations
- 4. Necropsy
- 5. Fixation and Histologic Procedures

- 6. Specialized Histologic Techniques
- 7. Histopathologic Evaluation
- 8. Artifacts versus Lesions
- 9. Diagnostic Challenges in Anatomic Toxicologic Pathology
- 10. Conclusions
- **Chapter 10. Clinical Pathology in Nonclinical Toxicity Testing**
- 1. Introduction
- 2. Clinical Pathology Parameters Commonly Included in Protocols for General Toxicity Studies
- 3. Nonstandard Biomarkers
- 4. Conclusions
- **Chapter 11. Special Techniques in Toxicologic Pathology**
- 1. Introduction
- 2. Immunohistochemistry
- 3. Enzyme Histochemistry
- 4. In Situ Hybridization
- 5. Flow Cytometry
- 6. Laser Capture Microdissection
- 7. Confocal Microscopy
- 8. Electron Microscopy
- 9. Stereology
- 10. Digital Pathology
- 11. Conclusions
- Glossary
- **Chapter 12. Digital Pathology and Tissue Image Analysis**
- 1. Introduction
- 2. Whole-Slide Imaging
- 3. Tissue Image Analysis
- 4. Regulatory Considerations for Digital Pathology Evaluation
- 5. Related Topics
- 6. Conclusion

- **Chapter 13. In Vivo Small Animal Imaging: A Comparison to Gross and Histopathologic Observations in Animal Models**
- 1. Introduction
- 2. Magnetic Resonance Imaging and Magnetic Resonance Microscopy
- 3. Computed Tomography
- 4. Radionuclide-based Imaging: PET and SPECT
- 5. Optical Imaging
- 6. Ultrasound
- 7. Translational Application, Safety Assessment, and Drug Screening with In Vivo or Ex Vivo Imaging
- Abbreviations for Imaging Modalities
- **Chapter 14. Biomarkers: Discovery, Qualification, and Application**
- 1. Introduction
- 2. Categories of Biomarkers
- 3. Strategies for Discovery of Biomarkers
- 4. Methods for Biomarker Measurement and Quantitation
- 5. Qualification of Biomarkers: Major Considerations
- **Chapter 15. Toxicogenomics: A Primer for Toxicologic Pathologists**
- 1. Introduction
- 2. Basics of Toxicogenomics
- 3. Overview of Toxicogenomic Technologies
- 4. Key Considerations for Conducting Toxicogenomic Studies
- 5. Goals and Applications of Toxicogenomic Studies
- 6. Sample Considerations
- 7. Applications of Toxicogenomics
- 8. Regulatory Considerations
- 9. Conclusions
- Glossary
- **Chapter 16. Experimental Design and Statistical Analysis for Toxicologic Pathologists**
- 1. Introduction
- 2. Considerations Made Before Designing the Experiment

- 3. Experimental Design
- 4. Designs Commonly Used in Toxicologic Pathology
- 5. Functions of Statistical Analyses
- 6. Prerequisites to Statistical Analysis
- 7. Statistical Methods
- 8. Interpretation of Results
- 9. Data Analysis Applications in Toxicologic Pathology
- 10. Assumptions of Statistical Tests
- 11. Summary and Conclusions
- Glossary
- **Part 3. Animal and Alternative Models in Toxicologic Research**
- **Chapter 17. Animal Models in Toxicologic Research: Rodents**
- 1. Introduction
- 2. Rodent Model Selection
- 3. Issues in Extrapolation of Rodent Data for Human Risk Assessment
- 4. Basic Biological Characteristics of Common Rodent Stocks and Strains
- 5. Common Pathologic Findings in Rodents
- 6. Conclusion
- **Chapter 18. Animal Models in Toxicologic Research: Rabbit**
- 1. Introduction
- 2. Model Selection
- 3. Basic Biological Characteristics and Common Breeds
- 4. Regulatory Aspects and Examples of Use of Rabbits in Biomedical Research
- 5. Pharmacokinetic and Toxicity Studies
- 6. Major Disease and Functional Models (Other than Safety)
- 7. Spontaneous Findings in the Experimental NZW Rabbit
- **Chapter 19. Animal Models in Toxicologic Research: Dog**
- 1. Introduction
- 2. History and Derivation of Beagles
- 3. Use of Dogs in Biomedical Research

- 4. Predictivity of Dog Toxicity Data to Humans
- 5. Comparative Toxicology of the Dog
- 6. Spontaneous Background Pathology in the Beagle (Refer to Woicke et al., 2021)
- 7. Use of the Dog as a Model of Human Diseases
- 8. Regulatory Considerations for Toxicity Studies
- 9. Ethics of Use of the Dog as a Laboratory Animal Species
- 10. Summary
- **Chapter 20. Animal Models in Toxicologic Research: Pig**
- 1. Introduction
- 2. Genetics of Pigs and Background for Their Use in Research
- 3. Use of Pigs in Toxicological Studies
- 4. Pigs as Organ Source for Xenotransplantation
- 5. Spontaneous Background Pathology in Swine
- 6. Use of the Pig as a Model System for Medical Devices and of Human Diseases
- 7. Regulatory Aspects
- 8. Ethics and Animal Welfare
- 9. Summary
- **Chapter 21. Animal Models in Toxicologic Research: Nonhuman Primate**
- 1. Introduction
- 2. History and Biological Characteristics of Nonhuman Primates
- 3. Selection of Nonhuman Primates for Toxicologic Research and Study Design Considerations
- 4. Predictivity of Nonhuman Primate Toxicity Data to Humans
- 5. Nonhuman Primate Models in Biomedical Research (see also (Abee, Mansfield, Tardif, & Morris, 2012))
- 6. Background Findings in Nonhuman Primates and Use of Historical Control Data
- 7. Conclusion
- **Chapter 22. Animal Models in Toxicologic Research: Nonmammalian**
- 1. Introduction

- 2. Nonmammalian Animal Taxa
- 3. Utilization of Nonmammalian Animals
- 4. Study Design Considerations
- 5. Data Extrapolation
- 6. Conclusions
- **Chapter 23. Genetically Engineered Animal Models in Toxicologic Research**
- 1. Fundamentals of Genetically Engineered Animal Models
- 2. Analysis of Genetically Engineered Animal Models
- 3. Genetically Modified Models for Hazard Identification and Safety Assessment
- 4. Limitations in Using Genetically Modified Animals for Hazard Identification and Safety Assessment
- 5. Special Considerations in Safety Assessment of Products Derived from Genetically Engineered Animals
- 6. Summary
- Glossary
- **Chapter 24. Alternative Models in Biomedical Research: In Silico, In Vitro, Ex Vivo, and Nontraditional In Vivo Approaches**
- 1. Introduction
- 2. Nontraditional Models in Toxicity Research
- 3. In Vitro and Ex Vivo Models
- 4. In Silico Models and Data Analytics
- 5. In Vivo Models Using Alternative Mammalian and Nonmammalian Species
- 6. Regulatory Perspective on Alternative Models
- 7. Conclusions and Perspectives
- **Part 4. Practice of Toxicologic Pathology**
- **Chapter 25. Nomenclature and Diagnostic Resources in Anatomic Toxicologic Pathology**
- 1. Introduction
- 2. The Need for Standardized Nomenclature
- 3. Components in Nomenclature

- 4. Challenges in Standardizing Nomenclature
- 5. Recommended Practices
- 6. Harmonization of Nomenclature
- 7. Conclusions
- **Chapter 26. Pathology Peer Review**
- 1. Introduction
- 2. Peer Review Timing and Pathology Raw Data
- 3. Peer Review Process
- 4. National Toxicology Program Review Process
- 5. Regulatory Aspects of Pathology Peer Review
- 6. Use of Digital/Whole-Slide Images in Pathology Peer Review
- 7. Conclusion
- **Chapter 27. Pathology and GLPs, Quality Control, and Quality Assurance**
- 1. Introduction
- 2. Overview of Good Laboratory Practice Standards
- 3. GLP and Pathology Data
- 4. Clinical Pathology Assessment in the GLP Environment
- 5. Ultrastructural Assessment in the GLP Environment
- 6. Noninvasive Imaging Applications in the GLP Environment
- 7. In the Spirit of GLP
- 8. GLP Criticism
- 9. Conclusions
- **Chapter 28. Practices to Optimize Generation, Interpretation, and Reporting of Pathology Data from Toxicity Studies**
- 1. Introduction
- 2. Practices that Prevent or Mitigate the Introduction of Pathology-Related Issues During Study Design and Protocol Preparation
- 3. Practices that Prevent or Mitigate the Introduction of Pathology-Related Issues Arising During the In-Life Phase
- 4. Practices that Prevent or Mitigate Issues Arising from Pathology Assessment and Reporting
- 5. Conclusions

- Glossary
- **Chapter 29. Issues in Laboratory Animal Science That Impact Toxicologic Pathology**
- 1. Introduction
- 2. Trends in Global Research Animal Care and Use
- 3. Regulatory Issues
- 4. Euthanasia of Research Animals
- 5. Selection of Animal Models
- 6. Animal Health Considerations
- 7. Microbiome and Microbial Effects on Pathophysiology and Study Outcomes
- 8. Housing and Husbandry Issues
- 9. The Role of Diet in Toxicity Studies
- **10. 3R's and In-Life Study Conduct for the Toxicologic Pathologist**
- 11. Description of Animal Studies in Scientific Publications
- 12. Conclusion
- Index.