Therapeutic Delivery Solutions

Edited By **Chung Chow Chan, Kwok Chow, Bill McKay & Michelle Fung**

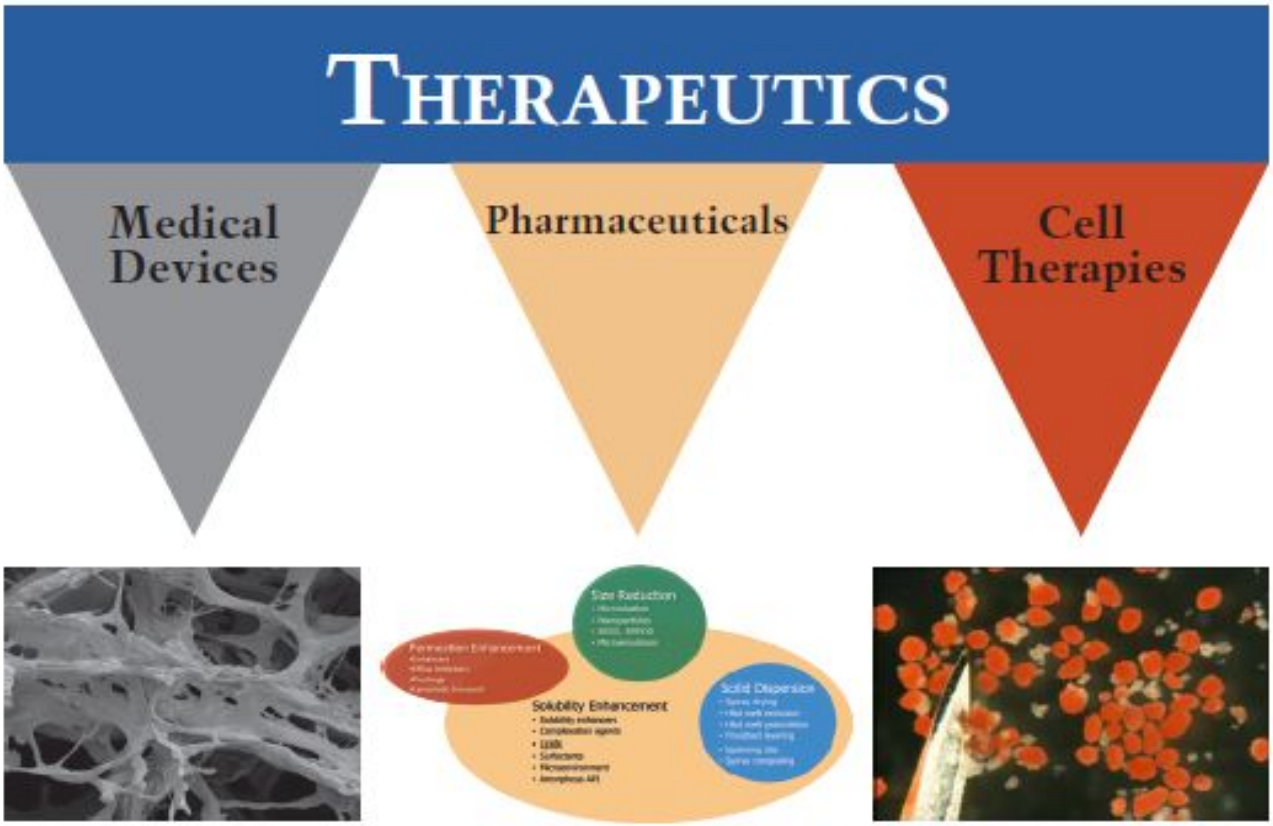

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Figure 12.11 pH-dependent calculated Do for 80 mg gliclazide dose. Dotted lines represent the critical Do for GLK (conservative upper limit of Do = 1 and the calculated value of Do = 14.5).Reproduced from Ref. 82, with permission of Springer Science and Business Media

Figure 12.12 Dissolution of montelukast sodium in different dissolution media using USP apparatus 2 and a flow-through cell. The profiles were used in GastroPlus to simulate the *in vivo* performance. Reproduced from Ref. 45, with permission of Elsevier.

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Preface

The technologies for the administration of therapeutic agents have been traditionally led by the pharmaceutical industry that develops drug molecules (both small and large molecules) in various dosage forms. The medical device industry has also evolved to apply its technologies to deliver drugs to various target sites.

Cellular therapy is now rapidly emerging as a new therapeutic solution platform, analogous to dosage form design and device development, in the last few decades. Under the Executive Order 13505 of March 9, 2009, in the United States, President Obama's Administration is committed to supporting and conducting ethically responsible, scientifically worthy human stem cell research, including human embryonic stem cell research. "National Institutes of Health Guidelines for Human Stem Cell Research" (Guidelines), effective July 7, 2009, applies to research using human embryonic stem cells and certain uses of human-induced pluripotent stem cells that have the potential to improve our understanding of human biology and aid in the discovery of new ways to prevent and treat illness. Researches in cellular therapy, for example, stem cells, have had very promising results as therapeutic solutions to diseased states and organ transplants.

This textbook provides a convergent link between traditional dosage form design, medical device development, and cellular therapeutics. It attempts to bring these three platforms of therapeutic delivery solution development together in one place to show the potential idiosyncrasies and common and dissimilar challenges that each platform faces to provide the best therapeutic delivery solution to the patient. Contemporary scientific and

medical information as well as the newly emerging regulatory scientific information are discussed. This textbook will provide development scientists and medical professionals more options to develop a therapeutic agent to its fullest potential and create better and more creative therapeutic solutions.

The content of the book is grouped into five sections. Section 1 (consisting of Chapter 1) introduces the requirements and issues encountered in regulatory submissions in the pharmaceutical, cellular/gene products, and medical device industries. Section 2 (consisting of Chapters 2 and 3) explains in detail the traditional pharmaceutical drug therapy development. Section 3 (consisting of Chapters 4–6) provides an overview, current trends, and strategies of special medical device development. Section 4 (consisting of Chapters 7–9) introduces the reader to the latest advances and innovations in cellular and stem cell therapeutic delivery. Section 5 (consisting of Chapters 10–14) provides information on the analytical support needed for the research and development in Sections 2–4.

Chapter 1 provides an overview of the current regulatory requirements for the development of the three platforms of therapeutic solution and new FDA initiatives to ensure that innovative products reach the patients who need them and when they need them.

An overview of the approach and strategies for development of immediate release tablets after a drug candidate is selected is provided in Chapter 2. Chapter 3 discusses the strategies (with examples) for the development of low aqueous solubility drug products.

Chapter 4 starts with an overview, key trends, and drivers for drug delivery medical devices. Chapter 5 focuses on the local growth factor delivery to address metabolic bone

disorders. “From glass syringes to feedback-controlled patch pumps”, Chapter 6 discusses the amazing accomplishment for the pharmaceutical and medical device industries with the insulin pump to continuously deliver precise amounts of insulin 24 h a day.

Cell-based biologic therapies have a long history. Simple blood transfusions and tissue transplants are commonly utilized in medical practice. Chapter 7 reviews the history of islet transplantation, procedural issues, current outcomes, and future directions. Chapter 8 provides an overview of the latest developments of cell-based biologic therapies and discusses the future outlook for these novel treatment modalities, for example, cancer, infection, and autoimmune disorders. Chapter 9 reviews the history of stem cell research and development, sources of various stem cells (e.g., neonatal, adult, reprogrammed), technical and regulatory issues of stem cell therapy, and the prospect of industrialization of stem cell technology into future medical therapy.

Chapters 10 to 14 provide the analytical support needed in the development of the three platforms of therapeutic solution delivery. Chapter 10 summarizes the specifications setting and stability studies requirements for development work. Chapter 11 shows how LC–MS techniques have been used in all stages of the drug development process including discovery, preclinical, clinical, and manufacturing. Chapter 12 discusses the importance of biorelevant methods and how to achieve them. Chapter 13 provides information and importance of ICH guidelines for development and global harmonization. In the development of therapeutic solution, there will be situations when out of specification (OOS) or aberrant data are obtained. Chapter 14 looks at how the use of sound scientific judgment and good documentation can lead to a successful OOS/atypical

result investigation in a case study according to current guidance.

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Section 1
Requirements and Issues encountered in Regulatory Submissions in the Pharmaceutical, Cell Therapy and Medical Device Industries