

## "Clinical Trials Handbook"

Shayne Cox Gad, editor, 2009, 1,225 pages, John Wiley & Sons, \$195.00

Review by Norman M. Goldfarb

"Clinical Trials Handbook" includes the customary chapters on the history, regulation, ethics and statistics of clinical trials. Its strength lies in chapters on trials in 14 therapeutic areas, plus emergency, bridging and special population (healthy subject) studies. However, these chapters are not entirely specific to their therapeutic areas; much of the material applies to clinical research in general. Six chapters cover trials from proof-of-concept to post-

marketing. One chapter discusses the business and operational aspects of clinical trials. Several chapters discuss advanced or specialized topics, such as adaptive research, analysis of adverse events, and biomarkers.

This book has been selected for  
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Essential reading for clinical research professionals

The following examples illustrate some of the book's insights in specific therapeutic areas:

- It is essential [in cancer trials] that induction therapy and local treatment with surgery and/or radiotherapy are part of the same treatment protocol with precisely defined timing and as short a gap as possible between systemic and local treatment. Tumors that shrink during induction therapy will often regrow rapidly. If the interval between induction therapy and local treatment is too long, accelerated repopulation of the tumor may quickly annihilate all the benefits of combined treatment.
- Dermatology is unique in that people who have skin conditions are able to identify their own diseases. As a result, subject recruitment outside of the clinic setting is a common and successful approach. Unlike other areas of medicine that recruit subjects from clinic patient populations, dermatology clinical trials are often advertised to the general public in the newspaper or in flyers. This method provides a great advantage to subject enrollment strategies since it reaches a much greater sample population.
- A major issue that has plagued [dental] caries trials is high rates of subject dropout. Earlier caries trials commonly reported findings based on a per-protocol analysis rather than using some method to impute data for dropouts. Use of a per-protocol analysis that ignores subject dropouts risks introduction of unknown bias. For example, if a test mouth rinse, which has an unpleasant taste and stains the teeth, is compared to a pleasant tasting, nonstaining control rinse, test subjects who use the rinse regularly may be more likely to drop out of the study than irregular users because of the unpleasant side effects. This would introduce a bias against finding a favorable effect. By using data imputation methods, such as an intention-to-treat analysis, one may minimize the effects of unknown bias in a trial. There are many other methods available to impute missing data from dropouts that are covered elsewhere in this text.

The book consists of 52 chapters by 175 contributors, with an average of 23 pages per chapter:

- Introduction to Clinical Trials
- Regulatory Requirements for Investigational New Drugs

- Preclinical Assessment of Safety in Human Subjects
- Predicting Human Adverse Drug Reactions from Nonclinical Safety Studies
- History of Clinical Trial Development and the Pharmaceutical Industry
- Adaptive Research
- Organization and Planning
- Process of Data Management
- Clinical Trials Data Management
- Clinical Trials and the Food and Drug Administration
- Phase I Clinical Trials
- Phase II Clinical Trials
- Designing and Conducting Phase III Studies
- Phase IV: Postmarketing Trials
- Phase IV and Postmarketing Clinical Trials
- Regulatory Approval
- New Paradigm for Analyzing Adverse Drug Events
- Research in Therapeutic Areas (14 chapters)
- Emergency Clinical Trials
- Special Population Studies (Healthy Patient Studies)
- Bridging Studies in Pharmaceutical Safety Assessment
- Methods of Randomization
- Randomized Controlled Trials
- Cross-Over Designs
- Biomarkers
- Biomarkers in Clinical Drug Development: Parallel Analysis of Alzheimer Disease and Multiple Sclerosis
- Review Boards
- Size of Clinical Trials
- Blinding and Placebo
- Pharmacology
- Modeling and Simulation in Clinical Trial Development
- Data Monitoring
- Inference Following Sequential Clinical Trials
- Statistical Methods for Analysis of Clinical Trials
- Explanatory and Pragmatic Clinical Trials
- Ethics of Clinical Research in Drug Trials
- Ethical Issues in Clinical Research
- Regulation
- Future Challenges in Design and Ethics of Clinical Trials
- Proof-of-Principle/Proof-of-Concept Trials in Drug Development

The book is available in bookstores.

**Reviewer**

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