DRUGS AND THE PHARMACEUTICAL SCIENCES VOLUME 139

New Drug Approval Process

Fourth Edition
Accelerating Global Registrations

edited by
Richard A. Guarino, M.D.

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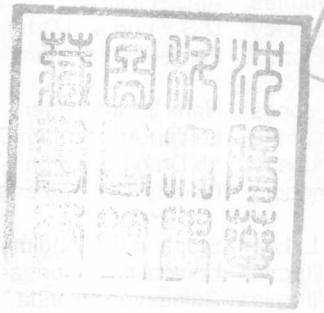

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To the victims of the tragic events of September 11, 2001, and to all our brave military who gave their lives and who proudly serve to protect our freedom and democracy. Let us never forget.

Preface

The impact of the global registration concept is still in the neonatal phase. The International Committee on Harmonization (ICH) and the subsequent implementation of its outcome will take time before the approvals of worldwide registrations for new pharmaceutical products can occur simultaneously. The interchange of information and the acceptance and adaptation of guidelines and regulations specific to drug, device, and biological product development need to be completely understood before the ideal common technical document can be readily accepted on an international scale.

This fourth edition of *New Drug Approval Process*, subtitled *Accelerating Global Registrations*, approaches each aspect of the processes required to obtain new product approval globally. Included is a comprehensive presentation of regulatory, clinical, and statistical mechanics involved in completing New Pharmaceutical Product Applications for prescription and generic drugs, devices, and biologics. Congruently, we address the way to expedite these processes and the strategic discipline necessary to achieve these difficult tasks.

We discuss the systems in which the dissemination of information to achieve a uniform way to educate the personnel involved in completing these duties. The authors selected to address the new drug approval process not only are knowledgeable in the academic writing of their specialties but also have the practical knowledge that can only come from years of successes and failures. They impart this knowledge so that readers can apply and use this information in their jobs with a clear understanding of their scientific and legal responsibilities.

The content, assembly, and strategic approach in filing U.S. and global submissions of Investigational and New Drug Applications (INDs/NDAs), Biologic License Applications (BLAs), Abbreviated New Drug Applications (ANDAs), and Supplemental New Drug Applications (SNDAs) are detailed in a step-by-step format. The essential aspects of the nonclinical, preclinical, and clinical development of products are carefully detailed and are integrated with the regulatory requirements for expediting new drug approvals. Within

these submissions, Chemistry, Manufacturing, and Controls (CMC) become one of the most important issues. Therefore special attention is devoted to the CMC section for NDAs and ANDAs.

Good Clinical Practice (GCP) regulations in the United States and the ICH guidelines, which meet safety, ethical and efficacy requirements, are comprehensively covered in the clinical research development chapters. Investigator, sponsor, and monitor obligations are detailed and applied practically. Institutional Review Boards (IRBs), Independent Ethics Committees (IECs), and Informed Consent (IC) will be discussed fully along with the sponsors', investigators', and monitors' legal responsibilities in the approval, implementation, and retention of the legal documents required for these processes. The Health Insurance Portability and Accountability Act (HIPAA) has become an essential consideration in the recruitment, identification, prescreening, and retention of subjects involved in clinical research. This edition addresses the impact HIPAA will have on the handling of patient data and on the use of existing databases.

The way we communicate electronically, coupled with new concepts and methodologies in global clinical development, will dramatically influence how pharmaceutical products are registered worldwide. Educating different societies on the techniques to meet international regulations will not be an easy task and will require immediate attention. The common technical document (CTD) and guidelines of the ICH are getting us closer to this goal, but there are still many differences to resolve. Educating the personnel involved in new product development and how this can be accomplished through technology change and e-learning is discussed in chapters on effective methodologies in expediting new product approvals.

New Drug Approval Process, Fourth Edition, addresses all the essentials, latest requirements, and techniques necessary to submit new pharmaceutical product applications globally. The text details the regulations, guidelines, and procedures that must be incorporated and adhered to in order to expedite and gain product approval. Moreover, it introduces a new approach of how to communicate effectively and integrate the world of pharmaceutical personnel on all aspects of new drug development. The future of international regulatory requirements and new product submissions is considered from every aspect by each contributing author. Readers will gain an education as well as an understanding of how to apply their research capabilities resourcefully now and in the future.

I sincerely thank the authors and contributors who have cooperated in the preparation of this fourth edition of *New Drug Approval Process*. In particular, a special thanks goes to Patricia Birkner and Barbara Connizzaro for their diligent efforts and insight in the preparation of this edition.

Richard A. Guarino, M.D.

Introduction

The global discovery and approval of new drugs, devices, and biologics will revolutionize the availability of health care products worldwide. The crucial areas of vaccines and blood safety, critical to our public health, coupled with such cutting-edge biologic scientific areas as gene therapy and tissue transplant will play a major part in these new product discoveries. These must be made available to the entire world population. The pharmaceutical industry's aggressiveness in marketing these products will also be a major factor in how fast these products become available internationally. Bureaucratic agencies regulating these products will also play a part in how fast they are approved for the global market.

The opportunity to accomplish this task has been greatly enhanced with the introduction of guidelines and recommendations formulated by the International Committee of Harmonization (ICH). This committee established safety, efficacy, and quality guidelines for new drug development in order to expedite international registrations. These guidelines give a basis for uniformity of data, developed for pharmaceutical products, that will be used as evidence for product approvals.

Notwithstanding these guidelines, which create the foundation necessary for new product approval internationally, each country's regulations for new product approval must be considered and incorporated within global submissions. For example, in the United States, the Food and Drug Administration expects that all U.S. and foreign data supporting safety and efficacy for new product submissions meet the regulatory standards required by this agency. Other countries might require that a percentage of clinical research be conducted in that country before approval of products is granted. In conjunction with these demands, regulatory and clinical personnel are con-

tinually confronted with the challenge of submitting data that will meet and support the requirements for global new product approvals. Each person who plays a role in the process of new product development is aware of what must be done to meet these regulatory requirements and puts forth a great deal of time, effort, and expense to achieve these goals. However, in many instances they are not entirely in agreement on *how to do it*.

Pharmaceutical companies and related industries are actively seeking new ways to decrease the time and costs for the development and approval of new products. The ability to submit applications for new products simultaneously in more than one country would greatly ease these goals. Bureaucratic agencies that approve these products are also cooperating by reviewing submissions more rapidly, with a new emphasis on accepting international data in order to avail new products to the world population. Personnel involved in new product development are working more closely with regulatory agencies to facilitate their needs and requests so that less time is involved in the approval process. Therefore a thorough understanding of all the regulations and guidelines and of how to effectively implement the intricate steps in new drug development is vital.

There are many components in the drug, device, and biologic approval process that must be defined, documented, and understood. The knowledge one may gain from reading a book or taking a course can only be considered a basis of what is needed in getting a new product approved. It is only from experience of trial and error and constant training and retraining that one is capable of expressing enough understanding to hope for a successful product submission and approval.

The personnel working in the pharmaceutical industries are of a particular breed. Above all, they *must love detail*. Detail, in this industry, is the underlying key to achieving many of these components. Every facet of new drug development must be examined and reexamined with the greatest care and understanding. Each regulatory aspect must be seriously applied in the overall product development. All clinical research must reflect the primary goal of human safety and investigator and sponsor integrity. The sponsors must assure the quality of all the data within the submissions. Lastly, the constant changes in the process of new product development must be rapidly distributed and applied.

These golden guidelines are detailed, defined, explained, resolved and practically applied in this new edition of *New Drug Approval Process*.

Richard A. Guarino, M.D.

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