Regulatory Perspectives On Extractables And Leachables

Quality management (QM) practices are the basis for the successful implementation and maintenance of any QM system. Quality control (QC) is identified as a QM component. Therefore, QM effectiveness is dependent on the QC strategy. QC practice is more or less complex depending on the type of production. The book is focused on new trends and developments in QM and QC in several types of industries from a worldwide perspective. Its content has been organized into two sections and seven chapters written by well-recognized researchers worldwide. Several approaches are debated based on sample traceability, analytical method validation, required parameters, class of exponential regression-type estimators of the population means, determination of impurities, viewpoints, and case studies.

A practical and science-based approach for addressing toxicological concerns related to leachables and extractables associated with inhalation drug products Packaging and device components of Orally Inhaled and Nasal Drug Products (OINDP)—such as metered dose inhalers, dry powder inhalers, and nasal sprays—pose potential safety risks from leachables and extractables, chemicals that can be released or migrate from these components into the drug product. Addressing the concepts, background, historical use, and development of safety thresholds and their utility for qualifying leachables and extractables in OINDP, the Leachables and Extractables Handbook takes a practical approach to familiarize readers with the recent recommendations for safety and risk assessment established through a joint effort of scientists from the FDA, academia, and industry. Coverage includes best practices for the chemical evaluation and management of leachables and extractables throughout the pharmaceutical product life cycle, as well as: Guidance for pharmaceutical professionals to qualify and risk-assess container closure system leachables and extractables in drug products Principles for defining toxicological safety thresholds that are applicable to OINDP and potentially applicable to other drug products Regulatory perspectives, along with an appendix of key terms and definitions, case studies, and sample protocols Analytical chemists, packaging and device engineers, formulation development scientists, component suppliers, regulatory affairs specialists, and toxicologists will all benefit from the wealth of information offered in this important text.

The papers assembled in this volume were originally presented at the joint meeting of the Phytochemical Society of North America and the Mid-Atlantic Plant Molecular Biology Society, in August 2000. The symposium from which these chapters were prepared was entitled "Regulation of Phytochemicals by Molecular Techniques" and was organised by James Saunders and Ben Matthews. This joint meeting was timely because of recent landmark advances in molecular biology and genomics as well as the renewed interest in phytochemistry as a rich source of nutraceuticals, drugs, and alternatives to synthetic agriculture pesticides. Progress in genome sequencing in plants such as Arabidopsis and rice has been remarkable, as have expressed sequence tag (EST) projects in other plants, including maize and soybean. Recently, private and public sector participants of the Human Genome Project announced that a rough draft of the human genome has been constructed. These advances directly influence phytochemical investigations by providing both insight and tools for exploring and manipulating genomes. The chapters cover a wide range of applications from molecular biology to phytochemistry, and from basic studies on promoters and gene expression to pathway regulation and engineering with transformed plants. A number of noteworthy aspects emerge from this volume: applications of molecular biology to phytochemical practical problems are succeeding; newly emerging molecular tools promise to open new doors to discovery; and remarkable progress has already occurred in phytochemical pathway engineering.

Food contact materials such as packaging, storage containers and processing surfaces can pose a substantial hazard to both food manufacturer and consumer due to the migration of chemicals or other substances from the material to the food, which can cause tainting of flavours and other sensory characteristics, or even illness. This book reviews the main materials used for food contact in terms of the global legislation in place to ensure their safe and effective use. Part One provides an overview of food contact legislation issues such as chemical migration and compliance testing. Part Two looks in detail at the legislation for specific food contact materials and their advantages, hazards and use in industry. Includes global coverage of food contact legislation Features expert analysis of future trends in global food packaging regulation Focus on specific materials such as plastic, paper and rubber materials in contact with food

Dosage Form Design Parameters, Volume II, examines the history and current state of the field within the pharmaceutical sciences, presenting key developments. Content includes drug development issues, the scale up of formulations, regulatory issues, intellectual property, solid state properties and polymorphism. Written by experts in the field, this volume in the Advances in Pharmaceutical Product Development and Research series deepens our understanding of dosage form design parameters. Chapters delve into a particular aspect of this fundamental field, covering principles, methodologies and the technologies employed by pharmaceutical scientists. In addition, the book contains a comprehensive examination suitable for researchers and advanced students working in pharmaceuticals, cosmetics, biotechnology and related industries. Examines the history and recent developments in drug dosage forms for pharmaceutical sciences Focuses on physicochemical aspects, prefomulation solid state properties and polymorphism Contains extensive references for further discovery and learning that are appropriate for advanced undergraduates, graduate students and those interested in drug dosage design

Residue Reviews

Continuous Biomanufacturing

Global Legislation for Food Contact Materials

Characterization of Drug Products, Packaging, Manufacturing and Delivery Systems, and Medical Devices

Practical Toxicology

Encyclopedia of Pharmaceutical Technology

This is the most comprehensive treatise of this topic available, providing invaluable information on the technological and economic benefits to be gained from implementing continuous processes in the biopharmaceutical industry. Top experts from industry and academia cover the latest technical developments in the field, describing the use of single-use technologies alongside perfusion production platforms and downstream operations. Special emphasis is given to process control and monitoring, including such topics as 'quality by design' and automation. The book is supplemented by case studies that highlight the enormous potential of continuous manufacturing for biopharmaceutical production facilities.

Compatibility of Pharmaceutical Products and Contact Materials Dennis Jenke Important safety aspects of compatibility for therapeuticproducts and their manufacturing systems, delivery devices, andcontainers Compatibility of Pharmaceutical Products and ContactMaterials helps pharmaceutical, toxicology, analytical, andregulatory affairs professionals assess the safety of leachable andextractable chemicals associated with drug product packaging,manufacturing systems, and devices. The most comprehensive resourceavailable, its coverage includes the strategies, tactics, andregulatory requirements for performing safety assessments, alongwith the means for interpreting results. Structured around a logical framework for an extractables andleachables safety assessment and closely linked to thepharmaceutical product development process, Compatibility ofPharmaceutical Products and Contact Materials directlyaddresses the fundamental questions of "what activities need to beperformed to completely, efficiently, and effectively address theissue of product safety from an extractables and leachablesperspective?" and "when do the various required activities need tobe performed?" Specifically, the chapters describe: Pertinent regulations and practical ways to meetguidelines Coordinating manufacturing, storage, and delivery systemsdevelopment and qualification with therapeutic productdevelopment Materials characterization and the materials screeningprocess Component and/or system qualification (illustrated by severalcase studies) Performing validation/migration studies and interpreting andreporting the results Creating a product registration dossier and putting it throughregulatory review Product maintenance (Change Control) from an extractables andleachables perspective Likely future developments in extractables and leachablesassessment Additionally, the book's appendix provides a database, includingCAS registry numbers, chemical formulas and molecular weights ofextractable/leachable substances that have been reported in thechemical literature. Detailing the interconnected roles played by analyticalchemistry, biological science, toxicology, and regulatory science,Compatibility of Pharmaceutical Products and ContactMaterials supplies a much-needed, comprehensive resource to allthose in pharmaceutical product or medical device development.

An up-to-date, sequenced approach to drug dosage formulation, design and evaluation. This edition offers new chapters on regulatory aspects of the pharmaceutical industry in the European Union, the pharmaceutical needs of special populations, target-oriented drug delivery systems and more.

Practical Toxicology: Evaluation, Prediction, and Risk, Third Edition shows how to conduct a program of safety evaluation and testing and then to interpret and apply the resulting data and information in the real world, beginning with the basic concepts in toxicology and progressing to the interpretation of the resulting data. Revised and updated chapters on risk assessment guide the reader to setting the foundations necessary for submission to regulatory authorities. In addition, a new chapter in the book reviews the errors in toxicology, mistakes, misuse, mismanagement, and misunderstanding with a view to avoiding these in the future. New Chapters in the Third Edition: Toxicology in silico Errors in Toxicology Safety Assessment of Extractables and Leachables. This new edition follows a practical sequence from introducing the basics of toxicology (including the vital concept of normality in controls) to describing a test program and then interpreting the data and translating that to risk assessment that can be used in a number of real world situations where safety and secure risk assessment are essential. Although written primarily from the perspective of pharmaceutical development, the test designs and toxicological problems encountered in that field are entirely relevant to those with other classes of chemicals, the only difference being the regulatory context. Toxicology is an international discipline and the book has been written to take into account some of the differences in regulatory nuance between the main regions of the world. Completely revised and written in an easily accessible style, the text address several audiences—from students and post-graduates coming to the subject for the first time to established professionals who find themselves needing to learn about toxicology, toxicity testing, interpretation of the results, and risk assessment. It is intended primarily as a textbook, with case studies and information on where to go to ask questions, but can also be used as a practical reference book. It covers all the basics of toxicology and the main aspects of safety evaluation testing and risk assessment while reviewing critically the current state of the discipline. It also provides a foundation for those seeking registration or certification.

Authoritative guide to the principles, characteristics, engineering aspects, economics, and applications of disposables in the manufacture of biopharmaceuticals The revised and updated second edition of Single-Use Technology in Biopharmaceutical Manufacture offers a comprehensive examination of the most-commonly used disposables in the manufacture of biopharmaceuticals. The authors—noted experts on the topic—provide the essential information on the principles, characteristics, engineering aspects, economics, and applications. This authoritative guide contains the basic knowledge and information about disposable equipment. The author also discusses biopharmaceuticals' applications through the lens of case studies that clearly illustrate the role of manufacturing, quality assurance, and environmental influences. This updated second edition revises existing information with recent developments that have taken place since the first edition was published. The book also presents the latest advances in the field of single-use technology and explores topics including applying single-use devices for microorganisms, human mesenchymal stem cells, and T-cells. This important book: • Contains an updated and end-to-end view of the development and manufacturing of single-use biologics • Helps in the identification of appropriate disposables and relevant vendors • Offers illustrative case studies that examine manufacturing, quality assurance, and environmental influences • Includes updated coverage on cross-functional/transversal dependencies, significant improvements made by suppliers, and the successful application of the single-use technologies Written for biopharmaceutical manufacturers, process developers, and biological and chemical engineers, Single-Use Technology in Biopharmaceutical Manufacture, 2nd Edition provides the information needed for professionals to come to an easier decision for or against disposable alternatives and to choose the appropriate system.

Safety Evaluation, Qualification, and Best Practices Applied to Inhalation Drug Products

Perspectives on Motivation

Nonclinical Safety Assessment

Sterile Product Development

Modern Pharmaceutics, Fourth Edition Revised and Expanded

The Challenge of CMC Regulatory Compliance for Biopharmaceuticals

Disposable Technology and Single-Use Systems. Regulatory Perspective, Best Practices and Future Trends of Extractables and LeachablesGRIN Verlag

This book will update the original edition published in 1997. Since the publication of the first edition, the biotechnology and biologics industries have gained extensive knowledge and experience in downstream processing using chromatography and other technologies associated with recovery and purification unit operations. This book will tie that experience together for the next generation of readers. Updates include: - sources and productivity - types of products made today - experiences in clinical and licensed products - economics - current status of validation - illustrations and tables - automated column packing - automated systems New topics include: - the use of disposables - multiproduct versus dedicated production - design principles for chromatography media and filters - ultrafiltration principles and optimization - risk assessments - characterization studies - design space - platform technologies - process analytical technologies (PATs) - biogenerics - comparability assessments Key Features: - new approaches to process optimiaztion - use of patform technologies - applying risk assessment to process design

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.

Have you ever been frustrated that arbitration folk aren't more numerate? The Guide to Damages in International Arbitration is a desktop reference work for those who'd like greater confidence when dealing with the numbers. This second edition builds upon last year's by updating and adding several new chapters on the function and role of damages experts, the applicable valuation approach, country risk premium, and damages in gas and electricity arbitrations.This edition covers all aspects of damages - from the legal principles applicable, to the main valuation techniques and their mechanics, to industry-specific questions, and topics such as tax and currency. It is designed to help all participants in the international arbitration community to discuss damages issues more effectively and communicate them better to tribunals, with the aim of producing better awards. The book is split into four parts: Part I - Legal Principles Applicable to the Award of Damages; Part II - Procedural Issues and the Use of Damages Experts; Part III - Approaches and Methods for the Assessment and Quantification of Damages; Part IV - Industry-Specific Damages Issues

A step-by-step, integrated approach for successful, FDA-approved combination drug products Using a proven integrated approach to combination drug development, this book guides you step by step through all the preclinical, clinical, and manufacturing stages. Written from an FDA regulatory perspective, the book not only enables you to bring a successful combination drug product to market, it also sets forth the most efficient and effective path to FDA approval. The book begins with an introductory chapter presenting definitions and basic regulatory principles of combination products. Next, it reviews manufacturing and controls, preclinical testing models, pharmacology, clinical testing, regulatory submissions, FDA reviews, and approvals. Among the key topics examined are: * The pharmacology, safety pharmacology, and toxicology supporting human clinical trials of combination products * Approaches to clinical trial protocol design and execution * Chemical, physicochemical, and analytical aspects of manufacturing controls and validation that lead to stable components for combination products * Key sponsor/FDA meetings and negotiations essential for approval and commercialization Case studies involving such actual combination products as Mylotarg, Herceptin, and HercepTest help you better understand how to implement the author's practical guidelines. References at the end of each chapter enable you to find more information on any stage of the development, manufacturing and approval processes. This book is ideal for researchers, regulators, academics, project managers, and executives involved in the complex process of combination product development. Not only does itoffer a comprehensive guide to the technical aspects of the field, it also integrates all ofthese technical aspects into a unified, effective approach to help ensure a successful, approved product.

Guide to Damages in International Arbitration

Biomaterials, Medical Devices, and Combination Products

Extractables & Leachables Europe 2012 Conference Proceedings

Pharmaceutical Suspensions

Disposable Bioreactors II

Parenteral Medications, Third Edition. 3 Volume Set

A practical and science-based approach for addressingtoxicological concerns related to leachables and extractablesassociated with inhalation drug products Packaging and device components of Orally Inhaled and Nasal DrugProducts (OINDP)—such as metered dose inhalers, dry powderinhalers, and nasal sprays—pose potential safety risks fromleachables and extractables, chemicals that can be released ormigrate from these components into the drug product. Addressing theconcepts, background, historical use, and development of safetythresholds and their utility for qualifying leachables andextractables in OINDP, the Leachables and Extractables Handbooktakes a practical approach to familiarize readers with the recentrecommendations for safety and risk assessment established througha joint effort of scientists from the FDA, academia, and industry.Coverage includes best practices for the chemical evaluation andmanagement of leachables and extractables throughout thepharmaceutical product life cycle, as well as: Guidance for pharmaceutical professionals to qualify andrisk-assess container closure system leachables and extractables indrug products Principles for defining toxicological safety thresholds that areapplicable to OINDP and potentially applicable to other drugproducts Regulatory perspectives, along with an appendix of key terms anddefinitions, case studies, and sample protocols Analytical chemists, packaging and device engineers, formulationdevelopment scientists, component suppliers, regulatory affairsspecialists, and toxicologists will all benefit from the wealth ofinformation offered in this important text.

Set to be the biggest and best European Extractables and Leachables conference to date, Smithers Rapra are bringing E&L 2012 to Vienna on 12-13 December. The conference programme will feature a comprehensive representation of best practice examples in pharmaceutical packaging, as well as the latest regulatory and working group updates, analytical chemist perspectives, and technical innovations from top pharmaceutical companies and materials suppliers.

The International Conference of Harmonization (ICH) has worked on har- nizing the stability regulations in the US, Europe, and Japan since the early 1990s. Even though the Stability Guidelines Q1A (R2) was issued over a decade ago, issues surrounding this arena continue to surface as the principles described in the guideline are applied to different technical concentrations. As a result, the stability community has continued to discuss concerns and find ways of harmonizing regulatory requirements, streamlining practices, improving processes in order to bring safe and effective medical supplies to the patients around the world. In 2007, the American Association of Pharmaceutical Scientists (AAPS) Stability Focus Group organized two workshops – the Stability Workshop and the Degradation Mechanism Workshop. These meetings attracted many industry scientists as well as representatives from several regulatory agencies in the world to discuss important topics related to pharmaceutical stability practices. Recognizing the importance of documenting these discussions and with the permission of AAPS, I have worked with speakers to assemble a collection of 30 articles from presentations given at these two meetings, mainly the Stability Workshop. I trust that this book will be beneficial to all of you in providing guidance and up-to-date information for building quality stability programs. v Freedom of our mind is Mother of all inventions.

This book gives pharmaceutical scientists an up-to-date resource on protein aggregation and its consequences, and available methods to control or slow down the aggregation process. While significant progress has been made in the past decade, the current understanding of protein aggregation and its consequences is still immature. Prevention or even moderate inhibition of protein aggregation has been mostly experimental. The knowledge in this book can greatly help pharmaceutical scientists in the development of therapeutic proteins, and also instigate further scientific investigations in this area. This book fills such a need

by providing an overview on the causes, consequences, characterization, and control of the aggregation of therapeutic proteins.
The suspension dosage form has long been used for poorly soluble active ingre- ents for various therapeutic indications. Development of stable suspensions over the shelf life of the drug product continues to be a challenge on many fronts. A good understanding of the fundamentals of disperse systems is essential in the development of a suitable pharmaceutical suspension. The development of a s- pension dosage form follows a very complicated path. The selection of the proper excipients (surfactants, viscosity imparting agents etc.) is important. The particle size distribution in the finished drug product dosage form is a critical parameter that significantly impacts the bioavailability and pharmacokinetics of the product. Appropriate analytical methodologies and instruments (chromatographs, visco- ters, particle size analyzers, etc.) must be utilized to properly characterize the s- pension formulation. The development process continues with a successful scale-up of the manufacturing process. Regulatory agencies around the world require cli- cal trials to establish the safety and efficacy of the drug product. All of this devel- ment work should culminate into a regulatory filing in accordance with the regulatory guidelines. Pharmaceutical Suspensions, From Formulation Development to Manufacturing, in its organization, follows the development approach used widely in the pharmaceutical industry. The primary focus of this book is on the classical disperse system - poorly soluble active pharmaceutical ingredients s- pended in a suitable vehicle.
Handbook of Process Chromatography
A Guide to International Pharmaceutical Regulations
Pharmaceutical Dosage Forms
Disposable Technology and Single-Use Systems. Regulatory Perspective, Best Practices and Future Trends of Extractables and Leachables
Biocompatibility Testing and Safety Assessment
Extractables and Leachables
Presenting authoritative and engaging articles on all aspects of drug development, dosage, manufacturing, and regulation, this Third Edition enables the pharmaceutical specialist and novice alike to keep abreast of developments in this rapidly evolving and highly competitive field. A dependable reference tool and constant companion for years to com
Biomaterials, Medical Devices, and Combination Products is a single-volume guide for those responsible for-or concerned with-developing and ensuring patient safety in the use and manufacture of medical devices.The book provides a clear presentation of the global regulatory requirements and challenges in evaluating the biocompatibility and clinical
While the safety assessment (“biocompatibility”) of medical devices has been focused on issues of local tissue tolerance (irritation, sensitization, cytotoxicity) and selected quantal effects (genotoxicity and acute lethality) since first being regulated in the late 1950s, this has changed as devices assumed a much more important role in healthcare and became more complex in both composition and in their design and operation. Add to this that devices now frequently serve as delivery systems for drugs, and that drugs may be combined with devices to improve device performance, and the problems of ensuring patient safety with devices has become significantly more complex. A part of this, requirements for ensuring safety (once based on use of previously acceptable materials – largely polymers and metals) have come to requiring determining which chemical entities are potentially released from a device into patients (and how much is released). Then an appropriate and relevant (yet also conservative) risk assessment must be performed for each identified chemical structure. The challenges inherent in meeting the current requirements are multifold, and this text seeks to identify, understand, and solve all of them. • Identify and verify the most appropriate available data. • As in most cases such data is for a different route of exposure, transform it for use in assessing exposure by the route of interest. • As the duration (and rate) of exposure to moieties released from a device are most frequently different (longer) than what available data speaks to, transformation across tissue is required. • As innate and adaptive immune responses are a central part of device/patient interaction, assessing potential risks on this basis are required. • Incorporating assessments for special populations such as neonates. • Use of (Q)SAR (Quantitative Structure Activity Relationships) modeling in assessments. • Performance and presentation of integrative assessments covering all potential biologic risks. Appendices will contain summarized available biocompatibility data for commonly used device materials (polymers and metals) and safety assessments on the frequently seen moieties in extractions from devices.
Biopharmaceuticals (i.e., biological medicines sourced from genetically-engineered living systems) for treatment of human diseases have become a significant percentage of the pharmaceutical industry. And not just the recombinant DNA-derived proteins and monoclonal antibodies (both from the innovators and biosimilars); but now, an increasing awareness of the importance of gene therapy and genetically engineered cellular medicinal products. These biopharmaceuticals are being developed by many companies whose Chemistry, Manufacturing & Control (CMC) teams have varying degrees of familiarity or experience with the CMC strategy and regulatory compliance requirements for these challenging products. Companies clearly plan out the strategy for their clinical study plans, but frequently, the development of a strategy for CMC is an afterthought. Coupled with the complexity of the biopharmaceutical manufacturing processes and products, and this can be a recipe for disaster. The third edition of this book provides insights and practical guidance for the CMC teams to develop an acceptable cost-effective, risk-based CMC regulatory compliance strategy for all biopharmaceuticals (recombinant proteins, monoclonal antibodies, genetically engineered viruses and genetically engineered human cells) from early clinical stage development through market approval. The third edition of this book provides added coverage for the biosimilars, antibody drug conjugates (ADCs), bispecific antibodies, genetically engineered viruses, and genetically engineered cells. This third edition of the book also addresses the heightened pressure on CMC regulatory compliance timelines due to the introduction of expedited clinical pathways moving the clinical development closer to a seamless phase process (e.g., FDA Breakthrough Therapy designation, CBER Regenerative Medicine Advanced Therapy (RMAT) designation, EMA Priority Medicines (PRIME) designation). The Challenge of CMC Regulatory Compliance for Biopharmaceuticals is essential, practical information for all pharmaceutical development scientists, Manufacturing and Quality Unit staff, Regulatory Affairs personnel, and senior management involved in the manufacture of biopharmaceuticals.
Worldwide concern in scientific, industrial, and governmental com munities over traces of toxic chemicals in foodstuffs and in both abiotic and biotic environments has justified the present triumvirate of specialized publications in this field: comprehensive reviews, rapidly published progress reports, and archival documentations. These three publications are integrated and scheduled to provide in international communication the coherency essential for nonduplicative and current progress in a field as dynamic and complex as environmental contamination and toxicology. Until now there has been no journal or other publication series reserved exclusively for the diversified literature on "toxic" chemicals in our foods, our feeds, our geographical surroundings, our domestic animals, our wild life, and ourselves. Around the world immense efforts and many talents have been mobilized to technical and other evaluations of natures, locales, magnitudes, fates, and toxicology of the persisting residues of these chemicals loosed upon the world. Among the sequelae of this broad new emphasis has been an inescapable need for an articulated set of authorita tive publications where one could expect to find the latest important world literature produced by this emerging area of science together with documentation of pertinent ancillary legislation.
The Comprehensive Guide to the Correct Feeding of Your Horse
Pharmaceutical Stability Testing to Support Global Markets
Development, Manufacturing, Validation and Economics
A Regulatory Perspective
New Trends and Developments
Evaluation, Prediction, and Risk, Third Edition
EXTRACTABLES AND LEACHABLES Learn to address the safety aspects of packaged drug products and medical devices Pharmaceutical drug products and medical devices are expected to be effective and safe to use. This includes minimizing patient, user or product exposure to impurities leached from these items when the drug product is administered or when the medical device is used. Clearly, patient or user exposure to leachables must not adversely impact their health and safety. Furthermore, these impurities must not adversely affect key quality attributes of the drug product or medical device, including its manufacturability, stability, efficacy, appearance, shelf-life and conformance to standards. Extractables and leachables are derived from the drug product’s packaging, manufacturing systems and/or delivery systems or from the medical device’s materials of construction. It is imperative to understand and quantify the release of extractables from these items, the accumulation of leachables in drug products and the release of leachables from medical devices. Once extractables and leachables have been discovered, identified and quantified, their effect on the key product or device quality attributes, including safety, must be systematically and scientifically established according to recognized, rigorous and relevant regulatory and compendial standards and industry-driven best practices. In Extractables and Leachables, the chemical compatibility (including safe use) of drugs (and their containers, delivery devices and manufacturing systems) and medical devices is examined at length, focusing particularly on how trace-level extractables and leachables affect the quality and safety of a medical product and how to assess the magnitude of the effect. This is accomplished by addressing the two critical activities required to develop, register and commercialize safe, effective and affordable clinical therapies; measuring extractables and leachables (chemical characterization) and assessing their impact (for example, toxicological safety risk assessment). Each of these activities is addressed in-depth, based on the existing and developing international regulations and guidelines, current published literature and the author’s extensive personal experience. Written by a key contributor to standards, guidelines, recommended practices and the scientific literature, the book provides “insider” insights beyond those gained by merely reading the relevant texts. Given that the rapidly evolving extractables and leachables landscape, this book provides the most current and crucial information on new and forthcoming regulations and best practices. Extractables and Leachables readers will also find: A thorough summary of regulatory and compendial guidelines and the steps required to meet them A detailed and in-depth review of essential scientific principles and recommended best practices for the design, implementation, interpretation and reporting of chemical characterization studies A practical resource for optimizing the development, registration, and commercialization of safe and effective medical products A helpful tool to maximize product development and successful regulatory outcomes Extractables and Leachables is the essential reference for pharmaceutical scientists, analytical chemists, regulatory affairs professionals, engineers, and toxicologists in areas such as product research and development, product registration and approval, regulatory affairs, analytical science, quality control, and manufacturing.
An international team of investigators presents thought-provoking reviews of bioreactors for stem cell expansion and differentiation and provides cutting-edge information on different bioreactor systems. The authors offer novel insights into bioreactor-based culture systems specific for tissue engineering, including sophisticated and cost-effective manufacturing strategies geared to overcome technological shortcomings that currently preclude advances towards product commercialization. This book in the fields of stem cell expansion, bioreactors, bioprocessing, and bio and tissue engineering, gives the reader a full understanding of the state-of-art and the future of these fields. Key selling features: Describes various bioreactors or stem cell culturing systems Reviews methods for stem cell expansion and differentiation for neural, cardiac, hemopoietic, mesenchymal, hepatic and other tissues cell types Distinguishes different types of bioreactors intended for different operational scales of tissue engineering and cellular therapies Includes contributions from an international team of leaders in stem cell research
Appearing on the hundredth anniversary of the teaching of psychology at the University of Nebraska, this volume represents a return to an earlier preoccupation with motivation and reflects a resurgence of interest in it.øEight professionals in psychology discuss the many sides of motivation. Mortimer Appley, president emeritus of Clark University, sees equilibrium, or homeostasis, as the fundamental motivational process. Douglas Derryberry and Don M. Tucker of the University of Oregon present a broad and basic model of motivation, viewing it as a product of the evolution and neural architecture of the human brain. Carole S. Dweck of Columbia University approaches personality development through motivational concepts, in particular goals related to self-image. Bernard Weiner of the University of California, Los Angeles, discusses the importance of one?s perception of control over the causes of a situation or problem and over its management or solution. Albert Bandura of Stanford University is concerned with short- and long-term goals as they are affected by emotional states and a sense of self-efficacy. Similarly, Edward L. Deci and Richard M. Ryan of the University of Rochester consider the bearing of self-determination on motivation and achievement.
Parenteral Medications is an authoritative, comprehensive reference work on the formulation and manufacturing of parenteral dosage forms, effectively balancing theoretical considerations with practical aspects of their development. Previously published as a three-volume set, all volumes have been combined into one comprehensive publication that addresses the plethora of changes in the science and considerable advances in the technology associated with these products and routes of administration. Key Features: Provides a comprehensive reference work on the formulation and manufacturing of parenteral dosage forms Addresses changes in the science and advances in the technology associated with parenteral medications and routes of administration Includes 13 new chapters and updated chapters throughout Contains the contributors of leading researchers in the field of parenteral medications Uses full color detailed illustrations, enhancing the learning process The fourth edition not only reflects enhanced content in all the chapters but also highlights the rapidly advancing formulation, processing, manufacturing parenteral technology including advanced delivery and cell therapies. The book is divided into seven sectionss: Section 1 - Parenteral Drug Administration and Delivery Devices; Section 2 - Formulation Design and Development; Section 3 - Specialized Drug Delivery Systems; Section 4 - Primary Packaging and Container Closure Integrity; Section 5 - Facility Design and Environmental Control; Section 6 - Sterilization and Pharmaceutical Processing; Section 7 - Quality Testing and Regulatory Requirements
Pharmaceutical Dosage Forms: Parenteral Medications explores the administration of medications through other than the enteral route. First published in 1984 (as two volumes) and then last revised in 1993, this three-volume set presents the plethora of changes in the science and considerable advances in the technology associated with these products
Integrated Safety and Risk Assessment for Medical Devices and Combination Products
Pharmaceutical Dosage Forms - Parenteral Medications
Volume 3: Regulations, Validation and the Future
Compatibility of Pharmaceutical Solutions and Contact Materials
Parenteral Medications, Fourth Edition
From Formulation Development to Manufacturing
This comprehensive book encompasses various facets of sterile product development. Key concepts relevant to the successful development of sterile products are illustrated through case studies and are covered under three sections in this book: • Formulation approaches that discuss a variety of dosage forms including protein therapeutics, lipid-based controlled delivery systems, PEGylated biotherapeutics, nasal dosage form, and vaccines • Process, container closure and delivery considerations including freeze-thaw process challenges, best practices for technology transfer to enable commercial product development, innovations and advancement in aseptic fill-finish operations, approaches to manufacturing lyophilized parenteral products, pen / auto-injector delivery devices, and associated container closure integrity testing hurdles for sterile product closures • Regulatory and quality aspects in the areas of particulate matter and appearance evaluation, sterile filtration, admixture compatibility considerations, sterilization process considerations, microbial contamination investigations and validation of rapid microbiological methods, and dry and moist heat sterilizers This book is a useful resource to scientists and researchers in both industry and academia, and it gives process and product development engineers insight into current industry practices and evolving regulatory expectations for sterile product development.
An In-Depth Introduction to Geothermal EnergyAddressing significant changes in the energy markets since the first edition, Geothermal Energy: Renewable Energy and the Environment, Second Edition expounds on the geothermal industry, exploring the expansion, growth, and development of geothermal systems. This text covers every area of geothermal ener
Master's Thesis from the year 2015 in the subject Medicine - Biomedical Engineering, grade: 1.1, , course: MSc. Industrial Pharmaceutical Science, language: English, abstract: With the adoption of Disposable and Single-use manufacturing equipment on the rise, it is logical there is an industry push to develop a standardised set of testing requirements to thoroughly evaluate the impact of extractable and leachable (E&L) contaminants on patient safety. The main objectives of this work are to critically evaluate the preliminary research previously undertaken on the subject area of Single-Use Systems (SUS) with emphasis on the data currently generated from vendors of single-use systems, the need for harmonised supplier data, current methodologies and best practices employed for E&L testing, and also identification of key areas that warrant further study. This will be accomplished using both quantitative and qualitative research methods where primary data is sourced directly from interviews with experienced professionals in the field. The secondary information is obtained from the critical analysis of scientific publications, scholarly articles, databases, and use of statistical data generated from recent surveys on the challenges E&L present and how industry have addressed this matter thus far. From an extractables and leachables viewpoint the regulatory outlook is still quite uncertain. Some SUS suppliers deliver a very strong data package which satisfies the needs of the drug product manufacturer while others fail in this regard. So, in that sense the evaluation of extractables and leachables remains a grey area at present. The challenge for the industry now is to achieve uniformity of data across multiple single-use vendors to facilitate end user risk assessment and compliance for future regulatory submissions and better patient care.
This book focuses on cell culture-produced viral vaccines to meet the needs of the rapidly expanding research and development in academia and industry in the field. This book introduces the basic principles of vaccination and the manufacturing of viral vaccines. Bioprocessing of Viral Vaccines, will provide an overview of the advanced strategies needed to respond to the challenges of new and established viral infection diseases. The first few chapters cover the basics of virology and immunology as essential concepts to understand the function and design of viral vaccines. The core of the content is dedicated to process development, including upstream processing and cell culture of viral vaccines, downstream processing, and extensive analytical technologies specific to viral vaccines. Advanced process analytical technologies (PAT) and Quality by Design (QbD) concepts are also introduced in the context of vaccine manufacturing. The case studies included cover inactivated, attenuated vaccines exemplified by influenza vaccines, sub-unit vaccines exemplified by Virus Like Particles (VLPs: HPV vaccines) and sub-unit vaccines (Flublock), vectored vaccines: adenoviruses and Vesicular stomatitis Virus (VSV) vectored vaccines, genomic vaccines (DNA and mRNA) vaccines as developed for COVID-19 response in particular and a review of COVID-19 vaccines approved or in advanced clinical trials. This book is aimed at graduate engineers and professionals in the fields of vaccinology, bioprocessing, and biomanufacturing of viral vaccines.
Bringing a new drug to market is a costly time-consuming process. Increased regional and international regulation over the last twenty years, while necessary, has only served to amplify these costs. In response to this escalation, developmental strategies have shifted towards a more global approach. In order to create the most cost-effective and safe processes, it is critical for those bringing drugs to market to understand both the globally accepted regulations and the local variations. Nonclinical Safety Assessment: A Guide to International Pharmaceutical Regulations provides a practical description of nonclinical drug development regulations and requirements in the major market regions. It includes: ICH – the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use National regulations, including US FDA, Canada, Mercosur and Brazil, South Africa, China, Japan, India and Australia Repeated dose toxicity studies Carcinogenicity; Genotoxicity; Developmental and reproductive toxicology; Immunotoxicology Biotechnology-derived pharmaceuticals Vaccine development Phototoxicity and photocarcinogenicity Degradants, impurities, excipients and metabolites Primarily intended for those professionals actively involved in the nonclinical and clinical development of a pharmaceutical product, including toxicologists, pharmacologists, clinicians and project managers, this book provides a roadmap for successful new drug approval and marketing.
Volume 6

Aggregation of Therapeutic Proteins
Regulatory Aspects of Gene Therapy and Cell Therapy Products
Single-Use Technology in Biopharmaceutical Manufacture
Bioreactors for Stem Cell Expansion and Differentiation
The pace of new research and level of innovation repeatedly introduced into the field of drug delivery to the lung is surprising given its state of maturity since the introduction of the pressurized metered dose inhaler over a half a century ago. It is clear that our understanding of pulmonary drug delivery has now evolved to the point that inhalation aerosols can be controlled both spatially and temporally to optimize their biological effects. These abilities include controlling lung deposition, by adopting formulation strategies or device technologies, and controlling drug uptake and release through sophisticated particle technologies. The large number of contributions to the scientific literature and variety of excellent texts published in recent years is evidence for the continued interest in pulmonary drug delivery research. This reference text endeavors to bring together the fundamental theory and practice of controlled drug delivery to the airways that is unavailable elsewhere. Collating and synthesizing the material in this rapidly evolving field presented a challenge and ultimately a sense of achievement that is hopefully reflected in the content of the volume.
This book discusses the different regulatory pathways for gene therapy (GT) and cell therapy (CT) medicinal products implemented by national and international bodies throughout the world (e.g. North and South America, Europe, and Asia). Each chapter, authored by experts from various regulatory bodies throughout the international community, walks the reader through the applications of

nonclinical research to translational clinical research to licensure for these innovative products. More specifically, each chapter offers insights into fundamental considerations that are essential for developers of CT and GT products, in the areas of product manufacturing, pharmacology and toxicology, and clinical trial design, as well as pertinent "must-know" guidelines and regulations. Regulatory Aspects of Gene Therapy and Cell Therapy Products: A Global Perspective is part of the American Society of Gene and Cell Therapy sub-series of the highly successful Advances in Experimental Medicine and Biology series. It is essential reading for graduate students, clinicians, and researchers interested in gene and cell therapy and the regulation of pharmaceuticals.

This three-volume set of Pharmaceutical Dosage Forms: Parenteral Medications is an authoritative, comprehensive reference work on the formulation and manufacture of parenteral dosage forms, effectively balancing theoretical considerations with the practical aspects of their development. As such, it is recommended for scientists and engineers in the pharmaceutical industry and academia, and will also serve as an excellent reference and training tool for regulatory scientists and quality assurance professionals. First published in 1984 (as two volumes) and then last revised in 1993 (when it grew to three volumes), this latest revision will address the plethora of changes in the science and considerable advances in the technology associated with these products and routes of administration. The third edition of this book maintains the features that made the last edition so popular but comprises several brand new chapters, revisions to all other chapters, as well as high quality illustrations. Volume three presents: An in-depth discussion of regulatory requirements, quality assurance, risk assessment and mitigation, and extractables/leachables. Specific chapters on parenteral administrations devices, injection site pain assessment, and parenteral product specifications and stability testing. Forward-thinking discussions on the future of parenteral product manufacturing, and siRNA delivery systems. New chapters covering recent developments in the areas of visual inspection, quality by design (QbD), process analytical technology (PAT) and rapid microbiological methods (RMM), and validation of drug product manufacturing process.

This book highlights the challenges facing quality assurance/quality control (QA/QC) in today's biopharmaceutical environment and presents the strategic importance and value generated by QA/QC for their involvement in control of manufacturing. It will put into perspective the need for a graded approach to QA/QC from early clinical trials through market approval. Since the first edition published in 2004, there have been more than 50 new regulatory guidances released by the Food and Drug Administration (FDA), European Medicines Agency (EMA) and ICH that affect the CMC regulatory compliance of biopharmaceuticals; also the application of biosimilars has been developed in Europe and is under development in the USA. The revised update will be broadened to include not only biopharmaceuticals (biotech drugs) but also other biologics (vaccines, cell therapy, plasma-derived proteins, etc.)

Compatibility of Pharmaceutical Products and Contact Materials Dennis Jenke Important safety aspects of compatibility for therapeutic products and their manufacturing systems, delivery devices, and containers Compatibility of Pharmaceutical Products and Contact Materials helps pharmaceutical, toxicology, analytical, and regulatory affairs professionals assess the safety of leachable and extractable chemicals associated with drug product packaging, manufacturing systems, and devices. The most comprehensive resource available, its coverage includes the strategies, tactics, and regulatory requirements for performing safety assessments, along with the means for interpreting results. Structured around a logical framework for an extractables and leachables safety assessment and closely linked to the pharmaceutical product development process, Compatibility of Pharmaceutical Products and Contact Materials directly addresses the fundamental questions of "what activities need to be performed to completely, efficiently, and effectively address the issue of product safety from an extractables and leachables perspective?" and "when do the various required activities need to be performed?" Specifically, the chapters describe: Pertinent regulations and practical ways to meet guidelines Coordinating manufacturing, storage, and delivery systems development and qualification with therapeutic product development Materials characterization and the materials screening process Component and/or system qualification (illustrated by several case studies) Performing validation/migration studies and interpreting and reporting the results Creating a product registration dossier and putting it through regulatory review Product maintenance (Change Control) from an extractables and leachables perspective Likely future developments in extractables and leachables assessment Additionally, the book's appendix provides a database, including CAS registry numbers, chemical formulas and molecular weights of extractable/leachable substances that have been reported in the chemical literature. Detailing the interconnected roles played by analytical chemistry, biological science, toxicology, and regulatory science, Compatibility of Pharmaceutical Products and Contact Materials supplies a much-needed, comprehensive resource to all those in pharmaceutical product or medical device development.

A Global Perspective

Dosage Form Design Parameters

Reviews of Environmental Contamination and Toxicology

Safety Assessments of Extractables and Leachables for Pharmaceutical Products

Geothermal Energy

Renewable Energy and the Environment, Second Edition

Updated and revised throughout. Second Edition explores the chromatographic methods used for the measurement of drugs, impurities, and excipients in pharmaceutical preparations--such as tablets, ointments, and injectables. Contains a 148-page table listing the chromatographic data of over 1300 drugs and related substances--including sample matrix analyzed, sample handling procedures, column packings, mobile phase, mode of detection, and more.

Innovative Technologies and Methods

Bioprocessing of Viral Vaccines

Formulation, Process, Quality and Regulatory Considerations

Controlled Pulmonary Drug Delivery

Development and Approval of Combination Products

Chromatographic Analysis of Pharmaceuticals