

TABLE OF CONTENTS

Chapter 1 Laboratory Animal Management	1
<i>Joseph C. Siglin and Georgene M. Rutledge</i>	
Chapter 2 Acute, Subchronic, and Chronic Toxicology	51
<i>Carol S. Auletta</i>	
Chapter 3 Dermal Irritation and Sensitization	105
<i>Rusty E. Rush, Kimberly L. Bonnette, Deborah A. Douds, and Todd N. Merriman</i>	
Chapter 4 Toxicology of the Eye	163
<i>Brendan J. Dunn</i>	
Chapter 5 Inhalation Toxicology	217
<i>Paul E. Newton</i>	
Chapter 6 Neurotoxicity	277
<i>Gene E. Schulze</i>	
Chapter 7 Preclinical Immunotoxicity Assessment	293
<i>Peter T. Thomas and Robert V. House</i>	
Chapter 8 Renal Toxicology: Renal Function Parameters for Adult Fischer-344, Sprague-Dawley, and Wistar Rats	317
<i>William J. Powers, Jr.</i>	
Chapter 9 Genetic Toxicology	337
<i>Donald L. Putman, Richard H. C. San, C. Anita H. Bigger, and David Jacobson-Kram</i>	
Chapter 10 Carcinogenesis	357
<i>Michael J. Derelanko</i>	
Chapter 11 Reproductive Toxicology	379
<i>Donald J. Ecobichon</i>	
Chapter 12 Developmental Toxicology	403
<i>Karen M. MacKenzie and Richard M. Hoar</i>	
Chapter 13 Animal Histopathology	451
<i>John C. Peckham</i>	

Chapter 14	
Animal Clinical Pathology	517
<i>Barry S. Levine</i>	
Chapter 15	
Metabolism and Toxicokinetics of Xenobiotics	539
<i>Mohamed B. Abou-Donia</i>	
Chapter 16	
Risk Assessment.....	591
<i>Michael J. Derelanko</i>	
Chapter 17	
Human Clinical Toxicology	677
<i>Jill Dolgin</i>	
Chapter 18	
Regulatory Toxicology in the United States: An Overview.....	709
<i>Michael J. Derelanko</i>	
Chapter 19	
Environmental Protection Agency: TSCA.....	713
<i>Henry C. Fogle</i>	
Chapter 20	
U. S. Food and Drug Administration: Pharmaceutical Regulatory Toxicology	751
<i>William J. Powers, Jr.</i>	
Chapter 21	
Notification of New Substances in the European Community.....	763
<i>Michael J. Derelanko</i>	
Chapter 22	
Appendices: Tables of Toxicological Importance.....	771
<i>Mannfred A. Hollinger</i>	
Index	921

DEDICATION

for MJD

To my wife, Patricia and my sons, Michael and Robert, for their patience and understanding.

To my parents, Anne and Frank, for their encouragement and support.

To my mentors, Dr. Joseph Lobue and the late Drs. Albert Gordon and Robert Kelly, for the example they set.

for MAH

To Georgia Lee Hollinger, Randolph Alan Hollinger, and Christopher Hastings Hollinger for being special contributors in their own ways.

Chapter 1

Laboratory Animal Management

Joseph C. Siglin, M.S., D.A.B.T. and Georgene M. Rutledge, A.H.T., L.A.T.G.

CONTENTS

Section 1. Introduction	3
Section 2. Animal Husbandry	3
Section 3. Regulations and Guidelines	3
A. Animal Welfare Act	3
B. Public Health Service Regulations	4
C. Guide for the Care and Use of Laboratory Animals	5
Section 4. Institutional Programs	6
A. AAALAC	6
B. IACUC	6
Section 5. Professional and Governmental Organizations	7
A. AALAS	7
B. ACLAM	7
C. ASLAP	8
D. AVMA	8
E. ICLAS	8
F. ILAR	8
G. SCAW	8
H. NIH	9
I. DEA	9
J. FDA	9
K. OPRR	9
L. APHIS	9
M. AWI	9
N. AWIC	9
O. CAAT	9
P. NABR	9
Section 6. Organizations That Oppose the Use of Animals in Research	10
Section 7. Animal Pain	10
Section 8. Animal Models and Alternatives	11
Section 9. Animal Facility Safety	11
Section 10. Zoonotic Diseases	11
A. Hepatitis	12
B. Herpesvirus B	12
C. Rabies	12
D. Lymphocytic Choriomeningitis	12
E. Other Zoonoses	12
Table 1. Other Zoonotic Diseases	13
Section 11. Recognition and Control of Disease	15
Table 2. Abnormal Conditions in Laboratory Animals	15
Section 12. Animal Nutrition	16
Table 3. Types and Sources of Commercial Laboratory Diets	16
Table 4. Nutritional Deficiencies of Laboratory Animals	17
A. Food and Water Requirements	17
Table 5. Approximate Daily Food and Water Requirements for Various Species	17
B. Fasting	18
Section 13. Anesthesia and Analgesia	18

A. General Considerations	18
B. Controlled Substances	18
C. Relevant Definitions	18
D. General Principles Regarding Anesthesia, Analgesia, and Tranquilization	18
E. Stages of Anesthesia	19
F. Methods of Administration	19
G. Commonly Used Anesthetic, Analgesic, and Tranquilizing Agents	19
Table 6. Typical Routes and Dosages of Several Sedative, Analgesic, and Anesthetic Agents	20
H. Species Peculiarities and Contraindications	21
Section 14. Euthanasia	22
A. Modes of Action	22
B. Euthanasia Methods and Agents	22
Table 7. Acceptable and "Conditionally Acceptable" Methods for Euthanasia of Several Common Laboratory Species	23
Table 8. Summary of the Characteristics of Several Euthanasia Methods	24
Section 15. Sources of Laboratory Animals	26
Table 9. Names, Addresses, and Phone Numbers of Several Animal Suppliers	26
Section 16. Species Data	28
A. Mouse (<i>Mus musculus</i>)	28
Table 10. Common Strains of Laboratory Mice	29
Table 11. Minimum Cage Space Requirements for Mice	30
Table 12. Physical and Physiological Parameters of Mice	30
Table 13. Identification, Bleeding, Anesthesia, and Euthanasia Methods for Laboratory Mice	31
Table 14. Various Diseases and Adverse Health Conditions of Laboratory Mice	31
B. Rat (<i>Rattus norvegicus</i>)	32
Table 15. Common Strains of Laboratory Rats	33
Table 16. Minimum Cage Space Requirements for Rats	33
Table 17. Physical and Physiological Parameters of Rats	34
Table 18. Identification, Bleeding, Anesthesia, and Euthanasia Methods for Laboratory Rats	35
Table 19. Various Diseases and Adverse Health Conditions of Laboratory Rats	35
C. Guinea Pig (<i>Cavia porcellus</i>)	36
Table 20. Minimum Cage Space Requirements for Guinea Pigs	37
Table 21. Physical and Physiological Parameters of Guinea Pigs	37
Table 22. Identification, Bleeding, Anesthesia, and Euthanasia Methods for Laboratory Guinea Pigs	38
Table 23. Various Diseases and Adverse Health Conditions of Guinea Pigs	38
D. Rabbit (<i>Oryctolagus cuniculus</i>)	39
Table 24. Minimum Cage Space Requirements for Rabbits	40
Table 25. Physical and Physiological Parameters of Rabbits	40
Table 26. Identification, Bleeding, Anesthesia, and Euthanasia Methods for Laboratory Rabbits	41
Table 27. Various Diseases and Adverse Health Conditions of Rabbits	41
E. Dog (<i>Canis familiaris</i>)	43
Table 28. Minimum Cage Space Requirements for Dogs	45
Table 29. Physical and Physiological Parameters of Dogs	46
Table 30. Identification, Bleeding, Anesthesia, and Euthanasia Methods for Laboratory Dogs	46
Table 31. Various Diseases and Adverse Health Conditions of Dogs	47
References	49