Methods in Pharmacology and Toxicology

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Process Simulation and Data Modeling in Solid Oral Drug Development and Manufacture

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Preface

The need for a more structured approach to process and product development has been recently identified in the pharmaceutical industry in order to consistently guarantee quality and value to processes and products. This need has been formally identified by the pharmaceutical industry as the Quality by Design (QbD) initiative and has been in the center of attention over the last few years. To enable the implementation of this concept, there is a need for quantitative characterization of process and product performance.

The goal of this handbook is to provide pharmaceutical engineers with an introduction to the current state of the art in modeling and simulation of pharmaceutical processes and to summarize a number of practical applications of such methodologies in drug product development. Chapters include reviews of the simulation and modeling methodologies, data collection and analysis, development of novel sensing techniques, development and integration of individual unit models, optimization approaches for data-based models, design space evaluation techniques, informatics-based methodologies, and emerging topics in pharmaceutical process development.

The first chapter focuses on examples of more mechanistic models developed in pharmaceutical manufacturing and specifically addresses the modeling of fluid bed granulation, tablet coating, and spray drying. The importance of the integration of such models in existing manufacturing workstreams is highlighted. Chapter 2 provides a detailed review of Population Balance Models (PBM) as one of the most promising alternatives to represent particulate systems. The distributed nature of the PBM makes it an appropriate modeling framework for pharmaceutical powder-based drug manufacturing.

Material properties and how they affect product and process performance are discussed in Chap. 3. In particular, specific properties of raw materials and the techniques used to measure them are described, and the state of the art of applying this information to define product formulation is also presented.

Chapter 4 reviews one of the most commonly used mechanistic approaches to model particular systems, which is Discrete Element Method (DEM). The main advantage of this approach is that it can capture mechanistic, particle-scale information such as velocity and collision profiles.

In pharmaceutical manufacturing, it is important to establish the right procedures to guarantee the consistency in process performance. Chapter 5 reviews the procedures used for the development of near infrared (NIR) spectroscopic methods and describes examples of the most recently developed approaches based on partial least squares (PLS) calibration methods that minimize the number of samples used. Following the ideas on latent-variable modeling techniques, Chap. 6 presents how those approaches can be used to support pharmaceutical development and manufacturing activities.

Chapter 7 is dedicated to control strategies required to support the switch from batch to continuous models of operations for the production of pharmaceutical products. A general methodology required to design and implement a control system is presented together with the required software and hardware of the control platform. Chapters 8 and 9 focus on the importance of mathematical modeling for process simulation, optimization, and the development of the design space for pharmaceutical process operations. In particular, Chap. 8 reviews the approaches that are used to define process feasibility and how

those are applied for pharmaceutical manufacturing. Chapter 9 provides a review of the optimization methodologies that have been applied to achieve better performance in pharmaceutical manufacturing. Finally, Chapter 10 provides a very detailed step-by-step description of the manufacturing stages involved in the production of solid dosage forms. Process analytical technology (PAT) devoted to the continuous manufacturing of solid-based drugs is also described.

It is hoped that the collection of these papers will promote research into the process systems methodologies and their application in pharmaceutical product and process development, which will undoubtedly become an increasingly important area in the future.

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