

# Preface

The initial seed for publishing a book on FDA's bioequivalence standards was implanted at the "2008 American Association of Pharmaceutical Scientists Annual Meeting and Exposition" in Atlanta, Georgia. It was in November—the climate was pleasantly cool and gentle, but inside the convention center the mood was hot and lively because of the discourse among a group of pharmaceutical scientists from around the world regarding FDA's bioequivalence guidance. While appraising FDA's bioequivalence guidance for specific drug products, many of the attendees raised inquiries about the bioequivalence of highly variable drugs, a topic that has been in controversy for decades. The discussions revealed a need—in particular, a need for some sort of literature to make available to the public that would systematically and transparently expound on FDA's rationale on bioequivalence. After stepping out of the room where the discussion was taking place, a thought sparkled in the editors' minds: what about a book?

The desire to publish a book on FDA's bioequivalence standards continued to grow in 2009 and 2010, a vigorous period when FDA implemented the partial area under the plasma concentration time curve (AUC) approach for drugs with complex pharmacokinetic profiles and initiated discussions on bioequivalence for narrow therapeutic index drugs. Meanwhile, debates on bioequivalence approaches for locally acting gastrointestinal drugs indicated that the public bore tremendous misunderstanding of the FDA's bioequivalence approaches. Although papers and books touching on these topics were published over that period of time, the information was delivered sporadically and in an unsystemic manner.

With the recent development of bioequivalence approaches for locally acting gastrointestinal drugs, liposomes, and inhalation products, as well as the issuance of FDA guidance on bioanalytical method validation, the editors of this book felt it was time—in fact, even essential to publish a book that summarized the origin, current development, and future trends of FDA's bioequivalence standards. To date, no book had been published that systemically communicated FDA's bioequivalence approaches to the public.

*FDA Bioequivalence Standards* features a comprehensive selection: 16 chapters of the most current regulatory sciences in the bioequivalence area. These chapters are

scrupulously selected to construct broad yet thorough coverage of the relevant topics in the field of bioequivalence. Chapter 1 discusses the origin of bioequivalence and reviews recent developments. Chapters 2 and 3 describe fundamentals of bioequivalence and detail statistical considerations. Chapter 4 explains the science of food effect on bioequivalence studies and elaborates on the study details. Chapter 5 discusses conditions for waivers of bioequivalence study, the Biopharmaceutics Classification Systems (BCS), and the Biopharmaceutics Drug Disposition Classification System (BDDCS). These five chapters are the foundation of bioequivalence. We recommend that beginning learners of this subject matter refer to these five chapters to garner the fundamentals of bioequivalence.

Chapters 6–8 introduce FDA approaches for highly variable drugs, the partial AUC concept, and narrow therapeutic index drugs. Chapters 9 and 10 focus on bioequivalence approaches with pharmacodynamics and clinical endpoints. Chapters 11–14 discuss the individual product classes that are considered more complex because the conventional pharmacokinetic approach alone is not sufficient to establish their bioequivalence. Because of their complexity, new approaches are developed to establish bioequivalence. The products discussed in these chapters are liposome, locally gastrointestinal drug products, topical products, and nasal and inhalation products. Chapter 15 is devoted to modeling and simulation, an area that has recently received considerable attentions as a tool in the demonstration of bioequivalence. Finally, Chapter 16 discusses the current best practices in bioanalytical method validation, introduces recent developments in bioanalysis, and highlights the challenges in bioanalysis.

These chapters are written, at least with our hopes and emphasis, in such way that beginning learners of bioequivalence can pick up a chapter, read through a subject of interest, and understand its overall contour and generate an outline of profile. Meanwhile, readers with years of experience in the bioequivalence area, when encountered with a puzzle, will be able to consult this book to help them find their answer. As such, we strived to ensure that the breadth and depth were appropriately measured.

FDA scientists who themselves develop regulatory policies and conduct regulatory assessment of bioequivalence studies contributed all of the chapters in this volume. Thus, fundamental sciences, as well as practical case studies, are highlighted in these chapters. The original contributions were then reviewed by renowned scientists who are respected experts in their fields to ensure the quality of the contributions. Herein, we would like to thank our chapter reviewers for their valuable time and effort. It was an intellectually gratifying experience to collaborate with them on this book.

We believe that the publication of this book will bring the most state-of-the-art regulatory science in bioequivalence and provide invaluable information to worldwide scientists who work in the pharmaceutical industry, regulatory agencies, and academia. Meanwhile, we affirm it will also serve as a valuable education resource for undergraduate and graduate students.

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