

"Guide to Drug Development: A Comprehensive Review and Assessment"

Bert Spilker, 2009, 1,277 pages, Lippincott, Williams & Wilkins, \$199

Review by Norman M. Goldfarb

"Guide to Drug Development: A Comprehensive Review and Assessment" gives justice to the entire drug development process in this massive volume. The prose is straightforward, with concise, insightful and pragmatic expositions on hundreds, if not thousands, of important issues. The 27-page index is likely to come in handy.

The book consists of 11 sections:

- Introduction and Overview of a Company and the Industry
- Basic Principles, Strategies and Approaches
- Corporate Organization and Management Issues
- External Corporate Relationships and Interactions
- Research and Development Organization, Management and Assessments
- Clinical Activities and Issues
- Regulatory Affairs Activities and Issues
- Marketing Activities, Issues and Interactions with Medical Affairs
- Functional Activities and Issues
- Overview of Current and Future Development
- Case Studies in Clinical Development, Regulatory Affairs, and the Management of Drug Development

This book has been selected for
[The First Clinical Research Bookshelf](#)
Essential reading for clinical research professionals

The 252-page section on clinical activities and issues consists of 25 chapters:

- Introduction to Clinical Trials
- Creating a Clinical Strategy and Development Plan for a New Drug or Indication
- Designing and Implementing a Clinical Trial
- Questions to Ask about a Clinical Trial Protocol
- Dose-Response Relationships in Clinical Trials
- Collecting and Interpreting Life Events Data in Clinical Trials
- Quality of Life and Pharmacoeconomics in Clinical Trials
- Overview of Phase 4 and Postapproval Clinical Activities
- Phase 4 Trials and Postapproval Pharmacovigilance
- Feasibility of Multinational Trials
- Groups that Influence Protocol Design
- Monitoring and Auditing a Clinical Trial
- Electronic Data Collection and E-clinical Trials
- Principles of Patient Recruitment and Retention
- Surrogate Endpoints and Biomarkers

- Contract Research Organizations and Outsourcing Strategies
- Conducting Clinical Trials Efficiently and Rapidly
- Clinical Significance
- Incorporating Benefit-to-Risk Determinations in Drug Development
- Interactions between Clinicians and Statisticians for Analysis and Interpretation of Clinical Data
- The Concept of Normalcy
- Recruiting and Training Clinical Investigators
- Human Subject Protection and Ethical Issues in Clinical Trials
- Improving the Standards of Clinical Trial Publications
- Registries and Directories of Clinical Trials, plus Disclosure of Their Results and Archiving Their Data

Representative excerpts from the text include:

Trial design issues when the use of placebos is unethical. One of the reasons that using a placebo is unethical in some trials is that the IRB/EC wants to ensure that patients will not deteriorate physically. In this situation, it may be possible to inform the IRB that, if patients are randomized to placebo or active drug, then any patients who deteriorate when assessed at Day X will be dropped from the trial and given the standard therapy for their disease. On the other hand, the issue may be that the IRB wants to go further and assure patients that they will improve and not simply remain stable. In this situation, the protocol can read that all patients will be assessed on Day X and any who have not improved by a predefined amount will be dropped from the trial. Both of these examples are referred to as fail-safe designs because anyone who fails to meet the standards at any clinic visit will be removed from the trial and placed on active therapy.

Pharmaceutical industry requirements of new investigators. The primary requirement is an ability (and interest) to pay compulsive attention to detail in adhering to both the protocol and recordkeeping that are part of Good Clinical Practices and FDA standards. An investigator becomes part of a team of professionals, whether there is a single or many investigators and one or many sites involved in the trial. These attributes create an issue for many academic or private practice physicians, who feel that the patient's interests come first and cannot be compromised, even in the interests of adhering to the protocol used in a clinical trial.

Determining the reason(s) for poor enrollment before adding sites. While there are some trials where additional sites are required to enroll more patients, it is often the last approach that should be considered because often there are other reasons for the lower-than-planned number of patients enrolled. This is mentioned because the author still hears from companies that want to add new sites to a trial as soon as they learn that recruitment is slower than desired, but they have not investigated the reasons for this situation. The primary principle is to identify the real cause(s) of the recruitment problem and to see whether the issue is the same at each site or varies from site to site. If some sites are performing well, then seek to learn what they are doing that other sites are not.

Patient associations. While patient associations are fairly well understood for their roles in helping recruit patients for clinical trials and to help in launching a new drug of importance to their members, these associations may also play a role in the protocol that is designed in their disease area. An excellent example of this is the

case of Genentech being approached and eventually allowing the breast cancer patient association to have input into clinical trials to test Herceptin. In some cases, it behooves a company to allow a patient association to review a proposed trial's protocol to build relationships and to see whether the association can provide information and suggestions that would help improve the protocol. In doing so, a company must be sensitive to the needs of patients, and the patient organization must be sensitive as well to provide input of significant value that does not delay the development program.

Sponsor management of CROs. Some sponsors do not monitor a CRO sufficiently enough, while others may try to micromanage the CRO to maintain a high degree of control over the CRO's operations to ensure that the CRO performs as it is contracted to do. To optimize the relationship with a CRO, it is important for the sponsor to have a number of performance metrics as a guide to know when more interaction to resolve issues or problems is appropriate. If monitoring is done appropriately, most issues will never become problems.

The book is available in bookstores.

Reviewer

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