# Biopharmaceutics Classification System A Regulatory Approach

FDA Bioequivalence Standards
Solid Oral Dosage Forms
Estimation of Solubility, Permeability, Absorption and Bioavailability
Applied Biopharmaceutics and Pharmacokinetics
Biopharmaceutics Modeling and Simulations
Solid Oral Dosage Forms, Second Edition
Preparing for Future Products of Biotechnology
The Challenge of CMC Regulatory Compliance for Biopharmaceuticals
Principles and Practice of Clinical Trial Medicine
Drug Delivery Approaches
From Fundamentals to Industrial Practice
Pharmaceutical Product Development
Oral Formulation Roadmap from Early Drug Discovery to Development
Biological, Physicochemical, and Computational Strategies
Excipient Applications in Formulation Design and Drug Delivery
Dosage Form Design Considerations
Homogeneous and Heterogeneous Approaches
Drug Bioavailability
In Vitro-In Vivo Correlations
Generic Drug Product Development
Generic Drug Product Development
Regulatory Affairs in the Pharmaceutical Industry
Excipient Development for Pharmaceutical, Biotechnology, and Drug Delivery Systems
Dissolution and Drug Release
In Vitro-In Vivo Correlation
Oral Drug Delivery for Modified Release Formulations
Design and Development at Early Stage
Theory, Practice, Methods, and Applications
Developing Solid Oral Dosage Forms
Biopharmaceutics Applications in Drug Development
Poorly Soluble Drugs
Biopharmaceutics Classification System (BCS)
Drug bioequivalence
Innovative Dosage Forms
Oral Colon-Specific Drug Delivery
Pharmaceutical Medicine and Translational Clinical Research
Biopharmaceutics
Perspectives from Pharmacokinetics and Pharmacodynamics
Generic Drug Product Development

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**FDA Bioequivalence Standards** Springer
Biopharmaceutics Classification System (BCS)Development, Implementation, and GrowthWiley
Solid Oral Dosage Forms Wiley
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.
Estimation of Solubility, Permeability, Absorption and Bioavailability Springer
A absorção oral de um fármaco é fundamentalmente dependente da solubilidade aquosa e da permeabilidade gastrintestinal. Estes são fatores determinantes da biodisponibilidade e, consequentemente, da eficácia clínica de um medicamento. O Sistema de Classificação Biofarmacêutica (SCB), fundamentado nas propriedades de solubilidade e permeabilidade, consolidou-se nos últimos anos como ferramenta de auxílio na predição da biodisponibilidade de fármacos e tem sido empregado no desenvolvimento de formas farmacêuticas, contendo novos fármacos ou não, bem como no registro de medicamentos genéricos. O emprego do SCB para a isenção dos estudos de biodisponibilidade relativa/bioequivalência para algumas classes de fármacos vem sendo adotado e discutido, uma vez que os ensaios de biodisponibilidade apresentam limitações técnicas, econômicas e éticas. Assim, nos últimos anos, Agências Regulatórias têm utilizado o SCB para permitir que testes de dissolução in vitro sejam usados para estabelecer bioequivalência no caso de fármacos altamente solúveis e altamente permeáveis. O presente trabalho tem como objetivos revisar e reunir a literatura relacionada ao SCB com vistas a discutir a possibilidade de isenção dos estudos de biodisponibilidade relativa / bioequivalência para os medicamentos. Com esta proposta, foram pesquisadas as bases de

dados Pubmed, Medline, Legislações Brasileiras indexadas no Visalegis e Legislação Internacional. Buscou-se a literatura pertinente publicada no período entre 1980 e o primeiro semestre de 2009. Desde a introdução do SCB existe uma relutância na aplicação das bioisenções para o registro de genéricos uma vez que as indústrias farmacêuticas não querem arriscar uma rejeição à sua solicitação nos países onde esse sistema ainda não é aceito, principalmente devido à falta de harmonização da legislação global. No Brasil, o SCB não é aceito para isenção de estudos de biodisponibilidade relativa/bioequivalência, pois os dados de permeabilidade são escassos n.

Applied Biopharmaceutics and Pharmacokinetics
Academic Press
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

*Biopharmaceutics Modeling and Simulations*
CRC Press
Oral Colon-Specific Drug Delivery covers approaches used to deliver a variety of drugs to the colon. Anatomy and physiology of the gastrointestinal tract as it affects colonic drug delivery and pharmacokinetics are reviewed, as well as drug absorption from the colon. The book presents valuable information on a variety of topics, including oral peptide/protein delivery, dextran-based delivery systems, glycoside/glycosidase-based delivery, azo-bond prodrugs, hydroxypropyl methacrylamide copolymers for colonic delivery, and matrices for colonic drug delivery. Special emphasis is placed on delivery systems, especially biochemical approaches to delivery, such as the use of degradable polymers and both low and high molecular weight prodrugs. Oral Colon-Specific Drug Delivery will provide a valuable reference resource for gastroenterologists, pharmaceutical scientists, and other researchers working with drug delivery to the colon.

**Solid Oral Dosage Forms, Second Edition**
McGraw-Hill/Appleton & Lange
Provides a comprehensive review of all types of

medical therapeuticdelivery solutions from traditional pharmaceutical therapydevelopment to innovative medical device therapy treatment to therecent advances in cellular and stem cell therapy development • Provides information to potentially allow futuredevelopment of treatments with greater therapeutic potential andcreativity • Includes associated regulatory requirements for thedevelopment of these therapies • Provides a comprehensive developmental overview ontherapeutic delivery solutions • Provides overview information for both the general reader as well as more detailed references forprofessionals and specialists in the field

**Preparing for Future Products of Biotechnology** Springer Science & Business Media

Developing Solid Oral Dosage Forms: Pharmaceutical Theory and Practice, Second Edition illustrates how to develop high-quality, safe, and effective pharmaceutical products by discussing the latest techniques, tools, and scientific advances in preformulation investigation, formulation, process design, characterization, scale-up, and production operations. This book covers the essential principles of physical pharmacy, biopharmaceutics, and industrial pharmacy, and their application to the research and development process of oral dosage forms. Chapters have been added, combined, deleted, and completely revised as necessary to produce a comprehensive, well-organized, valuable reference for industry professionals and academics engaged in all aspects of the development process. New and important topics include spray drying, amorphous solid dispersion using hot-melt extrusion, modeling and simulation, bioequivalence of complex modified-released dosage forms, biowaivers, and much more. Written and edited by an international team of leading experts with experience and knowledge across industry, academia, and regulatory settings Includes new chapters covering the pharmaceutical applications of surface phenomenon, predictive biopharmaceutics and pharmacokinetics, the development of formulations for drug discovery support, and much more Presents new case studies throughout, and a section completely devoted to regulatory aspects, including global product regulation and international perspectives

Springer Science & Business Media

The peroral application (swallowing) of a medicine means that the body must first resorb the active substance before it can begin to take effect. The efficacy of drug uptake depends on the one hand on the chemical characteristics of the active substance, above all on its solubility and membrane permeability. On the other hand, it is determined by the organism's ability to absorb pharmaceuticals by way of specific transport proteins or to excrete them. Since many pharmacologically active substances are poorly suited for oral intake, a decisive criterion for the efficacy of a medicine is its so-called bioavailability. Written by an international team from academia and the pharmaceutical industry, this book covers all

aspects of the oral bioavailability of medicines. The focus is placed on methods for determining the parameters relevant to bioavailability. These range from modern physicochemical techniques via biological studies in vitro and in vivo right up to computer-aided predictions. The authors specifically address possibilities for optimizing bioavailability during the early screening stage for the active substance. Its clear structure and comprehensive coverage make this book equally suitable for researchers and lecturers in industry and teaching.

**The Challenge of CMC Regulatory Compliance for Biopharmaceuticals**

Wiley

Between 1973 and 2016, the ways to manipulate DNA to endow new characteristics in an organism (that is, biotechnology) have advanced, enabling the development of products that were not previously possible. What will the likely future products of biotechnology be over the next 5â€"10 years? What scientific capabilities, tools, and/or expertise may be needed by the regulatory agencies to ensure they make efficient and sound evaluations of the likely future products of biotechnology? Preparing for Future Products of Biotechnology analyzes the future landscape of biotechnology products and seeks to inform forthcoming policy making. This report identifies potential new risks and frameworks for risk assessment and areas in which the risks or lack of risks relating to the products of biotechnology are well understood.

Principles and Practice of Clinical Trial Medicine CRC Press

In this age of combinatorial chemistry and high-throughput technologies, bioactive compounds called hits are discovered by the thousands. However, the road that leads from hits to lead compounds and then to pharmacokinetically optimized clinical and drug candidates is very long indeed. As a result, the screening, design, and optimization of pharmacokinetic properties has become the bottleneck and a major challenge in drug research. To shorten the time-consuming develop-ment and high rate of attrition of active compounds ultimately doomed by hidden pharmacokinetic defects, drug researchers are coming to incorporate structure-permeation, structure-distribution, structure-metabolism, and structure-toxicity relations into drug-design strategies. To this end, powerful biological, physicochemical, and computational approaches are being developed whose objectives are to increase the clinical relevance of drug design, and to eliminate as soon as possible compounds with unfavorable physicochemical properties and pharmacokinetic profiles. Toxicological issues are also of utmost importance in this paradigm. There was, hence, an urgent need for a book covering this field in an authoritative, didactic, comprehensive, factual, and conceptual manner. In this work of unique breadth and depth, international authorities and practicing experts from academia and industry present the most modern biological, physicochemical, and computational strategies to optimize gastrointestinal absorption, protein

binding and distribution, brain permeation, and metabolic profile. The biological strategies emphasized in the book include cell cultures and high-throughput screens. The physicochemical strategies focus on the determination and interpretation of solubility, lipophilicity, and related molecular properties as factors and predictors of pharmacokinetic bahavior. Particular attention is paid to the lipophilicity profiles of ionized compounds, to lipophilicity measurements in anisotropic media (liposomes/water, IAM columns), and to permeability across artificial membranes. Computational strategies comprise virtual screening, molecular modelling, lipophilicity, and H-bonding fields and their importance for structure-disposition relations. This book is both about theoretical and technological breakthroughs. Thus, molecular properties are contemplated from a dual perspective, namely a) their interpretation in biological and/or physicochemical terms, and b) their value in screening, lead optimization, and drug-candidate selection. In addition to its 33 chapters, the book includes a CD-ROM containing the invited lectures, oral communications and posters (in full version) presented at the Second LogP Symposium, 'Lipophilicity in Drug Disposition—Practical and Computational Approaches to Molecular Properties Related to Drug Permeation, Disposition and Metabolism', held at the University of Lausanne in March 2000.

Drug Delivery Approaches

CRC Press

This book is the first text to provide a comprehensive assessment of the application of fundamental principles of dissolution and drug release testing to poorly soluble compounds and formulations. Such drug products are, vis-à-vis their physical and chemical properties, inherently incompatible with aqueous dissolution. However, dissolution methods are required for product development and selection, as well as for the fulfillment of regulatory obligations with respect to biopharmaceutical assessment and product quality understanding. The percentage of poorly soluble drugs, defined in classes 2 and 4 of the Biopharmaceutics Classification System (BCS), has significantly increased in the modern pharmaceutical development pipeline. This book provides a thorough exposition of general method development strategies for such drugs, including instrumentation and media selection, the use of compendial and non-compendial techniques in product development, and phase-appropriate approaches to dissolution development. Emerging topics in the field of dissolution are also discussed, including biorelevant and biphasic dissolution, the use on enzymes in dissolution testing, dissolution of suspensions, and drug release of non-oral products. Of particular interest to the industrial pharmaceutical professional, a brief overview of the formulation and solubilization techniques employed in the development of BCS class 2 and 4 drugs to overcome solubility challenges is provided and is complemented by a collection of chapters that survey the approaches

and considerations in developing dissolution methodologies for enabling drug delivery technologies, including nanosuspensions, lipid-based formulations, and stabilized amorphous drug formulations.

From Fundamentals to Industrial Practice CRC Press

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.

**Pharmaceutical Product Development** Springer

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.

*Oral Formulation Roadmap from Early Drug Discovery to Development* CRC Press

This book presents a novel modeling approach to biopharamceutics, pharmacokinetics and pharmacodynamic phenomena. 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. Throughout, many examples are used to illustrate the intrinsic complexity of drug administration related phenomena in the human, justifying the use of advanced modeling methods.

*Biological, Physicochemical, and Computational Strategies* John Wiley & Sons

Detailing formulation approaches by stage of discovery to early development, this book gives a “playbook” of practical and efficient strategies to formulate drug candidates with the least chance of failing in clinical development. • Comes from contributing authors with experience developing formulations on the frontlines of the pharmaceutical industry • Focuses on pre (or non-) clinical and early stage development, the phases where most compounds are used in drug research • Features case studies to illustrate practical challenges and solutions in formulation selection • Covers regulatory filing, drug metabolism and physical and chemical properties, toxicology formulation, biopharmaceutics classification system (BCS), screening approaches, early stage clinical formulation development, and outsourcing

*Excipient Applications in Formulation Design and Drug Delivery* John Wiley & Sons

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.

*Dosage Form Design Considerations* CRC Press

Although the Bioequivalence (BE) requirements in many global jurisdictions have much in common, differences in certain approaches and requirements such as definitions and terms, choice of comparator (reference) product, acceptance criteria, fasted and fed studies, single and multi-dose studies, biowaivers and products not intended for absorption into the systemic circulation (locally acting medicines and dosage forms), amongst others, provide food for thought that standardisation should be a high priority objective in order to result in a harmonized international

process for the market approval of products using BE. An important objective of Bioequivalence Requirements in Various Global Jurisdictions is to attempt to gather the various BE requirements used in different global jurisdictions to provide a single source of relevant information. This information from, Brazil, Canada, China, European Union, India, Japan, MENA, Russia South Africa, the USA and WHO will be of value to drug manufacturers, regulatory agencies, pharmaceutical scientists and related health organizations and governments around the world in the quest to harmonize regulatory requirements for the market approval of generic products.
Homogeneous and Heterogeneous Approaches Frontiers Media SA
A comprehensive introduction to using modeling and simulation programs in drug discovery and development Biopharmaceutical modeling has become integral to the design and development of new drugs. Influencing key aspects of the development process, including drug substance design, formulation design, and toxicological exposure assessment, biopharmaceutical modeling is now seen as the linchpin to a drug's future success. And while there are a number of commercially available software programs for drug modeling, there has not been a single resource guiding pharmaceutical professionals to the actual tools and practices needed to design and test safe drugs. A guide to the basics of modeling and simulation programs, Biopharmaceutics Modeling and Simulations offers pharmaceutical scientists the keys to understanding how they work and are applied in creating drugs with desired medicinal properties. Beginning with a focus on the oral absorption of drugs, the book discusses: The central dogma of oral drug absorption (the interplay of dissolution, solubility, and permeability of a drug), which forms the basis of the biopharmaceutical classification system (BCS) The concept of drug concentration How to simulate key drug absorption processes The physiological and drug property data used for biopharmaceutical modeling Reliable practices for reporting results With over 200 figures and illustrations and a peerless examination of all the key aspects of drug research—including running and interpreting models, validation, and compound and formulation selection—this reference seamlessly brings together the proven practical approaches essential to developing the safe and effective medicines of tomorrow.
Drug Bioavailability John Wiley & Sons
This is a well thought-out, highly practical text covering contemporary ‘in vitro’ techniques for drug absorption studies. Starting at the molecular level of investigation, it continues with cell monolayer models (both primary and cell lines) and culminates with in situ techniques as a final testing format. In addition, chapters on high-throughput assays, in vitro-in vivo correlation, bioinformatics and regulatory issues are covered, giving a comprehensive overview of available models and techniques. Moreover, an appendix consisting of a number of practical

protocols is available online, updated as needed, and should prove very helpful to apply the techniques directly to the benchside.

**In Vitro-In Vivo Correlations** John Wiley & Sons

Oral Drug Absorption, Second Edition thoroughly examines the special equipment and methods used to test whether drugs are released adequately when administered orally. The contributors discuss methods for accurately establishing and validating in vitro/in vivo correlations for both MR and IR formulations, as well as alternative approaches for MR an