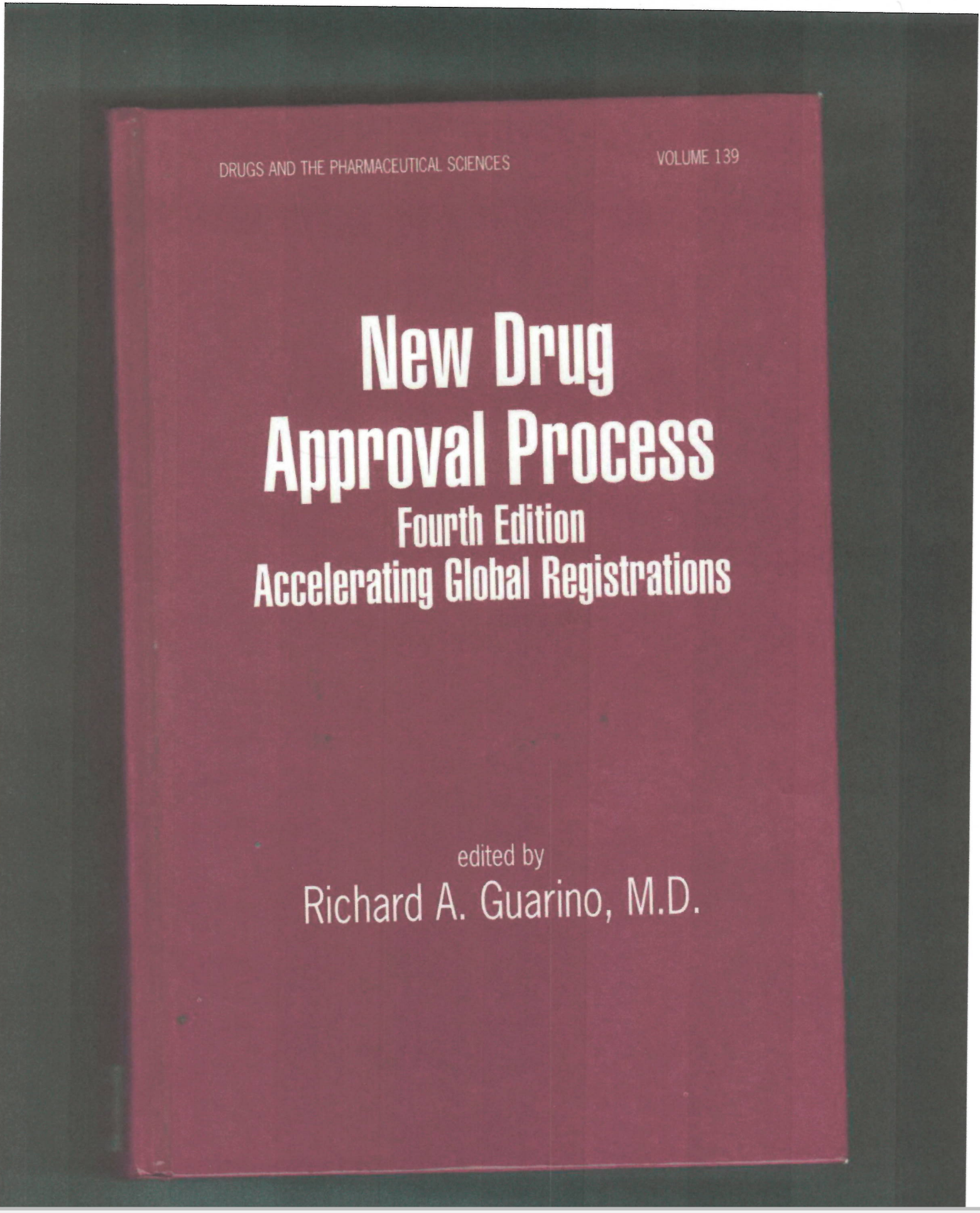

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New Drug Approval Process

Fourth Edition

Accelerating Global Registrations

edited by

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10
Clinical Research Protocols

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I. INTRODUCTION

The practice of clinical research—to establish safety and efficacy for new drugs, devices, and biologicals—is considered the most important part of the new drug approval process by many individuals in the FDA, sponsor companies, and users of pharmaceutical products. Accomplishing this task requires careful strategic planning to meet research objectives, an available subject population that meets the criteria of trial requirements, and experienced well trained clinical investigators who can evaluate the trial subjects following the protocol design.

Clinical research protocols are key to assuring successful approvals of new products in the health care industry. The protocol becomes the Bible for each research program. It must be followed exactly, without deviations, and must be the reference for any discussions that arise during the course of the investigation. This chapter will give instructions on how to write a clinical protocol for all phases of clinical research. It will include all necessary FDA requirements for confirming safety and efficacy for products marketed for human use. The format for protocol development is recommended on the basis of its successful use in clinical research. The recommendations throughout this chapter may not always be applicable to all clinical programs.

The objective of most clinical trials is to record scientific data concerning the efficacy and safety of a treatment for a specific disease on which valid conclusions can be drawn. The degree of success in achieving this objective depends largely, but not entirely, on the quality of the basic trial

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design. Faulty execution, due either to sloppiness or (in rare instances) dishonesty, can undermine the validity and usefulness of the data generated from a particular trial site. All investigators and their staffs must be meticulous in observing and reporting their clinical observations. On the other hand, even if a lengthy trial is carried out with the utmost care, the data generated will be useless if the protocol has not been designed intelligently. Overall, it must include all the necessary ingredients so that the eventual clinical results will support IND and NDA submissions.

Because the framework of every clinical research trial relies on a number of interdependent disciplines, the development of a clinical trial protocol is ideally a multidisciplinary task. Teamwork, coordinated by one experienced person in clinical research with good knowledge of the regulatory requirements for new drug development, is essential. The protocol design team should also include input, recommendations, and review by the following:

A chemist who is fully conversant with the physical and chemical properties of the investigational drug

A pharmacologist and/or toxicologist with a full understanding of the pharmacology and toxicology of the drug in animals and the expected effective dose, therapeutic effects, and possible adverse experiences in humans

A medical monitor, preferably one who specializes in the condition or illness to be studied, and who is experienced in the logistics and practicalities of clinical trials

A statistician who will address those aspects of trial design that determine the form the trial data will take for analysis and the types of analyses that will be applied to the data

A data management person who will be both involved in coding and in charge of data entry

A potential investigator or consultant who understands the indication to be researched and the objectives of the protocol and procedures to be followed

A capable program manager who can coordinate the multidisciplinary effort to form a final protocol and effect practical execution in the clinical setting straight through to data analysis and final write-up

Together, these specialists can provide both the criteria for all aspects of the trial and the rationale used to develop them. Once the specific objectives of the protocol have been established, it is customary for a protocol introduction to summarize these objectives, give a brief overview of the information found in the Investigator's Brochure (referencing the Brochure), and state the purpose of conducting the trial. The rationale for the criteria to be used for subject selection, exclusion, and randomization (if any) and the clinical variables to be monitored during the trial should also be stated.

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