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"Principles of Good Clinical Practice"

Michael J. McGraw, Adam N. George, Shawn P. Shearn, and Rigel L. Hall, editors, 2010, 256 pages, Pharmaceutical Press, $64.99

Review by Norman M. Goldfarb

"Principles of Good Clinical Practice" is a readable introductory summary of Good Clinical Practice (GCP) for pharmaceutical studies based on U.S. regulations and ICH E6 guidelines, which FDA has adopted as guidance. The reviewer is not qualified to comment on the applicability of the book to GCP outside the U.S.

For the large population of GCP novices, the book strikes a good balance between too much and too little detail. The book covers some topics, e.g., informed consent, in some depth; others, e.g., financial disclosure, only briefly; and others, e.g., unanticipated problem reporting, not at all. Most citations are to entire regulations, e.g., 21 CFR 312, rather to specific sections, e.g., 21 CFR 312.23(5)(iv), a practice that minimizes clutter but also the reader's ability to find the specific rule under discussion.

Broadly speaking, GCP consists not just of the rules, but also the customary interpretations and practices that have grown up around the rules. The book summarizes, for example:

> IRB membership is also influenced by the population eligible to participate in the protocol. Vulnerable populations specifically addressed in the DHHS, FDA or ICH regulations include children, prisoners, pregnant women, fetuses, and the handicapped and mentally impaired. In order to review research that includes these participant groups, the regulations require that individuals with expertise about those populations and who understand how they might be vulnerable be included on the committee.

However, 21 CFR 56.107 states:

> If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with those subjects.

In other words, the pertinent expertise is a "consideration," not a legal "requirement." Fetuses are not included in the list, but are covered by the phrase, "such as." ICH E6 states: "Special attention should be paid to trials that may include vulnerable subjects" (3.1.1) and provides a different list of vulnerable categories, including, but not limited to, "patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors and those incapable of giving consent." (1.61)

On the other hand, 21 CFR 56.111 states:

> In order to approve research, the IRB must determine that all of the following requirements are satisfied:… when some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to

> coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects…

In other words, an IRB should add a member with the expertise to ensure that vulnerable subjects of any type are protected, provided the IRB concludes that adding such a member is a good way to accomplish the objective.

This type of regulatory discussion delights GCP experts but probably need not concern the novice. It does, however, emphasize the necessity of both reading the rules firsthand and obtaining interpretative advice.

Also, for the record, the U.S. and E.U. have not codified the ICH guidelines as regulations.

The book consists of 12 essays, contributed by 27 authors:

- Introduction to Good Clinical Practice
- Regulatory Requirements
- Informed Consent
- Investigator Responsibilities
- Sponsor Responsibilities
- Clinical Trial Design
- Site Monitoring
- Institutional Review Boards and Independent Ethics Committees
- Pharmacovigilance
- Clinical Trial Registration and Reporting
- Quality Assurance
- Future Implications of Good Clinical Practice

The book is available in bookstores.

Reviewer

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