Calcium Hypothesis of Aging and Dementia. Edited by John F. Disterhoft (Northwestern University Medical School), William H. Gispen (Rudoph Magnus Institute), Jorg Traber (Tropenwerke, GmBH), and Zaven S. Khachaturian (National Institute on Aging, NIH). Annals of the New York Academy of Sciences: New York, 1995. 482 pp. $130.00. ISBN 0-89766-878-2.

This book is the result of a meeting on the Calcium Hypothesis of Aging and Dementia which was held on the campus of the National Institutes of Health in Bethesda, MD, on December 15−17, 1993. The book presents the work of leading scientists to advance the understanding of the role of calcium on the aging process and in the development of neural states of dementia. It examines the slight imbalances of calcium, which, sustained over a long period, could lead to cellular deterioration and ultimately death, and presents reviews ranging from considerations of calcium channel function at the molecular level to the role of altered calcium levels in behavior.

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Development and Validation of Analytical Methods. Edited by Christopher M. Riley (Du Pont Merck Pharmaceutical Co.) and Thomas W. Rosanske (Hoechst Marion Roussel, Inc.). Elsevier: Oxford, U.K., 1996. x + 352 pp. $88.00. ISBN 0-08-0427928.

This is a very important reference book for anyone that needs to meet regulatory requirements for analytical methods, in terms of methods development, optimization, and especially validation. Any analyst working in a pharmaceutical or biotechnology company, analytical service laboratory, government regulatory laboratory, or outside laboratory working for any of the above organizations must eventually learn about many of the topics contained within this book. In chapters in a previous publication by Riley, Lough, and Wainer, entitled *Pharmaceutical and Biomedical Applications of Liquid Chromatography* (Pergamon Press, Elsevier, 1994), an orientation toward methods development, and to some extent, validation were also covered. The current book attempts, and at times succeeds, to turn its attention more to method validation, and well as contains some chapters on method development and optimization. In our teaching of this subject matter via various short courses, workshops, tutorials, and undergraduate and graduate formal courses at a university, it is clear that there is a tremendous interest and a need to learn the very subject matter of this text. The question is whether or not this book really does discuss, in the main, method development and validation of analytical methods?

There is no question but that this subject is vitally important to a large segment of the chemical community, especially analytical chemists involved in any regulated environment. There is a crying need within academia to learn more about method validation, especially when we are training analytical chemists to work in private industry or government laboratories. During most academic preparation, the students are never even introduced to the basic subject matter, at either the undergraduate or graduate level. Though there are numerous texts and review papers that appear on a regular basis involving analytical chemistry, HPLC, HPCE, mass spectrometry, and other analytical areas, most of these do not even introduce the subject matter of the current text. At the graduate level, virtually no analytical courses cover this subject matter either. At the undergraduate level, usually less is discussed about method validation than any other subject in the analytical chemistry curriculum. Why is that the case today? This book attempts to address this dire lack of attention, concern, education, and learning. There are very few books, in part or whole, that really discuss, in depth, the basic subject matter of validation for analytical methods. It is as if this is not a subject matter worthy of discussion in a formal analytical chemistry text nor course. How can we overlook such a terribly important and vital subject until the time comes when we must actually validate a method ourselves for the FDA, EPA, or another regulatory authority?

This book certainly fills a basic need in this area; however, it has some basic flaws, not the least of which is that it does not really discuss method validation the way that it could and perhaps should be discussed. At the same time, there are perhaps chapters in the book that are out of place, such as Chapter 2 on statistical parameters and analytical figures of merit, which are perhaps better found in a general analytical chemistry text, rather than one devoted to analytical method development and validation. Though Chapter 1 does discuss assay validation and interlaboratory transfer, it does so without going into the basic, specific (individual) techniques involved in true method validation. It also does not lead the reader through the process of different levels of validation at different stages of the drug development life cycle or of an analytical method's utility at a given time/place. Chapter 1 should have been the very heart of the book, yet it is given less than a total of 12 pages. On the other hand, the chapter on statistical parameters and analytical figures of merit is given a total of almost 60 pages. There should have been a reversal in the page allocation for these first two chapters.

The next section, Part Two: Regulatory Considerations, consisting of Chapters 3−5, deals with an overview of current, worldwide regulations involving analytical methods validation. However, not enough emphasis is placed on the current, up-to-date International Conference on Harmonization (ICH) guidelines. The ICH guidelines are about to supplant virtually all other government regulatory guidelines in the pharmaceutical area and may (it appears today) eventually be adopted by our USP with full FDA sanctions. Thus, at least one entire chapter on ICH alone might have been apropos for a book of this type and scope. The other two chapters in this Part Two are devoted to the Barr decision, which together consist of about 30 pages. These chapters could be considered irrelevant to the scope and intent of the book. The Barr decision does not relate to analytical method development, optimization, nor validation, but rather to the use of analytical statistics and good laboratory practices in a pharmaceutical laboratory environment.

Part Three has chapters that deal with bulk drug substances and finished products, dissolution studies, robotics and automatic workstations, biotechnology products, biological samples, analytical methods for cleaning procedures, and computer systems and computer-aided validation. These chapters discuss the development of analytical methods and their optimization for various types of samples and pharmaceutical products or processes. They do not, by and large, deal with method validation for any of these products or processes or stages of a drug's development. Though the USP guidelines for method validation are mentioned at various places in Part Three, there is not enough discussion of each parameter. In addition, there is no logical, sequential order of when/where/how to demonstrate each of the USP figures of merit for method validation, nor how much USP method validation is required as a function of the stage of the drug development process.

Of all the chapters in Part Three, perhaps the best was that by Srivatsa dealing with biotechnology products. In this chapter, he discusses the basic biopharmaceutical industry, specific regulatory requirements of biopharmaceuticals, analytical requirements of biopharmaceuticals, and validation of various analytical biotechnology techniques. This is an excellent overview of the basic biotechnology industry, with emphasis on the types of methods that need to be developed, but again with very little discussion of method validation, per se.

The references, by and large, are very up-to-date, thorough, complete, on-target, and comprehensive. We suspect, however, given the title, that the reader may expect more basic validation procedural information than what has been provided. However, the book accomplishes its goal of discussing issues that need to be considered and serves as a guide to considerations that must be attended to in any analytical process. In this regard, these reviewers consider the book a valuable resource for those working in a regulated environment.

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