dx.doi.org/10.14227/DT160109P41

Book Review

Pharmaceutical Dosage Forms: Tablets (Third Edition), Volume 3: Manufacture and Process Control

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Published by Informa Healthcare USA, Inc.

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As the editors indicate in the forward, this book is intended to continue in the fine tradition of Lieberman, Lachman, and Schwartz, editors of previous editions of *Pharmaceutical Dosage Forms: Tablets*. This edition expands upon the last edition, published in 1990, and devotes many pages to new technologies and emerging trends in pharmaceutical development. The 311 pages comprise eleven chapters covering a broad range of topics related to tablets: development, manufacture, characterization, regulatory considerations, and intellectual property. The authors of the chapters are well chosen and are able to provide not only concise descriptions of the current state of technology and modern practices but also insight into emerging trends.

As the title of the book indicates, the text is primarily about manufacture and process control of tablets, still the most popular dosage form. However, some of the chapters branch out into other areas. For example, the dissolution and dissolution specifications chapters discuss approaches for other dosage forms; the chapter on intellectual property uses biologicals frequently in examples. Some chapters are general enough to apply to the development of any dosage form, such as the discussion of the change in manufacturing paradigms in Chapter 3 and cGMPs for the 21st century, covered in Chapter 8. So, the reader will enjoy a good review of the state of the art in the pharmaceutical industry that is somewhat broader than the title might imply.

Consistent with the current state of pharmaceutical manufacturing, the book is peppered with the language and concepts of Quality by Design (QbD). In most of the chapters, the authors describe the integration of this new paradigm into their respective fields. This topic is also a focus of Chapter 8, "cGMPs for the 21st Century and ICH Quality Initiatives." The consistency of the QbD message makes the book relevant and valuable for modern-day pharmaceutical manufacturing.

Chapter 1, "Tooling for Pharmaceutical Processing" by Dale Natoli, begins with the history of the tablet press and quickly moves to modern-day technology. The chapter provides very practical advice on advantages and disadvantages of tooling shapes, choice of fonts, tool care, and even how to purchase tools. Readers new to the field will appreciate the "terminology" section, and anyone trying to troubleshoot a tableting problem will appreciate the two "problem–possible cause–corrective action" tables for issues with tablet quality and tooling. Chapter 2, "Tablet Press Instrumentation in the Research and Development Environment" by Gary E. Bubb, is also closely tied to the equipment aspect of tablet manufacture. This chapter discusses transducers, in general, and strain gauges, in particular. The theory and electronics of strain gauges is discussed in some detail, including problems and methods of calibration. The chapter concludes with some examples of data from tablet presses fitted with transducers.

Chapters 3 and 4 take a broader perspective and discuss the scale-up and manufacturing processes. Chapter 3, "Pharmaceutical Manufacturing: Changes in Paradigms" by Jean-Marie Geoffroy and Denise Rivkees, describes manufacturing process flow including supply chain, materials, engineering, packaging, validation, quality, and regulatory affairs. The second half of the chapter is devoted to new concepts such as QbD, data integration, and process understanding. The authors provide examples illustrating that new approaches such as process analytical technology can help improve process understanding and reduce the amount of time spent on troubleshooting. Chapter 4, "A Forward-Looking Approach to Process Scale-Up for Solid Dose

Manufacturing" by Fernando J. Muzzio, Marianthi Ierapetritou, Patricia Portillo, Marcos Llusa, Michael Levin, Kenneth R. Morris, Josephine L.P. Soh, Ryan J. McCann, and Albert Alexander, begins with general discussions of approaches to scale-up. It rather quickly moves into discussions of unit operations, specifically addressing the complex process of mixing. The authors of this chapter provide the reader with an understanding of the problems with scale-up in terms of material properties. A discussion of the current practice of scale-up by size enlargement precedes an explanation of the advantages of scale-up by time extension via continuous process techniques. A continuous process case study is presented to illustrate the point.

Readers of *Dissolution Technologies* will likely find Chapters 5 and 6 the most relevant to their work. Chapter 5, "Dissolution and Drug Release Testing" by Vivian A. Gray, covers all the highlights of dissolution testing in about 38 pages. The chapter is written with several historical explanations of current practices and references many helpful sources of information, including a convenient list of relevant FDA guidance documents. All compendial dissolution apparatus are described along with their typical uses. The section on method validation concentrates on the aspects related to the dissolution test itself and leaves the validation of the analytical endpoint to other sources. Instrument calibration is covered here, but the chapter does not include a description of the emerging trend of mechanical calibration of Apparatus 1 and 2. Chapter 6, "Setting Dissolution Specifications" by Patrick J. Marroum, is well written by an author with an FDA perspective. This chapter covers topics that are generally already covered in FDA guidance documents; however, the author explains helpful details and interpretations that are typically missing from guidance documents. The section on setting a *Q* value and selecting the specification time point is straightforward and practical. The author also gives insight into a more difficult theoretical question: should all lots that meet a dissolution specification be bioequivalent? The specification strategies presented in this chapter cover a wide array of dosage forms: immediate release, modified release (with and without in vitro–in vivo correlation), and non-tablet types.

Chapter 7, "Mechanical Strength of Tablets" by Göran Alderborn and Göran Frenning, gives a detailed description of the theoretical and practical considerations of tablet strength. This chapter provides a description of tensile strength for tablets and for agglomerates. The second half of the chapter is devoted to powder and granule compactability and how it is impacted by material properties.

Chapter 8, mentioned above, by Moheb M. Nasr, Donghao (Robert) Lu, and Chi-wan Chen, covers the topics of QbD that are by now familiar to those who have been following the evolution of this initiative. This chapter is valuable because it nicely summarizes many of the documents that have been written on QbD and new quality principles by different organizations. Many have heard about the need for QbD; this chapter gives historical reasons and recent data to illustrate that point. A nice summary of ICH Q8, Q9, and Q10 documents is given. The reorganization of the FDA Office of New Drug Chemistry to better align with the review of QbD submissions is also described.

Chapter 9, "Intellectual Property, Patent, and Patenting Process in the Pharmaceutical Industry" by Keith K. H. Chan and Albert W. K. Chan, covers most of the intellectual property (IP) considerations that would be of concern to a pharmaceutical scientist. The industry uses many types of IP: patents, trade secrets, trademarks, and copyrights, and they are all covered in this chapter. International considerations are also addressed. The patenting process is described by explaining each of the required elements along with several examples to illustrate the point.

The book finishes with two chapters on techniques for tablet and powder characterization. Chapter 10, "Near-Infrared Chemical Imaging for Characterizing Pharmaceutical Dosage Forms" by Gerald M. Sando, Linda H. Kidder, and E. Neil Lewis, begins with a basic overview of the techniques and instrumentation and then moves on to several examples to illustrate mapping techniques, useful metrics, and data reduction techniques. The integration of the techniques in a high-throughput setting is also discussed. Chapter 11, "Surface Area, Porosity and Related Physical Characteristics" by Paul A. Webb, uses the analogy of a bound book to explain the concepts of particle surface area and porosity. A significant portion of the chapter is devoted to both gas adsorption/desorption and the measurement techniques utilizing these physical phenomena. The common theories of gas sorption, including more advanced techniques such as density functional theory and molecular dynamics simulations, are explained. Mercury porosimetry is introduced along with the techniques for extraction of many physical parameters from the intrusion curve data. The chapter concludes with gas pycnometry.

Overall, I found the book pleasant to read and a wealth of information in only 300 pages. It is generally well written, although the writing style varies from chapter to chapter. I noticed only a few editorial errors, which are not significant enough to detract from the book's usefulness. It is written at a level such that a scientist just starting in the pharmaceutical industry could use the book to learn the fundamentals of tablet development. Alternatively, it is also a good source for someone who has been in a different part of the industry for some time and is looking for an introduction to tablet manufacture. The popularity of the previous editions of this series indicates the value to those practicing in the pharmaceutical industry. Similarly, I would recommend Volume 3 of the third edition to anyone seeking a definitive summary of tablet manufacture and process control.