

Book Review

Specification of Drug Substances and Products Development and Validation of Analytical Methods

Edited by Christopher M. Riley, Thomas W. Rosanske, and Shelley R. Rabel Riley
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Gregory P. Martin

Complectors Consulting LLC, Pottstown, PA 19465

e-mail: greg.martin@complectors.com

The establishment of specifications for a new drug product, whether for a new drug entity or a generic product, can involve challenging dialogue with regulatory agencies. This text provides an excellent, comprehensive overview of the approach to developing specifications for these products. It will be a valuable tool in the scientists' arsenal, particularly for those new to the process of establishing specifications and those in smaller companies where the necessary expertise may not be readily at hand.

The authors lead the reader down a logical path that addresses various aspects of specifications and the associated analytical methods starting with an Introduction and sections on Universal Tests, Drug Substance, and Drug Product. These are followed by sections addressing special areas that may not be applicable to all products: pharmacopeial methods, microbial methods, and testing of biological fluids.

The introduction addresses general principles behind the regulatory basis for specifications, the application of quality by design (QbD) to analytical methods, and validation of methods. This section provides insight into the interplay among the guidelines published by the International Conference on Harmonization (ICH), the pharmacopeial monographs and general chapters, and the regulatory authorities. The use of statistics to aid in selection of acceptance criteria and trending are also introduced. Use of design of experiments (DOE) and risk assessment, as part of a QbD approach, is discussed. Validation of methods is presented in the context of the current guidelines from ICH and *USP* General Chapter <1225>, with additional guidance on using a lifecycle approach, especially for issues such as method revalidation or transfer.

The section on Universal Tests addresses the often-underrated tests for appearance and identity, tests for assay and related substances that apply to virtually every

sample, and tests for general impurities of residual solvents and elemental impurities (which must be controlled since they can enter the process from a host of sources but generally do not benefit the patient).

Properties important to drug substances (crystal structure, chirality, and moisture content) and to drug products (dissolution and extractables/leachables) are covered in the next sections. Since it is impossible for any text to address these comprehensively, the authors have wisely chosen to focus on areas that can be critical to the materials.

The final sections on pharmacopeial, microbial, and biological fluid methods are especially valuable to those who need to learn more about these areas. The pharmacopeias are widely used, and it is very useful to have a clear explanation of the similarities and differences among the three major pharmacopeias (*United States Pharmacopeia*, *European Pharmacopoeia*, and *Japanese Pharmacopoeia*) and the efforts to harmonize them. The section on microbiology introduces the current standards for microbial testing and then focuses on some of the emerging technology that uses rapid or alternative tests to speed up the generation of results. In the final section, it becomes obvious that testing of biological fluids includes many complexities that are not present when testing chemical samples, and practical advice on how to develop and validate these methods is offered.

Overall, this book provides a broad overview of pharmaceutical drug substance and drug product testing. It ably accomplishes its primary objective of providing a critical and comprehensive assessment of the approaches used to identify key quality attributes, select and validate appropriate analytical methods, and establish specifications. I highly recommend this book, especially for those new to the industry, new to product development, or in smaller companies where this resource can be especially valuable.