A Mab A Case Study In Bioprocess Development

Approaches to the Purification, Analysis and Characterization of Antibody-Based Therapeutics provides the interested and informed reader with an overview of current approaches, strategies and considerations relating to the purification, analytics and characterization of therapeutic antibodies and related molecules. While there are obviously other books published in and around this subject area, they seem to be either older (c.a. year 2000 publication date) or are more limited in scope. The book will include an extensive bibliography of the published literature in the respective areas covered. It is not, however, intended to be a how-to methods book. Covers the vital new area of R&D on therapeutic antibodies Written by leading scientists and researchers Up-to-date coverage and includes a detailed bibliography Edited by three pioneers in the field, each with longstanding experience in the biotech industry, and a skilled scientific writer, this is the first book to cover every step in the development and production of immunoglobulin Fc-fusion proteins as therapeutics for human disease: from choosing the right molecular design, to pre-clinical characterization of the purified product, through to batch optimization and quality control for large-scale cGMP production. The whole of the second part is devoted to case studies of Fc-fusion proteins that are now commercially successful products. In this section, the authors, several of whom were personally involved in clinical development of the products themselves, detail the product?s background and give insight into issues that were faced and how these issues were overcome during clinical development. This section also includes a chapter on promising new developments for the future. An invaluable resource for professionals already working on Fc-fusion proteins and an excellent and thorough introduction for physicians, researchers, and students entering the field.

Since the publication of the first edition in 2000, there has been an explosive growth of literature in biopharmaceutical research and development of new medicines. This encyclopedia (1) provides a comprehensive and unified presentation of designs and analyses used at different stages of the drug development process, (2) gives a well-balanced summary of current regulatory requirements, and (3) describes recently developed statistical methods in the pharmaceutical sciences. Features of the Fourth Edition: 1. 78 new and revised entries have been added for a total of 308 chapters and a third volume has been added to encompass the increased number of chapters. 2. Revised and updated entries reflect changes and recent developments in regulatory requirements for the drug review/approval process and statistical designs and methodologies. 3. Additional topics include multiple-stage adaptive trial design in clinical research, translational medicine, design and analysis of biosimilar drug development, big data analytics, and real world evidence for clinical research and development. 4. A table of contents organized by stages of biopharmaceutical development provides easy access to relevant topics. About the Editor: Shein-Chung Chow, Ph.D. is currently an Associate Director, Office of Biostatistics, U.S. Food and Drug Administration (FDA). Dr. Chow is an Adjunct Professor at Duke University School of Medicine, as well as Adjunct Professor at Duke-NUS, Singapore and North Carolina State University. Dr. Chow is the Editor-in-Chief of the Journal of Biopharmaceutical Statistics and the Chapman & Hall/CRC Biostatistics Book Series and the author of 28 books and over 300 methodology papers. He was elected Fellow of the American Statistical Association in 1995.

Biopharmaceuticals are emerging as frontline medicines to combat several life-threatening and chronic diseases. However, such medicines are expensive to develop and produce on a commercial scale, contributing to rising healthcare costs. Developability of Biotherapeutics: Computational Approaches describes applications of computational and molecular modeling techniques that improve the overall process of discovery and development by removing empiricism. The concept of developability involves making rational choices at the pre-clinical stages of biopharmaceutical drug development that could positively impact clinical outcomes. The book also addresses a general lack of awareness of the many different contributions that computation can make to biopharmaceutical drug development. This informative and practical reference is a valuable resource for professionals engaged in industrial research and development, scientists working with regulatory agencies, and pharmacy, medicine, and life science students and educators. It focuses primarily on the developability of monoclonal antibody candidates, but the principles described can also be extended to other modalities such as recombinant proteins, fusion proteins, antibody drug conjugates and vaccines. The book is organized into two sections. The first discusses principles and applications of computational approaches toward discovering and developing biopharmaceutical drugs. The second presents best practices in developability assessments of early-stage biopharmaceutical drug candidates. In addition to raising awareness of the promise of computational research, this book also discusses solutions required to improve the success rate of translating biologic drug candidates into products available in the clinic. As such, it is a rich source of information on current principles and practices as well as a starting point for finding innovative applications of computation towards biopharmaceutical drug development.

Oil Spill Environmental Forensics Case Studies includes 34 chapters that serve to present various aspects of environmental forensics in relation to “real-world oil spill case studies from around the globe. Authors representing academic, government, and private researcher groups from 14 countries bring a diverse and global perspective to this volume. Oil Spill Environmental Forensics Case Studies addresses releases of natural gas/methane, automotive gasoline and other petroleum fuels, lubricants, vegetable oils, paraffin waxes, bitumen, manufactured gas plant residues, urban runoff, and, of course, crude oil, the latter ranging from light Bakken shale oil to heavy Canadian oil sands oil. New challenges surrounding forensic investigations of stray gas in the shallow subsurface, volatiles in air, dissolved chemicals in water (including passive samplers), and biological tissues associated with oil spills are included, as are the effects and long-term oil weathering, long-term monitoring in urbanized and non-urbanized environments, fate and transport, forensic historical research, new analytical and chemical data processing and interpretation methods. Presents cases in each chapter on the application of specific oil spill environmental forensic techniques Features chapters written by international

experts from both academia and industry Includes relevant concepts and theories elucidated for each theme
The need to validate an analytical or bioanalytical method is encountered by analysts in the pharmaceutical industry on an almost daily basis, because adequately validated methods are a necessity for approvable regulatory filings. What constitutes a validated method, however, is subject to analyst interpretation because there is no universally accepted industry practice for assay validation. This book is intended to serve as a guide to the analyst in terms of the issues and parameters that must be considered in the development and validation of analytical methods. In addition to the critical issues surrounding method validation, this book also deals with other related factors such as method development, data acquisition, automation, cleaning validation and regulatory considerations. The book is divided into three parts. Part One, comprising two chapters, looks at some of the basic concepts of method validation. Chapter 1 discusses the general concept of validation and its role in the process of transferring methods from laboratory to laboratory. Chapter 2 looks at some of the critical parameters included in a validation program and the various statistical treatments given to these parameters. Part Two (Chapters 3, 4 and 5) of the book focuses on the regulatory perspective of analytical validation. Chapter 3 discusses in some detail how validation is treated by various regulatory agencies around the world, including the United States, Canada, the European Community, Australia and Japan. This chapter also discusses the International Conference on Harmonization (ICH) treatment of assay validation. Chapters 4 and 5 cover the issues and various perspectives of the recent United States vs. Barr Laboratories Inc. case involving the retesting of samples. Part Three (Chapters 6 - 12) covers the development and validation of various analytical components of the pharmaceutical product development process. This part of the book contains specific chapters dedicated to bulk drug substances and finished products, dissolution studies, robotics and automated workstations, biotechnology products, biological samples, analytical methods for cleaning procedures and computer systems and computer-aided validation. Each chapter goes into some detail describing the critical development and related validation considerations for each topic. This book is not intended to be a practical description of the analytical validation process, but more of a guide to the critical parameters and considerations that must be attended to in a pharmaceutical development program. Despite the existence of numerous guidelines including the recent attempts by the ICH to be implemented in 1998, the practical part of assay validation will always remain, to a certain extent, a matter of the personal preference of the analyst or company. Nevertheless, this book brings together the perspectives of several experts having extensive experience in different capacities in the pharmaceutical industry in an attempt to bring some consistency to analytical method development and validation.
Current Developments in Biotechnology and Bioengineering: Bioprocesses, Bioreactors and Controls provides extensive coverage of new developments, state-of-the-art technologies, and potential future trends, reviewing industrial biotechnology and bioengineering practices that facilitate and enhance the transition of processes from lab to plant scale, which is becoming increasingly important as such transitions continue to grow in frequency. Focusing on industrial bioprocesses, bioreactors for bioprocesses, and controls for bioprocesses, this title reviews industrial practice to identify bottlenecks and propose solutions, highlighting that the optimal control of a bioprocess involves not only maximization of product yield, but also taking into account parameters such as quality assurance and environmental aspects. Describes industrial bioprocesses based on the reaction media Lists the type of bioreactors used for a specific bioprocess/application Outlines the principles of control systems in various bioprocesses
Monoclonal antibodies (mAbs) are naturally occurring complex biomolecules. New engineering methods have turned mAbs into a leading therapeutic modality for addressing immunotherapeutic challenges and led to the rise of mAbs as the dominant class of protein therapeutics. mAbs have already demonstrated a great potential in developing safe and reliable treatments for complex diseases and creating more affordable healthcare alternatives. Developing mAbs into well-characterized antibody therapeutics that meet regulatory expectations, however, is extremely challenging. Obstacles to overcome include the determination and development of physiochemical characteristics such as aggregation, fragmentation, charge variants, identity, carbohydrate structure, and higher-order structure (HOS). This book dives deep into mAbs structure and the array of physiochemical testing and characterization methods that need to be developed and validated to establish a mAb as a therapeutic molecule. The main focus of this book is on physiochemical aspects, including the importance of establishing quality attributes such as glycosylation, primary sequence, purity, and HOS and elucidating the structure of new antibody formats by mass spectrometry. Each of the aforementioned quality attributes has been discussed in detail; this will help scientists in researching and developing biopharmaceuticals and biosimilars to find practical solutions to physicochemical testing and characterization. Describes the spectrum of analytical tests and characterization methods necessary for developing and releasing mAb batches Details antibody heterogeneity in terms of size, charge, and carbohydrate content Gives special focus to the structural analysis of mAbs, including mass spectrometry analysis Presents the basic structure of mAbs with clarity and rigor Addresses regulatory guidelines - including ICH Q6B - in relation to quality attributes Lays out characterization and development case studies including biosimilars and new antibody formats
The biotechnology/biopharmaceutical sector has tremendously grown which led to the invention of engineered antibodies such as Antibody Drug Conjugates (ADCs), Bispecific T-cell engager (BITES), Dual Variable Domain (DVD) antibodies, and fusion proteins that are currently being used as therapeutic agents for immunology, oncology and other disease conditions. Regulatory agencies have raised the bar for the development and manufacture of antibody-based products, expecting to see the use of Quality by Design (QbD) elements demonstrating an in-depth understanding of product and process based on sound science. Drug delivery systems have become an increasingly important part of the therapy and most biopharmaceuticals for self-administration are being marketed as combination products. A survey of the market indicates that there is a strong need for a new book that will provide “one stop shopping” for the latest information and knowledge of the scientific and engineering advances made over the last few

years in the area of biopharmaceutical product development. The new book entitled Development of Biopharmaceutical Drug Device Products is a reference text for scientists and engineers in the biopharmaceutical industry, academia or regulatory agencies. With insightful chapters from experts in the field, this new book reviews first principles, covers recent technological advancements and provides case studies and regulatory strategies relating to the development and manufacture of antibody-based products. It covers topics such as the importance of early preformulation studies during drug discovery to influence molecular selection for development, formulation strategies for new modalities, and the analytical techniques used to characterize them. It also addresses important considerations for later stage development such as the development of robust formulations and processes, including process engineering and modeling of manufacturing unit operations, the design of analytical comparability studies, and characterization of primary containers (pre-filled syringes and vials).Finally, the latter half of the book reviews key considerations to ensure the development and approval of a patient-centered delivery system design. This involves the evolving regulatory framework with perspectives from both the US and EU industry experts, the role of international standards, design control/risk management, human factors and its importance in the product development and regulatory approval process, as well as review of the risk-based approach to bridging between devices used in clinical trials and the to-be-marketed device. Finally, case studies are provided throughout.The typical readership would have biology and/or engineering degrees and would include researchers, scientific leaders, industry specialists and technology developers working in the biopharmaceutical field.
FRESHNEY'S CULTURE OF ANIMAL CELLS THE NEW EDITION OF THE LEADING TEXT ON THE BASIC METHODOLOGY OF CELL CULTURE, FULLY UPDATED TO REFLECT NEW APPLICATIONS INCLUDING IPSCS, CRISPR, AND ORGAN-ON-CHIP TECHNOLOGIES Freshney's Culture of Animal Cells is the most comprehensive and up-to-date resource on the principles, techniques, equipment, and applications in the field of cell and tissue culture. Explaining both how to do tissue culture and why a technique is done in a particular way, this classic text covers the biology of cultured cells, how to select media and substrates, regulatory requirements, laboratory protocols, aseptic technique, experimental manipulation of animal cells, and much more. The eighth edition contains extensively revised material that reflects the latest techniques and emerging applications in cell culture, such as the use of CRISPR/Cas9 for gene editing and the adoption of chemically defined conditions for stem cell culture. A brand-new chapter examines the origin and evolution of cell lines, joined by a dedicated chapter on irreproducible research, its causes, and the importance of reproducibility and good cell culture practice. Throughout the book, updated chapters and protocols cover topics including live-cell imaging, 3D culture, scale-up and automation, microfluidics, high-throughput screening, and toxicity testing. This landmark text: Provides comprehensive single-volume coverage of basic skills and protocols, specialized techniques and applications, and new and emerging developments in the field Covers every essential area of animal cell culture, including lab design, disaster and contingency planning, safety, bioethics, media preparation, primary culture, mycoplasma and authentication testing, cell line characterization and cryopreservation, training, and troubleshooting Features a wealth of new content including protocols for gene delivery, iPSC generation and culture, and tumor spheroid formation Includes an updated and expanded companion website containing figures, artwork, and supplementary protocols to download and print The eighth edition of Freshney's Culture of Animal Cells is an indispensable volume for anyone involved in the field, including undergraduate and graduate students, clinical and biopharmaceutical researchers, bioengineers, academic research scientists, and managers, technicians, and trainees working in cell biology, molecular biology, and genetics laboratories.
This introductory text explains both the basic science and the applications of biotechnology-derived pharmaceuticals, with special emphasis on their clinical use. It serves as a complete one-stop source for undergraduate/graduate pharmacists, pharmaceutical science students, and for those in the pharmaceutical industry. The Fifth Edition completely updates the previous edition, and also includes additional coverage on the newer approaches such as oligonucleotides, siRNA, gene therapy and nanotech and enzyme replacement therapy.
A practical guide to Quality by Design for pharmaceutical product development Pharmaceutical Quality by Design: A Practical Approach outlines a new and proven approach to pharmaceutical product development which is now being rolled out across the pharmaceutical industry internationally. Written by experts in the field, the text explores the QbD approach to product development. This innovative approach is based on the application of product and process understanding underpinned by a systematic methodology which can enable pharmaceutical companies to ensure that quality is built into the product. Familiarity with Quality by Design is essential for scientists working in the pharmaceutical industry. The authors take a practical approach and put the focus on the industrial aspects of the new QbD approach to pharmaceutical product development and manufacturing. The text covers quality risk management tools and analysis, applications of QbD to analytical methods, regulatory aspects, quality systems and knowledge management. In addition, the book explores the development and manufacture of drug substance and product, design of experiments, the role of excipients, multivariate analysis, and include several examples of applications of QbD in actual practice. This important resource: Covers the essential information about Quality by Design (QbD) that is at the heart of modern pharmaceutical development Puts the focus on the industrial aspects of the new QbD approach Includes several illustrative examples of applications of QbD in practice Offers advanced specialist topics that can be systematically applied to industry Pharmaceutical Quality by Design offers a guide to the principles and application of Quality by Design (QbD), the holistic approach to manufacturing that offers a complete understanding of the manufacturing processes involved, in order to yield consistent and high quality products.
This book introduces fundamental principles and practical application of techniques used in the scalable production of biopharmaceuticals with animal cell cultures. A broad spectrum of subjects relevant to biologics production and manufacturing are reviewed, including the generation of robust cell lines, a survey of functional genomics for a better understanding of cell lines and processes, as well as advances in regulatory compliant upstream and downstream development. The book is an essential reference for all those interested in translational animal cell-based pharmaceutical biotechnology.
Promoting a continued and much-needed renaissance in biopharmaceutical manufacturing, this book covers the different strategies and assembles top-tier technology experts to address the challenges of antibody purification. • Updates existing topics and adds new ones that include purification of antibodies produced in novel production systems, novel separation technologies, novel antibody formats and alternative scaffolds, and strategies for ton-scale manufacturing • Presents new and updated discussions of different purification technologies, focusing on how they can address the capacity crunch in antibody purification • Emphasizes antibodies and innovative chromatography methods for processing
Still the most comprehensive reference source on the development, production and therapeutic application of antibodies, this

second edition is thoroughly updated and now has 30% more content. Volume 1 covers selection and engineering strategies for new antibodies, while the second volume presents novel therapeutic concepts and antibodies in clinical study, as well as their potential. Volumes 3 and 4 feature detailed and specific information about each antibody approved for therapeutic purposes, including clinical data. This unique handbook concludes with a compendium of marketed monoclonal antibodies and an extensive index. Beyond providing current knowledge, the authors discuss emerging technologies, future developments, and intellectual property issues, such that this handbook meets the needs of academic researchers, decision makers in industry and healthcare professionals in the clinic.

Deep Reinforcement Learning with Python - Second Edition will help you learn reinforcement learning algorithms, techniques and architectures – including deep reinforcement learning – from scratch. This new edition is an extensive update of the original, reflecting the state-of-the-art latest thinking in reinforcement learning.

Medicinal chemistry is both science and art. The science of medicinal chemistry offers mankind one of its best hopes for improving the quality of life. The art of medicinal chemistry continues to challenge its practitioners with the need for both intuition and experience to discover new drugs. Hence sharing the experience of drug research is uniquely beneficial to the field of medicinal chemistry. Drug research requires interdisciplinary team-work at the interface between chemistry, biology and medicine. Therefore, the topic-related series Topics in Medicinal Chemistry covers all relevant aspects of drug research, e.g. pathobiochemistry of diseases, identification and validation of (emerging) drug targets, structural biology, drugability of targets, drug design approaches, chemogenomics, synthetic chemistry including combinatorial methods, bioorganic chemistry, natural compounds, high-throughput screening, pharmacological in vitro and in vivo investigations, drug-receptor interactions on the molecular level, structure-activity relationships, drug absorption, distribution, metabolism, elimination, toxicology and pharmacogenomics. In general, special volumes are edited by well known guest editors

Biopharmaceuticals, medicines made by or from living organisms (including cells from living organisms), are extremely effective in treating a broad range of diseases. Their importance to human health has grown significantly over the years as more biopharmaceutical products have entered the market, and now the biggest selling drugs in the world are biopharmaceuticals. Biopharmaceutical Manufacturing: Principles, Processes and Practices provides concise, comprehensive, and up-to-date coverage of biopharmaceutical manufacturing. Written in a clear and informal style, the content has been influenced by the authors' substantial industry experience and teaching expertise. That expertise enables the authors to address the many questions posed over the years both by university students and professionals with experience in the field. Consequently, the book will appeal both to undergraduate or graduate students using it as a textbook and specialized industry practitioners seeking to understand the big picture of biopharmaceutical manufacturing. This book:

Biopharmaceutical Processing: Development, Design, and Implementation of Manufacturing Processes covers bioprocessing from cell line development to bulk drug substances. The methods and strategies described are essential learning for every scientist, engineer or manager in the biopharmaceutical and vaccines industry. The integrity of the bioprocess ultimately determines the quality of the product in the biotherapeutics arena, and this book covers every stage including all technologies related to downstream purification and upstream processing fields. Economic considerations are included throughout, with recommendations for lowering costs and improving efficiencies. Designed for quick reference and easy accessibility of facts, calculations and guidelines, this book is an essential tool for industrial scientists and managers in the biopharmaceutical industry. Offers a comprehensive, go-to reference for daily work decisions Covers both upstream and downstream processes Includes case studies that emphasize financial outcomes Presents summaries, decision grids, graphs and overviews for quick reference

Endotoxin detection and control is a dynamic area of applied science that touches a vast number of complex subjects. The intersection of test activities includes the use of an ancient blood system from an odd "living fossil" (Limulus). It is used to detect remnants of the most primitive and destructive forms of life (prokaryotes) as contaminants of complex modern systems (mammalian and Pharma). Recent challenges in the field include those associated with the application of traditional methods to new types of molecules and manufacturing processes. The advent of "at will" production of biologics in lieu of harvesting animal proteins has revolutionized the treatment of disease. While the fruits of the biotechnology revolution are widely acknowledged, the realization of the differences in the means of production and changes in the manner of control of potential impurities and contaminants in regard to the new versus the old are less widely appreciated. Endotoxin as an ancient, dynamic interface between lifeforms, provides a singular perspective from which to view the parallel development of ancient and modern organisms as well as the progress of man in deciphering the complexity of their interactions in his efforts to overcome disease.

The premise of Quality by Design (QbD) is that the quality of the pharmaceutical product should be based upon a thorough understanding of both the product and the manufacturing process. This state-of-the-art book provides a single source of information on emerging statistical approaches to QbD and risk-based pharmaceutical development. A comprehensive resource, it combines in-depth explanations of advanced statistical methods with real-life case studies that illustrate practical applications of these methods in QbD implementation.

Dynamic Single-Use Bioreactors Used in Modern Liter- and m3- Scale Biotechnological Processes: Engineering Characteristics and Scaling Up, by Christian Löffelholz, Stephan C. Kaiser, Matthias Kraume, Regine Eibl , Dieter Eibl. Orbitally Shaken Single-Use Bioreactors, by Wolf Klöckner, Sylvia Diederichs, Jochen Büchs. Therapeutic Human Cells: Manufacture for Cell Therapy/Regenerative Medicine by Christian van den Bos, Robert Keefe, Carmen Schirmaier, Michael McCaman. Fast Single-Use VLP Vaccine Productions Based on Insect Cells and the Baculovirus Expression Vector System: Influenza as Case Study by Regine Eibl, Nina Steiger, Sabine Wellnitz, Tiago Vicente, Corinne John, Dieter Eibl. Microbial High Cell Density Fermentations in a Stirred Single-Use Bioreactor by Thomas Dreher, Bart Walcarius, Ute Husemann, Franziska Klingenberg, Christian Zahnow, Thorsten Adams, Davy de Wilde, Peter Casteels, Gerhard Greller. Quorus Bioreactor: A New Perfusion-Based Technology for Microbial Cultivation by Sheena J. Fraser, Christian Endres. Cultivation of Marine Microorganisms in Single-Use Systems by Friederike Hillig, Maciej Pilarek, Stefan Junne, Peter Neubauer. Flexible Biomanufacturing Processes that Address the Needs of the Future by Bernhard Diel, Christian Manzke, Thorsten Peuker. An Approach to Quality and Security of Supply for Single-Use Bioreactors by Magali Barbaroux, Susanne Gerighausen, Heiko Hackel. A Risk Analysis for Production Processes with Disposable Bioreactors by Tobias Merseburger, Ina Pahl, Daniel Müller, Markus Tanner.

Process Validation in Manufacturing of Biopharmaceuticals, Third Edition delves into the key aspects and current practices of process validation. It includes discussion on the final version of the FDA 2011 Guidance for Industry on Process Validation Principles and Practices, commonly referred to as the Process Validation Guidance or PVG, issued in final form on January 24, 2011. The book also provides guidelines and current practices, as well as industrial case studies illustrating the different approaches that can be taken for successful validation of biopharmaceutical processes. Case studies include Process validation for membrane chromatography Leveraging multivariate analysis tools to qualify scale-down models A matrix approach for process validation of a multivalent bacterial vaccine Purification validation for a therapeutic monoclonal antibody expressed and secreted by Chinese Hamster Ovary (CHO) cells Viral clearance validation studies for a product produced in a human cell line A much-needed resource, this book presents process characterization techniques for scaling down unit operations in biopharmaceutical manufacturing, including chromatography, chemical modification reactions, ultrafiltration, and microfiltration. It also provides practical methods to test raw materials and in-process samples. Stressing the importance of taking a risk-based approach towards computerized system compliance, this book will help you and your team ascertain process validation is carried out and exceeds

expectations.
Comprehensive Biotechnology, Third Edition unifies, in a single source, a huge amount of information in this growing field. The book covers scientific fundamentals, along with engineering considerations and applications in industry, agriculture, medicine, the environment and socio-economics, including the related government regulatory overviews. This new edition builds on the solid basis provided by previous editions, incorporating all recent advances in the field since the second edition was published in 2011. Offers researchers a one-stop shop for information on the subject of biotechnology Provides in-depth treatment of relevant topics from recognized authorities, including the contributions of a Nobel laureate Presents the perspective of researchers in different fields, such as biochemistry, agriculture, engineering, biomedicine and environmental science
Monoclonal antibodies represent one of the fastest growing areas of new drug development within the pharmaceutical industry. Several blockbuster products have been approved over the past several years including Rituxan, Remicade, Avastin, Humira, and Herceptin. In addition, over 300 new drugs are currently in clinical trials. With both large, established biotechnology companies and small start-ups involved in the development of this important class of molecules, monoclonal antibodies products will become increasingly prevalent over the next decade. Recently the regulatory review of monoclonal antibodies has been moved from Center for Biologics and Research to the Center for Drug Evaluation and Research (CDER) division of the US Food and Drug Administration. It is anticipated that CDER will expect a certain minimal amount of data to be provided as more of these products move through the regulatory pipeline. Current Trends in Monoclonal Antibody Development and Manufacturing will provide readers with an understanding of what is currently being done in the industry to develop, manufacture, and release monoclonal antibody products and what will be required for a successful regulatory submission.
Presents Practical Applications of Mass Spectrometry for Protein Analysis and Covers Their Impact on Accelerating Drug Discovery and Development Covers both qualitative and quantitative aspects of Mass Spectrometry protein analysis in drug discovery Principles, Instrumentation, Technologies topics include MS of peptides, proteins, and ADCs , instrumentation in protein analysis, nanospray technology in MS protein analysis, and automation in MS protein analysis Details emerging areas from drug monitoring to patient care such as Identification and validation of biomarkers for cancer, targeted MS approaches for biomarker validation, biomarker discovery, and regulatory perspectives Brings together the most current advances in the mass spectrometry technology and related method in protein analysis
This practical guide for advanced students and decision-makers in the pharma and biotech industry presents key success factors in R&D along with value creators in pharmaceutical innovation. A team of editors and authors with extensive experience in academia and industry and at some of the most prestigious business schools in Europe discusses in detail the innovation process in pharma as well as common and new research and innovation strategies. In doing so, they cover collaboration and partnerships, open innovation, biopharmaceuticals, translational medicine, good manufacturing practice, regulatory affairs, and portfolio management. Each chapter covers controversial aspects of recent developments in the pharmaceutical industry, with the aim of stimulating productive debates on the most effective and efficient innovation processes. A must-have for young professionals and MBA students preparing to enter R&D in pharma or biotech as well as for students on a combined BA/biomedical and natural sciences program.
Case Studies in Infectious Disease presents forty case studies featuring the most important human infectious diseases worldwide. Written for students of microbiology and medicine this book describes the natural history of infection from point of entry of the pathogen through pathogenesis, followed by clinical presentation, diagnosis and treatment. Five core sets of questions are posed in each case. What is the nature of the infectious agent, how does it gain access to the body, what cells are infected, and how does the organism spread? What are the host defense mechanisms against the agent and how is the disease caused? What are the typical manifestations of the infection and the complications that can occur? How is the infection diagnosed and what is the differential diagnosis? How is the infection managed, and what preventative measures can be taken to avoid infection? This standardized approach provides the reader with a logical basis for understanding these diverse and medically important organisms, fully integrating microbiology and immunology throughout.
The American Anti-Vivisection Society (AAVS) petitioned the National Institutes of Health (NIH) on April 23, 1997, to prohibit the use of animals in the production of mAb. On September 18, 1997, NIH declined to prohibit the use of mice in mAb production, stating that "the ascites method of mAb production is scientifically appropriate for some research projects and cannot be replaced." On March 26, 1998, AAVS submitted a second petition, stating that "NIH failed to provide valid scientific reasons for not supporting a proposed ban." The office of the NIH director asked the National Research Council to conduct a study of methods of producing mAb. In response to that request, the Research Council appointed the Committee on Methods of Producing Monoclonal Antibodies, to act on behalf of the Institute for Laboratory Animal Research of the Commission on Life Sciences, to conduct the study. The 11 expert members of the committee had extensive experience in biomedical research, laboratory animal medicine, animal welfare, pain research, and patient advocacy (Appendix B). The committee was asked to determine whether there was a scientific necessity for the mouse ascites method; if so, whether the method caused pain or distress; and, if so, what could be done to minimize the pain or distress. The committee was also asked to comment on available in vitro methods; to suggest what acceptable scientific rationale, if any, there was for using the mouse ascites method; and to identify regulatory requirements for the continued use of the mouse ascites method. The committee held an open data-gathering meeting during which its members summarized data bearing on those questions. A 1-day workshop (Appendix A) was attended by 34 participants, 14 of whom made formal presentations. A second meeting was held to finalize the report. The present report was written on the basis of information in the literature and information presented at the meeting and the workshop.
This book examines statistical techniques that are critically important to Chemistry, Manufacturing, and Control (CMC) activities. Statistical methods are presented with a focus on applications unique to the CMC in the pharmaceutical industry. The target audience consists of statisticians and other scientists who are responsible for performing statistical analyses within a CMC environment. Basic statistical concepts are addressed in Chapter 2 followed by applications to specific topics related to development and manufacturing. The mathematical level assumes an elementary understanding of statistical methods. The ability to use Excel or statistical packages such as Minitab, JMP, SAS, or R will provide more value to the reader. The motivation for this book came from an American Association of Pharmaceutical Scientists (AAPS) short course on statistical methods applied to CMC applications presented by four of the authors. One of the course participants asked us for a good reference book, and the only book recommended was written over 20 years ago by Chow and Liu (1995). We agreed that a more recent book would serve a

need in our industry. Since we began this project, an edited book has been published on the same topic by Zhang (2016). The chapters in Zhang discuss statistical methods for CMC as well as drug discovery and nonclinical development. We believe our book complements Zhang by providing more detailed statistical analyses and examples.

Translational Medicine: Tools and Techniques provides a standardized path from basic research to the clinic and brings together various policy and practice issues to simplify the broad interdisciplinary field. With discussions from academic and industry leaders at international institutions who have successfully implemented translational medicine techniques and tools in various settings, readers will be guided through implementation strategies relevant to their own needs and institutions. The book also addresses regulatory processes in USA, EU, Japan and China. By providing details on omics sciences techniques, biomarkers, data mining and management approaches, case reports from industry, and tools to assess the value of different technologies and techniques, this book is the first to provide a user-friendly go-to guide for key opinion leaders (KOLs), industry administrators, faculty members, clinicians, researchers, and students interested in translational medicine. Includes detailed and standardized information about the techniques and tools used in translational medicine Provides specific industry case scenarios Explains how to use translational medicine tools and techniques to plan and improve infrastructures and capabilities while reducing cost and optimizing resources

The concepts, applications, and practical issues of Quality byDesign Quality by Design (QbD) is a new framework currently beingimplemented by the FDA, as well as EU and Japanese regulatoryagencies, to ensure better understanding of the process so as toyield a consistent and high-quality pharmaceutical product. QbDbreaks from past approaches in assuming that drug quality cannot betested into products; rather, it must be built into every step ofthe product creation process. Quality by Design: Perspectives and Case Studies presentsthe first systematic approach to QbD in the biotech industry. Acomprehensive resource, it combines an in-depth explanation ofbasic concepts with real-life case studies that illustrate thepractical aspects of QbD implementation. In this single source, leading authorities from thebiotechnology industry and the FDA discuss such topics as: The understanding and development of the product's criticalquality attributes (CQA) Development of the design space for a manufacturingprocess How to employ QbD to design a formulation process Raw material analysis and control strategy for QbD Process Analytical Technology (PAT) and how it relates toQbD Relevant PAT tools and applications for the pharmaceuticalindustry The uses of risk assessment and management in QbD Filing QbD information in regulatory documents The application of multivariate data analysis (MVDA) toQbD Filled with vivid case studies that illustrate QbD at work incompanies today, Quality by Design is a core reference forscientists in the biopharmaceutical industry, regulatory agencies,and students.

This volume explores the application of Quality by Design (QbD) to biopharmaceutical drug product development. Twenty-eight comprehensive chapters cover dosage forms, liquid and lyophilized drug products. The introductory chapters of this book define key elements of QbD and examine how these elements are integrated into drug product development. These chapters also discuss lessons learned from the FDA Office of Biotechnology Products pilot program. Following chapters demonstrate how QbD is used for formulation development ranging from screening of formulations to developability assessment to development of lyophilized and liquid formats. The next few chapters study the use of small-scale and surrogate models as well as QbD application to drug product processes such as drug substance freezing and thawing, mixing, sterile filtration, filling, lyophilization, inspection and shipping and handling. Later chapters describe more specialized applications of QbD in the drug product realm. This includes the use of QbD in primary containers, devices and combination product development. The volume also explores QbD applied to vaccine development, automation, mathematical modeling and monitoring, and controlling processes and defining control strategies. It concludes with a discussion on the application of QbD to drug product technology transfer as well as overall regulatory considerations and lifecycle management. Quality by Design for Biopharmaceutical Drug Product Development is an authoritative resource for scientists and researchers interested in expanding their knowledge on QbD principles and uses in creating better drugs.

State-of-the-Art and Emerging Technologies for Therapeutic Monoclonal Antibody CharacterizationMonoclonal Antibody Therapeutics: Structure, Function, and Regulatory SpaceMonoclonal Antibody ProductionNational Academies Press

This book is an indispensable tool for anyone involved in the research, development, or manufacture of new or existing vaccines. It describes a wide array of analytical and quality control technologies for the diverse vaccine modalities. Topics covered include the application of both classical and modern bio-analytical tools; procedures to assure safety and control of cross contamination; consistent biological transition of vaccines from the research laboratory to manufacturing scale; whole infectious attenuated organisms, such as live-attenuated and inactivated whole-cell bacterial vaccines and antiviral vaccines using attenuated or inactivated viruses; principles of viral inactivation and the application of these principles to vaccine development; recombinant DNA approaches to produce modern prophylactic vaccines; bacterial subunit, polysaccharide and glycoconjugate vaccines; combination vaccines that contain multiple antigens as well as regulatory requirements and the hurdles of licensure.

Volumes are organized topically and provide a comprehensive discussion of developments in the respective field over the past 3-5 years. The series also discusses new discoveries and applications. Special volumes are dedicated to selected topics which focus on new biotechnological products and new processes for their synthesis and purification. In general, special volumes are edited by well-known guest editors. The series editor and publisher will however always be pleased to receive suggestions and supplementary information. Manuscripts are accepted in English.

Developing a bioprocess model can not only reduce cost and time in process development, but now also assist the routine manufacturing and guarantee the quality of the final products through Quality by Design (QbD) and Process Analytical Technology (PAT). However, these activities require a model based process design to efficiently direct, identify and execute optimal experiments for the best bioprocess understanding and optimisation. Thus an integrated model based process design methodology is desirable to significantly accelerate bioprocess development. This will help meet current urgent clinical demands and also lower the cost and time required. This thesis examines the feasibility of a model based process design for bioprocess optimisation. A new process design approach has been proposed to achieve such optimal design solutions quickly, and provide an accurate process model to speed up process understanding. The model based process design approach includes bioprocess modelling, model based experimental design and high throughput microwell experimentation. The bioprocess design is based on experimental data and a computational framework with optimisation algorithm. Innovative model based experimental design is a core part in this approach. Directed by the design objectives, the method uses D-optimal design to identify the most information rich experiments. It also employs Random design and Simplex to identify extra experiments to increase the accuracy, and will iteratively improve the process design solutions. The modelling and implementation method by high throughput experimentation was first achieved and applied to an antibody fragment (Fab') precipitation case study. A new precipitation model based on phase equilibrium has been developed using the data from microwell experimentation, which was further validated by statistical tests to provide high confidence. The precipitation model based on good data accurately describes not only the Fab' solubility but also the solubility of impurities treated as a pseudo-single protein, whilst changing two critical process conditions: salt concentration and pH. The comparison study has shown the model was superior to other published models. The new precipitation model and the Fab' microwell data provided the basis to test the efficiency and

robustness of the algorithms in model based process design approach. The optimal design solution with the maximum objective value was found by only 5 iterations (24 designed experimental points). Two parameterised models were obtained in the end of the optimisation, which gave a quantitative understanding of the processes involved. The benefit of this approach was well demonstrated by comparing it with the traditional design of experiments (DoE). The whole model based process design methodology was then applied to the second case study: a monoclonal antibody (mAb) precipitation process. The precipitation model was modified according to experimental results following modelling procedures. The optimal precipitation conditions were successfully found through only 4 iterations, which led to an alternative process design to protein A chromatography in the general mAb purification platform. The optimal precipitation conditions were then investigated at lab scale by incorporating a depth filtration process. The final precipitation based separation process achieved 93.6% (w/w) mAb yield and 98.2 % (w/w) purity, which was comparable to protein A chromatography. Polishing steps after precipitation were investigated in microwell chromatographic experimentation to rapidly select the following chromatography steps and facilitate the whole mAb purification process design. The data generated were also used to evaluate the process cost through process simulations. Both precipitation based and protein A chromatography based processes were analysed by the process model in the commercial software BioSolve under several relevant titre and scale assumptions. The results showed the designed precipitation based processes was superior in terms of process time and cost when facing future process challenges.

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.

Authored by two professionals in the medical and science fields, Ebola: An Emerging Infectious Disease Case Study analyzes the recent outbreak of the virus from a variety of angles and provides context for our understanding of emerging infectious diseases, how they are treated, and how agencies and governments respond to them.