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Book reviews

Good Laboratory Practice Regulations, 2nd edn., edited by S. Weinberg, Marcel Dekker, New York, 1995, 294 pp., US$125.00. ISBN 0-8247-9377-3.

Good Laboratory Practice regulations (GLPs) are issued by the Commissioner of the FDA, and establish standards for the conduct of studies designed to demonstrate the safety of pharmaceutical products. It goes without saying that the entire range of development science practiced today falls to some degree under GLPs, and therefore every worker in the field ought to have a basic understanding as to what is proper and what is not. This volume is designed to give the reader that degree of knowledge, and certainly succeeds in its task.

The first chapter (Jean Taylor and Gary Stein) sets the stage for the other chapters by reviewing the history of GLPs, beginning with the first perspective and regulations of FDA, and ending with the revisions of the 1980's. The second chapter covers the current FDA/GLP regulations, and is by far the longest in the book (86 pages). This chapter is most thorough in its coverage, and absolutely the most useful to practitioners in the United States. Wendell Peterson has written a general discussion of the GLP regulations as amended to 9/13/91, and discusses all critical parts in depth. He defines what type of studies need to be GLP, and which ones do not. I was particularly pleased with the clarity of his definitions, and found that the important terms are amply defined. He goes through all requirements of the GLPs, and expands on what the regulations actually mean, or even imply. Peterson's chapter is worth the price of the book.

The remainder of the chapters in this volume deal with other GLP considerations. Carl Morris and Frederick Snyder discuss the GLP regulations as they exist for the Environmental Protection Agency and in foreign counteries (an interesting coupling). The next two chapters cover special topics which pertain to various analytical laboratories. Barbara Sutter discusses how to implement GLPs in a non-GLP setting (Chapter 4), while John Fitzgerald and James Bower discuss how to align an automated laboratory into compliance (Chapter 5). This latter chapter is particularly interesting in that many analytical laboratories are turning towards automation to improve their productivity, while finding questions of validation akin to barbed wire and buried mines. Sandy Weinberg rounds out the special topics section by providing a particularly clear exposition of computer systems validation (Chapter 6).

Chapter 7 was written by George James, and covers the GLP inspection program of FDA. Unfortunately, this chapter is less than 20 pages and yet discusses an extraordinarily important area to the pharmaceutical industry. The chapter contains a basic outline as to the purpose of FDA inspections, the aim and focus of audits, and the content of a typical inspection report. The problem with this chapter is that it does not treat the atypical case. It would have been better if the author could have expanded his chapter with a few actual case histories, especially if enough issues of non-compliance existed so that they would have served as instances as to how facilities ought not to operate. Remember that there is no such thing as a failed experiment, for it can always be used as a bad example.

The volume ends with a brief discussion by Sandy Weinberg as to the necessity of GLPs, and why they will not disappear in the foreseeable future. Since this is certainly a correct perspective, the present volume is of value and should be on

the shelf of (and also read by) every individual having responsibility in a Quality Control function.

H.G. Brittain

Pharmacokinetics, 2nd edn., edited by P.G. Welling and F.L.S. Tse, Marcel Dekker, New York, 1995, 528 pp., US$175.00. ISBN 0-8247-9378-1.

The title of this volume does not do its subject matter justice, as it suggests that the book is mainly concerned with methodology to track the concentrations of drug substances in the body. The editors have chosen to place this science within the larger context of drug delivery, and have therefore succeeded in producing a far superior product. The more comprehensive scope of the chapter structure gives the reader a much better appreciation of classical pharmacokinetics, pharmacodynamics, and drug metabolism.

The first chapter (Dexter Goldman) presents the regulatory aspects of the subject matter, and outlines the principles of Good Laboratory Practice regulations as these are applied to pharmacokinetics. The chapter discusses in sufficient length the pertinent sections of 21 CFR 58 which define the regulatory requirements for such work. The author correctly points out that the GLPs have nothing to do with the science and design of pharmacokinetic studies, but are concerned with the prudent management of studies and with the integrity of data. It is his conclusion that compliance is cost-effective, since conduct of work ensures that studies would not be repeated due to insufficient documentation or questionable practices.

The next several chapters present an excellent overveiw of topics which precede the introduction of a drug into the circulatory system. Karen Habucky contributed an overview of the in vitro and in situ methods which can be used to assess the degree of drug absorption. Christopher Rhodes has provided a critical evaluation of the situation which has arisen whereby the science of drug delivery is now strongly influenced by pharmacokinetic principles. His overview is strong, but the strength of this chapter lies in the author's choice to be frank in his opinions and suggestive as to where the field ought to be headed. Vincent Lee follows with a discussion of the particular challenges associated with the delivery of peptides and proteins, focusing on both the preemptive barriers and on the systematic clearance of these drugs. To place a drug at its desired site requires transport across cell membranes, and the topic of membrane transport is addressed by Ernest Wright. The drug delivery section of the book concludes with a contribution by William Banks and Abba Kastin, discussing the blood-brain barrier and the special concerns of peptide drugs.

The next major section of the book begins with a description of the methodology used to model the relationships existing between pharmacokinetics and pharmacodynamics (Meindert Danhof and Jaap Mandema), and provides a particularly strong summary of models relating to the time course of pharmacological effects. Immediately following are chapters oriented toward drug metabolism topics: spatial imaging of radioactivity in animal tissues and organs (Alain Schweitzer), an outline of experimental methods used in studies of drug metabolism (Roger Hayes, William Pool, Michael Sinz, and Thomas Woolf), and the use of hepatic microsomes as in vitro models for drug metabolism (Thomas Kronbach).

Following the drug metabolism section, several reviews of the application of pharmacokinetic principles during various stages of drug development are presented. Peter Welling presents an overview of three approaches where pharmacokinetics could be totally integrated into all phases of the drug discovery and development process, amply discussing the pros and cons of each proposal. Francis Tse follows with a review of the goals and objectives associated with nonclinical pharmacokinetic studies, focusing on support for pharmacology, support for toxicology, prediction of human pharmacokinetics, and the screening of drug formulations. This chapter is followed by an equally detailed summary of the use of pharmacokinetics during the conduct of clinical studies, where Horst Schran and James Jaffe provide a lucid description of exactly what is to be learned during the three phases of clinical development. This section concludes with an exposition of the