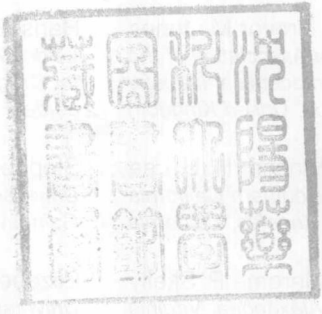
DRUGS AND THE PHARMACEUTICAL SCIENCES VOLUME 144

The Pharmaceutical Regulatory Process

edited by
Ira R. Berry

The Pharmaceutical Regulatory Process



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Preface

Welcome to the world of regulations and controls over the pharmaceutical industry. This is not necessarily a negative concept but is rather a necessary framework under which pharmaceutical products can be assured to provide safe and efficacious use. This book will trace the development and history of pharmaceutical regulations from their early beginnings to the present time. The process is never ending in that regulatory agencies such as the U.S. Food and Drug Administration (FDA), and industry, are constantly striving to improve the regulatory process – through the enactment of legislation and revised regulations and guidances.

The book is divided into two sections – the legal basis for regulation and FDA requirements for product approvals and after. In the pharmaceutical regulatory process, there are a legal basis, government regulatory requirements, academia influence and industry perspective. The needs and bases for these groups must be directed toward the same common goal – to provide safe and effective medicines. It is in this framework that the book aims to provide the reader with a basic understanding of the process by which pharmaceutical products are approved by the Food and Drug Administration for commercial sale and marketing in the United States. The book is intended to be an introduction to the regulatory requirements and procedures utilized by pharmaceutical companies to comply with these requirements. In addition, the book is intended to be a tool and source of information for the pharmaceutical industry professional who wishes more advanced training in pharmaceutical regulations.

The first section of the book deals with chapters that discuss the legal background and history of the product approval process. A chapter on "Pharmaceutical Regulation Before and After the Food, Drug, and Cosmetic Act" describes the creation of FDA and the reasons for its existence – to protect the consumer in sustaining a high level of public health by monitoring pharmaceutical product safety and efficacy. The next chapters deal with pharmaceutical company, or sponsor, requirements for preparing product submissions in compliance with regulatory requirements. The chapter, "New Drug Approval Process: Before and After 1962" follows. The year 1962 was very significant as a turning point for regulations pertaining to the pharmaceutical industry and this chapter traces the changes in the regulatory requirements of the approval process for "new" drugs, or new chemical entities. Following this chapter, is the "FDA Regulation of Biological Products" that describes the requirements for biological products as compared to pharmaceutical chemical products. Following these are the chapters "Generic Drug Approval Process: Pre-1984 History Concerning Generic Drugs" and "Generic Drug Approval Process: Post 1984: Hatch-Waxman Reform" that describe the corresponding requirements to obtain regulatory approval of "generic" drugs.

The chapter, "Food and Drug Administration Modernization Act", addresses the efforts that have been underway to streamline the regulatory process, as expressed by Congress – with a specific example applicable to antibiotic products. Product approval requirements for antibiotics followed a different pathway in earlier years and are described in the chapter "FDA's Antibiotic Regulatory Scheme: Then and Now". Patent issues influence the approval process for all pharmaceutical products and are described in the next chapter, "Pioneer and Generic Drugs: Balance Between Product Life Cycle Extension and Anti-Competitive Behavior". With the approval timelines associated with pharmaceutical products being as long as they are, and with efforts to shorten the approval times by providing FDA with additional resources, the next chapter focuses on "The Influence of the Prescription Drug User Fee Act on the Approval Process". Pharmaceutical products are not approved by FDA without demonstration of bioavailability or bioequivalence, perhaps as part of a clinical research program, and the next chapter addresses "Clinical Research Requirements for New Drug Applications".

The second section of the book addresses the FDA Requirements for Product Approvals and After. The section begins with a chapter on "Active Pharmaceutical Ingredients". There are specific requirements for manufacturers of active pharmaceutical ingredients (or bulk pharmaceutical chemicals), mostly contained in Drug Master Files and expressed by Good Manufacturing Practice for APIs, in order that a drug product license application may be approved. The next chapter deals with the process for "Obtaining Approval of New Drug Applications and Abbreviated New Drug Applications from a Chemistry, Manufacturing, and Controls Perspective", i.e., the requirements for a new drug product sponsor in preparing a product submission for approval. Following is a chapter describing the process of a generic drug sponsor in "Obtaining Approval of a Generic Drug". A drug product license application will not be approved without consideration being given to the compliance profile and manufacturing practices followed by the listed manufacturers in the application and "Current Good Manufacturing Practice and the Drug Approval Process" is the chapter that follows. In preparation of a product application for approval, attention is given to anticipating any changes that may be required to the manufacturing and control process after the product application is approved. This matter is discussed in the chapter "CMC Post-Approval Regulatory Affairs: Constantly Managing Change". The next chapter deals with "The Influence of the USP on the Drug Approval Process". In keeping with all these requirements for product approval, it is appropriate to next consider "Ways and Means to U.S. Registration of Foreign Drugs". In today's world, it is imperative to address the issues of registration of pharmaceutical products in the global marketplace and the next chapter deals with the "Common Technical Document – Quality (M4-Q): One Regulatory Participant's Perspective". In addition, computerization is becoming more prominent in today's standards and we consider "21 CFR Part 11 Compliance and Beyond". We must consider also the methods used in promoting pharmaceutical products, which are very different today as compared to past years, and the following chapter does this, "Marketing and Advertising/Promotion: The Impact of Government Regulations". The major emphasis in this book is on the process and issues relating to the approval process for registration of prescription drugs; however, we have a very important sector of the health care market devoted to over-the-counter drugs so the next

chapter focuses on "Approval and Marketing of Nonprescription or OTC Human Drugs".

The totality of the book has presented a comprehensive review of the history and background for the current pharmaceutical regulatory process in the U.S., in a global environment. With the background in place, the book further describes the steps and current requirements to obtain regulatory approval. It can be used as a training tool for individuals beginning to work in regulatory affairs, compliance and quality as well as to provide a general understanding of the regulatory process to all pharmaceutical industry and regulatory agency personnel.

I want to extend my personal gratitude to the contributing authors who have given their personal time to write this book and provide an education that is not attainable otherwise.

Ira R. Berry

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