Bioequivalence And Pharmacokinetic Evaluation Of Ijcpr

Olesja Rissling analyzes the potential interaction of mycophenolic acid (MPA) and pantoprazole. MPA is used as an immunosuppressive drug to prevent acute organ rejections after organ transplantation. Pantoprazole, known to interact with the bioavailability of drugs, is used to prevent upper gastrointestinal disorders. The author performed a clinical pharmacokinetic study in renal transplant patients to evaluate a potential interaction of MPA and pantoprazole. The bioavailability

and the maximum concentration of MPA were determined with or without pantoprazole intake. An influence on the immunosuppressive effect was evaluated by measuring the target enzyme activity. Overall, no significant change in the bioavailability or the maximum concentration was found. Similar results were obtained for the target enzyme activity after pantoprazole intake with MPA. The results suggest that the interaction of pantoprazole with MPA does not compromise the immunosuppressive effect to a clinically meaningful extent.
"Provides a comprehensive summary of the continuously growing literature and research activities on the regulatory

requirements, scientific and practical issues, and statistical methodology of the design and analysis of bioavailability and bioequivalence studies. Includes several new chapters."
Generic Drug Product Development: Specialty Dosage Forms explores the issues related to providing evidence of pharmaceutical equivalence and bioequivalence for specialty drug products. It describes various scientific approaches and regulatory requirements for manufacturers who need to demonstrate the therapeutic equivalence of generic specialty drug products to brand name alternatives. The contributors discuss measurement of drug product quality and performance,

as well as the regulatory and scientific requirements of topical, nasal and inhalation, and transdermal drug delivery products, along with generic biologics and modified release parenteral drug products. The book is essential reading for specialists and researchers in pharmaceutical drug development, regulation, manufacturing, and others in the pharmaceutical sciences. Knowledge of pharmacokinetics is critical to understanding the absorption, distribution, metabolism, and excretion of drugs. It is therefore vital to those engaged in the discovery, development, and preclinical and clinical evaluation of drugs, as well as practitioners involved in the clinical use of drugs. Using different approaches

accessible to
Pharmaceutical Theory and Practice
Controlled Pulmonary Drug Delivery
Specialty Dosage Forms

Pharmacokinetic Evaluation and Modeling of Clinically Significant Drug Metabolites

This open access book presents the history, pharmacokinetics and pharmacodynamics of levothyroxine, discussing its role in the thyroid pathophysiology of patients of various ages and during pregnancy. It also describes the influence of levothyroxine on heart, bone and in cancer. When it was first synthesized in 1949, levothyroxine represented a significant advance in the treatment

of hypothyroidism, providing a safe and effective treatment option for millions of hypothyroid patients around the globe. This synthetic form of thyroxine is now one of the most prescribed drugs in the world. Levothyroxine was first introduced by Merck KGaA,Darmstadt, Germany, in 1972, and since then the company has remained actively engaged in research on this mainstay of hypothyroidism treatment. This book is intended for healthcare professionals.

Pharmaceutical formulations have evolved from simple and traditional systems to more modern and complex novel dosage forms. Formulation development is a

tedious process and requires an enormous amount of effort from many different people. Developing a stable novel dosage form and further targeting it to the desired site inside the body has always been a challenge. The purpose of this book is to bring together scholarly articles that highlight recent developments and trends in pharmaceutical formulation science. Each article has been written by authors specializing in the subject area and hailing from top institutions around the world. The book has been written in a systematic and lucid style explaining all basic concepts and fundamentals in a very simple way. This book aims to serve the need of all

individuals involved at any level in the pharmaceutical dosage form development. I sincerely hope that the book will be liked by inquisitive students and learned colleagues.
The state of the art in Biopharmaceutics, Pharmacokinetics, and Pharmacodynamics Modeling is presented in this new second edition book. It shows how advanced physical and mathematical methods can expand classical models in order to cover heterogeneous drug-biological processes and therapeutic effects in the body. The book is divided into four parts; the first deals with the fundamental principles of fractals, diffusion and

nonlinear dynamics; the second with drug dissolution, release, and absorption; the third with epirical, compartmental, and stochastic pharmacokinetic models, with two new chapters, one on fractional pharmacokinetics and one on bioequivalence; and the fourth mainly with classical and nonclassical aspects of pharmacodynamics. The classical models that have relevance and application to these sciences are also considered throughout. This second edition has new information on reaction limited models of dissolution, non binary biopharmaceutic classification system, time varying models, and

interface models. Many examples are used to illustrate the intrinsic complexity of drug administration related phenomena in the human, justifying the use of advanced modeling methods. This book will appeal to graduate students and researchers in pharmacology, pharmaceutical sciences, bioengineering, and physiology. Reviews of the first edition: "This book presents a novel modelling approach to biopharmaceutics, pharmacokinetics and pharmacodynamic phenomena. This state-of-the-art volume will be helpful to students and researchers in pharmacology, bioengineering, and physiology. This book is a must

for pharmaceutical researchers to keep up with recent developments in this field." (P. R. Parthasarathy, Zentralblatt MATH, Vol. 1103 (5), 2007) "These authors are the unique (or sole) contributors in this area that are working on these questions and bring a special expertise to the field that is now being recognized as essential to understanding biological system and kinetic/dynamic characteristics in drug development...This text is an essential primer for those who would envision the incorporation of heterogeneous approaches to systems where homogeneous approaches are not sufficient to describe the system." (Robert R.

Bies, Journal of Clinical Pharmacology, Vol. 46, 2006)

This book represents the invited presentations and some of the posters presented at the conference entitled "In Vitro-In Vivo Relationship (IVIVR) Workshop" held in Sep tember, 1996. The workshop was organized by the IVIVR Cooperative Working Group which has drawn together scientists from a number of organizations and institutions, both academic and industrial. In addition to Elan Corporation, which is a drug delivery com pany specializing in the development of ER (Extended Release) dosage forms, the IVIVR Cooperative Working Group

consists of collaborators from the University of Maryland at Baltimore, University College Dublin, Trinity College Dublin, and the University of Not tingham in the UK. The principal collaborators are: Dr. Jackie Butler, Elan Corporation Prof. Owen Corrigan, Trinity College Dublin Dr. lain Cumming, Elan Corporation Dr. John Devane, Elan Corporation Dr. Adrian Dunne, University College Dublin Dr. Stuart Madden, Elan Corporation Dr. Colin Melia, University of Nottingham Mr. Tom O'Hara, Elan Corporation Dr. Deborah Piscitelli, University of Maryland at Baltimore Dr. Araz Raoof, Elan Corporation Mr. Paul Stark, Elan Corporation

Dr. David Young, University of Maryland at Baltimore The purpose of the workshop was to discuss new concepts and methods in the devel opment of in vitro-in vivo relationships for ER products. The original idea went back ap proximately 15 months prior to the workshop itself. For some time, the principal collaborators had been working together on various aspects of dosage form development.

Basic Pharmacokinetics

Handbook of Bioequivalence Testing, Second Edition

Commerce Business Daily

The bioequivalence of oral clarithromycin formulations. Pharmacokinetic and statistic

evaluation

Modeling in Biopharmaceutics, Pharmacokinetics and Pharmacodynamics

The breadth of the pharmaceutical medicine can be daunting, but this book is designed to navigate a path through the speciality. Providing a broad overview of all topics relevant to the discipline of pharmaceutical medicine, it gives you the facts fast, in a user-friendly format, without having to dive through page upon page of dense text. With 136 chapters spread across 8 sections, the text offers a thorough grounding in issues ranging from medicines regulation to clinical trial design and data management. This makes it a useful revision aid for exams as well as giving you a taster of areas of pharmaceutical medicine adjacent to your current role.

For healthcare professionals already working in the field, this book offers a guiding hand in difficult situations as well as supplying rapid access to the latest recommendations and guidelines. Written by authors with experience in the industry and drug regulation, this comprehensive and authoritative guide provides a shoulder to lean on throughout your pharmaceutical career. Preeminent Experts Update a Well-Respected BookTaking into account the regulatory and scientific developments that have occurred since the second edition, Design and Analysis of Bioavailability and Bioequivalence Studies, Third Edition provides a complete presentation of the latest progress of activities and results in bioavailability and bioequiva
Clinical trials are an important part of medicine and healthcare today, deciding

which treatments we use to treat patients. Anyone involved in healthcare today must know the basics of running and interpreting clinical trial data. Written in an easy-to-understand style by authors who have considerable expertise and experience in both academia and industry, Principles and Practice of Clinical Trial Medicine covers all of the basics of clinical trials, from legal and ethical issues to statistics, to patient recruitment and reporting results. Jargon-free writing style enables those with less experience to run their own clinical trials and interpret data Book contains an ideal mix of theory and practice so researchers will understand both the rationale and logistics to clinical trial medicine Expert authorship whose experience includes running clinical trials in an academic as well as industry settings Numerous illustrations reinforce and elucidate key

concepts and add to the book's overall pedagogy

Pharmacokinetics has evolved from its origin into a complex discipline with numerous subspecialties and applications in patient management, drug development, and regulatory issues. This expansion has made it difficult for any one individual to become a full-fledged expert in all areas. Fulfilling the need for a wide-ranging guide to the many existing subspecialties in this field, Pharmacokinetics in Drug Discovery and Development details the different areas in the field providing the ideal comprehensive, quick access text and reference. After an introduction of basic principles, the book is divided into sections that cover industrial and regulatory applications, clinical applications, and research applications. The following sections cover such topics

as PK/PD approaches, clinical pharmacokinetic monitoring, population pharmacokinetics, linear systems approaches, and more. Fourteen authors, each an expert in his/her area of expertise, provide an extensive background into the subspeciality with emphasis on the section's theme. Covering the many sub-disciplines and providing pharmacokinetic concepts, terminology, and approaches, Pharmacokinetics in Drug Discovery and Development serves as a resource for professionals throughout this field.

FDA Bioequivalence Standards

Essentials of Biopharmaceutics and Pharmacokinetics - E-Book

In Vitro-In Vivo Correlations

Drug Discovery and Evaluation: Methods in Clinical Pharmacology

Pharmacokinetics in Drug Discovery and Development

This book deals with the Pharmacokinetic evaluation of Sitagliptin, which is an oral DPP-4 inhibitor for the treatment of Type 2 Diabetes. This book provides the information about bio-analytical method development and validation of drugs by high performance liquid chromatography. The developed method for Sitagliptin in this book might be applicable to bioavailability and bioequivalence studies. Users of this book will be provided the simple, sensitive and validated bio-analytical method for the estimation of Sitagliptin in plasma and its applications to the pharmacokinetic studies.
Developing Solid Oral Dosage Forms is intended for pharmaceutical professionals engaged in research and

development of oral dosage forms. It covers essential principles of physical pharmacy, biopharmaceutics and industrial pharmacy as well as various aspects of state-of-the-art techniques and approaches in pharmaceutical sciences and technologies along with examples and/or case studies in product development. The objective of this book is to offer updated (or current) knowledge and skills required for rational oral product design and development. The specific goals are to provide readers with: Basics of modern theories of physical pharmacy, biopharmaceutics and industrial pharmacy and their applications throughout the entire process of research and development of oral dosage forms

Tools and approaches of preformulation investigation, formulation/process design, characterization and scale-up in pharmaceutical sciences and technologies New developments, challenges, trends, opportunities, intellectual property issues and regulations in solid product development The first book (ever) that provides comprehensive and in-depth coverage of what's required for developing high quality pharmaceutical products to meet international standards It covers a broad scope of topics that encompass the entire spectrum of solid dosage form development for the global market, including the most updated science and technologies, practice, applications, regulation, intellectual property

protection and new development trends with case studies in every chapter A strong team of more than 50 well-established authors/co-authors of diverse background, knowledge, skills and experience from industry, academia and regulatory agencies

Published in 1994: This text focuses on the determination of bioequivalence between formulations that are pharmaceutically equivalent and manufactured using acceptable chemistry, manufacturing and controls and in accordance with Good Manufacturing Practices.

A study was instituted in sheep to compare efficacy against Soman and the pharmacokinetics of atropine and HI-6 by wet/dry autoinjector and by syringe. The

efficacy in sheep against Soman of Atropine/HI-6 delivered by wet/ dry autoinjector was also compared to the efficacy of atropine/pralidoxime chloride when syringe. The aging rate of GD was also determined in sheep erytrocytes. There were no statistical differences in the LD50's of sheep treated with atropine/HI-6 using syringes of wet/dry autoinjectors. A PR was determined for atropine/HI-6 treatment. Based on analyses of HI-6 and atropine pharmacokinetic parameters there were no statistically significant differences in the two injection techniques. The aging rate of sheep RBC's is highly dependent upon the GD-AChE incubation temperature.
Interaction of Mycophenolic Acid and Pantoprazole
Pharmacokinetics and

Toxicokinetic Considerations - Vol II
The bioequivalence of oral losartan formulations. Pharmacokinetic and statistic evaluation
Homogeneous and Heterogeneous Approaches
New and Alternative Approaches to the Assessment of Pharmacokinetic and Pharmacodynamic Equivalence
As the generic pharmaceutical industry continues to grow and thrive, so does the need to conduct efficient and successful bioequivalence studies. In recent years, there have been significant changes to the statistical models for evaluating bioequivalence, and advances in the analytical technology used to detect drug and metabolite levels have made
The third edition of this introductory

text covers the factors which influence the release of the drug from the drug product and how the body handles the drug. A stronger focus has been placed on the basics with clear explanations and illustrated examples. There is also more information on statistics and population pharmacokinetics and new chapters on drug distribution, computer applications, enzyme kinetics and pharmacokinetics models.

Drug Discovery and Evaluation has become a more and more difficult, expensive and time-consuming process. The effect of a new compound has to be detected by in vitro and in vivo methods of pharmacology. The activity

spectrum and the potency compared to existing drugs have to be determined. As these processes can be divided up stepwise we have designed a book series "Drug Discovery and Evaluation" in the form of a recommendation document. The methods to detect drug targets are described in the first volume of this series "Pharmacological Assays" comprising classical methods as well as new technologies. Before going to man, the most suitable compound has to be selected by pharmacokinetic studies and experiments in toxicology. These preclinical methods are described in the second volume "Safety and Pharmacokinetic Assays". Only

then are first studies in human beings allowed. Special rules are established for Phase I studies. Clinical pharmacokinetics are performed in parallel with human studies on tolerability and therapeutic effects. Special studies according to various populations and different therapeutic indications are necessary. These items are covered in the third volume: "Methods in Clinical Pharmacology".

Due to a worldwide need for lower cost drug therapy, use of generic and multi-source drug products have been increasing. To meet international patent and trade agreements, the development and sale of these products must

conform to national and international laws, and generic products must prove that they are of the same quality and are therapeutically equivalent to the brand name alternative. However, many countries have limited resources to inspect and verify the quality of all drug products for sale in their country. This title discusses the worldwide legislative and regulatory requirements for the registration of generic and multi-source drug products.

Issues in Biologicals, Therapies, and Complementary and Alternative Medicine: 2011 Edition

Applied Biopharmaceutics and Pharmacokinetics

Pharmaceutical Medicine

Pharmacokinetic Assessment Of Sitagliptin By HPLC
Evaluation of Curve Comparison Metrics Applied to Pharmacokinetic Profiles and Relative Bioavailability and Bioequivalence
Pharmacokinetics and Toxicokinetic Considerations explains the central principles, cutting-edge methodologies, and incipient thought processes applied to toxicology research. As part of the Advances in Pharmaceutical Product Development and Research series, the book provides expert literature on dose, dosage regimen and dose adjustment, medication errors, and approaches for its

prevention, the concept of pharmacotherapy, and managed care in clinical interventions. It expounds on strategies to revamp the pharmacokinetics of the drug and the factors affecting the stability of drugs and their metabolites in biological matrices. Finally, the book offers focused elaborations on various bioanalytical methods for bioavailability and bioequivalence assessment and integrates the wide-ranging principles and concepts shared by toxicokinetics and pharmacodynamics as mutual crosstalk rather than isolated observations. It will be helpful

to researchers and advanced students working in the pharmaceutical, cosmetics, biotechnology, food, and related industries including toxicologists, pharmacists, and pharmacologists. Allows readers to systematically integrate up-to-date research findings into their laboratory work Presents focused explorations of bioanalytical methods for bioavailability and bioequivalence assessment Provides clinical applications of concepts

Issues in Biologicals, Therapies, and Complementary and Alternative Medicine: 2011 Edition is a ScholarlyEditions™

eBook that delivers timely, authoritative, and comprehensive information about Biologicals, Therapies, and Complementary and Alternative Medicine. The editors have built Issues in Biologicals, Therapies, and Complementary and Alternative Medicine: 2011 Edition on the vast information databases of ScholarlyNews.™ You can expect the information about Biologicals, Therapies, and Complementary and Alternative Medicine in this eBook to be deeper than what you can access anywhere else, as well as consistently reliable, authoritative, informed, and

relevant. The content of Issues in Biologicals, Therapies, and Complementary and Alternative Medicine: 2011 Edition has been produced by the world's leading scientists, engineers, analysts, research institutions, and companies. All of the content is from peer-reviewed sources, and all of it is written, assembled, and edited by the editors at ScholarlyEditions™ and available exclusively from us. You now have a source you can cite with authority, confidence, and credibility. More information is available at http ://www.ScholarlyEditions.com/. Essentials of Biopharmaceutics

and Pharmacokinetics Kar's Essentials of Biopharmaceutics and Pharmacokinetics deals with how a drug exerts its action in the human body through the fundamentals of absorption, distribution, metabolism and excretion. The book adopts a growth-oriented format and design that is developed systematically and methodically. The book interrelates five different sections: Section 1 Biopharmaceutics and Pharmacokinetics: What Do They Mean? Section 2 Biopharmaceutics Section 3 Pharmacokinetics Section 4 Clinical Pharmacokinetics

Section 5 Bioavailability and Bioequivalence Each section starts with a basic theory and fields of application, focuses on model-independent pharmacokinetic analyses, expatiates various biopharmaceutical aspects of dosage form and evaluation, provides an altogether new approach in understanding both dosage regimen design and individualization, and explains modification in drug molecules related to the pharmacokinetics. Undoubtedly, the unique blend of fundamental principles and latest breakthroughs in the field will certainly provide

sufficient subject matter to the students of pharmacy, pharmacology, medicinal chemistry scientists, who need a simple as well as detailed introduction in theory and application.

Studies in bioequivalence are the commonly accepted method to demonstrate therapeutic equivalence between two medicinal products. Savings in time and cost are substantial when using bioequivalence as an established surrogate marker of therapeutic equivalence. For this reason the design, performance and evaluation of bioequivalence studies have

received major attention from academia, the pharmaceutical industry and health authorities. Bioequivalence Studies in Drug Development focuses on the planning, conducting, analysing and reporting of bioequivalence studies, covering all aspects required by regulatory authorities. This text presents the required statistical methods, and with an outstanding practical emphasis, demonstrates their applications through numerous examples using real data from drug development. Includes all the necessary pharmacokinetic background

information. Presents parametric and nonparametric statistical techniques. Describes adequate methods for power and sample size determination. Includes appropriate presentation of results from bioequivalence studies. Provides a practical overview of the design and analysis of bioequivalence studies. Presents the recent developments in methodology, including population and individual bioequivalence. Reviews the regulatory guidelines for such studies, and the existing global discrepancies. Discusses the designs and analyses of drug-

drug and food-drug interaction studies. Bioequivalence Studies in Drug Development is written in an accessible style that makes it ideal for pharmaceutical scientists, clinical pharmacologists, and medical practitioners, as well as biometricians working in the pharmaceutical industry. It will also be of great value for professionals from regulatory bodies assessing bioequivalence studies.
70 Years of Levothyroxine
Recent Practices
Bioequivalence Issues
Pharmaceutical Formulation Design
Methods and Applications

Maintaining a practical perspective, Bioequivalence and Statistics in Clinical Pharmacology, Second Edition explores statistics used in day-to-day clinical pharmacology work. The book is a starting point for those involved in such research and covers the methods needed to design, analyze, and interpret bioequivalence trials; explores when, how, and why these studies are performed as part of drug development; and demonstrates the methods using real world examples. Drawing on knowledge gained directly from working in the pharmaceutical industry, the authors set the stage by

describing the general role of statistics. Once the foundation of clinical pharmacology drug development, regulatory applications, and the design and analysis of bioequivalence trials are established, including recent regulatory changes in design and analysis and in particular sample-size adaptation, they move on to related topics in clinical pharmacology involving the use of cross-over designs. These include, but are not limited to, safety studies in Phase I, dose-response trials, drug interaction trials, food-effect and combination trials, QTc and

other pharmacodynamic equivalence trials, proof-of-concept trials, dose-proportionality trials, and vaccines trials. This second edition addresses several recent developments in the field, including new chapters on adaptive bioequivalence studies, scaled average bioequivalence testing, and vaccine trials. Purposefully designed to be instantly applicable, Bioequivalence and Statistics in Clinical Pharmacology, Second Edition provides examples of SAS and R code so that the analyses described can be immediately implemented. The authors have made extensive use of

the proc mixed procedures available in SAS.
The landmark textbook on the theoretical and practical applications of biopharmaceutics and pharmacokinetics—now fully updated. Explains how to detect clinical pharmacokinetic problems and apply basic pharmacokinetic principles to solve them Helps you critically evaluate biopharmaceutic studies involving drug product equivalency and unequivalency Chapters have been revised to reflect the latest clinical perspectives on drug performance, bioavailability, bioequivalence,

pharmacokinetics, pharmacodynamics, and drug therapy The field's leading text for more than three decades, Applied Biopharmaceutics & Pharmacokinetics gets you up to speed on the basics of the discipline like no other resource. Practical problems and clinical examples with discussions are integrated within each chapter to help you apply principles to patient care and drug consultation situations. In addition, outstanding pedagogy, including chapter objectives, chapter summaries, and FAQs, plus additional application questions, identify and

focus on key concepts. Written by authors who have both academic and clinical experience, Applied Biopharmaceutics & Pharmacokinetics shows you how to use raw data and formulate the pharmacokinetic models and parameters that best describe the process of drug absorption, distribution, and elimination. The book also helps you work with pharmacokinetic and biopharmaceutic parameters to design and evaluate dosage regimens of drugs. In the seventh edition of this must-have interactive learning tool, most of the chapters are updated to

reflect our current understanding of complex issues associated with safe and efficacious drug therapy.

Pharmacokinetic Evaluation and Modeling of Clinically Significant Drug MetabolitesFrontiers Media SAEvaluation of Curve Comparison Metrics Applied to Pharmacokinetic Profiles and Relative Bioavailability and BioequivalencePharmacokineti c Assessment Of Sitagliptin By HPLCEstimation of Sitagliptin by HPLCLAP Lambert Academic Publishing

A unique, unifying treatment for statistics and science in clinical trials What sets

this volume apart from the many books dealing with clinical trials is its integration of statistical and clinical disciplines. Stressing communication between biostatisticians and clinical scientists, this work clearly relates statistical interpretation to clinical issues arising in different stages of pharmaceutical research and development. Plus, the principles presented here are universal enough to be easily adapted in non-biopharmaceutical settings. Design and Analysis of Clinical Trials tackles concepts and methodologies. It not only covers

*statistical basics such as uncertainty and bias, design considerations such as patient selection, randomization, and the different types of clinical trials but also deals with various methods of data analysis, group sequential procedures for interim analysis, efficacy data evaluation, analysis of safety data, and more. Throughout, the book: * Surveys current and emerging clinical issues and newly developed statistical methods * Presents a critical review of statistical methodologies in various therapeutic areas * Features case studies from*

*actual clinical trials * Minimizes the mathematics involved, making the material widely accessible * Offers each chapter as a self-contained entity * Includes illustrations to highlight the text This monumental reference on all facets of clinical trials is important reading for physicians, clinical and medical researchers, pharmaceutical scientists, clinical programmers, biostatisticians, and anyone involved in this burgeoning area of clinical research. It can also be used as a textbook in graduate-level courses in the field. Bioequivalence Studies in*

Drug Development
Bioequivalence and Statistics in Clinical Pharmacology
Developing Solid Oral Dosage Forms
Bioavailability, Bioequivalence and Pharmacokinetics : International Conference of F.I.P. "Bio-International '92" Held in Bad Homburg, Germany, May 20-22, 1992
Development and Evaluation of a Physiologically Based Pharmacokinetic Model of Fentanyl in Dogs

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 comprehensive reference provides an in-depth discussion on state-of-the-art regulatory science in bioequivalence. In sixteen chapters, the volume explores a broad range of topics pertaining to bioequivalence, including its origin and principles, statistical considerations, food

effect studies, conditions for waivers of bioequivalence studies, Biopharmaceutics Classification Systems, Biopharmaceutics Drug Disposition Classification System, bioequivalence modeling/simulation and best practices in bioanalysis. It also discusses bioequivalence studies with pharmacodynamic and clinical endpoints as well as bioequivalence approaches for highly variable drugs, narrow therapeutic index drugs, liposomes, locally acting gastrointestinal drug products, topical products and nasal and inhalation products. FDA Bioequivalence Standards is written by FDA regulatory scientists who develop regulatory

policies and conduct regulatory assessment of bioequivalence. As such, both practical case studies and fundamental science are highlighted in these chapters. The book is a valuable resource for scientists who work in the pharmaceutical industry, regulatory agencies and academia as well as undergraduate and graduate students looking to expand their knowledge about bioequivalence standards.

The assessment of bioequivalence is an important process whereby the bioavailability of a generic drug product is compared with its brand-name counterpart. Generic pharmaceutical products must be approved as therapeutic

equivalents to the brand name alternative in order to be interchangeable. The demonstration of bioequivalence is an important component of therapeutic equivalence. Bioequivalence studies are very expensive, time consuming and always have the possibility of failure. The objective of this textbook is to describe some of those specific bioequivalence issues which need to be considered for the design and conduct of bioequivalence studies. By exploring scientific, legal, and international regulatory challenges, Generic Drug Development, discusses the use of alternative approaches to the measurement of plasma drug concentrations for the

demonstration of bioequivalence, and covers bioequivalence procedures for drug products that are not easily assessed - based upon the physical and chemical properties of the active drug and the nature of the drug product. Bioequivalence is a surrogate measure of safety and efficacy in different stages of drug development process with the most pronounced significance in the development of generic drugs. Bioequivalence, among other standards, ensures that generic drugs are equivalent to their approved innovator or reference products in terms of clinical efficacy and safety while circumventing the lengthy-time course and high cost of animal and clinical trials in patients

required for innovator drugs. Despite the advancements in development of robust bioequivalence approaches over the past decades, there are still controversies in the current practice of bioequivalence. The aim of this thesis is to explore some of these controversies and address them by putting forward new and alternative approaches. One of the most controversial issues in the current practice of bioequivalence is the extrapolation of bioequivalence study results from one population to another. The majority of bioequivalence studies for systemic effective oral dosage forms are conducted based on pharmacokinetic endpoints in healthy volunteers whilst the

targeted population is patients. This is based on the assumption that if two products are bioequivalent in one population, they should be bioequivalent in another one. The extrapolation of bioequivalence study results is not limited to that from healthy volunteers to patients. Since 2007, an ever-increasing proportion of pharmacokinetic bioequivalence studies for North American or European generic submissions have been performed in geographical/ethnic populations other than the intended ones, due to the lower cost of these studies outside North America and Europe. In the first part of this thesis, we investigated whether the bioequivalence results obtained in

one geographical or ethnic population can be extrapolated to another one. To this purpose, we extracted pharmacokinetic bioequivalence studies results from generic submissions to Health Canada and the US Food and Drug Administration. We calculated food effect for ten different reference drug products and compared the results for each product between two ethnic populations, Indians and North Americans. This is based on the reasoning that if food effect is found to be the same between the Indian and North American populations, then the generic product and its reference that were found to be bioequivalent in the Indian population should also be bioequivalent in North

American population. For 90% of the study drugs, statistically significant difference was detected in the food effect between two populations. For 30% of these drugs, the difference was found to be of possible clinical relevance. The results of this study raised a flag for extrapolating the bioequivalence results from one population to another. Challenges in the context of bioequivalence are not always limited to the pivotal studies where the performance of a generic product is compared to that of Reference. Prior to pivotal bioequivalence studies, a pilot study may be conducted to establish an appropriate study design for the pivotal bioequivalence study.

Therefore, inaccurate results from a pilot study, such as inaccurate estimation of time point or dose duration for comparison of test versus reference, can affect the bioequivalence outcomes adversely. An example to this case is the comparison of the extent of skin blanching, the pharmacological effect of generic versus reference products of topical dermatological corticosteroids at specific dose duration, DD50, where the effect is half maximal. This dose duration should initially be determined in a pilot study. The US FDA 1995 Guidance document recommends the use of non-linear mixed effect population modeling for the estimation of DD50, irrespective of the method

of analysis. Given the availability of different types of non-linear mixed effect modeling methods, each sponsor could choose a different one. In the second part of this thesis we investigated whether the same DD50 estimates can be obtained when different non-linear mixed effect modeling methods are used. To this purpose, we fitted the skin blanching data from eleven studies with two different non-linear mixed effect modeling methods, the Maximum Likelihood Expectation Maximization (MLEM) and the First Order Conditional Estimation (FOCE). The results favored MLEM given its lower population DD50 estimates that would locate in a more discriminative portion of the

Emax curve and better minimization of inter-individual variability. Although the pharmacokinetic-based bioequivalence approach has contributed significantly to the development of high-quality generic versions of systemic effective oral dosage form, the availability of generic versions of topical dermatological products remains constrained due to the limited methods accepted for bioequivalence evaluation of these products. In the third part of this thesis, a novel approach for the bioequivalence assessment of topical acyclovir cream formulations was developed based on the model-based analysis of local exposure data recovered from tape

stripping of the skin at a single dose duration, DD50. Conducting the stripping procedure only at DD50 not only ensured that the PK data was collected at the dose duration that is most discriminative of formulation differences, but it also decreased the number of samples to be analyzed significantly. More importantly, our novel approach in generating the local PK profile in the skin (dermatopharmacokinetic profile) and the implementation of population compartmental analysis circumvented the numerous assumptions and sophisticated calculations that were inherent to previous methods, while yielding the PK parameters relevant for topical

bioavailability and bioequivalence assessment (rate and extent of exposure to the skin). This method successfully concluded bioequivalence and its absence.

Principles and Practice of Clinical Trial Medicine

Estimation of Sitagliptin by HPLC A Pharmacokinetic Crossover Study

Generics and Bioequivalence

Handbook of Bioequivalence Testing

As the generic pharmaceutical industry continues to grow and thrive, so does the need to conduct adequate, efficient bioequivalence studies. In recent years, there have been significant changes to the

statistical models for evaluating bioequivalence. In addition, advances in the analytical technology used to detect drug and metabolite levels have made bioequivalence testing more complex. The second edition of Handbook of Bioequivalence Testing has been completely updated to include the most current information available, including new findings in drug delivery and dosage form design and revised worldwide regulatory requirements. New topics include: A historical perspective on generic pharmaceuticals New guidelines governing submissions related to

bioequivalency studies, along with therapeutic code classifications Models of noninferiority Biosimilarity of large molecule drugs Bioequivalence of complementary and alternate medicines Bioequivalence of biosimilar therapeutic proteins and monoclonal antibodies New FDA guidelines for bioanalytical method validation Outsourcing and monitoring of bioequivalence studies The cost of generic drugs is rising much faster than in the past, partly because of the increased costs required for approval–including those for bioequivalence testing. There is

a dire need to re-examine the science behind this type of testing to reduce the burden of development costs–allowing companies to develop generic drugs faster and at a lower expense. The final chapter explores the future of bioequivalence testing and proposes radical changes in the process of biowaivers. It suggests how the cost of demonstrating bioequivalence can be reduced through intensive analytical investigation and proposes that regulatory agencies reduce the need for bioequivalence studies in humans. Backed by science and

updated with the latest research, this book is destined to spark continued debate on the efficacy of the current bioequivalence testing paradigm.

Task 89-06: Determination of the Bioequivalence of HI-6 and Atropine When Delivered by Wet/Dry Autoinjector Or Syringe in Sheep: A Pharmacokinetic and Efficacy Evaluation

Design and Analysis of Clinical Trials

Design and Analysis of Bioavailability and Bioequivalence Studies

Generic Drug Product Development

Concept and Methodologies