Nonclinical Development Of Novel Biologics Biosimilars Vaccines And Specialty Biologics

A single-source reference with a broad and holistic overview of nonclinical studies, this book offers critical training material and describes regulations of nonclinical testing through guidelines, models, case studies, practical examples, and worldwide perspectives. The book: Provides a complete overview of nonclinical study organization, conduct, and reporting and describes the roles and responsibilities of a Study Director to manage an effective study Covers regulatory and scientific concepts, including international testing and Good Laboratory Practice (GLP), compliance with guidelines, and animal models Features a concluding chapter that compiles case studies / lessons learned from those that have served as a Study Director for many years Addresses the entire spectrum of nonclinical testing, making it applicable to those in the government, laboratories and those actively involved in in all sectors of industry

Drug repurposing or drug repositioning is a new approach to presenting new indications for common commercial and clinically approved existing drugs. For example, chloroquine, an old antimalarial drug, showed promising results for treating COVID-19, interfering with MDR in several types of cancer, and chemosensitizing human leukemic cells.This book focuses on the hypothesis, risk/benefits, and economic impacts of drug repurposing on drug discovery in dermatology, infectious diseases, neurological disorders, cancer, and orphan diseases. It brings together up-to-date research to provide readers with an informative, illustrative, and easy-to-read book useful for students, clinicians, and the pharmaceutical industry.

A Comprehensive Guide to Toxicology in Preclinical Drug Development is a resource for toxicologists in industry and regulatory settings, as well as directors working in contract resource organizations, who need a thorough understanding of the drug development process. Incorporating real-life case studies and examples, the book is a practical guide that outlines day-to-day activities and experiences in preclinical toxicology. This multi-contributed reference provides a detailed picture of the complex and highly interrelated activities of preclinical toxicology in both small molecules and biologics. The book discusses discovery toxicology and the international guidelines for safety evaluation, and presents traditional and nontraditional toxicology models. Chapters cover development of vaccines, oncology drugs, botanic drugs, monoclonal antibodies, and more, as well as study development and personnel, the role of imaging in preclinical evaluation, and supporting materials for IND applications. By incorporating the latest research in this area and featuring practical scenarios, this reference is a complete and actionable guide to all aspects of preclinical drug testing. Chapters written by world-renowned contributors who are experts in their fields Includes the latest research in preclinical drug testing and international guidelines Covers preclinical toxicology in small molecules and biologics in one single source

This unique volume traces the critically important pathway by which a "molecule" becomes an "anticancer agent. " The recognition following World War I that the administration of toxic chemicals such as nitrogen mustards in a controlled manner could shrink malignant tumor masses for relatively substantial periods of time gave great impetus to the search for molecules that would be lethal to specific cancer cells. Weare still actively engaged in that search today. The question is how to discover these "anticancer" molecules. Anticancer Drug Development Guide: Preclinical Screening, Clinical Trials, and Approval, Second Edition describes the evolution to the present of preclinical screening methods. The National Cancer Institute's high-throughput, in vitro disease-specific screen with 60 or more human tumor cell lines is used to search for molecules with novel mechanisms of action or activity against specific phenotypes. The Human Tumor Colony-Forming Assay (HTCA) uses fresh tumor biopsies as sources of cells that more nearly resemble the human disease. There is no doubt that the greatest successes of traditional chemotherapy have been in the leukemias and lymphomas. Since the earliest widely used in vivo drug screening models were the murine L 1210 and P388 leukemias, the community came to assume that these murine tumor models were appropriate to the discovery of "antileukemia" agents, but that other tumor models would be needed to discover drugs active against solid tumors.

Good Research Practice in Non-Clinical Pharmacology and Biomedicine

Introduction to Biological and Small Molecule Drug Research and Development

Regenerative Medicine Technology

Improving and Accelerating Therapeutic Development for Nervous System Disorders

On-a-Chip Applications for Disease Modeling, Drug Discovery and Personalized Medicine

From Gene to Bioactive Product

Preclinical Safety Evaluation of Biopharmaceuticals

Comprehensive Toxicology, Third Edition, discusses chemical effects on biological systems, with a focus on understanding the mechanisms by which chemicals induce adverse health effects. Organized by organ system, this comprehensive reference work addresses the toxicological effects of chemicals on the immune system, the hematopoietic system, cardiovascular system, respiratory system, hepatic toxicology, renal toxicology, gastrointestinal toxicology, reproductive and endocrine toxicology, neuro and behavioral toxicology, developmental toxicology and carcinogenesis, also including critical sections that cover the general principles of toxicology, cellular and molecular toxicology, biotransformation and toxicology testing and evaluation. Each section is examined in state-of-the-art chapters written by domain experts, providing key information to support the investigations of researchers across the medical, veterinary, food, environment and chemical research industries, and national and international regulatory agencies. Thoroughly revised and expanded to 15 volumes that include the latest advances in research, and uniquely organized by organ system for ease of reference and

diagnosis, this new edition is an essential reference for researchers of toxicology. Organized to cover both the fundamental principles of toxicology and unique aspects of major organ systems Thoroughly revised to include the latest advances in the toxicological effects of chemicals on the immune system Features additional coverage throughout and a new volume on toxicology of the hematopoietic system Presents in-depth, comprehensive coverage from an international author base of domain experts

Translational Medicine: Optimizing Preclinical Safety Evaluation of Biopharmaceuticals provides scientists responsible for the translation of novel biopharmaceuticals into clinical trials with a better understanding of how to navigate the obstacles that keep innovative medical research discoveries from becoming new therapies or even making it to clinical trials. The book includes sections on protein-based therapeutics, modified proteins, oligonucleotide-based therapies, monoclonal antibodies, antibody–drug conjugates, gene and cell-based therapies, gene-modified cell-based therapies, combination products, and therapeutic vaccines. Best practices are defined for efficient discovery research to facilitate a science-based, efficient, and predictive preclinical development program to ensure clinical efficacy and safety. Key Features: Defines best practices for leveraging of discovery research to facilitate a development program Includes general principles, animal models, biomarkers, preclinical toxicology testing paradigms, and practical applications Discusses rare diseases Discusses "What-Why-When-How" highlighting different considerations based upon product attributes. Includes special considerations for rare diseases About the Editors Joy A. Cavagnaro is an internationally recognized expert in preclinical development and regulatory strategy with an emphasis on genetic medicines.. Her 40-year career spans academia, government (FDA), and the CRO and biotech industries. She was awarded the 2019 Arnold J Lehman Award from the Society of Toxicology for introducing the concept of science-based, case-by-case approach to preclinical safety evaluation, which became the foundation of ICH S6. She currently serves on scientific advisory boards for advocacy groups and companies and consults and lectures in the area of preclinical development of novel therapies. Mary Ellen Cosenza is a regulatory toxicology consultant with over 30 years of senior leadership experience in the biopharmaceutical industry in the U.S., Europe, and emerging markets. She has held leadership position in both the American College of Toxicology (ACT) and the International Union of Toxicology (IUTOX) and is also an adjunct assistant professor at the University of Southern California where she teaches graduate-level courses in toxicology and regulation of biologics.

In recent years, the costs of new drug development have skyrocketed. The average cost of developing a new approved drug is now estimated to be $1.3 billion (DiMasi and Grabowski, 2007). At the same time, each year fewer new molecular entities (NMEs) are approved. DiMasi and Grabowski report that only 21.5 percent of the candidate drugs that enter phase I clinical testing actually make it to market. In 2007, just 17 novel drugs and 2 novel biologics were approved. In addition to the slowing rate of drug development and approval, recent years have seen a number of drugs withdrawn from the market for safety reasons. According to the Government Accountability Office (GAO), 10 drugs were withdrawn because of safety concerns between 2000 and March 2006 (GAO, 2006). Finding ways to select successful drug candidates earlier in development could save millions or even billions of dollars, reduce the costs of drugs on the market, and increase the number of new drugs with improved safety profiles that are available to patients. Emerging scientific knowledge and

technologies hold the potential to enhance correct decision making for the advancement of candidate drugs. Identification of safety problems is a key reason that new drug development is stalled. Traditional methods for assessing a drug's safety prior to approval are limited in their ability to detect rare safety problems. Prior to receiving U.S. Food and Drug Administration (FDA) approval, a drug will have been tested in hundreds to thousands of patients. Generally, drugs cannot confidently be linked to safety problems until they have been tested in tens of thousands to hundreds of thousands of people. With current methods, it is unlikely that rare safety problems will be identified prior to approval. Emerging Safety Science: Workshop Summary summarizes the events and presentations of the workshop.

Nonclinical Development of Novel Biologics, Biosimilars, Vaccines and Specialty Biologics is a complete reference devoted to the nonclinical safety assessment of novel biopharmaceuticals, biosimilars, vaccines, cell and gene therapies and blood products. This book compares and contrasts these types of biologics with one another and with small molecule drugs, while incorporating the most current and essential international regulatory documents. Each section discusses a different type of biologic, as well as early characterization strategies, principles of study design, preclinical pharmacokinetics and pharmacodynamics and preclinical assays. An edited book that is authored by leading experts in the field, this comprehensive reference provides critical insights to all researchers involved in early through late stage biologics. Provides in-depth coverage of the process of nonclinical safety assessment and comprehensive reviews of each type of biopharmaceutical Contains the most pertinent international regulatory guidance documents for nonclinical evaluation Covers early de-risking strategies and designs of safety assessment programs for novel biopharmaceuticals and vaccines, as well as follow-on biologics or "biosimilars" A multi-authored book with chapters written by qualified experts in their respective fields

Pharmaco-Imaging in Drug and Biologics Development

A Comprehensive Guide to Toxicology in Nonclinical Drug Development

A Strategic Approach

ADME and Translational Pharmacokinetics / Pharmacodynamics of Therapeutic Proteins

Development and Strategies

Chapter 5. Similarities and differences in the discovery and use of biopharmaceuticals and small-molecule chemotherapeutics

A Regulatory Overview

"The goal is to provide a comprehensive reference book for thepreclinicaldiscovery and development scientist whoseresponsibilities span target identification, lead candidateselection, pharmacokinetics, pharmacology, and toxicology, and forregulatory scientists whose responsibilities include the evaluationof novel therapies." –From the Afterword by Anthony D. Dayan Proper preclinical safety evaluation can improve the predictivevalue, lessen the time and cost of launching newbiopharmaceuticals, and speed potentially lifesaving drugs tomarket. This guide covers topics ranging from lead candidateselection to establishing proof of concept and toxicity testing tothe selection of the first human doses. With chapters

contributedby experts in their specific areas, Preclinical SafetyEvaluation of Biopharmaceuticals: A Science-Based Approach toFacilitating Clinical Trials: Includes an overview of biopharmaceuticals with information onregulation and methods of production Discusses the principles of ICH S6 and their implementation inthe U.S., Europe, and Japan Covers current practices in preclinical development andincludes a comparison of safety assessments for small moleculeswith those for biopharmaceuticals Addresses all aspects of the preclinical evaluation process,including: the selection of relevant species; safety/toxicityendpoints; specific considerations based upon class; and practicalconsiderations in the design, implementation, and analysis ofbiopharmaceuticals Covers transitioning from preclinical development to clinicaltrials This is a hands-on, straightforward reference for professionalsinvolved in preclinical drug development, including scientists,toxicologists, project managers, consultants, and regulatorypersonnel.

Nonclinical Development of Novel Biologics, Biosimilars, Vaccines and Specialty BiologicsAcademic Press

Here in a single source is a complete spectrum of ideas on the development of new anticancer drugs. Containing concise reviews of multidisciplinary fields of research, this book offers a wealth of ideas on current and future molecular targets for drug design, including signal transduction, the cell division cycle, and programmed cell death. Detailed descriptions of sources for new drugs and methods for testing and clinical trial design are also provided. One work that can be consulted for all aspects of anticancer drug development Concise reviews of research fields, combined with practical scientific detail, written by internationally respected experts A wealth of ideas on current and future molecular targets for drug design, including signal transduction, the cell division cycle, and programmed cell death Detailed descriptions of the sources of new anticancer drugs, including combinatorial chemistry, phage display, and natural products Discussion of how new drugs can be tested in preclinical systems, including the latest technology of robotic assay systems, cell culture, and experimental animal techniques Hundreds of references that allow the reader to access relevant scientific and medical literature Clear illustrations, some in color, that provide both understanding of the field and material for teaching

This book illustrates, in a comprehensive manner, the most current areas of importance to Safety Pharmacology, a burgeoning unique pharmacological discipline with important ties to academia, industry and regulatory authorities. It provides readers with a definitive collection of topics containing essential information on the latest industry guidelines and overviews current and breakthrough topics in both functional and molecular pharmacology. An additional novelty of the book is that it constitutes academic, pharmaceutical and biotechnology perspectives for Safety Pharmacology issues. Each chapter is written by an expert in the area and includes not only a fundamental background regarding the topic but also detailed descriptions of currently accepted, validated models and methods as well as innovative methodologies used in drug discovery.

A Handbook of Practice, Application, and Strategy

Protein Therapeutics

Biotechnology and Biopharmaceuticals

The Role of the Study Director in Nonclinical Studies
Formulation and Device Lifecycle Management of Biotherapeutics
Blue Biotechnology
Translational Medicine

This book describes the discovery of molecules from unexploited extreme marine environments, and presents new approaches in marine genomics. It combines the current state of knowledge in marine genomics and advanced natural products' chemistry to pursue the sustainable production of novel secondary metabolites (lead compounds), as well as pharmacologically active peptides/proteins, with antimicrobial, neuroprotective, anti-osteoporotic, anti-protozoan/anti-plasmodial, anti-ageing and immune-modulating effects. Further, it employs molecular-biology-based approaches and advanced chemical techniques to obtain and to select candidate compounds for pre-clinical and clinical studies.

Today, the pressure on healthcare costs and resources is increasing, and especially for biopharmaceuticals that require parenteral administration, the inherent complex and invasive dosing procedure adds to the demand for efficient medical management. In light of the COVID-19 pandemic the value of drug delivery technologies in enabling a flexible care setting is broadly recognized. In such a setting, patients and their caregivers can choose the place of drug administration based on individual preferences and capabilities. This includes not only dosing in the clinic but also supervised at-home dosing and self-administration for eligible patients. Formulation and Device Lifecycle Management of Biotherapeutics: A Guidance for Researchers and Drug Developers covers the various aspects of improving drug delivery of biological medicines with the ultimate goal to reduce dosing complexity associated with parenteral administration and, thus, enhance patient experience and drug administration-related healthcare capacity. The target audience are multidisciplinary researchers and drug developers in the pharmaceutical industry, biotech companies, and academia involved in formulation and device development. This includes pharmacology and medical experts in charge of generating nonclinical and clinical data to support approval of novel dosing regimens, and drug delivery scientists and engineers responsible for technical particulars of product optimizations. Moreover, professionals in market access and commercial functions are expected to benefit from the discussions about the impact of patient and healthcare provider needs and country-specific reimbursement models on realizing a truly convenient and cost and resource efficient drug delivery solution. Summarizes formulation and device lifecycle management activities that enable customer-centric and sustainable drug delivery for biotherapeutics Describes the pharmacokinetic-based clinical development pathway for subcutaneous dosing

alternatives to established intravenous formulations for monoclonal antibodies Details established clinical development pathways supporting the approval of automated subcutaneous injection devices and proposes novel concepts Discusses how to realize home- and self-administration of biotherapeutics in cancer care Highlights aspects of multidisciplinary formulation and device lifecycle management that can be leveraged across different disease areas and introduces a decision architecture on when and how drug developers should embark into related development activities

Biosimilars have the potential to change the way we think about, identify, and manage health problems. They are already impacting both clinical research and patient care, and this impact will only grow as our understanding and technologies improve. Written by a team of experienced specialists in clinical development, this book discusses various potential drug development strategies, the design and analysis of pharmacokinetics (PK) studies, and the design and analysis of efficacy studies.

Pharmaceutical Medicine and Translational Clinical Research covers clinical testing of medicines and the translation of pharmaceutical drug research into new medicines, also focusing on the need to understand the safety profile of medicine and the benefit-risk balance. Pharmacoeconomics and the social impact of healthcare on patients and public health are also featured. It is written in a clear and straightforward manner to enable rapid review and assimilation of complex information and contains reader-friendly features. As a greater understanding of these aspects is critical for students in the areas of pharmaceutical medicine, clinical research, pharmacology and pharmacy, as well as professionals working in the pharmaceutical industry, this book is an ideal resource. Includes detailed coverage of current trends and key topics in pharmaceutical medicine, including biosimilars, biobetters, super generics, and Provides a comprehensive look at current and important aspects of the science and regulation of drug and biologics discovery

Principles and Case Studies in Drug Development

Comprehensive Toxicology

Nonclinical Safety Assessment, Second Edition

Expediting Drug and Biologics Development

Preclinical Screening, Clinical Trials, and Approval

Pharmaceutical Medicine and Translational Clinical Research

Challenges in Protein Product Development

Discover how biomarkers can boost the success rate of drugdevelopment efforts As pharmaceutical companies struggle to improve the success

rateand cost-effectiveness of the drug development process, biomarkershave emerged as a valuable tool. This book synthesizes and reviewsthe latest efforts to identify, develop, and integrate biomarkersas a key strategy in translational medicine and the drugdevelopment process. Filled with case studies, the bookdemonstrates how biomarkers can improve drug development timelines,lower costs, facilitate better compound selection, reducelate-stage attrition, and open the door to personalizedmedicine. Biomarkers in Drug Development is divided into eightparts: Part One offers an overview of biomarkers and their role in drugdevelopment. Part Two highlights important technologies to help researchersidentify new biomarkers. Part Three examines the characterization and validation processfor both drugs and diagnostics, and provides practical advice onappropriate statistical methods to ensure that biomarkers fulfilltheir intended purpose. Parts Four through Six examine the application of biomarkers indiscovery, preclinical safety assessment, clinical trials, andtranslational medicine. Part Seven focuses on lessons learned and the practical aspectsof implementing biomarkers in drug development programs. Part Eight explores future trends and issues, including dataintegration, personalized medicine, and ethical concerns. Each of the thirty-eight chapters was contributed by one or moreleading experts, including scientists from biotechnology andpharmaceutical firms, academia, and the U.S. Food and DrugAdministration. Their contributions offer pharmaceutical andclinical researchers the most up-to-date understanding of thestrategies used for and applications of biomarkers in drugdevelopment.

This practical guide presents a road map for safety assessment as an integral part of the development of new drugs and therapeutics. Helps readers solve scientific, technical, and regulatory issues in preclinical safety assessment and early clinical drug development Explains scientific and philosophical bases for evaluation of specific concerns – including local tissue tolerance, target organ toxicity and carcinogenicity, developmental toxicity, immunogenicity, and immunotoxicity Covers the development of new small and large molecules, generics, 505(b)(2) route NDAs, and biosimilars Revises material to reflect new drug products (small synthetic, large proteins and cells, and tissues), harmonized global and national regulations, and new technologies for safety evaluation Adds almost 20% new and thoroughly updates existing content from the last edition

The very rapid pace of advances in biomedical research promises us a wide range of new drugs, medical devices, and clinical procedures. The extent to which these discoveries will benefit the public, however, depends in large part on the methods we choose for developing and testing them. Modern Methods of Clinical Investigation focuses on strategies for clinical evaluation and their role in uncovering the actual benefits and risks of medical innovation. Essays explore differences in our current systems for evaluating drugs, medical devices, and clinical procedures; health insurance databases as a tool for assessing treatment outcomes; the role of the medical profession, the Food and Drug Administration, and industry in stimulating the use of evaluative methods; and more. This book will be of special interest to policymakers, regulators, executives in the medical industry, clinical researchers, and physicians.

A Comprehensive Guide to Toxicology in Nonclinical Drug Development, Second Edition, is a valuable reference designed to provide a complete understanding of all aspects of nonclinical toxicology in the development of small molecules and biologics. This updated edition has been reorganized and expanded to include important topics such as stem cells in nonclinical toxicology, inhalation and dermal toxicology, pitfalls in drug development, biomarkers in toxicology, and more. Thoroughly updated to reflect the latest scientific advances and with

increased coverage of international regulatory guidelines, this second edition is an essential and practical resource for all toxicologists involved in nonclinical testing in industry, academic, and regulatory settings. Provides unique content that is not always covered together in one comprehensive resource, including chapters on stem cells, abuse liability, biomarkers, inhalation toxicology, biostatistics, and more Updated with the latest international guidelines for nonclinical toxicology in both small and large molecules Incorporates practical examples in order to illustrate day-to-day activities and the expectations associated with working in nonclinical toxicology

Nonclinical Statistics for Pharmaceutical and Biotechnology Industries

Accelerating Research and Development

A Science-Based Approach to Facilitating Clinical Trials

Applications in Drug Discovery and Development

Anticancer Drug Development

A Comprehensive Guide to Toxicology in Preclinical Drug Development

Tested and proven solutions to the challenges of biologicaldrug product development Biological drug products play a central role in combating humandiseases; however, developing new successful biological drugspresents many challenges, including labor intensive productionprocesses, tighter regulatory controls, and increased marketcompetition. This book reviews the current state of the science,offering readers a single resource that sets forth the fundamentalsas well as tested and proven development strategies for biologicaldrugs. Moreover, the book prepares readers for the challenges thattypically arise during drug development, offering straightforwardsolutions to improve their ability to pass through all theregulatory hurdles and deliver new drug products to the market. Biological Drug Products begins with generalconsiderations for the development of any biological drug productand then explores the strategies and challenges involved in thedevelopment of specific types of biologics. Divided into fiveparts, the book examines: Part 1: General Aspects Part 2: Proteins and Peptides Part 3: Vaccines Part 4: Novel Biologics Part 5: Product Administration/Delivery Each chapter has been prepared by one or more leading experts inbiological drug development. Contributions are based on acomprehensive review and analysis of the current literature as wellas the authors' first-hand experience developing and testing newdrugs. References at the end of each chapter serve as a gateway tooriginal research papers and reviews in the field. By incorporating lessons learned and future directions forresearch, Biological Drug Products enables pharmaceuticalscientists and students to improve their success rate in developingnew biologics to treat a broad range of human diseases.

Miniaturization in the fields of chemistry and molecular biology has resulted in the "lab-on-a-chip." Such systems are micro-fabricated devices capable of handling extremely small fluid volumes facilitating the scaling of single or multiple lab processes down to a microchip-sized format. The convergence of lab-on-a-chip technology with the field of cell biology facilitated the development of "organ-on-a-chip" systems. Such systems simulate the function of tissues and organs, having the potential to bypass some cell and animal testing methods. These technologies have generated high interest as applications for disease modeling and drug discovery. This book, edited by Drs. Sean Murphy and Anthony Atala, provides a comprehensive coverage of the technologies that have been used to develop organ-on-a-chip systems. Known leaders cover the basics to the most relevant and novel topics in the field, including micro-fabrication, 3D bio-printing, 3D cell culture techniques, biosensor design and microelectronics, micro-fluidics, data collection, and predictive analysis. The book describes specific tissue types amenable for disease modeling and drug discovery applications. Lung, liver, heart, skin and kidney "on-a-chip" technologies are included as well as a progress report on designing an entire "body-on-a-chip" system. Additionally, the book covers applications of various systems for modeling tissue-specific cancers, metastasis, and tumor microenvironments; and provides an overview of current and potential applications of these systems to disease modeling, toxicity testing, and individualized medicine.

Rare diseases collectively affect millions of Americans of all ages, but developing drugs and medical devices to prevent, diagnose, and treat these conditions is challenging. The Institute of Medicine (IOM) recommends implementing an integrated national strategy to promote rare diseases research and product development.

Biotechnology has given rise to a broad range of biotherapies or biologics, including biomolecular drugs, vaccines, cell or gene therapies. This chapter focuses on biomolecular drugs, namely monoclonal antibodies (Mabs), cytokines, tissue growth factors and therapeutic proteins. Prior to the US approval of recombinant human insulin in 1982, biomolecular drugs were extracted from natural sources. The tools of molecular biology have dramatically increased the discovery and development of new biopharmaceuticals. The most obvious difference between small-molecule drugs (SMDs) and biomolecular drugs is size, like the difference in weight between a bicycle and a business jet. SMDs and biomolecular drugs are compared in this chapter by structure, molecular weight, preparation, physicochemical properties, and route of

administration, as well as distribution, metabolism, serum half-life, dosing regimen, species reactivity, antigenicity & hypersensitivity, clearance mechanisms, drug-drug interactions, and pharmacology. This chapter reviews the differences and similarities in the various stages of drug discovery and development, with respect to cost, probability of success and cycle time. The clinical metrics of overall clinical success rate, stage-related success rate, and clinical cycle time are examined for SMDs and biomolecular drugs. The hybrid class of peptide drugs tends to be equated with biologics, due to their amino acid content and because oral activity is rare. But peptides truly bridge the gap between small molecules and biologics, in terms of physical properties, range of therapy areas and means of production. This chapter summarizes the similarities and differences of peptide drugs with SMDs and biomolecular drugs. The manner in which these agents compare as products with respect to manufacturing and pricing are considered. Two case studies are presented—the antagonists where small-molecule, peptide and Mab agents have competed in the market, and Her2 inhibitors where small-molecule and Mab agents may ultimately synergize as a combination product. Biomolecular drugs have levelled the playing field. All the "big Pharma" companies now have the capacity to develop both types of drugs. Conversely the larger biotech companies are developing the capacity for small-molecule synthesis. Now, with many blockbuster biologics nearing patent expiration, biosimilars are on the way. It's no longer a question of "choose which type"—one will need to know how to discover and develop either type of drug.

Pharmaceuticals, Chemicals, Medical Devices, and Pesticides

A Guidance for Researchers and Drug Developers

Biosimilar Clinical Development: Scientific Considerations and New Methodologies

Drug Repurposing

Nonclinical Drug Administration

Optimizing Preclinical Safety Evaluation of Biopharmaceuticals

Hypothesis, Molecular Aspects and Therapeutic Applications

Atkinson's Principles of Clinical Pharmacology, Fourth Edition is the essential reference on the pharmacologic principles underlying the individualization of patient therapy and contemporary drug development. This well-regarded survey continues to focus on the basics of clinical pharmacology for the development, evaluation and clinical use of pharmaceutical products while also addressing the most recent advances in the field. Written by leading experts in academia, industry, clinical and regulatory settings, the fourth edition has been thoroughly updated to provide readers with an ideal reference on the wide range of important topics impacting clinical pharmacology. Presents the essential knowledge for effective practice of clinical pharmacology Includes a new

chapter and extended discussion on the role of personalized and precision medicine in clinical pharmacology Offers an extensive regulatory section that addresses US and international issues and guidelines Provides extended coverage of earlier chapters on transporters, pharmacogenetics and biomarkers, along with further discussion on "Phase 0" studies (microdosing) and PBPK

In this practice-oriented two volume handbook, professionals from some of the largest biopharmaceutical companies and top academic researchers address the key concepts and challenges in the development of protein pharmaceuticals for medicinal chemists and drug developers of all trades. Following an introduction tracing the rapid development of the protein therapeutics market over the last decade, all currently used therapeutic protein scaffolds are surveyed, from human and non-human antibodies to antibody mimetics, bispecific antibodies and antibody-drug conjugates. This ready reference then goes on to review other key aspects such as pharmacokinetics, safety and immunogenicity, manufacture, formulation and delivery. The handbook then takes a look at current key clinical applications for protein therapeutics, from respiratory and inflammation to oncology and immune-oncology, infectious diseases and rescue therapy. Finally, several exciting prospects for the future of protein therapeutics are highlighted and discussed.

If we will ever achieve Paul Ehrlich's "magic bullet," that is, a molecule which goes with high selectivity to the therapeutic target site, does what it needs to do, and is subsequently cleared from the body, the practice of safety assessment will have to change. Nonclinical Drug Administration: Formulations, Routes and Regimens for Solving Drug Delivery Problems in Animal Model Systems seeks to address a trio of objectives that, though separate, are linked and central to biomedical science and, ultimately, medicine. Rather seeing these as separate "silos," those working in nonclinical safety assessment will have to view these three in an integrated manner and to regularly and thoughtfully incorporate new information and technology. The trio of objectives this book explores are: first, to present how to deliver more of a drug product systemically to facilitate the regulatory need for evaluating safety and efficacy in animal species (at elevated exposure levels) prior to advancing the drug to human testing; second is to achieve better tolerance to therapeutics administration in test animals and humans which achieves objectives 1 and 3; and third, to explore ways to improve on therapeutic target receptor delivery performance, therefore improving both clinical pharmacodynamics bioavailability and specificity. The book's ten chapters assemble the basic concepts, principles and hypotheses involved in quantitative receptor and chronological organism interaction dynamics central to the successful development of new therapeutics which depend on systemic administration to achieve desired therapeutic goals and in so doing avoid outcomes which limit, marginalize, or preclude the therapeutic use of so many molecules.

This book serves as a reference text for regulatory, industry and academic statisticians and also a handy manual for entry level Statisticians. Additionally it aims to stimulate academic interest in the field of Nonclinical Statistics and promote this as an important discipline in its own right. This text brings together for the first time in a single volume a comprehensive survey of methods important to the nonclinical science areas within the pharmaceutical and biotechnology industries. Specifically the Discovery and Translational sciences, the Safety/Toxiology sciences, and the Chemistry, Manufacturing and Controls sciences. Drug discovery and development is a long and costly process. Most decisions in the drug development process are made with incomplete information. The data is rife with uncertainties and hence risky by nature. This is therefore the purview of Statistics. As such, this book aims to introduce readers to important statistical thinking and its application in these nonclinical areas. The chapters provide as appropriate, a scientific background to the topic, relevant regulatory guidance, current statistical practice, and further research directions.

Transforming Proteins and Genes into Drugs

Biomarkers in Drug Development

Anticancer Drug Development Guide

Emerging Safety Science

Modern Methods of Clinical Investigation

Continuous Processing in Pharmaceutical Manufacturing

Formulations, Routes and Regimens for Solving Drug Delivery Problems in Animal Model Systems

With contributions from biotechnologists and bioengineers, this ready reference describes the state of the art in industrial biopharmaceutical production, with a strong focus on continuous processes. Recent advances in single-use technology as well as application guidelines for all types of biopharmaceutical products, from vaccines to antibodies, and from bacterial to insect to mammalian cells are covered. The efficiency, robustness, and quality control of continuous production processes for biopharmaceuticals are reviewed and compared to traditional batch processes for a range of different production systems.

This first ever coverage of the pharmacokinetic and pharmacodynamic characteristics of biopharmaceuticals meets the need for a comprehensive book in this field. It spans all topics from lead identification right up to final-stage clinical trials. Following an introduction to the role of PK and PD in the development of biotech drugs, the book goes on to cover the basics, including the pharmacokinetics of peptides, monoclonal antibodies, antisense oligonucleotides, as well as viral and non-viral gene delivery vectors. The second section discusses such challenges and opportunities as pulmonary delivery of proteins and peptides, and the delivery of oligonucleotides. The final section considers the integration of PK and PD concepts into the biotech drug development plan, taking as case studies the preclinical and clinical drug development of tasidotin, as well as the examples of cetuximab and pegfilgrastim. The result is vital reading for all pharmaceutical researchers.

With an emphasis on the fundamental and practical aspects of ADME for therapeutic proteins, this book helps readers strategize, plan and implement translational research for biologic drugs. • Details cutting-edge ADME (absorption, distribution, metabolism and excretion) and PKPD (pharmacokinetic / pharmacodynamics) modeling for biologic drugs • Combines theoretical with practical aspects of ADME in biologic drug discovery and development and compares innovator biologics with biosimilar biologics and small molecules with biologics, giving a lessons-learned perspective • Includes case studies about leveraging ADME to improve biologics drug development for monoclonal antibodies, fusion proteins, pegylated proteins, ADCs, bispecifics, and vaccines • Presents regulatory expectations and industry perspectives for developing biologic drugs in USA, EU, and Japan • Provides mechanistic insight into biodistribution and target-driven pharmacokinetics in important sites of action such as tumors and the brain

In this volume, the authors discuss the many significant challenges currently faced in biotechnology dosage form development, providing guidance, shared experience and thoughtful reflection on how best to address these potential concerns. As the field of therapeutic recombinant therapeutic proteins enters its fourth decade and the market for biopharmaceuticals becomes increasingly competitive, companies are increasingly dedicating resources to develop innovative biopharmaceuticals to address unmet medical needs. Often, the pharmaceutical development scientist is encountering challenging pharmaceutical properties of a given protein or by the demands placed on the product by stability, manufacturing and preclinical or clinical expectations, as well as the evolving regulatory expectations and landscape. Further, there have been new findings that require close assessment, as for example those related to excipient quality, processing, viscosity and device compatibility and administration, solubility and opalescence and container-closure selection. The literature varies widely in its discussion of these critical elements and consensus does not exist. This topic is receiving a great deal of attention within the biotechnology industry as well as with academic researchers and regulatory agencies globally. Therefore, this book is of interest for business leaders, researchers, formulation and process development scientists, analytical scientists, QA and QC officers, regulatory staff, manufacturing leaders and regulators active in the pharmaceutical and biotech industry, and expert reviewers in regulatory agencies.

Drug Safety Evaluation

Toxicologic Pathology

Fundamentals and Applications

Biological Drug Products

Oncology Biosimilars

Rare Diseases and Orphan Products

Workshop Summary

Following the success of the first edition, this book is designed to provide practical and timely information for toxicologic pathologists working in pharmaceutical drug discovery and development. The majority of the book (Organ Systems) will provide detailed descriptions of histopathological lesions observed in drug development. In addition, it will provide information to assist the pathologist in making determinations of the origin of lesions as well as its relevance to human risk. Toxicologic Pathology: Nonclinical Safety Assessment, Second

Edition includes 2 new concept chapters. The first of the new chapters address approaches for the evaluation of unique therapeutic modalities such as cell therapies, gene therapies, and gene expression knockdown therapies. While these still represent new developing therapeutic approaches, there has been significant experience with the therapeutic modalities in the last 5 years. The second new chapter addresses the nonclinical safety assessment of medical devices, a topic of increasing importance that was not addressed in a unique chapter in the first edition. The other concept chapters have been updated and cover important topics including the overview of drug development; principles of nonclinical safety assessment; an introduction to toxicologic pathology; techniques used in toxicologic pathology, clinical pathology, toxicokinetics, and drug development toxicogenomics; and spontaneous lesions. The 13 organ system chapters provide the specifics related to pathologic characteristics, differential diagnosis, and interpretation of toxic responses in each organ system. These chapters are specifically important for the bench pathologist but also for the toxicologist who interacts with pathologists and function as study toxicologists and project team representatives in the drug development arena.

Biotechnology and Biopharmaceuticals: Transforming Proteins and Genes into Drugs, Second Edition addresses the pivotal issues relating to translational science, including preclinical and clinical drug development, regulatory science, pharmaco-economics and cost-effectiveness considerations. The new edition also provides an update on new proteins and genetic medicines, the translational and integrated sciences that continue to fuel the innovations in medicine, as well as the new areas of therapeutic development including cancer vaccines, stem cell therapeutics, and cell-based therapies.

This publication is the only text on Biologics Development and Regulation in the Post-CBER/CDER Consolidation Era. Completely revised and updated to address the transfer of therapeutic biological products to CDER, this all-new edition provides the most comprehensive and up-to-date analysis of the FDA's emerging processes for regulating and approving biological products. Written by CDER and CBER officials and industry experts, Biologics Development: A Regulatory Overview offers an expansive examination of the FDA's regulation of biologic products, from preclinical testing to post-marketing regulatory requirements, and from user fees to electronic submissions. Better yet, this new text provides the first detailed look inside the re-invented FDA that will regulate and approve today's biological products.

The volume aim to be a comprehensive overview of the drug and biologic development process that is often called “the valley of death” (pre-IND through approval) where high costs of studies and high rates of product failure are part of the drug development landscape. Imaging tools can serve in this period by adding high value data, the images and the kinetic information they can provide, and cost-effective development alternative tools which potentially improve pivotal study designs. Imaging may identify safety issues early such as unwanted organ or tissue distributions, and then can serve advanced development with added certainty of a drug or biologic’s success to senior corporate management and investors. There are numerous textbooks, reference texts and treatises on medical imaging technologies, teaching tools on medical cases and physics books on the science of detector and computer interface systems. Rarely, in each of these are examples of medical imaging protocols and animal models of disease i.e. a text on methodology in drug development is currently unavailable.

Principles of Safety Pharmacology

Atkinson's Principles of Clinical Pharmacology

Pharmacokinetics and Pharmacodynamics of Biotech Drugs

Biologics Development

Nonclinical Development of Novel Biologics, Biosimilars, Vaccines and Specialty Biologics

This open access book, published under a CC BY 4.0 license in the Pubmed indexed book series Handbook of Experimental Pharmacology, provides up-to-date information on best practice to improve experimental design and quality of research in non-clinical pharmacology and biomedicine.

Improving and Accelerating Therapeutic Development for Nervous System Disorders is the summary of a workshop convened by the IOM Forum on Neuroscience and Nervous System Disorders to examine opportunities to accelerate early phases of drug development for nervous system drug discovery. Workshop participants discussed challenges in neuroscience research for enabling faster entry of potential treatments into first-in-human trials, explored how new and emerging tools and technologies may improve the efficiency of research, and considered mechanisms to facilitate a more effective and efficient development pipeline. There are several challenges to the current drug development pipeline for nervous system disorders. The fundamental etiology and pathophysiology of many nervous system disorders are unknown and the brain is inaccessible to study, making it difficult to develop accurate models. Patient heterogeneity is high, disease pathology can occur years to decades before becoming clinically apparent, and diagnostic and treatment biomarkers are lacking. In addition, the lack of validated targets, limitations related to the predictive validity of animal models - the extent to which the model predicts clinical efficacy - and regulatory barriers can also impede translation and drug development for nervous system disorders. Improving and Accelerating Therapeutic Development for Nervous

System Disorders identifies avenues for moving directly from cellular models to human trials, minimizing the need for animal models to test efficacy, and discusses the potential benefits and risks of such an approach. This report is a timely discussion of opportunities to improve early drug development with a focus toward preclinical trials.