INTRODUCTION

Over the years, the role of the clinical research investigator has changed dramatically. A once unsophisticated and relatively simple cottage industry, the clinical research enterprise of today is large, dynamic, complex, more regulated and far more sophisticated.

More than 125,000 government- and industry-sponsored clinical trials are conducted annually around the globe for a wide variety of medical conditions.[1] Industry sponsors include pharmaceutical, biological, biotechnology and medical device companies. The purpose of conducting a clinical trial is to gather safety and efficacy data for a marketing application in order to receive regulatory approval for marketing. Some clinical trials are conducted post-approval to collect actual use data and to expand a product's safety and efficacy data. Clinical trials are not limited to studies of medical treatments for the desperately ill, and they aren't all conducted at famous academic medical centers. Clinical trials are conducted at more than 9,000 locations worldwide, including physicians' offices, standalone clinical research centers, government-owned and -operated hospitals, private and public clinics and large academic medical centers.[2] A growing number of practice-based physicians now are involved in conducting clinical trials.

Although this book primarily is focused on industry-sponsored clinical trials, the same precepts hold for conducting research on humans in any kind of trial, including investigator-initiated or government-sponsored trials, or those funded by other entities. The regulations may vary somewhat, but the basics remain the same.

An estimated 10,500 promising new molecular entities now fill the research and development pipeline. This number is growing by 5% to 7% each year, largely due to the impact of new drug discovery technologies, including combinatorial chemistry, high throughput screening, genomics and proteomics.[3] Approximately one-third of drug candidates in the pipeline are under investigation in clinical trials involving human participation. Biopharmaceutical companies spend more than $60 billion to sponsor clinical research projects each year—of which an estimated $12 billion flows to clinical investigators as study grants to conduct trials among patient volunteers in

their communities.[4]

Striving to manage the rising costs of drug development, tighter regulatory scrutiny and a highly competitive marketplace, research sponsors increasingly rely on investigators to conduct clinical trials faster and under tightening budgets, while maintaining the highest quality standards. In order to meet these demands, today's clinical investigator must be able to perform a broad range of tasks—many of which fall outside his or her primary areas of training. Not only must the investigator be a good and ethical scientist, but he or she also must be a strong leader and operations manager, a proficient business development specialist and a sound business strategist and implementation expert.

It is an understatement to say today's clinical investigator must wear many hats. Not only must investigators evaluate and conduct complicated protocols, they must establish and adhere to standard operating procedures (SOPs) and good clinical practice (GCP) (as defined in applicable regulations, guidance documents and consensus standards), prepare and negotiate contracts and budgets, enroll and retain study volunteers and manage investigative site staffing, data collection technologies and financial operations.

The U.S. Food and Drug Administration (FDA) and its parent executive department the Department of Health and Human Services (HHS), along with regulatory agencies around the world, also have observed an increase in noncompliant practices among clinical investigators.

During the past several years, study staff and patients have filed record numbers of complaints against investigators for failure to follow protocols and proper informed consent procedures, poor record-keeping practices and lack of involvement in daily clinical research operations. In several well-documented cases, the Office for Human Research Protections (OHRP) and the FDA have been forced to suspend ethical review committees and disqualify individual investigators.

Facing the operating realities of today's clinical research enterprise, regulatory agencies and research sponsors are setting stricter guidelines with regard to investigator training and education. Already, many major academic institutions and biopharmaceutical companies are requiring mandatory GCP training for their clinical investigators. OHRP, the FDA, policy facilitators, patient advocacy groups and the general public have been exploring—and in some cases, demanding—the implementation of national certification for clinical investigators.

This book has been organized into three sections:

- A review of the roles and responsibilities of the clinical investigator and study staff
- An overview of the regulations and guidelines that govern clinical investigations
- A review of key practices that ensure effective and efficient study conduct.

The information contained in each of these three sections—including practical aspects of study conduct—has been gleaned from, and is tied to, GCP regulations and, as appropriate, selected guidance documents and consensus standards. The beginning of every chapter features core questions the reader should be able to answer once the chapter has been read.

In addition to reading and reviewing this book, investigators are encouraged to review and become familiar with the following FDA regulations and other related documents:

- 21 CFR Part 11—Electronic Records; Electronic Signatures
- 21 CFR Part 50—Protection of Human Subjects
- 21 CFR Part 54—Financial Disclosure by Clinical Investigators
- 21 CFR Part 56—Institutional Review Boards
- 21 CFR Part 312—Investigational New Drug Application
- 21 CFR Part 314 – Applications for FDA Approval to Market a New Drug
- 21 CFR Part 600—Biological Products: General
- 21 CFR Part 601—Applications for FDA Approval of a Biologic License
- 21 CFR Part 812—Investigational Device Exemptions
- 21 CFR Part 814—Premarket Approval of Medical Devices
- 45 CFR Part 46—Protection of Human Subjects
- 45 CFR Parts 160 and 164—HIPAA Privacy Rule
- Various FDA guidance documents for Institutional Review Boards and Investigators cited in this publication
- ICH Guideline for Good Clinical Practice (E6)
- ISO 14155: Clinical investigation of medical devices for human subjects—good clinical practice

Although the focus of this book is on U.S.-based trials and regulations, investigators in other countries who conduct trials that will be submitted for U.S. registration will find this information useful, as they must follow the same guidelines and regulations for their trials.

Clearly, a rapidly changing environment presents numerous challenges. Equally clear, clinical investigators must be well prepared to perform successfully in this changing environment, ultimately turning challenge into opportunity.

References

1. CenterWatch, 2013
2. CenterWatch, 2013
3. Tufts Center for the Study of Drug Development, 2012
4. CenterWatch, 2013