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Book Review

Antimicrobial Susceptibility Testing. Critical Issues for the 90s
(Advances in Experimental Medicine and Biology/349)
Edited by James A. Poupard, Lori R. Walsh and Bruce Kleger
Published 1994 Plenum Press, New York
xii + 191 pages
ISBN 0 306 44673 1 $69.50

To paraphrase an old joke, when two microbiologists are discussing sensitivity tests, there are three opinions. This diversity of views underpins the need for a book such as Antimicrobial Susceptibility Testing—Critical Issues for the 90s. It is correctly stated in this book that the cost of antibiotic therapy substantially exceeds the cost of the sensitivity test, so good prediction is very cost effective. This book originated from a symposium of the Eastern Pennsylvania Branch of the American Society of Microbiology and the bias is inevitably towards American susceptibility testing criteria which, surprisingly, can be different from European, thus the reader should beware.

The book is divided into chapters written by different authors. The first chapter is historical and, except for the student of such history, unlikely to thrill. The second chapter on testing methods and interpretative problems is much more stimulating. It questions why sensitivity tests are performed and makes the timely reminder that the sensitivity test measures the interaction between bacterium and antibiotic, and does not tell you whether the antibiotic will control the organism at the site of infection. The author discusses the merit of disc diffusion tests and microdilution assays and warns against the current trend towards the latter. R. C. Bartlett has a chapter on when we should use sensitivity tests and emphasizes how specimens should be taken and maintained, how care must be taken to avoid mixed cultures, and how the tests employed should be appropriate for the organism and the antibiotic; much of this should be basic knowledge for the diagnostic microbiologist. He does, however, discuss how much information should be provided; an important point as some specimens are now being sent to private laboratories that do not provide consultant recommendation. There is a particularly provocative piece by Janet Hindler on the actual execution of sensitivity tests and the pitfalls that can be encountered. This chapter is essential reading for all involved in any sensitivity test with antibiotics and she emphasizes the importance of quality control and adequate training. I found the latter part of her chapter on the potential inaccuracies very revealing. There are further chapters that examine new techniques for minimum inhibitory concentration (MIC) and sensitivity testing. These include automated systems such as VITEK and ALADIN; these techniques may be more common on the other side of the Atlantic, but our diagnostic laboratories have yet to adopt them. A section that should have been important was the one that discusses MIC testing by gradient techniques. The most important version of this in the UK at the moment is the E-test. It is actually mentioned on page 9 in the Introduction, but the author promises it will be discussed in more detail later on. This promise was not kept, for although the E-test was mentioned twice later in the book (pages 137 and 156), it was only in passing. This was a serious omission as the E-test is the centre of much current debate.

The book continues with a number of philosophical questions such as "Is One Laboratory In Town Enough?"; to which virtually every UK microbiologist will simply answer "NO". The last section of the book discusses a few of the posters presented at the meeting from which the book was taken. These are quite esoteric, though I personally found the one on β-lactamase combinations by Barry particularly illuminating.

I am lucky enough to have been given this book because I am reviewing it. Sensitivity testing interests me so I would have bought it. If the reader is looking for a book to tell all they want to know about sensitivity tests, including how to do them, then this is not the book for them. It dips into the subject, with some superb discussions on specific points, but it is, by no means, a comprehensive guide.

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Book Review

International Pharmaceutical Product Registration. Aspects of Quality, Safety and Efficacy
Edited by A. C. Cartwright and B. R. Matthews
Published 1994 Ellis Horwood, Chichester
xxxx + 928 pages
ISBN 0 13 474947 X £175.00

I must admit to some trepidation in approaching this book. At almost a thousand pages, the volume is considerably larger than any of its predecessors in the Ellis Horwood excellent series in pharmaceutical technology. Secondly, the title of the book is not one to set the pulses racing, with its promises of more paperwork for the pharmaceutical scientist. However, these initial apprehensions were eventually set aside and I can safely say that this is one of those rare books that actually delivers more than it promises.

The same editors had previously published a book in the same series, entitled *Pharmaceutical Product Licensing; Requirements for Europe*. The success of that book—a success which was inevitable given the obvious need for such a publication—has prompted the authors to tackle the world scene, not as a discourse on national differences, but with the firm intention of concentrating on the underlying scientific rationale of registration requirements, contributing to the eventual holy grail of the pharmaceutical industry; the Global Dossier.

Anybody who has been involved in assembling a registration dossier of any kind will be well aware of the enormous breadth of expertise that is reflected in the document, ranging from materials science to enzyme kinetics, and one of the difficulties in assembling a book on the subject is to ensure that the various chapters are written with authority, and stitched together with editorial skill. Not the least of the problem is to persuade a large number of busy scientists to produce well-considered, relevant pieces in a reasonable time. I don't know what methods the editors used to achieve this, but they have certainly been successful; no relevant area is missing from the coverage, and the chosen contributors have the experience to ensure the volume speaks with authority. The contributors comprise a mix of pharmaceutical scientists from industry and from regulatory authorities, indicating the

day-to-day involvement of the authors. Most of the contributors are European, perhaps reflecting that the present book is built on the earlier volume. One might expect more than the single contribution from the US Food and Drug Administration, but on second thoughts, the European arms of the major drug companies must have considerable experience in preparing dossiers for the US authorities.

The book is divided into four main sections, five if you count the lengthy introductory pages—forty of them before the page numbers proper begin! I include mention of the introduction as it is well worth reading as a lucid and informative introduction containing a considerable body of background information to the evolution of national guidelines and regulations.

Part I is entitled Chemistry, Pharmacy and Manufacturing with the authors of the earlier chapters giving comprehensive descriptions of what are, for the most part, well-defined topics—formulation (described as pharmaceutical development), packaging materials, manufacturing, active ingredients, excipients, control tests on finished products, and stability data. The later chapters on analytical validation, biopharmaceutics and radiopharmaceuticals illustrate the problem of trying to categorize the various parts of the wide spectrum of subjects that needs to be covered. Indeed, the chapter on analytical validation is subdivided into matters dealing with pure materials and matters dealing with pharmacokinetic and toxicokinetic validation, with different authors for the two subsections.

Part II, Preclinical Toxicology and Pharmacology, demonstrates the breadth of this subject with its chapters on preclinical testing strategy, toxicity protocols including reproductive toxicology, mutagenicity and carcinogenicity. Whereas Part I deals largely with non-controversial matters of compound purity, Part II covers the greyer areas of biology, where knowledge is changing rapidly and there may not always be agreement as to which procedures are scientifically justified. There is an important chapter on animal pharmacokinetics and toxicokinetics, which describes several of the newer issues which are exciting the interest of the regulators such as problems with chiral molecules; the authors point out that where new regulations are promulgated there should also be consideration of the continuing relevance of established procedures to avoid an unnecessary burden on the originators of the information.

Part III takes us into the clinical aspects, including pharmacodynamics and pharmacokinetics (again), ethnic factors, Good Clinical Practice, clinical trials and statistical treatment of data.

Finally, Part IV comprises two chapters written by officials of the UK regulatory authority, which deals with clinical and scientific aspects of biological products and biotechnology.

So why do I contend that the book delivers more than it promises? My opening remarks suggested that the book promised a check-list approach to compilation of a registration dossier, and it would be safe to assume that anyone using it as such would be well-guided. However, it is in the wealth of other detail that is provided that I believe the book has great value. Several of the chapters expounding basic theory could serve as basic textbook material on their own and probably deserve a wider readership than they will reach if confined to registration experts. Additionally, there is information here that might not be easily obtained in the general scientific literature.

Despite my initial reservations, I enjoyed reviewing this book and would suggest it is essential for registration departments and would also be useful as a general reference for all those involved in the development phases of drug research. The editors are to be congratulated, both for their own substantial contributions and for ensuring the rest of the volume is presented in such a readable and well-integrated form.

JOSEPH CHAMBERLAIN

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Book Review

Herbal Drugs and Phytopharmaceuticals
Edited by Norman Grainger Bisset
Published 1994 medpharm GmbH Scientific Publishers, Stuttgart, and CRC Press, Boca Raton
XVI + 566 pages
ISBN 3 88763 025 4 MSP
ISBN 0 8493 7192 9 CRC DM 298.00 FR 298.00

I took this book home at Christmas to read and review over the holiday. It was spotted by a member of the family and mistaken for a Christmas present. Indeed, this is such a book that is very attractive to the casual browser with an interest in herbal medicines. The book is beautifully and imaginatively illustrated with colour plates ranging from details of seeds or parts of the plant to thin-layer chromatographic analysis of extracts. This edition is the first English translation of a well-established German reference book with the more specific title of 'Teedrogen', or 'tea-drugs'. Max Wichtl's collection of 181 monographs was therefore almost wholly concerned with the properties of various herbal teas, including even instructions for making the infusions.

Although herbal teas are now becoming more readily available in the United Kingdom, their use has been much more prevalent on the continent for many years, including their acceptance in pharmacies. This English translation is therefore a timely reminder that it is not just the mysterious Orient that puts its faith in imprecisely defined natural products as part of the everyday tool-kit against illness and disease; indeed there are many who would suggest that the well-worn path of isolating active constituents from natural products, identifying them and going on to produce pure synthetic samples of the active compound or an analogue is not the way to make best advantage of these traditional medicines. A typical monograph in this work contains paragraphs on the plant source and country of origin, including countries where the plant may be cultivated, the main constituents of the natural product as used, indications for its use as a tea or other herbal preparation as well as side-effects, details of medicines arising from the same source, the regulatory status (especially in the UK) and useful references to the scientific literature.

The foreword and preface to this English edition make sad reading however; the translator and editor, Norman Grainger Bisset died unexpectedly before the English edition appeared. I can only add to the views of David Phillipson in the foreword and Max Wichtl in the preface that this book will be a lasting tribute to Professor Bisset's efforts.

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Book Review

Pharmaceutical and Biomedical Applications of Liquid Chromatography
(Progress in Pharmaceutical and Biomedical Analysis Volume 1)
Edited by Christopher M. Riley, W. John Lough and Irving W. Wainer
Published 1994 Elsevier Science Ltd, Oxford
x + 379 pages
ISBN 0 08 041009 X £85.00 $136.00

This is a multiauthor volume of some 11 chapters, covering a range of topics in the application of liquid chromatography to the separation and analysis of drugs in a variety of matrices. In this context it is worth noting that liquid chromatography in this volume includes capillary electrophoresis but not gas liquid, supercritical fluid or thin-layer chromatography to any significant extent.

The book is divided into four principle sections covering new technology, recent developments in the isolation of compounds from biological matrices, preparative methods and method validation. The authors themselves are drawn from a mixture of backgrounds which include the pharmaceutical industry, manufacturers and academics. As is to be expected with a multiauthor volume, some of the contributions are more satisfying than others, and the articles range in scope from broadly based critical reviews to articles which are essentially research papers.

Particular highlights of the new technology section was an excellent overview of the current state of the art of capillary electrophoresis by David Lloyd, which provided a lot of food for thought. The other articles in this section were an in depth discussion of the use of the derivatizing reagent NDA for primary amines, amino acids and peptides (Riley et al) and the use of fast liquid chromatography for the analysis of enantiomers (Perrin).

The section on developments in isolation techniques covers solid-phase extraction (SPE) (Zief & Kakodkar), the use of restricted-access stationary phases for the direct analysis of biological samples (Perry), on-line microdialysis (Riley et al) and multi-column chiral bioanalysis (Lough & Noctor). I found the SPE chapter disappointing with little in it that was new (only one reference post 1990). Considering the many exciting and new developments in SPE (e.g. graphitized carbon, new polymer-based adsorbents, membrane-bound adsorbents, antibody-mediated SPE, automation) this was a missed opportunity. The use of restricted-access media is described in the next chapter. This provides a useful review of progress with an alternative approach to SPE, the direct injection of plasma samples onto HPLC columns containing phases designed to stand up to this sort of treatment. This is followed by a good overview of the use of in-situ microdialysis for bioanalysis, with a comprehensive reference list to 1993. This section is then rounded off with a brief review of recent progress in the coupling of achiral and chiral separations for bioanalysis.

Chiral chromatography is also the subject of the article by Mical & Wuonola, but in this case the separations under consideration are preparative in nature. This is one of the chapters that provides details of the authors own experiences rather than reviewing the field, and some interesting separations (but no references to other work) are provided. There then follows a chapter which reviews the use of liquid chromatography for protein and peptide purification (Narayanan). The major topics in this area are covered and many references are provided (up to 1993).

The final section of the book contains two articles which describe the approaches that can be taken to ensure that methods provide valid results in the pharmaceutical (Bopp et al) and bioanalytical areas (Lang & Bolton). These provide interesting contributions to the continuing debate on this important subject.

Overall the book is well produced, with generally accepted figures and an adequate index. Future volumes in this series on capillary electrophoresis and validation are promised by the editors and I will look forward to these with interest.

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