

REVIEWS

Ethical Safeguards in Research on Humans. Vol. 5. Philosophy and Technology of Drug Assessment. Edited by JOSEPH D. COOPER and HERBERT L. LEY. Interdisciplinary Communication Associates, 1717 Massachusetts Ave., N.W., Washington, DC 20036, 1976. 235 pp. 14.5 × 23 cm. Price \$9.00.

This publication consists primarily of the transcripts of an April 1973 conference on "Ethical Problems in Drug Experimentation," which was the fifth in a series on the Philosophy and Technology of Drug Assessment. The 3-year time lag was due to the death of the coordinator, Dr. Joseph D. Cooper, following the seventh conference of the series in March 1975. Human research is a subject with many recent developments, and there are current publications that diminish the significance and timeliness of these proceedings.

The conference dialog was divided into several aspects of human research including surgical experimentation, patients and prisoners as subjects, state moratoriums on research, how to turn off an experiment, national and local review mechanisms, extrapolating results from animal to human, and payments and indemnification. Unfortunately, the majority of the book is merely transcripts of the dialog among the 22 nationally renowned medical scientists who are listed as the conference participants. Other than the brief introductory summaries of each chapter, the dialog is sometimes difficult to follow. With the emphasis on dialog, the book suffers from a lack of references that might be useful in documenting the seemingly anecdotal comments of the participants.

The most valuable portion of the book is the introductory "Background Notes on Issues in Experimentation with Human Subjects." This 32-page segment of preconference material summarizes the issues prior to 1973 rather well. The background includes 63 references and a selected bibliography of eight publications. Readers who are following the human experimentation issue very closely may be interested in this publication.

*Reviewed by William F. McGhan
College of Pharmacy
University of Minnesota
Minneapolis, MN 55414*

Drug Metabolism Reviews. Vol. 4. Edited by FREDERICK J. DiCARLO. Dekker, 270 Madison Ave., New York, NY 10016, 1976. 340 pp. 16 × 24 cm. Price \$32.50.

According to the press release for reviewers, "Volume 4 includes treatises on the disposition of used and abused drugs, the effects of liver disease upon drug disposition, the biotransformation of insecticides by insects, the clinical usefulness of organic nitrates and the logistics of drug metabolism studies." This is a factual and bald description of a fascinating volume.

The trend toward the complete integration of drug metabolism and pharmacokinetics continues and is very apparent in these reviews. We might as well stop referring to drug metabolism and pharmacokinetics and recognize that we are dealing with an integrated science of drug disposition. The term "drugs" does not just refer to human health products but also to animal health products, pesticides, industrial chemicals, and just about any other nonnutritive material that can enter any type of living organism.

There are three reviews on compounds that have been in use from centuries to millennia: morphine and heroin (Boerner, Abbot, and Roe), nitroglycerin (DiCarlo), and caffeine (Burg). It is always surprising to realize that, despite the length of their use, a great deal about each of them remains unknown. They present active and ongoing research problems of fundamental importance. The review on nitroglycerin is fun to read as well as informative. It got some "Gee whiz, I didn't

know that" reactions from me. I'd recommend it as a model for authors.

A great deal of experimental work has been done, and clinical experience exists concerning renal dysfunction and its effects on drug disposition. Much less information exists on the effects of dysfunction of the liver, the other major organ of drug elimination. Wilkinson and Schenker's review on drug disposition and liver disease plays its part in redressing this balance.

The two most important reviews in this volume were written by Ruelius and Weiner on the logistics of drug disposition studies. The discipline of drug disposition is of fundamental importance in industry, where it constitutes an important part of the safety evaluation process, *de facto* or *de jure*. This is not simply to meet regulatory requirements; the regulatory agencies can only lag and react to what is found in the research laboratory and in the field when a drug is in use. Drug disposition studies can occupy a central place in the development process and interact with screening studies, pathology, toxicology, and "clinical" development and use. An academically engendered desire to know all that there is possible to know must give way to the imposition of priorities and the use of finite resources to find out what is of fundamental but practical importance. The primary question must be: "Within what limits is this agent safe and effective?" Each new drug represents a different problem. It would be impractical and impossible to impose rigid checklists or rules of procedure on drug disposition studies. The only valid approach, which both Ruelius and Weiner adapted, is to discuss general principles and then to illustrate the application of those principles by case studies of the problems presented by specific compounds. Many times they are saying the same things but what they are saying needs a lot of repetition.

This book costs almost 10¢ a page but it's well worth it. Buy a copy through your library or your own budget or even personally (it is tax deductible). Once you've got a copy, read it!

*Reviewed by Morris Pfeffer
Bristol Laboratories
Syracuse, NY 13201*

Calculations in Pharmacy. Third Edition. By SUE H. ROUSE and M. GEORGE WEBBER. Lippincott, East Washington Square, Philadelphia, PA 19105, 1976. 264 pp. 15.5 × 23.5 cm. Price \$12.75.

The familiar strengths of this useful textbook in pharmaceutical calculations have for the most part remained intact in the second revision of the work. Substantially little has changed in format, content, or presentation of the third edition. Most helpful is its continued logical approach to the reasoned solution for pharmaceutical calculations in a way that deemphasizes rote methods and confusing proportionalities.

To accommodate newer concepts, nearly 800 revised practice problems with answers have been prepared, and "much of the emphasis on the 'art of compounding' has been reduced or neglected in favor of orientation toward patients." The art of the printer, however, is very much evident in the presentation of the book. The new table of contents is expanded in topical outline and detail. It visually organizes the material chapter by chapter, thereby eliminating any need for an index. Answers for sample problems in the text are always given and in many instances underlined for added clarity and emphasis. The use of unit labels is judiciously observed; and wherever factor reduction by cancellation occurs in the sample problems, smaller faced type indicates the results of the operation, thereby making this edition uniformly more readable and understandable for the student.

Chapter 6 contains useful additions contemplated for inclusion in the second edition (1968) but dropped because of a perceived overlap

with pharmacology. This edition more boldly and appropriately includes the material on dosage calculations based on body surface area and Fried's rule for the calculation of children's doses based upon age in months. Standard nomograms are included for the conversion of doses based on body weight to doses based on body surface.

Much less successful is the material added in the newly appended Chapter 14. The authors preface their book with an indication that the material contained in this last chapter results from acknowledgment of requests from many instructors. The appended chapter, prepared by two of the authors' colleagues, attempts to review important concepts from chemistry [milliequivalents, electrolyte replenishment, and operator p (pH and pK)], pharmaceuticals (alligation involving the HLB system), and mathematics (logarithms, unit label analysis, and elementary statistics), all within 18 pages and 29 practice problems! The task is hopelessly more global than the space allotted, with the result that nothing in the chapter works well. A seven-page section (with nine practice problems on the elements of statistics, the operator p , and the unit analysis) is totally inadequate and will confuse even the proficient student who turns to it for review. It has no potential as a teaching chapter and the authors would have been wiser in reapplying their reasoning from the preface of the second edition: to reject the inclusion of these materials in the third edition because of duplication with much more authoritative and useful treatments in other standard pharmaceutical textbooks, rather than blemish the new edition with so inadequate a treatment.

Ignoring at least portions of the newly appended chapter as a misplaced and nonfunctioning appendage to the book, Rouse and Webber have provided a useful third edition that will undoubtedly continue to serve as a mainstay textbook for traditional courses in pharmaceutical calculations and as a wealthy storehouse of reference material and practice problems for the student engaged in competency based self-directed study.

*Reviewed by Robert G. Mrtek
College of Pharmacy
University of Illinois at the Medical
Center
Chicago, IL 60680*

Amino-Acids, Peptides, and Proteins. Vol. 7. Edited by R. C. SHEPPARD. The Chemical Society, Burlington House, London, W1V 0BN, England, 1976. 431 pp. 14.5 × 22.5 cm. Price \$57.75.

This volume is the seventh in the series of literature reviews in the field of amino acids, peptides, and proteins. Under the leadership of Dr. Sheppard, a selected group of researchers summarize the developments during 1974 in six chapters. As with previous volumes, the reader can expect the high standards associated with publications of the Chemical Society.

The first four chapters are primarily concerned with an extensive review of the literature regarding amino acids, structural investigations of peptides and proteins, peptide synthesis, and peptides with structural features not typical of proteins. In addition to the usual format, the second chapter contains tables summarizing features of affinity chromatography separations, molecular weights and subunit composition of proteins, uses of chemical modifications of proteins, affinity labeling of proteins, and proteins whose partial or complete sequence was published in 1974. These tables are followed by a summary of references to authors and published articles in an orderly and useful fashion.

A most important feature of this seventh edition is Chapter 5, which covers enzymes for the first time in the series. Dr. Fersht, in a sophisticated yet enjoyable manner, reviews some of the more important papers published during 1974 that were concerned with chemical structure and biological activity of enzymes; very appropriately mentions earlier work done in the area; and presents all sides of current work and some current problems. Chapter 6 is the biennial review of metal derivatives of amino acids, peptides, and proteins. The format

is that followed by previous volumes, and the reader is given a survey of the literature for 1973-1974.

This seventh volume presents the reader with some interesting developments, with further applications of known chemistry, and some presentations of old principles which have been given ingenious new applications. This volume is certainly a comprehensive source of information to researchers interested in amino acids, peptides, proteins, and enzymes. The information should, of course, be supplemented by reading the original literature, especially by students.

*Reviewed by A. Kapoor
Department of Pharmaceutical Sciences
College of Pharmacy and
Allied Health Professions
St. John's University
Jamaica, NY 11439*

Advances in Mass Spectrometry In Biochemistry and Medicine. Vol. 1. Edited by ALBERTO FRIGERIO and NEAL CASTAGNOLI. Spectrum Publications, 86-19 Sancho St., Holliswood, NY 11423, 1976. 586 pp. 16 × 23.5 cm.

This volume is a compilation of 51 separate papers of varying quality, with titles ranging from "Biomedical Applications of Chemical Ionization" to "Gas Chromatography-Mass Fragmentography Pharmacokinetics of Antineoplastic Agents." The text was taken from the proceedings of the Second International Symposium of Mass Spectrometry in Biochemistry and Medicine at the Mario Negri Institute for Pharmacological Research, Milan, Italy, in June 1974. Each chapter was contributed by different authors, and each relates to a different potential application of mass spectrometry in biochemistry and medicine. The topics range in value from prime import to minimal interest. Most chapters contain illustrations such as normalized mass spectra, gas chromatographs, and fragmentation schemes. The illustrations are clearly presented and well labeled. Each chapter includes a thorough bibliography which would enable the reader to do further research on the given theme, if desired.

Topics such as mass fragmentography, gas chromatography-mass spectrometry, stable isotope measurements, field ionization, field desorption, chemical ionization, atmospheric pressure ionization, high-resolution studies, and data acquisition and processing are discussed. In particular, the major topics include detection and identification of drug metabolites and other biomedical applications including biosynthesis and toxicology studies. Applications of mass spectrometry to the study of such important groups of compounds as peptides, steroids, prostaglandins, nucleotides, carbohydrates, and many other natural products and medicinal agents are given. Although mass spectrometry is the principal means of identification of these compounds, various means of isolation and separation are discussed. Also described are derivatization techniques that not only enhance volatility but also generate more intense ions in their spectra.

The papers contained in this volume represent a large cross section of mass spectrometric techniques presently being developed over a broad range field of mass spectrometry. Owing to the scope of this book, it is impossible to evaluate all of the topics covered at one level of criticism. This book does, however, have definite merit, since various mass spectrometry systems represent one of the most powerful means of analysis now available for the study of samples of biologic origin.

This book should serve as a useful source of information to many chemists, biochemists, pharmacologists, and medical researchers. Mass spectrometrists, in particular, will find this book useful in keeping abreast of the many faceted advances in their technology.

*Reviewed by Charles F. Kuhlman
Wyeth Laboratories, Inc.
Research Division
Radnor, PA 19087*