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Introduction to the Book Reviews

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Over the past 15 years, the debate about what to teach in statistics courses for nonstatisticians, and how to teach such courses, has intensified, particularly in the academic community. There has been a shift in focus from the traditional lecture—discussion—homework—test, probability based, statistical methods course to the highly interactive, data driven, statistical reasoning course addressing real life problems (for example, see Bradstreet (1996) and Sapra (1997)). The emphasis in the former style is on mathematics, probability, and methods of computation, with the information transfer performed explicitly from teacher to student in a formal fashion. In the latter approach, the emphasis is on statistical reasoning and problem solving using statistical tools. This often takes the form of workshop-based courses where students get experience in asking questions, defining problems, formulating hypotheses and operational definitions, designing experiments and surveys, collecting data and dealing with measurement error, summarizing data, analyzing data and communicating findings, and planning follow-up experiments suggested by the findings (Hogg 1991). Therefore, much of what is learned in these courses is implicit rather than strictly explicit. Some of the relevant references in the debate can be found in Misra, S.C., Sahai, H., Gore, A.P., and Garrett, J.K. (1987) and Sahai, H., Khurshid, A., and Misra, S.C. (1996); in recently published *Proceedings of The Section on Statistical Education*, American Statistical Association; and in the ASA-sponsored *Journal of Statistics Education*.

With the change in attitude and course emphasis, it might be reasonable to expect similar changes in text and reference books. Indeed, in academic circles, the books by Rossman (1996) and Utts (1996) have emerged with others in the renovation of statistical education for nonstatisticians. Hopefully, text and reference books targeted for the statistical education of our clients in the pharmaceutical industry will follow as well, thus making statistical reasoning and methodology accessible to a greater proportion of our clients.

We provide here reviews of several recent books which, based upon their title and targeted audience, are candidates for use by our clients in the pharmaceutical industry. The reviewers, with one exception, each selected a book from a list of 15 books which I (quite arbitrarily) compiled and provided to them. It is recognized that the list that I provided is neither a random sample from the population of such books, nor is it necessarily representative of that population.

Our objective was to produce a coordinated set of book reviews for the readership of the *Biopharmaceutical Report*, primarily statisticians, who then might recommend (or not recommend) some of the books to their clients. These clients are the consumers of statistical information, not the generators of statistical theories and methodologies. Therefore, I provided the reviewers with "Guidelines for Book Reviewers" which I felt were relevant to our clients' needs. These guidelines are shown on page 2. Perhaps they will be useful to the readership of the *Biopharmaceutical Report* in assessing the relevance and potential usefulness of similar texts.

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Guidelines for Book Reviews

1. From a "bookkeeping" or "documentation" point-of-view, be sure to include the following:
   - **a.** Title
   - **b.** Authors/Editors
   - **c.** Year of Publication
   - **d.** Edition (if other than first)
   - **e.** Publisher
   - **f.** Number(s) of Pages
   - **g.** Price
   - **h.** ISBN
   - **i.** Be sure to end your review with a summary statement about the book containing either a recommendation for or against purchase, with justification for your opinion.

2. Consider and weigh the following issues, as are appropriate for your text:
   - **a.** Whom do the authors suggest that the book is for? Whom do you think the book is for? Are you in agreement with the authors? What level of subject matter and/or statistical sophistication should the reader have? Whom is the book not for?
   - **b.** How should the book be used? Reference book? Text book? Self-instruction? Primary or secondary source of information?
   - **c.** What is the scope of the book? What are the chapter titles and/or chapter contents? Are they arranged in a logical fashion? Are any chapters exceptional? Are any chapters disappointments? Could any chapters be skipped? What level of detail does the book provide? Is the book up to date?
   - **d.** Does the book stress statistical thinking and reasoning? Or methodology? Or both? Does the book present an exploratory data-analytic point of view? Or formal inference? Or both? Is the book data and example driven? Or is it the basic lecture format? Does the book focus on decision making? On computation? Or both? Does the book present (or dwell) on theory?
   - **e.** Is the book written well? Does the author engage and motivate the reader? Is there adequate sign-posting throughout? Does the author present one or many viewpoints? How well does the author communicate? Does the author provide insight? Is the writing style conversational and nonthreatening?
   - **f.** Are there enough examples? Are they clear? Are they relevant to the reader's subject matter expertise?
   - **g.** Are there enough graphics and tables? Are they effective in demonstrating concepts and techniques?
   - **h.** Are there problems, investigations, or demonstrations at the end of the chapters for the reader to ponder and carry out?
   - **i.** How is notation used? Sparingly? Extensively throughout? Effectively? Or confusingly?
   - **j.** Does the book discuss the limitations of statistical methodologies?
   - **k.** Does the book mention/demonstrate the use of software? Is there an accompanying diskette?
   - **l.** Does the book contain a bibliography? Other reference lists? Use of citations? Subject index? Author index? Appendices? Comment on their quality and quantity.
   - **m.** Are there previous books which this one can be compared with? How similar? How different? Where does the book fit into the literature? What will be the impact of the book?
   - **n.** What is the general appearance of the book? Choice of type? Size of type? Use of colors? Box offsets? And so forth? Is the book constructed well? Is it worth the money?
   - **o.** Comment on the severity and quantity of conceptual, technical, computational, and typographical errors. Provide brief examples if necessary.

3. Some professional courtesies:
   - **a.** Review the book primarily from the reader's viewpoint, not your own. To the reader, this may be the only point of view that matters.
   - **b.** Do not just paraphrase the description on the dust jacket. Provide your own insight.
   - **c.** Be fair to the author and publisher. Do not point out every inadequacy of the book; indicating the major ones will make your point.
   - **d.** Be constructive, even if you cannot recommend the book. Your helpful comments may salvage a less-than-adequate first edition to be an exemplary second edition. Remember, today's reviewers may be tomorrow's authors, and today's authors may be tomorrow's reviewers!

REVIEWS, *continued from page 1*

I also imposed a single-spaced, two type-written page constraint on the reviewers.

I thank each of the reviewers for their contribution to this endeavor. These books are of potential interest and use by our clients in the pharmaceutical industry. Thus, the reviewers provided to all of us a valuable and timely service.

The books which were on the candidate list but were not reviewed are shown below. Perhaps they will be reviewed by someone else.

Andersen, Bjørn (1990). *Methodological Errors In Medical Research*. Boston: Blackwell Scientific Publications.

Bailer, John C. and Mosteller, Frederick (1986). *Medical Uses of Statistics*. Waltham, Massachusetts: NEJM Books.

Dunn, Graham and Everitt, Brian (1995). *Clinical Biostatistics—An Introduction to Evidence-Based Medicine*. New York: Halsted Press.

Fisher, Lloyd D. and VanBelle, Gerald (1993). *Biostatistics—A Methodology for the Health Sciences*. New York: John Wiley and Sons.

Gonick, Larry and Smith, Woollcott (1993). *The Cartoon Guide to Statistics*. New York: Harper Collins Publishers.

Iman, Ronald L. (1995). *A Data-Based Approach to Statistics*. Belmont, CA: Duxbury Press.

Moore, David S. (1995). *The Basic Practice of Statistics*. New York: W.H. Freeman and Company.

Rossman, Alan J. (1996). *Workshop Statistics—Discovery With Data*. New York: Springer-Verlag.

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Bradstreet, T.E. (1996), "Teaching Introductory Statistics Courses So That Nonstatisticians Experience Statistical Reasoning," *The American Statistician*, 50, 69-78.

Hogg, R.V. (1991),"Statistical Education: Improvements Are Badly Needed," *The American Statistician*, 45, 342-343.

Misra, S.C., Sahai, H., Gore, A.P., and Garrett, J.K. (1987), "A Bibliography on the Teaching of Probability and Statistics," *The American Statistician*, 41, 284-310.

Rossman, A.J. (1996), *Workshop Statistics—Discovery With Data*, New York: Springer-Verlag.

Sahai, H., Khurshid, A., and Misra, S.C. (1996), "A Second Bibliography on the Teaching of Probability and Statistics," *Journal of Statistics Education*, 4 (3).

Sapra, S.K. (1997), "Comment by Sapra" on Bradstreet (1996), *The American Statistician*, 50, 389.

Utts, J.M. (1996), *Seeing Through Statistics*, Belmont, California: Duxbury Press.

Book Reviews

Review of: *Biostatistics—Experimental Design and Statistical Inference*

Zolman, James F (1993). New York: Oxford University Press. xv + 343 pp. $45.00. ISBN: 0-19-507810-1.

Reviewed by Charles L. Liss
Merck Research Labs

This book provides a rather unique approach to the problem of imparting statistical concepts to the experimental biologist. A result of over a decade of teaching experimental design and statistical inference to researchers in the biological sciences at the University of Kentucky College of Medicine, Department of Physiology and Biophysics, half of the book is devoted to 100 real research design problems and accompanying critiques.

Although ostensibly divided into four parts, the book really has two main sections. The first comprises 12 chapters on experimental design, statistical inference, and statistical tests. The latter part includes the aforementioned research problems, each of which is 1-2 pages in length. There are no problems at the end of each chapter as one would find in a typical textbook. An introductory chapter (Chapter A) provides some philosophy regarding the research enterprise and the role of the research biologist. Part I of the book, titled "Experimental Design" (60 pages), includes four chapters. The first, "Anatomy of an Experiment," gives an overview of the research enterprise and the contribution of statistics to that effort. A number of useful definitions are also provided. The next two chapters, "Anatomy of a Scientific Paper" (3 pages) and "Evaluation of a Scientific Article" (2 pages) are entirely too short to cover the intended material and seem to be thrown in as an afterthought. The final chapter in this section, "Experimental Design" (37 pages), provides some real meat. Again, all the basic definitions are covered and the between-subjects designs are explained in great detail. Within-subject designs are only briefly discussed, with numerous cautions. It is not clear that this is a great service to the intended audience.

Part II of the book (60 pages) includes chapters on statistical inference, analysis of variance (ANOVA) and post hoc analyses. The chapter on statistical inference (23 pages) provides the basics of hypothesis testing (null and alternative hypotheses, critical regions, type I and II errors, power and sample size), as well as an effective lead-in to the concepts required for the next chapter on ANOVA. Sections at the end of the chapter on regression analysis and correlation seem out of place. This is especially true considering that the relationship of regression and ANOVA models is never explored. The next chapter on an ANOVA analysis also provides a great amount of detail (31 pages) on this particular method, including testing of main effects and interactions, and multiple comparisons. Oddly, there is very little discussion of crossover designs. The final chapter "Post Hoc Analyses" (3 pages) also seems to be added as an afterthought. Cautions regarding post hoc analyses and a brief mention of combining data from multiple experiments (e.g., meta-analysis) are noted.

Part III (37 pages) includes five chapters on disparate subjects. The inappropriately titled chapter on parametric tests (3 pages) actually talks about methods for checking distributional assumptions, such as box-and-whisker and stem-and-leaf plots. The next chapter continues the exposition of ANOVA analyses. In particular, it discusses nested designs with examples using litters of animals. This would seem apropos to the intended audience, although it's not clear why it isn't covered earlier. Popular multiple comparison procedures are covered next. This chapter provides a nice review and good practical advice and may be the most useful for the practicing biologist. The next chapter on nonparametric tests is woefully short (5 pages) and provides only a brief introduction to this area of statistics. The final chapter in this part is a review and reference to the concepts covered earlier.

The greatest contribution of this book to the statistical literature for nonstatisticians is in the final part of the book

(148 pages). Here are provided the research problems and critiques. Examples are taken from cardiovascular, renal, exercise, respiratory and neuro-physiology, as well as pharmacology, toxicology, psychology, zoology, and the biomedical sciences. Careful reading of these will certainly aid the statistically naive in reviewing the research literature as well as avoiding many common pitfalls. Despite an introductory statement indicating that an attempt was made to avoid jargon, this reader found this not to be the case. Although the terms used here may be common to a research biologist, a statistical student would find this section rough going. A typical quote follows (Research Design Problem 10): "Expiratory neurons in the area of the nucleus retroambigualis were studied in 20 anesthetized cats to determine their responsiveness to the iontophoretic application of the putative neurotransmitter gamma-aminobutyric acid (GABA)."

Although touted as a strength of the book, the extensive cross-referencing of topics in the text is annoying when reading this book. The extensive number of figures and tables, albeit beautifully reproduced, are not particularly helpful in explaining the material in the text. The text is laid out well and typographical errors are few and far between. An adequate bibliography is provided at the end. As befitting a book which is to be used as a reference for researchers, an extensive index is also provided.

As noted in the introduction, this book is intended as a secondary reference to a research-oriented statistical book. The audience is students in biological research. The research problems would also be of interest to the practicing pre-clinical research scientist in the pharmaceutical industry. However, the usefulness of this volume is restricted to that group by the choice of topics covered and the examples. Only parametric methods are covered in any depth, particularly ANOVA. There is virtually no discussion of ordinal or bivariate data. Other special methods, such as survival analysis techniques, are completely absent. In addition, nearly all of the examples come from the pre-clinical arena. Given the caveats above and a fair amount of quantitative literacy, a research biologist with a penchant for self-taught tutorials may find this volume a useful reference.

Review of: *Intuitive Biostatistics*

Harvey Motulsky (1995). New York: Oxford University Press. 386 pp. ISBN: 0-19-508606-6.

Reviewed by Daniel Holder
Merck Research Labs

The book is composed of ten parts, each made up of a handful of chapters. The ten parts are as follows: Part I. Confidence Intervals, II. Comparing Groups with Confidence Intervals, III. Introduction to P Values, IV. Bayesian Logic, V. Correlation and Regression, VI. Designing Clinical Studies, VII. Common Statistical Tests, VIII. Introduction to Advanced Statistics, IX. Overviews, and X. Appendices.

A statistics book can be a little like a political candidate's stump speech. To one audience the ideas will resonate with wisdom, to another they may seem off the mark. I think a very large audience will find *Intuitive Biostatistics* to be a useful resource in sorting out the what and why of statistical methods. The book is aimed at anyone who reads published medical papers. Consequently, the book focuses on the ideas behind statistical methods rather than computational details. Some formulae and details are given. However, it is primarily a book for a consumer, not a producer, of statistical analyses. Those looking for technical details should look elsewhere.

This book has more breadth than depth. Although, certain basic topics like confidence intervals and *p*-values are covered thoroughly, explanation of most topics is short and to the point. Much of the latter part of the book is dedicated to short vignettes on advanced topics such as logistic regression, comparing survival curves, multiple comparisons. For the most part the synopses succeed in providing the motivating ideas behind these sophisticated statistical tools and methods. Some readers, particularly readers encountering these methods for the first time, may find the explanations too succinct. Coverage of statistical methods used with continuous data is ample. Except for binary data, coverage of techniques for categorical data is scant. For the most part, explanation of concepts are very clear, although occasionally precision is sacrificed for readability. One nice feature of the book is that when a particular statistical test is discussed the assumptions required for the test are enumerated clearly. This makes the book a handy reference. Examples used in the book are taken from the medical literature, injecting a dose of realism into the statistics. The number of examples is sufficient for explanation, but do not overwhelm the reader. A couple of unusual topics, like the "Will Rogers Effect" and the "Let's Make a Deal" problem spice up the text.

The book reads as if you are talking with a good statistical consultant. The tone is conversational and informal. This is consonant with the philosophy of the book. Estimation is emphasized over formal hypothesis testing. Motulsky gives sound advice, not decision rules. Like a good consultant, the author makes many ideas clearer with judicious use of graphs and charts. I especially enjoyed the chapter entitled "The Big Picture," in which Motulsky espoused some wise, but not often clearly stated, statistical advice. Among the suggestions are: look at the data, beware of very large and very small samples, beware of multiple comparisons, don't focus only on averages, non-Gaussian distributions are normal, garbage-in-garbage-out, confidence intervals are as informative as *p*-values, statistically significant does not mean scientifically important, and $p < 0.05$ is not sacred. In the first appendix, Motulsky provides a list of thirteen books. Rather than cite original sources for a particular topic, Motulsky provides this list with a grid matching the books with the topics. Thus, the interested reader can find further information without having to plow through a pile of original source material.

Although *Intuitive Biostatistics* is intended as a reference for medical researchers, with a little ingenuity it could be used effectively as a classroom text. A few problems with answers in the appendix are given at the end of each chapter. Most of the chapters are self-contained so it is easy to pick and choose from the contents. The author points out chapters that may be of greater interest to clinical researchers than basic scientists. The statistical output shown in the books is from a basic statistics package called Instat, by GraphPad Software, Inc. Although a student reading the book might find it convenient to have this companion software, it is not necessary. There is an appendix dedicated to analyzing data with a spreadsheet or other statistics program.

I think this book fills somewhat of a void in the literature. I do not know of another place where the reader can obtain the basic ideas behind such a large array of statistical tools, both simple and sophisticated, without having to struggle through a mountain of details. In terms of a book to recommend to the medical scientist who wishes to understand the statistical concepts necessary to interpret published analyses, *Intuitive Biostatistics* gets a strong vote of confidence.

Review of: *Planning Pharmaceutical Clinical Trials —Basic Statistical Principles*

William M. Wooding (1994). New York: John Wiley and Sons, Inc. xx + 539 pages. $94.95. ISBN: 0-471-62244-3.

Reviewed by Thomas E. Bradstreet
Merck Research Labs

The author wrote this book for professionals in the pharmaceutical industry who plan, run, and analyze industrial clinical trials. He assumes that readers will be physicians, nurses, CRAs, (and perhaps) biologists, pharmacologists, chemists, or physical chemists, who understand the fundamentals of undergraduate algebra and may have previous experience with scientific research.

The book is divided into five parts, each comprised of from one to five chapters, with a total of 15 chapters. Each chapter ends with a summary and reference list. The appendices contain tables and computer programs. In the bibliography, the references are sorted alphabetically within one of 15 topics, including "graphical data display," "computer software," and "guides to good writing."

Part I (Chapters 1-3; 54 pages) introduces the structure and content of the book, outlines the scientific method as applied to planning a good clinical trial, and describes working with the U.S. Food and Drug Administration on the submission and approval of new drugs.

Part II (Chapters 4-7; 113 pages) provides an overview of the clinical trials planning process. Topics discussed include clinical trial objectives, medical response variables, independent vs. dependent variables, scales of measurement, blinding, randomization, blocking, stratification, matching, multiplicity, random sampling, hypothesis testing, sample size, power, use or nonuse of baseline measurements, ANCOVA, early trial termination, and the writing of the protocol and clinical case report forms.

Part III (Chapters 8-12; 100 pages) reviews experimental designs which, in the author's opinion, are the most commonly used. These are the one factor completely randomized design, randomized block design, factorial designs, and changeover designs, with or without longitudinal data collection.

Part IV (Chapters 13 and 14; 100 pages) is consistent with planning a clinical trial with the end in mind. It covers the fundamental ideas of data analysis and some basic statistical methods. General topics include scales of data, randomization, hypothesis testing, confidence intervals, and evaluating assumptions. Specific testing procedures include one and two sample t-tests, the least significant difference procedure, one and two sample Wilcoxon tests, large sample continuity corrected 2 x 2 contingency table tests, Fisher's exact test, and multiple comparisons procedures.

Part V (Chapter 15; 45 pages) concerns sample size estimation. The author stresses estimating variability from pilot trials.

This book has two strengths. The first lies in some of the author's advice to the reader. For example, the author indicates (p. 33) that there are three essential features of a good clinical trial: concurrent controls, blinding, and randomization. He points out (p. 41-43) that the selection of clinics and patients for a clinical trial is not random, and the best we can hope for is to recruit a representative sample. When determining sample size, he recommends increasing from the calculated value to a starting value which plans for dropouts (p. 251), and provides adequate cell replication in factorial designs (p. 217-220). On randomization, the author states that its use avoids bias in the assignment of patients to treatment (p. 127), it ensures the validity of statistical tests and confidence intervals (p. 126), and the common practice of randomizing allocation numbers in blocks is seldom taken into account in the statistical analysis (p. 130). On statistical analysis, the author suggests using ANCOVA instead of ANOVA on change (p. 74-75), he insists that residuals analysis be routine (p. 386), and he chooses heteroscedasticity as more serious than nonnormality (p. 378). And, he identifies multiplicity issues.

The second strength is the author's conversational style and pedagogical repetition. He speaks directly to the reader as if engaged in a consulting session. Each topic is introduced early in the text, and then repeatedly developed in later chapters. Although there are more than occasional diversions from a stated topic, there is adequate signposting throughout the book. He uses statistical notation sparingly, and he highlights important words with bold and italics font. Graphics, charts, and tables were, in general, used adequately.

However, the author also makes several philosophical and technical statements which many statisticians will disagree with. For example, with few exceptions (e.g., p. 126-127), the reader is repeatedly given the impression (e.g., p. 121) that a major purpose of randomization in a given finite sample size clinical trial is to ensure the balance of covariates between treatment groups. The author recommends (p. 103) only the Bonferroni philosophy for addressing multiplicity; he dismisses any use of first or second period baseline measurements in the two period crossover design (p. 296); and he suggests (p. 313-317) that the randomization scheme for a randomized block design and its statistical analysis alleviates the problem of an unequal carryover effect in the two period crossover study. In addition, the author instructs (p. 468) the reader to obtain the two tailed p-value for Fisher's exact test by doubling the observed one tailed result; he links statistics to parameters only by least squares methodology (p. 106); and by example (p. 251), he favors analyzing the data from only the planned number of patients when a study is over-enrolled. Further, by example (p. 272), he recommends evaluating the consistency of multiclinic results by computing the overall average response across all factors (including treatments) within each clinic and then comparing the overall clinic averages between clinics. This procedure does not assess the consistency between clinics in the qualitative and quantitative relationships observed between the treatments within clinics. And, the author is emphatic (p. 198) that the nonstatistical client is always the best qualified person to choose the statistical study design.

Among the author's comments on hypothesis testing, several concepts and technical issues are either misunderstood or miscommunicated. For example, in interpreting the observed outcome of a two sample t-test calculated at the end of a planned trial, the author says (p. 357), "If you find significance, you will conclude that the difference between the two drugs (in the population) is delta, . . . " where delta is defined (p. 433) to be "the minimum population difference that you wish to be detectable . . ." And, he states (p. 435) that "Alpha is the probability that the difference between the observed means being tested could be as large as they are seen

to be if there were really no population difference." These statements are ironic since the author states (p. 336) about hypothesis testing that "It is widely misunderstood among nonstatistical professionals, partly because we statisticians rarely explain it very clearly."

The author's treatment of the average bioequivalence problem is dated. He seeks to obtain "a lack of significance between drugs" (p. 303), and there is no explicit discussion of confidence intervals and precision. Also, the author does not mention the assessment of individual bioequivalence. In fact, he ignores most Phase I and II issues and study designs [e.g., see Rodda, Tsianco, Bolognese, and Kersten (1988)]. Some of the book's pedagogical repetition should be exchanged for coverage of Phases I and II.

With regard to omissions, typographical errors, and the like, it is not surprising that a 539 page first edition (but second printing) would have a few. However, there are too many. Several graphics are not consistent with their descriptions in the text. For example, the upper end of the visual analogue scale in Figure 4.2 should be "Very Severe Pain;" Figure 14.2 is not a plot of residuals vs. fitted values; Figure 14.3 should be rotated 180 degrees; and a "Totals" column label is needed in Figures 14.3 and 14.4. The typographical errors come in several varieties, including incorrect spacing, duplication of text, omission of necessary notation, inconsistent notation, incorrect decimal use, and inconsistent hyphenation. Some references are cited in the text without their inclusion in either the chapter reference lists or the book's bibliography.

In summary, I cannot recommend the entire book; only parts of it. Prior to giving selected sections of the text to nonstatistical clients, it will be necessary for a consulting statistician to read the sections, in detail, to determine a comfort level with the author's presentation. This seems quite labor intensive, and, at $94.95 a copy, expensive for limited return on investment. For additional details and discussions, see the critiques by Senn (1994), Williams (1996), and Keiding (1996). They also provide mixed reviews of this book.

References

Keiding, N. (1996). Book review of *Planning Pharmaceutical Clinical Trials, Basic Statistical Principles* by William M. Wooding, *Statistics in Medicine* 15: 1709-1710.

Rodda, B.E., Tsianco, M.C., Bolognese, J.A., and Kersten, M.K. (1988). "Clinical Development," Chapter 6 in *Biopharmaceutical Statistics for Drug Development*, Karl E. Peace, editor, New York: Marcel Dekker, Inc.

Senn, S. (1994). Book review of *Planning Pharmaceutical Clinical Trials, Basic Statistical Principles* by William M. Wooding, *Statistical Methods in Medical Research* 3: 432-433.

Williams, G.W. (1996). Book review of *Planning Pharmaceutical Clinical Trials, Basic Statistical Principles* by William M. Wooding, *Controlled Clinical Trials* 17: 72-74.

Review of: *Seeing Through Statistics*

Jessica M. Utts (1996). Belmont, California: Duxbury Press. 464 pp. ISBN: 0-534-25776-3

Review by William H. Stewart
Hoechst Marion Roussel

Statisticians, teachers, students, and scientists have complained for eons that statistics textbooks do not contain relevant, interesting examples. O.K., here it is. Jessica Utts has written an interesting textbook, *Seeing Through Statistics*, which is loaded with relevant examples. Utts presents many scientific problems from medical science, government, business, and social science which are used to explain the science of statistical thinking. This book is extremely well written, reading easily even when explaining the more difficult statistical concepts, and is printed in a very pleasing format.

Utts takes an unusual strategy in the order which she presents the concepts. She begins first with examples of real studies and data, i.e., case studies. As she presents these, she raises questions to get the reader thinking about statistical issues. She then takes the reader through chapters that explain how to run a well-designed study. Here she discusses how to measure and collect relevant data, how to sample, and how to run an experiment. This section is not just an introduction; it takes up about 100 pages and includes 13 case studies. Next Utts develops descriptive statistics in conjunction with looking at data and continuing the thought process about how to draw conclusions. Then comes a relatively short section on probability with a focus on how to interpret it, not how to calculate it. Finally comes the unification of all these ideas into a section on statistical inference.

In all, 39 case studies are presented and constantly used to provide a scientific basis for the statistical concepts. Utts's goal is to "emphasize statistical ideas and their use in real life." I believe that this goal is accomplished by her approach and style. This is a book that can be read and understood without the help of an instructor. It uses the minimum amount of mathematics to teach statistical thinking. All the basic ideas of random sampling, sampling variability of a statistic, the normal distribution, correlation, confidence intervals, hypothesis testing and *p*-values are explained in plain language, but still in quite a lot of detail as they relate to the case studies. There are particularly good sections: distinguishing sample surveys, designed experiments, and observational studies; the role of randomization in both sample surveys and experiments; cause-and-effect vs. association; statistical significance vs. practical significance; Simpson's paradox; and meta-analysis. This is not a book to teach a variety of statistical methods; only simple statistics based on normal approximations are presented. (Not even the *t*-test is covered!) I was disappointed that randomization tests like Fisher's Exact Test were not covered. This was surprising to me, because that approach is the most basic and simple one for understanding inference for randomized experiments. I was also disappointed in not seeing very many historical references to famous statisticians who have developed the science.

This will be a useful book for a statistician to loan to clients who want to understand more about statistics. It is not a short book to read, so the statistician would do well to mark key chapters or case studies to help focus on the client's immediate problem. In reading parts of this book, it's quite possible the client's interest will be piqued to go on and read the whole thing! This book certainly would be the first choice for clients weak in mathematics, but still might be helpful to others wanting a big picture of the role of statistics in science. I recommend purchasing this book for its wealth of real life examples, its unique and pleasing style, its coverage of many basic statistical issues, and its potential for getting non-statisticians interested in statistics.

Review of: *Practical Statistics for Medical Research*

Douglas G. Altman (1991). London: Chapman & Hall, 611 pp. ISBN 0-412-27630-5.

Reviewed by Michael Ames
Hoechst Marion Roussel

According to the publisher's description, *Practical Statistics for Medical Research* includes methods, principles, design, analysis, interpretation, and presentation of results for "medical researchers and clinicians" as well as "medical students and statisticians entering the field." The book does not assume any statistical background by the reader. To meet these ambitious goals, Altman's text covers:

Chapter 1: An introduction to statistics and the text.
Chapter 2: Types of data, e.g., continuous, categorical.
Chapter 3: Summary statistics and visual displays. Means, medians, standard deviations, scattergrams, histograms, box-and-whisker plots.
Chapter 4: Probability and probability distributions. The binomial, normal, lognormal, Poisson, uniform distributions. Independence.
Chapter 5: Introduction to research designs: observational vs. experimental, prospective vs. retrospective, longitudinal vs. cross-sectional. Covers basics of bias, randomization, blinding, replication, sample selection, controls, and sample size. Pros and cons of case-control, cohort, and cross-sectional studies.
Chapter 6: Uses and misuses of computers. Data collection forms, data layout.
Chapter 7: Checks for outliers, missing data, preparatory to analysis.
Chapter 8: Estimation, hypothesis testing, parametric vs. non-parametric methods.
Chapter 9: Analysis of continuous data.
Chapter 10: Analysis of categorical data.
Chapter 11: Correlation and regression.
Chapter 12: Multiple regression, analysis of variance, logistic regression, discriminant analysis.
Chapter 13: Survival analysis.
Chapter 14: "Some common problems in medical research."
Chapter 15: Clinical trials. Design, sample size, analysis, interpretation, and presentation of results.
Chapter 16: Common statistical problems in medical literature.

There are exercises at the end of most chapters (with answers) and statistical tables at the end of the book. Quite a number of the exercises are from actual research studies. I found them very interesting and more challenging than those in most textbooks. The reference list is extensive, reflecting the number of real examples used in the text and exercises.

An idea of just how ambitious the book is can be seen by going through Chapter 9: "Comparing Groups—Continuous Data." There are sections on independent vs. paired data; the *t*-distribution, with a brief explanation of "degrees of freedom;" confidence intervals for the mean; one sample *t*-tests; confidence intervals for the median using non-parametric methods; the sign test, with the large sample normal approximation and continuity correction; Wilcoxon signed rank test, with the large sample normal approximation; methods for paired data; confidence intervals and two sample *t*-tests for unpaired data; the Mann-Whitney test, with the exact distribution and large sample normal approximation; *F*-test for equality of variances; analysis of skewed data using the logarithmic transformation; one-way analysis of variance; exploration of residuals; Bartlett's test; adjustments for multiplicity; trend tests; Kruskal-Wallis tests; non-parametric tests for ordered groups; replicates; and presentation of results. Formulae and tables are given to perform all these analyses, but no theoretical development is given for these or any methods presented in the book. Chapter 9 covers 45 pages, plus 6 pages of exercises.

The book has a number of strengths. The advantages of estimation are stressed over hypothesis testing. The logarithmic transformation for handling skewed data is given. The author reminds the reader that the goal of analysis is to make inference to a population from which the sample, hopefully, comes and not to the sample itself. The author also makes an important distinction when describing the analysis of repeated (serial) measurements that in this case the "patient is the unit of investigation" (experimental unit) rather than the individual observations. The author gives prominence to the aspects of statistics that do not focus on the use of formulae and graphs. Specifically, the author states that the design of an experiment is as important, if not more so, than the analysis, as a poorly analyzed experiment can always be reanalyzed, but a poorly designed experiment can never be reclaimed. His final chapter on statistics in the medical literature has a checklist for assessing journal articles that, he points out, can be used to guide original research as well. And most of these points do not address statistical methods. Rather they focus on whether the study design was appropriate to the stated objectives, whether the source and method of selection of subjects was representative of the population, whether the study was sufficiently powered to be able to arrive at worthwhile conclusions, and how drop-outs and other sources of bias were minimized (including randomization and blocking).

The book is fairly general in most aspects, except that the examples and exercises are from a medical background, and could be used by researchers in other disciplines. However, there are enough topics relating directly to medical research covered here that are not covered in more general texts that can make this text more useful to medical researchers. Chapter 15 is specifically on design and analysis of clinical trials. Chapter 14: "Some common problems in medical research" addresses method comparison studies; inter-rater agreement with kappa statistics; diagnostic tests including sensitivity and specificity, prevalence, Bayes' theorem, likelihood ratios and pre- and post-test odds ratios; reference ranges; and the kind of analyses of serial measurements that are most common in pharmacokinetic studies, e.g., area-under-the-curve, peak response, time to peak response, etc., but that are actually more widely applicable in medical studies.

The author makes some recommendations that not all statisticians will agree with: e.g., non-significant effects in an analysis of variance should be pooled with the residual error (p. 332), step-wise multiple regression methods are preferable to all-subset regressions (p. 345). His recommendation for handling the multiplicity in means comparisons (p. 211) ignores much of the complexity behind this problem. Bayesian methods are not even mentioned. There are other statements the author makes that are just incorrect, e.g., ". . . if the sample size is large enough the distribution of the means will be Normal regardless of the distribution of the data" (p. 154). "There is another class of statistical methods which do not involve distributional assumptions which are called distribution-free or non-parametric methods." This is a statement that the author, fortunately, contradicts elsewhere in the text, but it does tend to reinforce the mistaken impression that non-parametric methods (which the author equates with rank tests, exclusively) will work on any dataset. There are

other problems; e.g., "The slope is the parameter of main interest in a regression analysis, as it indicates the *strength* of the relationship between the two variables" (p. 306, emphasis added). This is a sloppy choice of words, given the author's insistence on the difference in goals between regression and correlation analysis. On the same page the author seems to imply that the confidence interval given in his figure can be used both as the confidence interval for the line and for a point on the line. The only description of contrasts to study multilevel designs, one of the most useful methods in statistics, is in an incomplete description of their use in trend tests.

The author's stated attempt was "to give prominence to the concepts and principles of statistical design and analysis before considering specific methods of analysing data" (p. 8). However, the author attempts to cover too many methods to succeed very well. I could not recommend this book to a reader who does not have the option of reviewing it first. It might have a place on some readers' shelves, especially for those looking for breadth in these topics rather than depth, if it is not the only statistics book there. And there exist other, more complete, material on the non-statistical aspects of medical research discussed from a statistian's perspective, such as Pocock's *Clinical Trials* (1983), that may be a better place to start for new medical researchers and new statisticians in medical research. Statisticians will not find any methods discussed here that they probably haven't a reference or text for already. Researchers who will be primarily consumers of statistics would have been better served with more examples of fewer methods without so much detail on calculations. There are separate sections of formulae in the chapters, but in other parts of the book the author tries to incorporate the calculations into the text. I couldn't say how successful the author is in this conversational approach, but my guess is that the medical researcher without a strong mathematical or statistical background will find these sections, in Chapters 3 and 4 especially, hard to follow. (Imagine trying to write a paragraph or two on how to calculate normal probabilities or construct a histogram.) For more experienced researchers with some statistics background, the text would be worth reading for its strengths and the author's perspective.

Reference

Stuart J. Pocock. (1983). *Clinical Trials—A Practical Approach.* New York: John Wiley & Sons.

Review of: *All That Glitters Is Not Gold—What Clinicians Need to Know About Clinical Trials*

Furberg, Bengt and Furberg, Curt (1994). Winston-Salem, North Carolina (Curt D. Furberg, Professor and Chair, The Bowman Gray School of Medicine, Medical Center Boulevard, Winston-Salem, North Carolina 27157-1063). 59 pp. $12.

Reviewed by Michael G. Wilson
Eli Lilly & Company

This delightful little book will pique the interest of beginning medical researchers. Attractive and thought-provoking, it contains the most-essential fundamentals of clinical trials. Though you will not find any discussion of statistical methodology, you will find purely stated epidemiological principles on how to interpret results from a clinical trial, spiced playfully with sometimes cavalier and often clichéd language.

People are so drawn to this book that they cannot help picking it up off your desk and wanting a copy of their own. My colleagues said they couldn't put it down. What makes this book so attractive is its friendly size; no-nonsense, easy-to-read prose; inviting chapter titles; and winsome cartoons. Fifty-nine pages encourages both the busy and the potentially intimidated reader to say, "I can handle this." Written by clinicians for clinicians, the pages engage and motivate the reader through good insight, common sense, and a non-threatening, conversational style. The chapter titles, stated as questions, draw the reader into thinking about the contextual fundamental point. Throughout, Nils Simonson has generously distributed cartoons that effectively buttress the point of the text.

Building one chapter upon the next, their well-thought-out order closely parallels a more complete and previous work entitled, *Fundamentals of Clinical Trials*. In this less in-depth book, the authors skillfully present the opposing forces and principles to consider when addressing the chapters' questions. The case-studies and examples clearly illustrate the main point; and those having taught clinical trial courses know how difficult this can be.

For such brevity, its contents are surprisingly extensive. The format and the general scope prohibit detailed discussion, but this is its strength. Few authors of clinical trial texts take a moment to back away from the details and give the overall broad picture. Therefore, this is a very useful book. The chapter titles are the top questions that clinicians ask, for example: Does publication in a scientific journal guarantee quality? Was the scientific question stated a priori? How are adverse experiences measured? Is it really possible to assess quality of life? What is the value of surrogate endpoints or biologic markers? Were the treatment groups comparable initially? Why is blinding so important? What happened to the patients who disappeared from the analysis? Is biostatistical training necessary to interpret scientific data? Do the trial results also apply to my patients? Do meta-analyses provide the ultimate truth? How much confidence can be placed in economic analysis? What is the road map for reading trial reports? This last chapter pleasantly and briefly provides criteria for evaluating medical journal articles.

The book's short, concise form is also its limitation. Sometimes it's difficult to take a short book with cartoons seriously. So you might at first think that the book comes dangerously close to making clinical trials look too easy. You do not find a single intimidating statistical formula anywhere in the text, but you also do not find discussion of some statistical concepts basic to clinical trials theory and implementation. You may have wanted the authors to review caveats about interim analyses rather than discussing economic analyses. Inspecting its contents, you find no reference to alpha and beta errors, or sample size. Upon further review, you find no tables, graphs, datasets, accompanying diskette, end of the chapter problems, or investigations. The text does not discuss the limitations of specific statistical methodologies; beware, however, you might get the feeling that it does discuss the limitations of biostatisticians. More examples used in the text could have been referenced. Also, the reference list is too short. However, by this time, you already approve of the book and you overlook these imperfections.

There are few instructional books on clinical trials that are this much fun! Get copies by ordering directly from the second author, Curt Furberg, at the above address. It's a bargain; this glittering book is worth its weight in gold!

Review of: *Clinical Epidemiology: The Essentials (Third Edition)*

Fletcher, Robert H, Fletcher, Suzanne W, and Wagner, Edward (1996). Baltimore: Williams & Wilkins. ix + 276 pp. $28.95. ISBN: 0-683-03269-0.

Reviewed by Brian L. Wiens
Merck Research Laboratories

This book, written "for clinicians who wish to develop a systematic understanding of how the evidence base for patient care is developed and assessed" (p. VI), is primarily intended for practicing physicians and students studying to become practicing physicians—the consumers of medical research information. Yet, the content and presentation of material in this book will also make it useful to clients in clinical research who desire to learn more about effectively using statistics in research. The title should not be allowed to deter some who would potentially benefit from the book.

The authors write with a very clear, readable style, and they rely on charts, tables, and graphics rather than mathematical formulae and advanced statistical theory to present their ideas on the use of quantitative methods in medical research. This is the strongest feature of the book. Further, many of these graphical aids come from published medical literature, introducing the reader to examples of the very items that she or he will need to create or interpret. Another helpful feature is the summary section at the end of every chapter which concisely restates the main ideas of the chapter. Each chapter also has a bibliography and a list of suggested readings for further study.

Except for an introductory first chapter and a summary last chapter, the order in which the book is read is of little importance. Consequently, the ten remaining chapters can be read and studied in any order with little loss of understanding. These ten chapters are entitled, respectively, "Abnormality," "Diagnosis," "Frequency," "Risk," "Prognosis," "Treatment," "Prevention," "Chance," "Studying Cases," and "Cause." All chapters are worthwhile reading.

Chapter 3 (entitled "Diagnosis") contains a clear and concise discussion of interpreting diagnostic tests in a clinical setting. It will also be helpful to clients in preclinical and clinical research who use lab tests, assays, and other analyses to measure safety or bioavailability, diagnose a disease, or quantify a biological response to a test drug. Sensitivity, specificity, receiver operator characteristic curves, and positive and negative predictive values are all discussed with examples. Another example discusses making conclusions based on a borderline test result. Odds, probability, and likelihood ratios are also discussed in this chapter, including some simple equations to compare these different concepts—one of the very few places in which a mathematical formula is used in the book.

One of the most important concepts that a medical researcher needs to understand is the concept of randomness. The concepts of chance and randomness are clearly presented throughout the book. The main focus on chance is in chapter 9 (entitled "Chance"), which includes a very good discussion of random events and how the idea of random events is used in statistical analysis and discussion. The chapter begins with a discussion of random error, then proceeds into a good discussion of hypothesis testing, alpha and beta errors, *p*-values, confidence intervals, and even multiple comparisons. (The discussion of *p*-values is an improvement over the second edition of the book, but the notation is still a little non-standard compared with the notation usually shown in statistics texts and in the medical literature.)

The authors spend a great amount of effort to discuss various forms of bias. (The index lists over 20 references to the various forms of bias.) Nearly every chapter has reference to bias of some sort. Three broad categories (selection bias, measurement bias, and confounding bias) are discussed in the introductory chapter and continually throughout the book. With each new concept described in the book, the ideas of how bias can enter are discussed (e.g., bias in case-control studies, bias in cohort studies, bias in diagnoses, bias in selecting a study sample, etc.).

There are many more excellent topics that the book describes, usually in less detail. To give an idea of the breadth of the book, a list of the subjects described in the book would have to include cost-benefit and cost-effectiveness; quality of life measurements; using qualitative results to establish the preferred treatment for an individual patient; effectiveness compared with efficacy; meta analysis; prevalence studies; randomized trials; uncontrolled trials; and finding and interpreting appropriate articles in the medical literature. Each of these topics is described only briefly, generally in a paragraph or up to a couple of pages. None of the subjects is covered in enough detail to make the reader an expert on the topic, but all are covered well enough so that the reader can discuss the topic intelligently with a consulting statistician.

I have very few criticisms of the book. One error I found in the book is that standard deviation, while defined correctly in the mathematical formula, is described as "the absolute value of the average difference of individual values from the mean" (page 31). This is wrong, of course, and it may be wrong enough to cause confusion. I will grant that it is quite difficult to define the standard deviation in words, and this is one place when relying on a description rather than on the formula has negatively affected the book. Another comment (more of a caution than a criticism) is that, as mentioned above, the book will not make the clinical reader an expert in statistical methodology. This book will be most effective if a reader has a statistical expert available with whom any missing or unclear details can be discussed. Finally, there is no discussion of pharmacokinetics, bioequivalence, or other early (Phase I) studies, so for our clinical clients in those areas of research this book may have limited direct value.

The differences between the previous edition and this Third Edition are minimal. Chapter 10 ("Studying Cases") seems to be the most different from the previous edition of the book, in which the chapter was entitled "Rare Disease." (This chapter discusses case reports and case-control, cohort, and prevalence studies.) Someone who already uses the previous edition would probably receive only minimal benefit from replacing it with the new edition.

In summary, I will recommend this book to a research client in Phase II and III clinical research who needs to know about using quantitative methods in medical research, as well as the practicing clinician who desires to know more about incorporating quantitative methods into medical practice. Pre-clinical researchers may also benefit from studying this book, but that benefit will be less direct since the examples are generally drawn from clinical areas. I also might recommend it to the entry-level statistician who has a thorough background in statistical theory but little experience in applying statistics to clinical research. It contains practical scientific information and will help the entry-level statistician understand the level of comprehension of statistical concepts that his or her clients should possess.

Review of: *Health and Numbers: Basic Biostatistical Methods*

Le, C.T. and Boen, J.R. (1995). New York: Wiley-Liss, Inc. 247 pp. (plus 22 pp. introduction). US $34.95. ISBN: 0-471-01248-3.

Reviewed by Nathan Enas

Amongst the plethora of introductory statistics texts available today, in their present work, Le and Boen attempt to "rectify the dilemma" that results when "professionals and students in medical and allied health fields need a working knowledge of the methods for statistical analysis" and yet are limited to "the dry language and complex formulas of most statistics texts." I believe that the authors achieve their objectives, though at the risk of oversimplifying the subject.

Organizationally, the book has some novel features. It is much shorter than other introductory statistics texts, yet there is still quite a bit of user-friendly "white space" throughout the presentation. The brevity seems to owe to the omission of details other authors may feel are necessary for sufficient statistical depth or statistical purity. Quite a few times, the authors stop discussing a particular topic, stating that further discussion would be beyond the scope of the book. Although debatable, such omissions do help to streamline the text. Another reason the text is shorter than others is the focus on fewer topics, with just enough discussion to make a point. This can be illustrated by an outline of the contents: summarizing discrete data (chapter 1), summarizing continuous data (chapter 2), probability and distributions (chapter 3), confidence estimation (chapter 4), hypothesis testing and statistical tests (chapter 5 and 6), and various topics (chapter 7, includes additional statistical graphics, sample size calculation, and some nonparametric tests). These chapters are surrounded by a useful introduction, conclusion, bibliography for data sets used (a very nice feature), a few probability tables, solutions to selected exercises, and an adequate index.

Each topic is described briefly, directly motivated and illustrated by many examples, and reinforced with several exercises. Pictures and graphics are used occasionally. Formulas and statistical notation are used regularly, but are usually provided in the context of an algorithm that describes how to apply them. The authors even introduce some formulas using prose. The algorithmic approach is a strength, considering that the target audience may be relatively nonmathematically oriented. However, it seems that a natural complement to this approach would have been to incorporate, or at least mention, the use of computer software to perform the necessary computations, even if only a hand-held calculator with statistical functions. In this way, the pedagogical benefits of seeing and using the formulas could be attained while also giving students exposure to tools that some might find themselves needing someday.

The content of the text is a mixed bag of pros and cons. The authors do an excellent job at engaging their intended audience. A lengthy introduction broken into digestible sections serves this purpose and addresses issues like the reasons why statistics is so hard for some people to learn, setting reasonable goals, and dealing with formulas. One can see that the authors have spent much time teaching statistics to students with "math phobia." In addition, the authors use a variety of interesting examples from various medical fields to illustrate concepts and provide practice for solving other problems. Another excellent feature is the diversity of applications introduced to the reader. Noteworthy topics include adjusted mortality rates, odds ratios, life-table methods, and sample size calculation, among others. Nonstatisticians in the pharmaceutical industry will find many useful examples and exercises that apply to both clinical trials and epidemiology

While I believe the authors will succeed in engaging their readers, I also feel that the book's brevity will leave students with some substantial questions unanswered. This is not so bad in an environment where the reader can find assistance from an instructor or statistician. However, this puts a greater burden on instructors and may require substantial additions during lectures or consultations to make up for what the text lacks in detail. Even if instructors don't mind this, the reader may find the text less useful as a future reference than some of the more thorough, yet longer, texts. This is the requisite tradeoff which authors must address somehow. In this text, the authors focus on methods with less elaboration on rationale. Having said this, there are some notable counterexamples in the text where the authors provide more rationale; i.e., in the "basic concepts" sections at the beginning of chapters 4 and 5.

Finally, I believe this is a useful and unique contribution to the superset of all introductory statistics texts. It is concise and lively, yet it covers both basic and some advanced topics to the point where the reader can get familiar with statistical thinking and methodologies. It seems particularly suited for a short course in biostatistics as might be offered by a corporation's statistics group wanting to help colleagues understand statistical thought and some of the tools of the trade. Readers who would like a second opinion may wish to consult a 1996 review by J. D. Dawson of the same book (see Book Reviews, *Stat Meth Med Res*, 5:1, pp. 102-3).

Editor's Note

The following review by Don Edwards of Jason Hsu's book on multiple comparisons is in a different category than the previous reviews. Please don't add this book to your list of those you plan to recommend to your non-statistical clients; you might get mostly blank stares for your efforts!

Review of: *Multiple Comparisons: Theory and Methods*

Hsu, Jason C. (1996). Chapman and Hall, 277 pp.

Reviewed by Don Edwards
University of South Carolina

The reader should be aware from the start that Jason Hsu was this reviewer's thesis advisor some 15 years ago, and that we have continued as good friends since then. That matters little in view of the fact that the circle of individuals active in multiple comparisons work is sufficiently small that any competent reviewer would necessarily be friends with Jason Hsu. Also (and this is the voice of experience), writing reviews of friends' books can be a good way to lose friends.

This book would be ideal as a text for a graduate statistics course in multiple comparisons (indeed, it grew out of notes from an American Statistical Association short course). Many readers of The *Biopharmaceutical Report* may find it a little technical unless they can bring themselves to read between the derivations. For those who can, the thought-provoking rewards will be substantial, as there are few individuals today who understand the issues and controversies of simultaneous inference as deeply as Professor Hsu. Real-data numerical examples with graphics are used often and effectively. These examples, predominantly in the health sciences, are also an excellent showcase of the currently available commercial software for multiple comparisons. So, despite its technical detail, this is a book for everyone who does multiple comparisons.

Most of the book deals with multiple comparisons in the classical one-way analysis of variance setting, under normally distributed errors, though there are regular references to nonparametric analogs. Emphasis throughout is on simultaneous confidence intervals and/or bounds, since these are generally more informative than multiple significance-test procedures. Stagewise tests are discussed, in appropriate depth, as alternatives to interval estimates. Chapters 1 and 2 establish preliminary definitions and concepts, and define several "standard" forms of multiple comparisons problems whose solution forms the bulk of the rest of the book. These are abbreviated MCC (multiple comparisons with a control, Chapter 3), MCB (multiple comparisons with the unknown "best" treatment, Chapter 4) and MCA (multiple comparisons for all pairwise differences between treatment means, Chapter 5). Many readers will associate the classical methods of Dunnett (1955) and Tukey (1953) with MCC and MCA, respectively.

The sixth chapter is a short "concepts" chapter, a "rogues gallery" of multiple comparisons abuses and misconceptions. Hopefully its location midway through the book will not cause it to go unnoticed, as it should be required reading material for all of us! The seventh and final chapter deals with traditional and cutting-edge methods for multiple comparisons in more complicated data-analytic settings such as multi-factor analysis of variance and covariance, and for non-standard types of comparisons. There are also five very useful appendices, two for mathematical background, one on determination of sample sizes for multiple comparisons, one on accessing computer code available over the internet, and (of course) one for tables of critical points.

What is most surprising is that all of these bases, and others, are covered in a remarkably thin, unintimidating, and attractive volume. This bears witness to the author's deep, well organized understanding of multiple comparisons.

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Tukey, J.W. (1953). "The Problem of Multiple Comparisons." Mimeo of 396 pages, Department of Statistics, Princeton University.

Section News

Chairman's Column

Bob Davis

At this very moment you may be sporting a handsome new Biopharmaceutical Section T-shirt as a reward for completing the Section's survey. Phil Pichotta and the other members of the survey team are to be congratulated for getting the survey completed so quickly and eliciting such a high response rate (64%). Either our members are interested in the Section or are desperate for free clothes!

The survey results will be summarized in detail at the annual meeting in Anaheim this summer, in the *Amstat News*, and in later issues of the *Biopharmaceutical Report*. However, in this and future articles, I want to address some of the comments you made in the open-ended survey questions.

Old Boys Network

One suggestion that really struck home was to "Get rid of the good ol' boys' network of leadership. The same people from the same companies always doing the same thing—primary self-aggrandizement." To respond to this comment, first I had to look up aggrandizement in my son's SAT word list. Aggrandizement means "making appear great or greater." I suppose there is a little self-aggrandizement motivation in us all, but my experience has been that volunteers in the Biopharm Section do a lot more work than the resulting glory would justify.

On the other hand, the complaint about the old boys, or in some cases old girls, probably is valid. For 15 years or so, my Merck colleagues and I would dutifully send in the ASA form indicating interest in serving on various committees but rarely would we be selected. It seemed as if the same familiar names were always on the committees. I was 50 years old when asked to be a candidate for Section Secretary-Treasurer, my first ASA job except for local Chapter positions. Then I turned around and appointed two more old boys, Bob Small and Sandy Heft, to the Section Executive Committee, since I had worked with, or for, them in previous lives and knew their capabilities.

Somehow, we need to make use of the wealth of talent in our membership of over 1,700 strong. Last fall when we were looking for a third editor of the *Biopharmaceutical Report*, nine members indicated interest via E-mail and the names of those not selected were passed on to committee chairs as possible volunteers. So now I'll make another request. We will need volunteers for:

- Leading roundtable luncheon discussions
- Reviewing papers for the Best Student Paper Awards
- Organizing an invited paper session
- Chairing contributed paper sessions
- Collecting data for the Best Paper presentations at the ASA Annual meeting
- Sponsoring nominations for ASA Fellow
- Serving as Webmaster or Assistant Webmaster for the Section's Web site
- Organizing or presenting at Section short courses
- Organizing or serving on a Section work group to explore a particular statistical topic

If you have an interest in any of these positions, or in something I have overlooked, please contact me at:

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Phone: (610) 695-1070
E-mail: bob.davis@astramerck.com

We will try to get you involved as soon as possible, and we will maintain a volunteer list. But, when volunteering, please consider your other obligations. If job or family considerations may keep you from devoting serious time to the Section's activities, wait until your plate is less full before signing up with the Section.

I look forward to hearing from you. Maybe there'll even be some aggrandizement for you!

1996 Best Contributed Paper Award Winners

Shein-Chung Chow

Bristol-Myers Squibb

The following papers were selected for the Best Contributed Biopharmaceutical Paper for the 1996 Joint Statistical Meetings:

First Place

Brian Wiens, Joseph Heyse, and Holly Mathews. *Similarity of Three Treatments, with Application to Vaccine Development.*

Second Place

Gregory Campbell. *Statistical Issues in Medical Devices: A Regulatory Perspective.*

Third Place

Karen M. Higgins. *The Effect of Serial Dilution Error on Assay Calibration.*

Minutes of the ASA Biopharmaceutical Section Executive Committee Meeting

August 6, 1996, Chicago, Illinois

Attendees:

Tom Capizzi	Sally Greenberg	Denise Roe
Shein-Chung Chow	Ken Koury	Steve Snapinn
Christy Chuang-Stein	Jeff Meeker	Lianng Yuh
Bob Davis	Gary Neidert	Wayne Weng
Chuck Davis	Phil Pichotta	Curtis Wiltse
Richard Entsuah		

Gary Neidert welcomed the members of the Executive Committee and introduced the newly-elected officers for 1997: Chair-Elect, Ken Koury; Program Chair-Elect, Tom Capizzi; and Section Representative to the Council of Sections, Chuck Davis.

Minutes

The minutes of the March 19, 1996, Executive Committee meeting in Richmond were approved with two corrections. Under the Council of Sections report of the presentation by Lorraine Denby to the Council, the paragraph discussing proposed presentations at the 1996 Joint Statistics Meeting, the statement "We [the Electronic Communications Committee of the Council of Sections] will plan a session on what is available on the web . . ." should be clarified by changing the wording to "There will be a session. . . ." Secondly, under the ASA and Biopharmaceutical Section Web site, the discussion on whether to include E-mail addresses of Section members should read whether to include E-mail addresses of Executive Committee members.

1996 Invited and Contributed Paper Sessions

Steve Snapinn reported there were no invited paper sessions sponsored at the 1996 ENAR meeting in Richmond. The problem appears to have been poor communications with the ENAR program committee. Gary Neidert has sent a letter to Scott Zeger, current ENAR president, outlining our concerns.

The Biopharmaceutical Section sponsored the following sessions at the 1996 Joint Statistics Meetings:

- the short course Designing and Implementing Economic Evaluation in Health Care, by Michael Drummond, Joe Heyse, and John Cook;

four invited paper sessions:

- Hidden Issues Concerning Lab Data Evaluation, organized by Christy Chuang-Stein
- Greater Efficiency in Clinical Trials while Preserving Statistical Validity, organized by Jay Andersen
- Methods for Analyzing Recurrent Events, organized by Katherine Lipschutz
- Statistical Analysis of Combination Drugs, organized by Sanat Sarkar;

three special contributed paper sessions:

- Statistical Issues in Multiple Sclerosis Trials, organized by James Koziol
- FDA Session on Special Statistical Issues, organized by Satya Dubey
- Statistical issues in Medical Device Studies, organized by Richard Kotz;

and 14 regular contributed paper sessions:

- Growth Models and Smoothing
- Assay
- Bioequivalence
- Applications of Clinical Trials
- Multivariate Methods
- Sequential Clinical Trials
- Categorical Data and Crossover Trials
- Analysis with Missing Data
- Survival Analysis
- Issues in Multiplicity
- Vaccine Clinical Trials and other Clinical Trial Issues
- Pharmacokinetics
- Combining Information
- Regression Models

It was noted that there have been problems in many of the sessions so far with facilities, specifically room size, shape, and location.

The Executive Committee thanked Steve for an excellent job.

1997 Invited and Contributed Paper Sessions

Lianng Yuh indicated two invited sessions are already being arranged for the 1997 Joint Statistics Meetings:

- ICH Guidelines, by Frank Rockhold
- Using Decision Analysis Approach to the Drug Development Process, by Jay Andersen.

Plans are to organize a couple more sessions during September and October to have them available if we are able to get additional slots. Two new ideas which are going to be tried next year include invited poster sessions and informal lunch presentations. Lianng solicited ideas for both the additional sessions and for the invited poster sessions.

Post Meeting Note: A third invited session is organized by Donald Berry on an overview of the applications of Bayesian methods in drug development.

1996 Joint Statistical Meetings Luncheon Round Tables

Christy Chuang-Stein indicated there are 10 luncheon round tables at the 1996 Joint Statistical Meetings:

- Janet Wittes, Reporting Adverse Events—What can we Statisticians Contribute?
- C. Thomas Lin, Use of Statistics in Pharmaceutical Product Development
- Carl Metzler, PK/PD Modeling in Drug Development
- Lisa Kammerman, Challenges in AIDS Clinical Trials: Study Design Issues
- Lora Schwab, CRO Statisticians: Significant Differences, Significant Opportunities
- Steven Piantadosi, Advising the FDA on Product Approval
- Donald Berry, Bayesian Methods and Ideas in Medical Research
- Roy Tamura, Adaptive Techniques in Clinical Trials
- Laura Meyerson, Are Double Blind, Placebo Controlled Studies Really Blinded?
- Perry Haaland, New Optimization Strategies for Complex Chemical, Biochemical, and Physical Processes.

Lianng Yuh will fill in for Carl Metzler. Richard Entsuah will coordinate the reports. He solicited ideas for next year's round tables.

Work Groups

Lianng Yuh indicated the Population Modeling Work Group is to be disbanded after six years in existence. The second publication of this work group, which evaluated different methodologies and software for population modeling, has been accepted by *Statistics in Medicine*. He acknowledged the hard work of the individual members. Currently, there are no work groups. There was some discussion on regenerating work groups. The original intention was to use round table discussions to generate work groups. Richard Entsuah has been appointed Work Group Coordinator.

Joint Sessions with other Organizations

Lianng Yuh brought up the possibility of organizing joint sessions with other organizations at their meetings. He mentioned the American Association of Pharmaceutical Scientists and the American Medical Association, both organizations with which we have liaisons.

Best Presented Contributed Paper Awards

Wayne Weng reported the winners for the Best Presentation of a Contributed Paper Award for papers presented at the 1994 Joint Statistical Meetings:

- **1st place:** Larry Gould and Joe Heyse. *Simple Methods for Managing Multiplicity*
- **2nd place:** Fred Whaley, John Schoenfelder, and Carl Pinsky. *Comparing a Standard Diagnostic Procedure to a Second Procedure Used in Combination with the Standard Procedure*
- **3rd place:** Dror Rom and Eunhee Hwang. *Testing the Equality of Treatment Effects by their Proportion of Similar Responses.*

The winners for the Best Presentation of a Contributed Paper Award for papers presented at the 1995 Joint Statistical Meetings were:

- **1st place:** Keith Soper. *Estimation of Median Lethal Dose (LD50) for Sequential Designs with Small Samples*
- **2nd place:** Lisa Suchower and Steven Snapinn. *The Use of Adjusted Means in Presenting Clinical Trial Data*
- **3rd place:** Thomas Bradstreet and Milton Parnes. *Distributions of Order K in Passive Avoidance Testing.*

The awards will be presented at the Section business meeting. Evaluation forms are being collected from the 17 contributed paper sessions at the 1996 Joint Statistical Meetings. Shein-Chung Chow said he hopes to have the process complete by October.

Best Student Paper Competition

Chuck Davis announced the winners of the 1996 Student Paper Competition Award (in alphabetical order):

- Li Chen, Department of Biostatistics, Harvard School of Public Health, *Analysis of Multivariate Survival Times with Non-Proportional Hazards Models*
- David Dunson, Department of Biostatistics, Emory University, *Dose Dependent Litter Size and Implications in Quantitative Risk Assessment for Developmental Toxicity*
- Karen Higgins, Department of Biostatistics, Harvard School of Public Health, *The Effect of Serial Dilution Error on Calibration Inference in Immunoassay*
- Qi Zeng, Department of Biostatistics, Harvard School of Public Health, *Bootstrap Calibrated 'Calibration' Confidence Limits for Immunoassay*
- Hongwei Zhao, Department of Biostatistics, Harvard School of Public Health, *A Consistent Estimator for the Distribution of Quality Adjusted Survival Times.*

The awards will be presented at the Biopharmaceutical Section business meeting. Fourteen papers were submitted, more than three times as many as in previous years. Two reasons were offered for the increase in submissions: a letter was sent to 119 U.S. and Canadian departments announcing the competition and the deadline for submitting papers was delayed to June 1. It was proposed and the Executive Committee concurred that both the letter should be sent again and the date would remain June 1.

Currently, two endorsements, the student's advisor and the department head, are required on the application. It was proposed to change the requirements so that only one endorsement would be required. Also, currently the student has to be the sole author of the paper. It was proposed to change this requirement so that the student must be the first author and the presenter. It was also proposed that we modify the description of the program to emphasize that papers including practical applications and examples are especially valued. These requirement changes are to be on the agenda for the transition meeting, so a decision can be made prior to next year's competition.

Lianng Yuh was appointed to form a committee for next year's awards. He was also charged to develop formal procedures for the award. The procedures would be placed on the August, 1997 agenda and would be finalized at the 1997 transition meeting.

Post-meeting note: Denise Roe, Shein-Chung Chow, and Christy Chuang-Stein agreed to also serve on the Committee.

Council of Sections Report

Denise Roe reported on the Council of Sections meeting on August 5:

- The cost-sharing algorithm between ASA and co-sponsors of continuing education courses has been changed so that ASA and the co-sponsors are sharing profits and losses. The Section may subsidize the cost of Section members and presenters. The Committee on Continuing Education is looking for more 2-3 hour workshops costing $25-$50.
- The Board of Directors has formed a Committee on Strategic Planning. That Committee is seeking input from any sources on a wide range of topics.
- Section surpluses have decreased. The Section financial plans and budgets are due by the end of the year.
- ASA ended 1995 with a surplus of approximately $113,000.
- ASA currently has approximately 18,500 members. Retention rate on members obtained through the various marketing campaigns is approximately 65%.
- Corporate Member Dues are increasing from $480 per year to $780 per year. The last price increase was in 1986. This may impact the Biopharmaceutical Section since our Industrial Members must be Corporate ASA Members. There will be a small increase in individual membership dues.
- ASA Board of Directors voted $7,000 for a survey of membership interest. The Council of Sections will have an opportunity to request information to be collected of their interest on the survey. It was pointed out that the ASA survey will not impact the proposed Biopharmaceutical Section census because of the breadth of the ASA survey.
- The ASA Board of Directors has formed a Committee on Applied Statistics to address issues of statisticians in applied areas. Jeff Meeker is a member of that Committee.

- Recommendations of nominees were requested for President-Elect and Vice President of the Council of Sections and Council of Sections Representative to the ASA Board of Directors.
- There was a discussion of various Section success stories. The Biopharmaceutical Section was one of those presented, stressing the Biopharmaceutical Report, the Adverse Events workshop, student paper awards, and contributed paper awards.

Sally Greenberg reported on Council of Sections discussion of the ASA Web site.

- The Sections have donated $32,000 for this project. Lorraine Denby extended her thanks to the Section executive committees. The Web site has shown steady growth in the number of accesses. In the past month it was accessed by 7,328 different computer systems.The newest features include:
  - The on-line membership listing is on, effective July 31.
  - The entire Web site (Web sites) have been revamped
  - Keyword search of ASA pages, Section, and Chapter sites
  - ASA deadlines and dates
  - Clickable Chapter map
  - Joint Statistical Meetings program, abstracts, and registration form
  - Thirteen of 20 Sections have Web sites
  - Seventeen chapters have Web sites
  - Six journals have information on the site.
- The ASA Board of Directors approved Mike Meyer and Bruce Trumbo as co-editors of the Web site.
- The Committee currently expires on January 1. There is still approximately $5,000 left. The ASA Electronic Communications Committee is still waiting to hear from some Sections who didn't answer the E-mail query. There are a few items the committee would like to implement prior to being disbanded, so pretty much all of the money will be used.
- It is requested that the Section liaisons continue to interface and attend committee meetings during the year. The Section needs to appoint a Web master.
- Sally Greenberg was appointed Web master for the Biopharmaceutical Section.
- As of August 1, 300 requests concerning the online directory had been received by the ASA office. Approximately one-third requested omission from the directory. Others were address or phone number corrections. Currently, the directory listing is all information or nothing. Eventually people will be able to pick and choose what is listed and which address is listed on the directory.
- Action Item: Each person should check their online directory entry and submit correction forms if necessary.

Sally also reported the following information from the Electronic Communications Liaison Meeting:

- Soon ASA will have secure server capability for credit card transactions.
- Electronic submission of abstracts for the 1997 Joint Statistical Meetings is planned, with the abstract simultaneously submitted to both ASA and the Section Program Chair. No mathematics will be possible, except in LATEX. Electronic submission of abstracts is expected to save the ASA office $20,000/year.
- Plans are for the Sections to maintain their own sites. They will be mirrored onto the ASA site, unless there are strong objections from the Section.
- Sections may want a non-technical committee to review the content of the Web site. Advertising, libel, copyright, sales, and lobbying are major concerns of ASA. Job ads are more or less fine as long as there are no financial benefits to the Section or the sponsor.
- Listserv use of the ASA computer will be discussed at a policy meeting of August 7.
- Electronic proceedings will need to be approved by the ASA office.

Business Meeting Agenda

Gary Neidert reviewed the agenda for the Biopharmaceutical Section business meeting. Several items were added.

1996 Section Financial Report

Jeff Meeker distributed the final 1995 financial statements received from ASA and the 1996 financial statements through June 30. It was noted that the annual increase in cash on hand has been stemmed and, if expenses scheduled for later in the year are incurred, the Section will come close to meeting its goal of reducing its cash on hand by $30,000 this year. Jeff also indicated several errors in the 1996 report, including incorrect figures for cash on hand and the omission of the annual budget, even though it had been submitted. Also, the ASA does not separate individual membership dues and industrial memberships. Several of the donations voted on by the Executive Committee during both 1995 and 1996 have not been made.

Assignment: Jeff Meeker will follow up with ASA staff to make sure the donations are made.

Jeff stressed the importance of both the budgeted loss on the Adverse Event Workshop and the Section membership census on meeting our goal of reducing cash on hand.

Biopharmaceutical Report

The second issue of the *Biopharmaceutical Report* was mailed just prior to the meetings. A third issue, centered on Adverse Events, is scheduled for September. The series of reviews of books for nonstatistical clients by Tom Bradstreet will appear early next year. A lead article on Data Monitoring Boards is planned. Curtis Wiltse and Bill Huster are considering putting together an Information for Authors document.

The Executive Committee commended Curt Wiltse and Bill Huster for an excellent job.

Adverse Events Workshop

Christy Chuang-Stein updated the Committee on the Adverse Events Workshop, scheduled on October 28-29 at the Hyatt Bethesda in Bethesda, Maryland. The program is almost complete. The Executive Committee approved $1000 from our travel budget to subsidize travel of one speaker from the U.K. Christy expressed appreciation of the Meetings staff at ASA for their help.

It is expected that the program will draw a large interest, but attendance is limited by the meeting space available. It was decided to give Biopharmaceutical Section members who register prior to September 15 priority. After that date, attendance will be on a first come, first served basis.

The Executive Committee expressed their thanks to the Program Committee for the excellent program. The committee, in addition to Christy, includes Thomas Lin, Robert Northington, and Curtis Wiltse.

Membership Committee—Membership Census

Phil Pichotta reported that the current version of the

proposed census has been distributed for review. There was a discussion of the timeliness of payments.

Assignment: Jeff Meeker will preauthorize payment with Penny Young for bills up to $10,000, as approved in the Section budget. Bills should be sent directly to Penny.

Phil has had no response to his request for help. A recommendation was made to try to recruit younger people to help. Jeff Meeker stressed the importance of completing the census by the end of 1996 in order for the Section to meet its financial objectives for the year.

Finance Committee—Brochure

Assignment: Gary will contact Spencer Hudson to determine whether the update of the Biopharmaceutical Section brochure is on tract.

Section Web Site

Sally Greenberg reported that the Biopharmaceutical Section Web site has been running since March. It now contains:

- The Executive Committee and Section Representatives Roster
- The 1996 Joint Statistics Meeting Biopharmaceutical Section Program
- The Adverse Events Workshop Program
- Part of the first issue of the *Biopharmaceutical Report* for 1996
- The Biopharmaceutical Section Charter.

The following are expected to be available soon:

- A page with links to other relevant sites
- A page with Section activities
- A page with Section benefits
- The remainder of the first issue of the *Biopharmaceutical Report* for 1996
- Access counters on all pages.

Future issues of the *Biopharmaceutical Report* can be put on the Web site if either:

1. Someone will convert them from Quark to ASCII
2. The ASA office changes its policy
3. The ASA office will convert it to Adobe Acrobat format
4. The versions on the Web site are based on the Word documents which we submit to ASA, rather than on the finished product.

Option 2 is unlikely and option 1 is dependent on the kindness of Mike Conlin, who has been developing the Web site for ASA.

A question was raised as to whether a committee should be formed for electronic communication. This item is to be on the agenda of the October Executive Committee meeting. It was decided to put a note in the *Biopharmaceutical Report* concerning the availability of the Section Web site.

1997 Budget

The 1997 budget must be finalized at the October meeting. An initial look at the budget indicates that we will still need to reduce our cash on hand by approximately $10,000 during 1997. A concern was raised that we not overshoot the amount we are required to reduce our cash on hand.

Amendment of Biopharmaceutical Report Editorship

Curt Wiltse and Bill Huster proposed a change in the editorship of the Biopharmaceutical Report so that a person will rotate through the positions of Associate Editor, Editor, and Past Editor, holding each position for one year. This would allow greater continuity. The Associate Editor would spend a year learning the editorship process before spending a year as editor. The Past Editor would serve as an advisor. A motion was passed to accept this proposal and that the necessary changes be made to the Manual of Operations. The appointment of an associate editor would be added to the list of appointments made by the Chair-Elect.

Assignment: Gary Neidert will make sure the necessary change is made to the Manual of Operations.

Assignment: Bob Davis, as Chair-Elect, will appoint an associate editor for 1997.

Section Electronic Mail List

Sally Greenberg proposed the creation of a Section E-mail list which will be open to all Section members (and only to Section members) for the following:

- Announcement of relevant meetings and workshops
- Announcements of relevant job openings and availability of candidates
- Discussion of issues relevant to Section members.

Only Section members can post to and receive mail from the list. As such, the list owner will manually subscribe and unsubscribe individuals. The names and E-mail addresses of subscribers will be made available to the list owner, but not to other subscribers. The mail being sent to the list will not be moderated unless an abuse occurs.

A motion was passed that the Section create an unmoderated Biopharmaceutical Section E-mail list which will be open to all Section members. Subscriptions to the list will be limited to Section members. Postings to the list will include items broadly related to topics of interest to the Biopharmaceutical Section and its members. There will be no advertising or selling of products or services. Violators of this policy will be unsubscribed.

Sally Greenberg volunteered to serve as list owner/moderator for a period of one year.

Assignment: Sally Greenberg will provide two documents for review by the Executive Committee prior to the creation of the mail list: Guidelines for subscribers which will be provided to a subscriber at the time of subscription, and the Responsibilities of the Moderator.

Sally recommended that the list be maintained on the ASA computer system, when that system can support the list. Until that time, she recommended an Internet Service Provider. Specifically, she recommended Best Internet Communications, Inc. The cost would be $30/month plus an initial set-up fee of $30. The Executive Committee agreed to allocate $500 for the first year of the list.

ASA Fellow Nominations

Proposals for nomination to ASA Fellow will be discussed at the October meeting. One Section member is to become a fellow this year.

Candidates for Section Offices for 1998

Suggestions were requested for individuals to run for Biopharmaceutical Section offices for 1998. The two positions to be elected in 1997 are 1998 Chair-Elect and 1998 Program Chair-Elect.

Transition Meeting

The transition meeting of the Biopharmaceutical Section Executive Committee will be October 30 at the Hyatt Bethesda in Bethesda, Maryland. This is scheduled in conjunction with the Adverse Events Workshop.

Minutes of the ASA Biopharmaceutical Section Executive Committee Meeting

October 30, 1996, Bethesda, Maryland

Attendees:

Bob Davis	Ken Koury	Bob Small
Chuck Davis	Jeff Meeker	Steve Snapinn
Richard Entsuah	Gary Neidert	Lianng Yuh
Sally Greenberg	Phil Pichotta	Curtis Wiltse
Sandy Heft		

Each member introduced themselves. Gary Neidert reviewed the agenda.

Transition Review

Gary reviewed each person's responsibility in transferring responsibilities to next year s Executive Committee. He distributed a list of the 1997 Executive Committee and a list of 1997 assignments.

Assignment: Jeff Meeker will update the *Biopharmaceutical Section* Manual of Operations, including the following changes: revise section on the Editor of the Biopharmaceutical Report; add the third Executive Committee (transition) meeting; and update the list of committees to add the Committee on Nominations and the Fellows Nominations Committee and to delete the Committee to recommend statisticians to FDA advisory committees.

Minutes

The minutes of the August 6 meeting were approved with a clarification of the third sentence of the fourth paragraph of Sally Greenberg's report on the Council of Sections discussion of the ASA Web site, to read "The ASA Electronic Communications Committee is . . ." Also, the organizer of one of the 1997 invited sessions for the Joint Statistical Meetings was specified correctly in the minutes, although his name was misspelled.

1996 Financial Statement

Jeff Meeker reviewed the September, 1996, financial statement. By that date, we have reduced our cash on hand from $82,786 to $66,195. The current estimate is by the end of 1996 we will have reduced our cash on hand by approximately $24,000 (of the budgeted $29,900), about $6,000 under our goal for 1996. The donations to the Tape Preservation Committee and the Deming Lecture Fund have been made. The donation to the Student Analysis Competition was not made because we did not know who to make it to. Since the analysis for this year has already occurred, we will not proceed.

1997 Budget

Jeff Meeker presented a preliminary 1997 budget. The budget is approximately $6,000 short of our targeted reduction in cash on hand. Sally Greenberg noted that the $500 for the Section Electronic Mail List was not included. Several options were proposed to spend the remaining $6,000, including sponsoring another workshop, publishing proceedings of the last workshop, and providing financial support to working groups.

Assignment: Jeff Meeker will finalize the 1997 budget and submit it to Gary for approval. He will then submit it to ASA.

Bob Davis presented a request to support the SPAIG initiative, a proposal which arose out of the meetings the ASA corporate representatives and the academic department heads to develop a workshop on academic/industry/government interaction. The Executive Committee agreed to made a $500 donation.

Biopharmaceutical Report

Anne Meibohm has been appointed Associate Editor. Three issues are proposed for next year. To date, six items are proposed for publication, including several book reviews coordinated by Tom Bradstreet and articles on Data Monitoring Board management by Steve Snapinn, dissolution by Stein-Chung Chow, data integrity by Bill Fairweather, ICH Guidelines for Clinical Study Reports by Dave Carlin, and pharmaceutical cost effectiveness by Bob Obenchain. Other suggestions included a member news column, the publication of the results of the survey, a column on the Section mail list, and a summary of Section activities. The deadline for the next issue is the end of 1996.

Section Survey

On the week of October 7, 1,770 surveys were sent to Section members, at a cost of $4,382.61. As of October 25, 540 post cards had been returned. Data entry of the survey will be provided by Medfocus, as long as we acknowledge them for services provided in the article. Entry should start the week after the meeting. The present estimate is that 700 cards will be returned.

T-shirts will cost $5.80 plus shipping for a total estimated cost of $5,670. 100% Cotton shirts will cost $1.00 more. The Executive Committee authorized an additional $2,000 to cover additional charges for XXL size, foreign postage, sales taxes, and 100% cotton shirts.

Assignment: Jeff Meeker will check with Lee Decker to see if any extra T-shirts can be sold as souvenirs at the Joint Statistical Meetings.

The Executive Committee decided that the results of the survey should be presented as an invited poster at the 1997 Joint Statistics Meeting. The full results will also be published in the *Biopharmaceutical Report* and a summary will be published in *Amstat News*.

Web Site

Sally Greenberg reported that major enhancements, including counters and change notification by E-mail, will be in place for all active pages by November 18. An electronic list sign-up page will be added by the end of the year. Eventually the Web site will be moved to Best, where the mailing list is. She indicated there is a need for people to submit material.

Assignment: New Executive Committee members need to provide information, including address, phone number, and E-mail address for the Web site as soon as possible. Also, any changes need to be provided.

Assignment: If any Executive Committee member with an E-mail address who doesn't want to have it published wants an alias set up on the Web site, please contact Sally.

Electronic Mailing List

Sally Greenberg reported the electronic mail list is called asabiopharm. The mailing list introductory message was circulated to all Executive Committee members and is finalized. Also, a document listing the responsibilities of the list owner/moderator was circulated for review to Executive Committee members. An account with Best Internet Communications, Inc. was established on September 13. The mailing list was defined on October 21. The mailing list will be up on November 4. Handouts and a sign-up list were available

at the Adverse Events Workshop. Eighteen people subscribed. An electronic mailing list sign-up Web site form will be available by the end of the year.

Once there are approximately 50 subscribers or by approximately November 7, Sally needs volunteers to begin some discussions. She also needs a volunteer to be a back-up moderator. That person should be someone with seven day E-mail capabilities, but no other computer sophistication is required. The primary task will be to subscribe/verify membership for people when the moderator is away from E-mail for a period of time. This will become important in early January.

Assignment: Sally will prepare a proposed section for the Manual of Operations for Web Master/Assistant Web Master.

Council of Sections Debriefing Meeting

Four items were noted as requiring potential action of the Council: the Health Policy Statistics Section wanted to co-publish proceedings with another Section and requested any interested Sections to contact them; there were problems with facilities at the meetings, including problems with round table facilities, room set-up, size, and noise levels; Penny Young claims that all internal funds transfers are up-to-date; and to avoid conflict with Section Executive Committee meetings, the Council of Sections meeting next year will be scheduled at 4 p.m. on Sunday. There was a lot of concern from the Sections about the timeliness of financial reports and the status of the ASA computer system transition. In addition to charges not showing on reports, numerous membership changes were lost. Several Sections expressed concern about drop outs and had questions about the general membership survey. There was a discussion on the cost of proceedings, electronic proceedings, co-publishing, and which Sections are making and losing money. There was a brief discussion of the annual meetings facilities and logistics, including concerns about the mixer, round tables, and Council of Sections meetings. Several Sections expressed interest in a fee structure which allows Section membership without belonging to ASA.

Jim Landwehr, of the ASA Constitutional Committee, asked Sections to address the following:

- Do Sections feel they are being adequately represented on the Board of Directors?
  —The Executive Committee felt yes.
- Do Sections feel people should be allowed to join Sections without necessarily being a member of ASA?
  —The Executive Committee felt no.
- Do Sections feel they have the autonomy and responsibility they need?
  —The Executive Committee felt autonomy was not an issue.

The Executive Committee also raised the question as to how Council of Sections representatives to the ASA Board of Directors were elected. The Executive Committee felt the representatives should be selected solely by members of Sections.

Assignment: Sally will communicate our responses and the additional question back to Jim Landwehr.

1997 Program

Three sessions have been arranged for the Biometric Society (ENAR) meeting in Memphis, March 23-26:

- Dilemmas of Regulation: Dtheorems for the FDA, organized by Peter Lachenbruch
- New Wine from Old Bottles, organized by Dave Salsburg
- Sample Size Reestimation in Medical Studies, organized by Gordon Lan.

Three invited paper sessions are arranged for the Joint Statistical Meetings:

- ICH-E9: A Review of International Biostatistics Guidelines in Drug Development, organized by Frank Rockhold
- Applications of Decision Analysis in the Pharmaceutical Industry, organized by Jan Andersen
- Applications of Bayesian Methods in Clinical Trials, organized by Don Berry.

We are competing for one more invited paper session which will be Therapeutic Equivalence, Bioequivalence, and Dissolution Similarity Testing with Multiple Variables, organized by Yi Tsong.

Post-Meeting Note: We lost in the competition.

One special contributed session is arranged on Statistical Issues on Health-Related Quality of Life Assessment in Cancel Clinical Trials, organized by Wayne Weng. There is also an invited poster session. The FDA has not responded on the FDA Special Invited Session.

Assignment: Anyone with recommendations for chairs of contributed paper sessions should give them to Lianng Yuh. The chairs will be expected to provide a 5 minute summary of the session.

There was a discussion of proposals for continuing education offerings for next year.

Assignment: Christy Chuang-Stein will find out the deadline for submitting Continuing Education proposals. Also, she will contact Bruce Rodda and Bob Starbuck to see if they are interested in repeating the course on Statistics in the Pharmaceutical Industry.

1997 Candidates

Bob Davis presented the proposed candidates for 1997 elections for Chair-Elect, Program Chair-Elect, and Publications Officer.

Fellows Nominating Committee

Gary Neidert is organizing a committee of current ASA fellows who will be charged with identifying potential candidates for ASA Fellows from the Biopharmaceutical Section, to identify the Fellow to write the cover letter for each candidate, and to find someone to put together the package, to be submitted by the deadline.

Post-Meeting Note: Bruce Rodda has agreed to chair the committee. The other members will be Charlie Goldsmith and Larry Gould.

1996 Best Paper Award Winners

Gary Neidert reported for Shein-Chung Chow that the following papers were selected for the Best Contributed Biopharmaceutical Paper for the 1996 Joint Statistical Meetings:

- **First Place:** Brian Wiens, Joseph Heyse, and Holly Mathews. *Similarity of Three Treatments, with Application to Vaccine Development.*
- **Second Place:** Gregory Campbell. *Statistical Issues in Medical Devices: A Regulatory Perspective.*
- **Third Place:** Karen M. Higgins. *The Effect of Serial Dilution Error on Assay Calibration.*

There was some discussion concerning the policies regarding this award. There was also a discussion concerning the lack of votes and proposals as to how to get more evaluations.

Post Meeting Note: A search for a written policy was made, although little was found. A written policy was proposed.

1997 Round Table Topics

The following topics were proposed for round table discussions at the 1997 Joint Statistics Meetings:

- Statistical Modeling of Dose Response Relationships
- Multiple Endpoints Issues in Clinical Trials
- Assessment of Onset of Treatment Effects in Clinical Trials
- Recent Developments in Generalized Linear Models
- Interim Analysis and Early Termination
- Adaptive Designs and Analysis in Clinical Trials
- Bayesian Approach to the Analysis of Clinical Trials
- Statistical Issues Involving Adverse Effects in Cross Over Designs
- Missing Data in Cross Over Designs
- Individual Bioequivalence
- In Vitro Dissolution vs. Bioequivalence.

A summary of 1996 round table discussions is needed for the *Biopharmaceutical Report.*

Assignment: Richard Entsuah will work with Christy Chuang-Stein to determine if any of the round tables can be expanded into work groups.

1997 Student Paper Competition

The proposals to modify the Student Paper Competition made at the August 6 meeting of the Executive Committee were approved, specifically: the requirements were changed so only one endorsement, the major professor or the department head, would be required rather than both as is currently the case; the student must be the first author and the presenter of the paper rather than the sole author; and the description of the competition will be modified to emphasize that papers including practical applications and examples are especially valued.

Adverse Event Workshop

There were approximately 160 who attended the Adverse Events Workshop, including approximately 30 who were in an overflow room. The attendees recommended against the use of an overflow room in the future, since it was hard to see presentations and participate. Otherwise, the workshop was considered a success. It was proposed that evaluation forms be used in the future. They were not this time. A proposal to publish the proceedings of the workshop was discussed. Another proposal was to organize a follow-up session at the Joint Statistical Meetings.

Assignment: Christy will provide a financial summary to Jeff and the Executive Committee.

Response from ENAR

Gary distributed the response from Scott Zeger to our letter concerning past difficulties with ENAR on the program for the Spring meeting. The Executive Committee discussed our reaction extensively. Lianng Yuh was appointed to work with the 1997 ENAR program chair to also develop a protocol for how the two program committees would interact in the future. The Executive Committee decided that, in addition, the Biopharmaceutical Section would request a specified number of dedicated sessions to be contributed by the Section.

Proposals for New Activities

The Executive Committee discussed a proposal to publish a series of how-to manuals, similar to the series published by ASQC for quality control personnel. The texts would be cook-book in approach. There was a mixed reaction from the Executive Committee.

Another symposium was also discussed. The question was raised as to whether we should provide a sequel to the Adverse Events symposium or another topic. It was pointed out that it is hoped a working group will be formed from the symposium. Another idea was to hold the Adverse Events workshop at another location.

Courses on statistical concepts for non-statisticians were also discussed. There is currently a proposal within PhRMA for a 2½ day course. Another idea was to cosponsor short courses at other societies. A committee was formed of Sandy Hetf (chair), Richard Entsuah, and Lianng Yuh to see if other societies are interested.

Section Brochure

The update of the Section brochure, on the 1996 budget, will not be completed. It will be added to the 1997 budget.

Future Executive Committee Meetings

The next Executive Committee meeting is scheduled for 8:00-12:30 on Tuesday, March 27, 1997 at the ENAR meetings in Memphis, Tennessee. It was requested that a report from one of the co-chairs of the Muncie meeting be on the agenda for that meeting.

Tuesday morning of the Joint Statistical Meetings in Anaheim in August was selected as a first choice for the Executive Committee meeting. Monday morning was selected as a second choice. The preferred time for the Section business meeting was Tuesday evening.

Biopharmaceutical Section Starts Electronic Mailing List

Sally Greenberg
Council of Sections Representative and Webmaster

Effective November 4th, the Biopharmaceutical Section began sponsoring an unmoderated electronic discussion list for exclusive use by members of the ASA Biopharmaceutical Section: asabiopharm@lists.best.com.

Only ASA Biopharmaceutical Section members who are subscribed to this list can post to and receive mail from this list. All ASA Biopharmaceutical Section members are welcome to join. The messages posted to this list represent the views of the authors and have no explicit or implicit endorsement by the Biopharmaceutical Section of ASA.

The primary purpose of this list is to foster communication among and disseminate information to the members of the ASA Biopharmaceutical Section. It may also be a forum for identifying topics for future technical sessions and workshops. As such, messages on the following topics are actively encouraged:

(1) Discussion of issues which are relevant to Section members (e.g., implementation of regulatory requirements and biopharmaceutical statistical methodology)

(2) Announcement of relevant meetings & workshops (regardless of the sponsoring group)

Occasional postings of relevant job advertisements also fall within the scope of this list. Postings which advertise products or services are expressly prohibited. Willful violators of this policy will be removed from the list.

The names and E-mail addresses of subscribers are available only to the ASA Biopharmaceutical Section Executive Committee.

To subscribe to the digest version of the list, Biopharmaceutical Section members should send an E-mail message as follows: Address the message to: asabiopharm-request@lists.best.com. The body of the message should contain the two lines:

 # your-name (as listed in the ASA directory)
subscribe

Digests (containing all messages since the previous digest) will be generated approximately once a day (assuming that one or more messages have been posted).

To subscribe to the individual message version of the list, rather than to the digest version, Section members should instead send an E-mail message as follows: Address the message to: asabiopharm-request@lists.best.com. The body of the message should contain the two lines:

 # your-name (as listed in the ASA directory)
subsingle

Section members who experience any difficulties with subscribing or posting should E-mail Sally Greenberg (asabp@best.com), who is the List-Owner/Moderator for asabiopharm.

Let's Hear from You!

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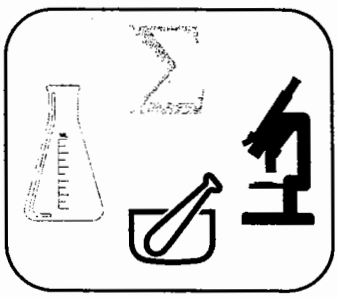

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