Book Reviews

Validation of Bulk Pharmaceutical Chemicals. Edited by Ira R. Berry and Daniel Harpasz. Interpharm Press: Buffalo Grove, IL. 1997. 496 pp. ISBN 1-57491-042-6. $209.00.

Over the last 10 to 15 years manufacturers of bulk pharmaceutical chemicals (BPCs) have had to cope with increasing attention from the regulatory authorities, particularly the U.S. Food and Drug Administration (FDA). In 1992 the situation became particularly acute, when the FDA began conducting preapproval site inspections for all new drug applications and insisting that processes be "validated" before such applications could be approved. Prior to this, process validation was a concern only at the stage of manufacturing dosage forms; now it was to be transplanted into the entirely different realm of chemical processing.

This book is therefore a timely contribution to discussion within the pharmaceutical and fine chemicals industries of this all-important topic. Until now virtually no published guidance to BPC manufacturers has been available, either from industrial experts or from the authorities themselves. There has been plenty of advice aimed at pharmacists, but chemists could only read between the lines and do their best to interpret drug formulation practice in the context of synthetic chemistry. While it was acknowledged that BPC manufacture was "different" from pharmaceutical formulations, there has been no consensus about how the eternal principles of process validation ought to be applied to BPCs.

Perversely though the book has appeared slightly too early. The book having been written just before the publication in late 1996 of the FDA's draft guidance to industry on "Manufacture, Processing or Holding of Active Pharmaceutical Ingredients", there was no opportunity for comment on this key document.

The book offers a series of essays by industrial and quality assurance experts, which overall provide an introduction to the topic and some food for thought. Two chapters, "BPC Validation: An Overview and Comparative Analysis" (Max S. Lazar) and "Quality Assurance Systems" (Fred C. Radford), put the issue in a historical and philosophical context. A further two chapters are dedicated to explaining the legal framework for the regulation of BPCs and for validation, including a summary of important court judgments (David F. Weeda, Arthur Y. Tsien, Neil F. O'Flaherty, Irving L. Wiesen). There are articles on specific issues such as "Cleaning for BPCs" (William E. Hall), "Microbiological Attributes of BPCs" (Karen Zink McCullough and John T. Shirtz), "Vendor Qualification and Certification" (Ira R. Berry), and "Drug Master Files" (Arthur B. Shaw). Topics of specialist interest are "Validation of Sterile BPCs" (Robert V. Kasubick), "Validation of Biotechnology BPCs" (Rob Murphy and Robert J. Seely), and "Excipients: Facility, Equipment and Processing Changes" (Irwin Silverstein). There is also a useful chapter on "BPC Terminology and Documentation" (Robert A. Nash). At the heart of the volume is a detailed case study (Nirmal Khanna) of the validation programme at a fictitious BPC manufacturing facility. About 100 pages are given over to this, including numerous appendices of associated documentation.

Overall I found the book accessible and informative, with a good index and many references to original papers. The chapter on "Cleaning for BPCs" in particular should be read by all manufacturers. On the other hand, those looking for the step by step "what to do" and "how to do it" promised in Interpharm's catalogue may be disappointed. The only BPC process referred to specifically is for aspirin. I would have liked some discussion on how to identify and set ranges for critical parameters in complex processes, or guidance on how far back in the synthesis to go with validation (other than listing FDA's own vague criteria). A few chapters written by process chemists themselves would have improved the book significantly.

Nonetheless I would recommend this book as essential reading for all involved with quality or process management in the BPC industry.

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