Stability Studies In Pharmaceutical Development Catalent

Pharmaceutical Quality by Design: Principles and Applications discusses the Quality by Design (QbD) concept implemented by regulatory agencies to ensure the development of a consistent and high-quality pharmaceutical product that safely provides the maximum therapeutic benefit to patients. The book walks readers through the QbD framework by covering the fundamental principles of QbD, the current regulatory requirements, and the applications of QbD at various stages of pharmaceutical product development, including drug substance and excipient development, analytical development, formulation development, dissolution testing, manufacturing, stability studies, bioequivalence testing, risk and assessment, and clinical trials. Contributions from global leaders in QbD provide specific insight in its application in a diversity of pharmaceutical products, including nanopharmaceuticals, biopharmaceuticals, and vaccines. The inclusion of illustrations, practical examples, and case studies makes this book a useful reference guide to pharmaceutical scientists and researchers who are engaged in the formulation of various delivery systems and the analysis of pharmaceutical product development and drug manufacturing process. Discusses vital QbD precepts and fundamental aspects of QbD implementation in the pharma, biopharma and biotechnology industries Provides helpful illustrations, practical examples and research case studies to explain QbD concepts to

readers Includes contributions from global leaders and experts from academia, industry and regulatory agencies 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. Solid-State Properties of Pharmaceutical Materials --

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The vast majority of drugs are organic molecular entities. A clear understanding of the organic chemistry of drug degradation is essential to maintaining the stability, efficacy, and safety of a drug product throughout its shelf-life. During analytical method development, stability testing, and pharmaceutical manufacturing troubleshooting activities, one of the frequently occurring and usually challenging events would be the identification of drug degradants and understanding of drug degradation mechanisms and pathways. This book is written by a veteran of the pharmaceutical industry who has first-hand experience in drug design and development, drug degradation mechanism studies, analytical development, and manufacturing process troubleshooting and improvement. The author discusses various degradation pathways with an emphasis on the mechanisms of the underlying organic chemistry, which should aid greatly in the efforts of degradant identification, formulation development, analytical development, and manufacturing process improvement. Organic reactions that are significant in drug degradation will first be reviewed and then illustrated by examples of drug degradation reported in the literature. The author brings the book to a close with a final chapter dedicated to the strategy for rapid elucidation of drug degradants with regard to the current regulatory requirements and guidelines. One chapter that should be given special

attention is Chapter 3, Oxidative Degradation. Oxidative degradation is one of the most common degradation pathways but perhaps the most complex one. This chapter employs more than sixty drug degradation case studies with in-depth discussion in regard to their unique degradation pathways. With the increasing regulatory requirements on the quality and safety of pharmaceutical products, in particular with regard to drug impurities and degradants, the book will be an invaluable resource for pharmaceutical and analytical scientists who engage in formulation development, analytical development, stability studies, degradant identification, and support of manufacturing process improvement. In addition, it will also be helpful to scientists engaged in drug discovery and development as well as in drug metabolism studies. Illustrating how stability studies play an important role in drug safety and quality assurance, Statistical Design and Analysis of Stability Studies presents the principles and methodologies in the design and analysis of stability studies. After introducing the basic concepts of stability testing, the book focuses on short-term stability studies and reviews several methods for estimating drug expiration dating periods, it then compares some commonly employed study designs and discusses both fixed and random batch statistical analyses. Following a chapter on the statistical methods for stability analysis under a linear mixed effects model, the book examines stability analyses with discrete responses, multiple components, and frozen drug products. In addition, the author provides statistical methods for dissolution testing and explores current issues and recent developments in

stability studies. To ensure the safety of consumers, professionals in the field must carry out stability studies to determine the reliability of drug products during their expiration period. This book provides the material necessary for you to perform stability designs and analyses in pharmaceutical research and development. Features, Introduces short-term stability studies, such as accelerated testing for obtaining a tentative drug shelf life, Describes various stability designs, such as bracketing and matrixing designs for new drug application stability studies, Focuses on the estimation of drug shelf life based on both fixed batch effects and random batch effects approaches, Summarizes current regulatory practices, including the US Pharmacopeia-National Formulary in vitro dissolution testing and dissolution profile testing, Discusses the recent developments of scale up and postapproval, mean kinetic temperature, and optimal criteria for choosing appropriate stability designs Book jacket.

Dosage Form Design Parameters, Volume I, 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 This book provides comprehensive information of the nanotechnology-based pharmaceutical product development including a diverse range of arenas such as liposomes, nanoparticles, fullerenes, hydrogels, thermally responsive externally activated theranostics (TREAT), hydrogels, microspheres, micro- and nanoemulsions and carbon nanomaterials. It covers the micro- and nanotechnological aspects for pharmaceutical product development with the product development point of view and also covers the industrial aspects, novel technologies, stability studies, validation, safety and toxicity profiles, regulatory perspectives, scale-up technologies and fundamental concept in the development of products. Salient Features: Covers micro- and nanotechnology approaches with current trends with safety and efficacy in product development. Presents an overview of the recent progress of stability testing, reverse engineering, validation and regulatory perspectives as per regulatory requirements. Provides a comprehensive overview of the latest research related to

micro- and nanotechnologies including designing, optimisation, validation and scale-up of micro- and nanotechnologies. Is edited by two well-known researchers by contribution of vivid chapters from renowned scientists across the globe in the field of pharmaceutical sciences. Dr. Neelesh Kumar Mehra is working as an Assistant Professor of Pharmaceutics & Biopharmaceutics at the Department of Pharmaceutics, National Institute of Pharmaceutical Education & Research (NIPER), Hyderabad, India. He received 'TEAM AWARD' for successful commercialisation of an ophthalmic suspension product. He has authored more than 60 peer-reviewed publications in highly reputed international journals and more than 10 book chapter contributions. He has filed patents on manufacturing process and composition to improved therapeutic efficacy for topical delivery. He guided PhD and MS students for their dissertations/research projects. He has received numerous outstanding awards including Young Scientist Award and Team Award for his research output. He recently published one edited book, 'Dendrimers in Nanomedicine: Concept, Theory and Regulatory Perspectives', in CRC Press. Currently, he is editing books on nano drug delivery-based products with Elsevier Pvt Ltd. He has rich research and teaching experience in the formulation and development of complex, innovative ophthalmic and injectable biopharmaceutical products including micro- and nanotechnologies for regulated market. Dr. Arvind Gulbake is working as an Assistant Professor at the Faculty of Pharmacy, School of Pharmaceutical &

Population Health Informatics, at DIT University, Dehradun, India. He has authored more than 40 peer-reviewed publications in highly reputed international journals, four book chapters and a patent contribution. He has received outstanding awards including Young Scientist Award and BRG Travel Award for his research. He is an assistant editor for IJAP. He guided PhD and MS students for their dissertations/research projects. He has successfully completed extramural project funded by SERB, New Delhi, Government of India. He has more than 12 years of research and teaching experience in the formulation and development of nanopharmaceuticals.

Keeping pace with the latest technologies in the field, this guide describes the development of solid oral generic drug products from project initiation to market approval. Focusing on immediate-release and modified-release dosage forms, the book collects in-depth discussions from more than 30 noted specialists on topics such as quality control, experimental formulation, pharmaceutical ingredients, and bioequivalence, and considers key elements in the formulation of generic drug products including the availability of raw materials, chemical purity. It also highlights constraints in generic drug development that differ from the formulation design of a brand name pharmaceutical product.

In the last few decades, the pharmaceutical industry has employed a quality by design (QbD) approach for conventional drug product development to minimize errors in product optimization and validation. Lately, this has been extended to novel pharmaceutical drug products (such as nanocrystalline and nanoamorphous drug products). The

present research emphasizes the design and development of stable nanocrystalline and nanoamorphous formulations of BCS class II and II/IV drugs via a comprehensive QbD approach. This approach was used to identify, optimize, validate and control different critical process parameters and critical formulation parameters of solid nano-formulations. The objectives of this research were to: (1) investigate any correlation between critical process parameters and critical formulation parameters as well as critical quality attributes using a comprehensive QbD approach; (2) investigate the effect of temperature and relative humidity during accelerated and/or long term stability studies; and (3) investigate drug-stabilizer interaction mechanisms. Based on proof-of-concept studies, BCS class II and II/IV drugs with different physicochemical properties were utilized for the successful development of stable and robust nanocrystalline and nanoamorphous formulations. Different top-down and bottom-up manufacturing techniques: wet media milling (nanocrystalline formulations); and sonoprecipitation (nanoamorphous formulations) followed by spray drying were used to prepare the solid nanoformulations. Based on the pre-formulation studies, drug-stabilizer interaction mechanisms were investigated via different solid-state tools (DSC, FTIR and PXRD). The DSC data was used to determine whether drug-stabilizer interactions occurred and the type of interaction was investigated using FTIR. PXRD was used to detect the solid-state form and any polymorphic transition in the drug-stabilizer complexes. Low and intermediate molecular weight polymers, high glass transition (Tg) sugars and anionic surfactants were determined to be the strong stabilizers during processing and storage stability of the solid nanoformulations. A quality by design approach was used to establish a correlation between critical process parameters, critical formulation parameters and critical quality attributes

for the development of the robust solid nanoformulations. Critical process parameters related to manufacturing techniques: wet media milling (milling speed, milling time, pump speed); sonoprecipitation (ultra-sonication speed, time); and spray drying (inlet temperature, aspirator rate, feed flow rate) were investigated. Critical formulation parameters: drug and stabilizer concentrations were investigated. The process speed, time, inlet temperature, flow rates, drug concentrations and stabilizer concentration significantly affected the particle size and total product yield of the solid nanoformulations. Following the DoE studies, validation was performed to ensure reproducibility and robustness of different CQAs (particle size, total product yield, drug loading, moisture content and zeta potential) of solid nanoformulations prepared using the optimized and predicted process and formulation parameters. Stability studies were performed at three different conditions: 4°C, 25°C/60% RH and 40°C/75% RH for different time-points (1, 3, 6 and 12 month/s) to investigate the effect of temperature and relative humidity on the nanoamorphous and nanocrystalline formulations. Stability studies revealed the following trend: 4°C (most stable) > 25°C/60% RH > 40°C/75% RH (least stable) for the optimized spray-dried nanocrystalline and nanoamorphous formulations in terms of physicochemical attributes, crystallinity and in vitro dissolution testing. An array of orthogonal solid-state tools (DSC, ATR-FTIR, PLM, PXRD and AFM) were utilized to characterize the solid-state form (crystalline, amorphous, semi-crystalline and semi-amorphous) and polymorphic transitions in the freshly prepared solid nanoformulations and those stored at different stability conditions. Particle size distribution and moisture content analysis were performed via Zetasizer (ZS90) and Karl fisher titration, respectively. RP-HPLC was used to detect drug loading in the solid nanoformulations. The solid

nano-formulations prepared via the comprehensive QbD approach resulted in a remarkably high total product yield (~70-80% w/w) with small, uniform and homogenous particle size (200-300 nm, 0.05-0.2 PDI). In vitro dissolution testing were performed to investigate the effect of pH, solid-state form, particle size, temperature and relative humidity on drug release from the solid nano-formulations. USP apparatus I and II were utilized to study and differentiate the drug release from the nanoamorphous and nanocrystalline formulations based on their solid-state form and particle size. Drug release from the solid nanoformulations followed a particle size dependent dissolution trend. Nanoamorphous and nanocrystalline formulations showed a high dissolution rate/kinetic solubility compared to the macro-sized formulations. To sum up, the comprehensive QbD approach performed in the present research delineates an important and time-saving strategy to develop successful, robust and stable solid nanoamorphous and nanocrystalline formulations with the desired physicochemical attributes/CQAs, solid-state form and in vitro and/or in vivo performance.

The US Food and Drug Administration's Report to the Nation in 2004 and 2005 indicated that one of the top reasons for drug recall was that stability data did not support existing expiration dates. Pharmaceutical companies conduct stability studies to characterize the degradation of drug products and to estimate drug shelf life. Illustrating how stability studies play an important role in drug safety and quality assurance, Statistical Design and Analysis of Stability Studies presents the principles and methodologies in the design and analysis of stability studies. After introducing the basic concepts of stability testing, the book focuses on short-term stability studies and reviews several methods for estimating drug expiration dating periods. It then compares some commonly employed study designs and discusses both fixed and

random batch statistical analyses. Following a chapter on the statistical methods for stability analysis under a linear mixed effects model, the book examines stability analyses with discrete responses, multiple components, and frozen drug products. In addition, the author provides statistical methods for dissolution testing and explores current issues and recent developments in stability studies. To ensure the safety of consumers, professionals in the field must carry out stability studies to determine the reliability of drug products during their expiration period. This book provides the material necessary for you to perform stability designs and analyses in pharmaceutical research and development.

The second edition of Pharmaceutical Stress Testing: Predicting Drug Degradation provides a practical and scientific guide to designing, executing and interpreting stress testing studies for drug substance and drug product. This is the only guide available to tackle this subject in-depth. The Second Edition expands coverage from chemical stability into the physical aspects of stress testing, and incorporates the concept of Quality by Design into the stress testing construct / framework. It has been revised and expanded to include chapters on large molecules, such as proteins and antibodies, and it outlines the changes in stress testing that have emerged in recent years. Key features include: A renowned Editorial team and contributions from all major drug companies, reflecting a wealth of experience. 10 new chapters, including Stress Testing and its relationship to the assessment of potential genotoxic degradants, combination drug therapies, proteins, oligonucleotides, physical changes and alternative dosage forms such as liposomal formulations Updated methodologies for predicting drug stability and degradation pathways Best practice models to follow An expanded Frequently Asked Questions section This is an essential reference book for Pharmaceutical Scientists and

those working in Quality Assurance and Drug Development (analytical sciences, formulations, chemical process, project management).

This Second Edition is an essential guide to preparing for FDA pre-approval inspections-taking into account current trends in FDA expectations and inspection activities, such as the GMPs of the 21st Century, quality systems-based approach to inspections, risk-based inspections, quality by design, process analytical technology, design space, etc. Th

Examining the implications and practical implementation of multi-disciplinary International Conference on Harmonization (ICH) topics, this book gives an integrated view of how the guidelines inform drug development strategic planning and decision-making. • Addresses a consistent need for interpretation, training, and implementation examples of ICH guidelines via case studies • Offers a primary reference point for practitioners addressing the dual challenge of interpretation and practical implementation of ICH guidelines • Uses case studies to help readers understand and apply ICH guidelines • Provides valuable insights into guidelines development, with chapters by authors involved in generating or with experience implementing the guidelines • Includes coverage of stability testing, analytical method validation, impurities, biotechnology drugs and products, and good manufacturing practice (GMP)

How to Develop Robust Solid Oral Dosage Forms from Conception to Post-Approval uses a practical and hands-on approach to cover the development process of solid oral dosage forms in one single source. The book details all of the necessary steps from formulation through the post-approval phase and contains industry case studies, real world advice, and troubleshooting tips. By merging the latest scientific information with practical instructions, this book provides pharmaceutical scientists in formulation research and

development with a concrete look at the key aspects in the development of solid oral dosage forms. Focuses on important topics, such as robustness, bioavailability, formulation design, continuous processing, stability tests, modified release dosage forms, international guidelines, process scale-up, and much more Part of the Expertise in Pharmaceutical Process Technology series edited by Michael Levin Discusses common, real-world problems and offers both theoretical and practical solutions to these everyday issues

Hot melt extrusion (HME) was evaluated as a processing technology for the manufacture of immediate as well as controlled release formulations for oral delivery of two model compounds. For immediate release applications lower molecular weight grades of Hydroxypropyl cellulose polymers, EF and ELF, were utilized as carrier matrices to form solid solutions of a poorly soluble compound, Ketoprofen (KPR). Thermal characterization techniques were used to confirm thermal stability, miscibility and setting up processing conditions for extrusion. Extruded matrices were pelletized to be filled into pellets or further milled and compressed into tablets. Pellets exhibited a carrier dependent release with ELF matrices releasing the drug at a faster rate than EF. Addition of Mannitol further enhanced the release with H4 formulation constituting KPR:MNT:ELF in a 1:1:1, releasing 88.5±1.5% drug in 1hr. Milled H4 matrices compressed into tablets exhibited rapid release with 90% drug release occurring in 15 min, similar to a marketed capsule formulation of the same dose. Stability studies performed utilizing mDSC, XRD, and SEM studies confirmed the physical stability of the drug, post storage at 25°C/60%RH and 40°C/75%RH. Extrusion process also imparts significant physical transformations to the component systems which find utility in tabletting applications. Extruded matrices were compressed

into tablets and tabletability profiles generated. Simultaneously tablet hardness evaluation was performed using conventional characterization techniques as well as using a texture analyzer. HME tablets were more compressible and plastic nature in comparison to un-extruded tablets. ELF polymers exhibited better tabletting properties than EF. The ability of HME to homogenously mix polymers and drug was utilized to manufacture custom controlled release film formulations of a water soluble model drug. Polymer blends comprising Klucel(TM) EF (HPC), Eudragit® RSPO and POLYOX® N10 (PEO) were evaluated. Effect of polymer particle size on release was evaluated using in vitro release testing and Near Infrared chemical imaging techniques. Manufactured films exhibited controlled release for ~24 hrs with HPC exhibiting a more pronounced effect than RSPO. A correlation of 90% was obtained between polymer concentration on fifty percent and eighty percent drug release, T50% and T0% respectively, suggesting its applicability to bring about tailored release profiles. Extruded films remained physically and chemically stable for a period of three months at 40°C/75%RH storage conditions. The ability of Cyclodextrin derivatives to enhance solubility of a poorly soluble drug, Clotrimazole was evaluated. Phase solubility studies were performed to assess the type of association between CT and 2-hydroxypropyl ß Cyclodextrin. An AL type curve was obtained suggesting a 1:1 association, which was further confirmed utilizing DSC, FTIR, XRD, NMR and SEM analysis. Gels formulated from complex exhibited a complete release in 92 hrs whereas pure CT gels exhibited only 60% release in the same amount of time. Similar results were obtained with antifungal testing, with complexed gels having a more pronounced fungistatic action.

This book describes the role modern pharmaceutical analysis plays in the development of new drugs. Detailed information

is provided as to how the quality of drug products is assured from the point of discovery until the patient uses the drug. Coverage includes state-of-the-art topics such as analytics for combinatorial chemistry and high-throughput screening, formulation development, stability studies, international regulatory aspects and documentation, and future technologies that are likely to impact the field. Emphasis is placed on current, easy-to-follow methods that readers can apply in their laboratories. No book has effectively replaced the very popular text, Pharmaceutical Analysis, that was edited in the 1960s by Tak Higuchi. This book will fill that gap with an up-to-date treatment that is both handy and authoritative.

A comprehensive introduction for scientists engaged in new drug development, analysis, and approvals Each year the pharmaceutical industry worldwide recruits thousands of recent science graduates—especially chemistry, analytical chemistry, pharmacy, and pharmaceutical majors—into its ranks. However, because of their limited background in pharmaceutical analysis most of those new recruits find making the transition from academia to industry very difficult. Designed to assist both recent graduates, as well as experienced chemists or scientists with limited regulatory, compendial or pharmaceutical analysis background, make that transition, Pharmaceutical Analysis for Small Molecules is a concise, yet comprehensive introduction to the drug development process and analysis of chemically synthesized, small molecule drugs. It features contributions by distinguished experts in the field, including editor and author, Dr. Behnam Davani, an analytical chemist with decades of technical management and teaching experience in compendial, regulatory, and industry. This book provides an introduction to pharmaceutical analysis for small molecules (non-biologics) using commonly used techniques for drug

characterization and performance tests. The driving force for industry to perform pharmaceutical analyses is submission of such data and supporting documents to regulatory bodies for drug approval in order to market their products. In addition, related required supporting studies including good laboratory/documentation practices including analytical instrument qualification are highlighted in this book. Topics covered include: Drug Approval Process and Regulatory Requirements (private standards) Pharmacopeias and Compendial Approval Process (public standards) Common methods in pharmaceutical analysis (typically compendial) Common Calculations for assays and impurities and other specific tests Analytical Method Validation, Verification, Transfer Specifications including how to handle out of specification (OOS) and out of trend (OOT) Impurities including organic, inorganic, residual solvents and elemental impurities Good Documentation Practices for regulatory environment Management of Analytical Laboratories Analytical Instrument Qualifications including IQ, OQ, PQ and VQ Due to global nature of pharmaceutical industry, other topics on both regulatory (ICH) and Compendial harmonization are also highlighted. Pharmaceutical Analysis for Small Molecules is a valuable working resource for scientists directly or indirectly involved with the drug development process, including analytical chemists, pharmaceutical scientists, pharmacists, and quality control/quality assurance professionals. It also is an excellent text/reference for graduate students in analytical chemistry, pharmacy, pharmaceutical and regulatory sciences.

This book comprehensively reviews drug stability and chemical kinetics: how external factors can influence the stability of drugs, and the reaction rates that trigger these effects. Explaining the important theoretical concepts of drug stability and chemical kinetics, and providing numerous

examples in the form of illustrations, tables and calculations, the book helps readers gain a better understanding of the rates of reactions, order of reactions, types of degradation and how to prevent it, as well as types of stability studies. It also offers insights into the importance of the rate at which the drug is degraded and/or decomposed under various external and internal conditions, including temperature, pH, humidity and light. This book is intended for researchers, PhD students and scientists working in the field of pharmacy, pharmacology, pharmaceutical chemistry, medicinal chemistry and biopharmaceutics.

This detailed volume collects numerous methods and protocols related to different aspects of stability programs that are followed in pharmaceutical development laboratories. Implementation of a successful stability program, vital in preventing product failures and recalls, requires critical and logical thinking that goes beyond the regular documented protocols and methods, so the experiences of the book's internationally-based expert contributors fill the chapters with practical guidance. As a volume in the Methods in Pharmacology and Toxicology series, this book presents the kind of real-world advice that is essential for advancing laboratory research. Authoritative and thorough, Methods for Stability Testing of Pharmaceuticals serves as a valuable addition to the existing armamentarium of resources available to stability testing personnel in research and industry.

Reversed-phase high-performance liquid chromatography (RP-HPLC) has become the most widely used method for pharmaceutical analysis, as it ensures accuracy, specificity and reproducibility for the quantification of drugs, while avoiding interference from any of the excipients that are normally present in pharmaceutical dosage forms. This book presents a simple methodology for developing stability-indicating methods and offers a 'how-to guide' to creating

novel stability-indicating methods using liquid chromatography. It provides the detailed information needed to devise a stability-indicating method for drug substances and drug products that comply with international regulatory guidelines. As such, it is a must-read for anyone engaged in analytical and bioanalytical chemistry: professionals at reference, test, and control laboratories; students and academics at research laboratories, and scientists working for chemical, pharmaceutical, and biotechnology companies.
The overall purpose of this contract was to perform chemical/physical analyses on bulk pharmaceutical substances and formulated drug products of interest to the USAMRMC Drug Development Program for parasitic and infectious diseases, chemical and biological defense, etc. Specific objectives were to design, develop, validate, and apply methods to determine chemical and physical characteristics on bulk drug and drug products. For the entire contract period, 1 August 1991 to 30 June 1997, 125 samples of bulk drugs and dosage formulations were analyzed for identity, purity or potency; 133 samples were studied for stability and solubility. Four chiral separation methods were developed and validated, and 11 other chemical assay methods were validated. Special projects included the development and application of assays for determining protein content, residual solvents, and other relevant components in microsphere vaccine preparations. A second special project was the development and application of an assay for determining bis(chloromethyl) ether in HI-6 bulk drugs. Posters were presented in the 1993 and 1996 Medical Defense Bioscience Reviews. One publication appeared in press and a second has been accepted for publication.
Accelerated Predictive Stability (APS): Fundamentals and Pharmaceutical Industry Practices provides coverage of both the fundamental principles and pharmaceutical industry

applications of the APS approach. Fundamental chapters explain the scientific basis of the APS approach, while case study chapters from many innovative pharmaceutical companies provide a thorough overview of the current status of APS applications in the pharmaceutical industry. In addition, up-to-date experiences in utilizing APS data for regulatory submissions in many regions and countries highlight the potential of APS in support of registration stability testing for certain regulatory submissions. This book provides high level strategies for the successful implementation of APS in a pharmaceutical company. It offers scientists and regulators a comprehensive resource on how the pharmaceutical industry can enhance their understanding of a product's stability and predict drug expiry more accurately and quickly. Provides a comprehensive, one-stop-shop resource for accelerated predictive stability (APS) Presents the scientific basis of different APS models Includes the applications and utilities of APS that are demonstrated through numerous case studies Covers up-to-date regulatory experience

This one-stop reference systematically covers key aspects in early drug development that are directly relevant to the discovery phase and are required for first-in-human studies. Its broad scope brings together critical knowledge from many disciplines, ranging from process technology to pharmacology to intellectual property issues. After introducing the overall early development workflow, the critical steps of early drug development are described in a sequential and enabling order: the availability of the drug substance and that of the drug product, the prediction of pharmacokinetics and -dynamics, as well as that of drug safety. The final section focuses on intellectual property aspects during early clinical development. The emphasis throughout is on recent case studies to exemplify salient points, resulting in an abundance

of practice-oriented information that is usually not available from other sources. Aimed at medicinal chemists in industry as well as academia, this invaluable reference enables readers to understand and navigate the challenges in developing clinical candidate molecules that can be successfully used in phase one clinical trials.

This handbook is the first to cover all aspects of stability testing in pharmaceutical development. Written by a group of international experts, the book presents a scientific understanding of regulations and balances methodologies and best practices.

In this era of increased pharmaceutical industry competition, success for generic drug companies is dependent on their ability to manufacture therapeutic-equivalent drug products in an economical and timely manner, while also being cognizant of patent infringement and other legal and regulatory concerns. Generic Drug Product Development: Solid Oral Dosage Forms, Second Edition presents in-depth discussions from more than 30 noted specialists describing the development of generic drug products—from the raw materials to the development of a therapeutic-equivalent drug product to regulatory approval. Major topics discussed include: Active pharmaceutical ingredients Experimental formulation development, including a new section on Quality by Design (QbD) Scale-up Commercial product formulation Quality control and bioequivalence Drug product performance ANDA regulatory process Post-approval changes Post-

marketing surveillance Legislative and patent challenges This second edition also contains a new chapter on the relationship between the FDA and the United States Pharmacopeia and in Chapter 4, using specific examples, the application of Quality by Design (QbD) during formulation development is examined.The book is a thorough guide to the development of solid oral generic dosage formulations. This textbook is ideal for the pharmaceutical industry, graduate programs in pharmaceutical sciences, and health professionals working in the area of generic drug development.

Stability testing is a critical piece of a drug development program that assesses a potential drug?s shelf life and required storage conditions. Pharmaceutical Stability Testing: A Practical Guide provides a comprehensive guide to the approaches and regulations covering stability testing. The book helps pharmaceutical personnel organize and conduct drug stability tests by describing the many different aspects of drug stability programs, the different types of study that are required, and the approaches pharmaceutical companies apply to ensure that their critical stability programs are secure.

An informative look at the intricacies of today's drug development process Once a discovery organization has identified a potential new drug candidate, it is the daunting task of synthetic organic chemists to

identify the chemical process suitable for preparation of this compound in a highly regulated environment. Only through a multi-layered chemical process that takes into account such factors as safety, environmental considerations, freedom to operate and cost-effectiveness can researchers begin to refine the drug in terms of quality and yield. This book covers both recent advances in the design and synthesis of new drugs, as well as the myriad other issues facing a new drug candidate as it moves through the development process. Utilizing recent case studies, the authors provide valuable insights into the complexities of the process, from designing new synthetic methodologies and applying new automated techniques for finding optimal reaction conditions to selecting the final drug form and formulation. Both novice and active researchers will appreciate the inclusion of chapters on such diverse topics as: * Cross-coupling methods * Asymmetric synthesis * Automation * Chemical Engineering * Application of radioisotopes * Final form selection * Formulations * Intellectual property A wealth of real-world examples and contributions from leading process scientists, engineers, and related professionals make this book a valuable addition to the scientific literature.

Monoclonal antibodies (MAbs) are currently the major class of protein bio therapeutic being developed by biotechnology and pharmaceutical

companies. Monoclonal Antibodies discusses the challenges and issues revolving around development of a monoclonal antibody produced by recombinant DNA technology into a therapeutic agent.This book covers downstream processing which includes design of processes to manufacture the formulation, formulation design, fill and finish into closure systems and routes of administration. The characterization of the final drug product is covered where the use of biophysical methods combined with genetic engineering is used to understand the solution properties of the formulation. The latter has become very important since many indications such as arthritis and asthma require the development of formulations for subcutaneous delivery (SC). The development of formulations for IV delivery is also important and comes with a different set of challenges. The challenges and strategies that can overcome these limitations are discussed in this book, starting with an introduction to these issues, followed by chapters detailing strategies to deal with them. Subsequent chapters explore the processing and storage of mAbs, development of delivery device technologies and conclude with a chapter on the future of mAbs in therapeutic remedies. Discusses the challenges to develop MAbs for intravenous (IV) and subcutaneous delivery (SC) Presents strategies to meet the challenges in development of MAbs for SC and IV administration

Discusses the use of biophysical analytical tools coupled with MAb engineering to understand what governs MAb properties at high concentration
Drug development is an iterative process. The recent publications of regulatory guidelines further entail a lifecycle approach. Blending data from disparate sources, the Bayesian approach provides a flexible framework for drug development. Despite its advantages, the uptake of Bayesian methodologies is lagging behind in the field of pharmaceutical development. Written specifically for pharmaceutical practitioners, Bayesian Analysis with R for Drug Development: Concepts, Algorithms, and Case Studies, describes a wide range of Bayesian applications to problems throughout pre-clinical, clinical, and Chemistry, Manufacturing, and Control (CMC) development. Authored by two seasoned statisticians in the pharmaceutical industry, the book provides detailed Bayesian solutions to a broad array of pharmaceutical problems. Features Provides a single source of information on Bayesian statistics for drug development Covers a wide spectrum of pre-clinical, clinical, and CMC topics Demonstrates proper Bayesian applications using real-life examples Includes easy-to-follow R code with Bayesian Markov Chain Monte Carlo performed in both JAGS and Stan Bayesian software platforms Offers sufficient background for each problem and detailed description of solutions suitable for

practitioners with limited Bayesian knowledge Harry Yang, Ph.D., is Senior Director and Head of Statistical Sciences at AstraZeneca. He has 24 years of experience across all aspects of drug research and development and extensive global regulatory experiences. He has published 6 statistical books, 15 book chapters, and over 90 peer-reviewed papers on diverse scientific and statistical subjects, including 15 joint statistical works with Dr. Novick. He is a frequent invited speaker at national and international conferences. He also developed statistical courses and conducted training at the FDA and USP as well as Peking University. Steven Novick, Ph.D., is Director of Statistical Sciences at AstraZeneca. He has extensively contributed statistical methods to the biopharmaceutical literature. Novick is a skilled Bayesian computer programmer and is frequently invited to speak at conferences, having developed and taught courses in several areas, including drug-combination analysis and Bayesian methods in clinical areas. Novick served on IPAC-RS and has chaired several national statistical conferences.

This text lists the necessary steps for meeting compliance requirements during the drug development process. It presents comprehensive approaches for validating analytical methods for pharmaceutical applications.

This book contains an overview of the scientific and

regulatory requirements for stability testing including the draft of the harmonised guideline for the stability testing in the EC, Japan and the USA. Therefore it will be possible to carry out stability testing in the most efficient way. This book may be of interest to scientists in the field of drug development in pharmaceutical industries, responsible for drug registration, responsible for quality control, and at universities.

Written specifically for biotechnology scientists, engineers, and quality professionals, this book describes and demonstrates the proper application of statistical methods throughout Chemistry, Manufacturing, and Controls (CMC). Filled with case studies, examples, and easy-to-follow explanations of how to perform statistics in modern software, it is the first book on CMC statistics written primarily for practitioners. While statisticians will also benefit from this book, it is written particularly for industry professionals who don't have access to a CMC statistician or who want to be more independent in the design and analysis of their experiments. Provides an introduction to the statistical concepts important in the biotechnology industry Focuses on concepts with theoretical details kept to a minimum Includes lots of real examples and case studies to illustrate the methods Uses JMP software for implementation of the methods Offers a text suitable for scientists in the industry with some quantitative

training Written and edited by seasoned veterans of the biotechnology industry, this book will prove useful to a wide variety of biotechnology professionals. The book brings together individual chapters that showcase the use of statistics in the most salient areas of CMC.

Handbook of Stability Testing in Pharmaceutical DevelopmentRegulations, Methodologies, and Best PracticesSpringer Science & Business Media

Teaches future and current drug developers the latest innovations in drug formulation design and optimization This highly accessible, practice-oriented book examines current approaches in the development of drug formulations for preclinical and clinical studies, including the use of functional excipients to enhance solubility and stability. It covers oral, intravenous, topical, and parenteral administration routes. The book also discusses safety aspects of drugs and excipients, as well as regulatory issues relevant to formulation. Innovative Dosage Forms: Design and Development at Early Stage starts with a look at the impact of the polymorphic form of drugs on the preformulation and formulation development. It then offers readers reliable strategies for the formulation development of poorly soluble drugs. The book also studies the role of reactive impurities from the excipients on the formulation shelf life; preclinical formulation assessment of new chemical entities; and regulatory aspects for formulation design. Other chapters cover innovative formulations for special indications, including oncology injectables, delayed release and

depot formulations; accessing pharmacokinetics of various dosage forms; physical characterization techniques to assess amorphous nature; novel formulations for protein oral dosage; and more. -Provides information that is essential for the drug development effort -Presents the latest advances in the field and describes in detail innovative formulations, such as nanosuspensions, micelles, and cocrystals -Describes current approaches in early pre-formulation to achieve the best in vivo results -Addresses regulatory and safety aspects, which are key considerations for pharmaceutical companies -Includes case studies from recent drug development programs to illustrate the practical challenges of preformulation design Innovative Dosage Forms: Design and Development at Early Stage provides valuable benefits to interdisciplinary drug discovery teams working in industry and academia and will appeal to medicinal chemists, pharmaceutical chemists, and pharmacologists.

Master's Thesis from the year 2011 in the subject Medicine - Pharmacology, grade: 8.0, , course: B.Pharm.,M.Pharm, language: English, abstract: A reverse phase high performance liquid chromatographic method (HPLC) has been developed for the method development validation of Carvedilol in bulk and pharmaceutical formulation by using YMC PACK PRO 4.6 X 150 mm (5?m Particle size). The mobile phase was Buffer: Acetonitrile: (70:30) and pH was adjusted to 2 pumped at a flow rate of 1 ml/min and the eluents were monitored at 320nm. Linearity was obtained in the concentration range of 10-90 ?g/ml. The retention time of

Carvedilol was found to be 3.2 minute. The method was validated for specificity, accuracy, precision, linearity, and limit of detection, limit of quantification, robustness and solubility stability. LOD and LOQ were found to be 0.001 ?g/ml and 0.011?g/ml respectively. The method was statistically validated and RSD was found to be less than 2% indicating high degree of accuracy and precision of the proposed HPLC method. Stability study report revealed that the drug is susceptible for acidic, alkaline, oxidative, photolytic and UV degradation. The drug is stable to thermal degradation. More over the degradants were well separated from its API. Due to its simplicity, rapidness, high precision and accuracy, the proposed HPLC method may be used for determining Carvedilol in bulk drug samples or in pharmaceutical dosage forms.

High pressure liquid chromatography–frequently called high performance liquid chromatography (HPLC or, LC) is the premier analytical technique in pharmaceutical analysis and is predominantly used in the pharmaceutical industry. Written by selected experts in their respective fields, the Handbook of Pharmaceutical Analysis by HPLC Volume 6, provides a complete yet concise reference guide for utilizing the versatility of HPLC in drug development and quality control. Highlighting novel approaches in HPLC and the latest developments in hyphenated techniques, the book captures the essence of major pharmaceutical applications (assays, stability testing, impurity testing, dissolution testing, cleaning validation, high-throughput screening). A complete reference guide to HPLC

Describes best practices in HPLC and offers 'tricks of the trade' in HPLC operation and method development Reviews key HPLC pharmaceutical applications and highlights currents trends in HPLC ancillary techniques, sample preparations, and data handling

Providing the guidance needed for formulation, handling, and quality control of photolabile drugs, Photostability of Drugs and Drug Formulations, Second Edition explores the significance of new information on drug photoreactivity in a pharmaceutical context. Completely revised and updated, with chapter authors drawn from an international panel of experts, the book supplies the background necessary for planning standardized photochemical stability studies as a part of drug development and formulation work. It contains comprehensive coverage of the physical and chemical aspects of drug photoreactivity, formulation, stability testing, and drug design/discovery in one resource. The contents have been reorganized to focus on the standardization of photostability testing of drug substances and products, in vitro photoreactivity screening of drugs, and various aspects of the formulation of photoreactive substances. The information on in vitro screening of drug photoreactivity is of great relevance for scientists who are developing and validating a set of testing protocols to address photosafety. Discussing kinetic and chemical aspects of drug photodecomposition as well as the practical problems frequently encountered in photochemical stability testing, this book helps you design a test protocol and interpret the results. Features Assists non-

experts in this field design a test protocol and interpret the results Covers in vitro and in vivo aspects of interactions between drugs and light Explores the kinetic and chemical aspects of drug photodecomposition Discusses the problems frequently encountered in photochemical stability testing Provides guidance on how to address photosafety assessments and labeling requirements of potentially photoreactive drugs Highlights the practical implications of drug photodecomposition from a pharmaceutical viewpoint Offers specific guidance in photostability testing and screening of drug photoreactivity

Focusing on the application of physical pharmacy, drug design, and drug regulations as they relate to produce effective dosage forms for drug delivery, Integrated Pharmaceutics provides a comprehensive picture of pharmaceutical product design, describing the science and art behind the concepts of dosage form development. Combining physical pharmacy, product design, and regulatory affairs issues in a single book, the authors address topics governing drug regulations of United States, European, and Japanese agencies and detail new regulatory guidelines, including quality by design, design space analysis, and blend sample uniformity.

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.

Master's Thesis from the year 2011 in the subject Medicine - Pharmacology, grade: 8.0, course: B.Pharm., M.Pharm, language: English, comment: This thesis was submitted in the year 2011 when I (Kishanta Kumar Pradhan) was lecturer at Royal College of Pharmacy and Helath Sciences, Berhampur, Odisha, India. The Project conducted under my guidance along with a person from industry. There after I have moved to Birla Institute of Technology, Mesra, Ranchi on 2012. I have been

awarded with GOLD MEDAL being topper amongst all M.Pharm students by Governer of Odisha in the year 2008. I have also qualified GATE-2005. I have 20 publications in various national and international journals., abstract: A reverse phase high performance liquid chromatographic method (HPLC) has been developed for the method development validation of Carvedilol in bulk and pharmaceutical formulation by using YMC PACK PRO 4.6 X 150 mm (5um Particle size). The mobile phase was Buffer: Acetonitrile: (70:30) and pH was adjusted to 2 pumped at a flow rate of 1 ml/min and the eluents were monitored at 320nm. Linearity was obtained in the concentration range of 10-90 g/ml. The retention time of Carvedilol was found to be 3.2 minute. The method was validated for specificity, accuracy, precision, linearity, and limit of detection, limit of quantification, robustness and solubility stability. LOD and LOQ were found to be 0.001 g/ml and 0.011 g/ml respectively. The method was statistically validated and RSD was found to be less than 2% indicating high degree of accuracy and precision of the proposed HPLC method. Stability study report revealed that the drug is susceptible for acidic, alkaline, oxidative, photolytic and UV degradation. The drug is stable to thermal degradation. More over the degradants were well separated from its API. Due to its simplicity, rapidness, high precision and accuracy, the proposed HPLC method may be used for determining Carvedilol in bulk drug samples or in pharmaceutical dosage fo"