selected. The book is highly recommended for graduate students and researchers in industry and academia looking for fundamental information on the exciting fields of skin absorption, skin toxicology, skin risk assessment, and skin pharmacology. It was a pleasure for me to go through the book!

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Mark C. Rogge, David R. Taft (Eds.), Preclinical Drug Development, Drugs and the Pharmaceutical Sciences Series (vol. 152, 2005, Taylor & Francis, Boca Raton) ISBN 0-8247-0293-X

The selection of drug molecules for development from an abundance of potential candidates is a key element of preclinical development programs. Effective molecule assessment programs facilitate more productive and informative absorption, disposition, and safety data, and help guard against unexpected pharmacokinetics and toxicities in clinical testing. Furthermore, experimental in vitro predictive methods for assessing tissue permeability, cellular transport, and organ toxicity have reduced the number of animals used in preclinical drug development while simultaneously providing further mechanistic insights into transport, metabolism, and toxicity of potential new candidate drugs. Thus, drug molecules periodically pass through decision gates predefined by carefully selected criteria as a strategy to terminate drug development as early as possible where appropriate to reduce unexpected late clinical stage failure and thus provide opportunities for more viable drug candidates to move forward in the development pipeline.

The scope of the text covers the general elements of preclinical drug development and introduces the reader to these scientific disciplines.

Chapter two encompasses interspecies differences in physiology and pharmacology between animal and human populations. The discussion also focusses on interspecies pharmacokinetic differences including absorption, metabolism, distribution, protein binding, and biliary excretion. Chapter three extends this discussion to the use of transgenic animals for preclinical drug development. This includes also disease models for evaluating biological activities of new drugs. Due to their fundamental differences, the pharmacokinetics/ADME of small and large molecules (protein pharmaceuticals) are described in separate chapters. Other chapters include preclinical pharmacokinetic–pharmacodynamic modeling and simulation, factors related to the formulation and route of administration influencing drug permeability and absorption, membrane transporters, and in vitro/isolated organ systems in the assessment of pharmacokinetics and non-clinical toxicity evaluations. Furthermore, the role of the ICH and the technical requirements for the registration of pharmaceuticals for human use in current toxicology practices is discussed including case studies of Celecoxib (Celebrex®), Trastuzumab (Herceptin®), Rituximab (Rituxan®), and Infliximab (Remicade®). Chapter 11 is a survey on the application of pathology in the safety assessment of compounds pointing out the involvement of pathologists during different phases of a toxicity/carcinogenicity study. It is demonstrated that, e.g., early microscopic assessment of nonhuman tissues may reveal subtle toxicity and subsequently lead to a timely discontinuation of the development project. Finally, in Chapter 12, the principles of toxicogenomics and its implications for preclinical drug development are discussed. Due to the fact that modulation of gene expression is of paramount importance in the mechanisms of drug-induced toxicity, major efforts are being made to determine the relevance of gene expression in response to drug exposure.

Overall, most chapters are starting points for understanding the scientific foundation needed to move a drug candidate into clinical trials. While there are additional textbooks that are more focussed and advanced on specific scientific disciplines, they should be regarded as complementary.

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Stanley H. Nusim (Ed.), Active Pharmaceutical Ingredients Development, Manufacturing, and Regulation, Drugs and the Pharmaceutical Sciences (vol. 151, 2005, Taylor & Francis, Boca Raton) ISBN 0-8247-0293-X

Organic chemicals (Active Pharmaceutical Ingredients, "APIs"), generally synthetic and not of biotechnological origin such as fermentation products, are the subject of this book. Historically these compounds are also referred to as Bulk Drug Substances (BDS) which are determined to be used in a final pharmaceutical dosage form.

Over the past century, significant changes have occurred in the pharmaceutical industry, causing equally significant changes for API suppliers. These changes are themselves a result of major direct and indirect alterations on the industry, including company consolidation, an increased role of quality, the significant intensification of regulatory bodies worldwide, the impact of the greatly increased potency of APIs and the broadening of the market worldwide. These changes suggested the need for a reference book for the manufacturing activity of APIs. The books focus is on three overall areas, that bring an API to market: the development of the chemical process including discussions on the process development cycle and introduction of the process into factory design engineering, the manufacturing activity utilizing that process, and the governmental regulations that control the approval of the product so that it may be commercially marketed. In the latter respect, quality control/assurance, and validation as well as the standard plant manufacturing operation activities including materials management, planning and maintenance are presented. In addition, basic information for those readers is provided to think through, understand, and effectively plan bulk manufacturing of an API. The material is organized in ten chapters: Introduction, Process Development, Bulk Drugs: Process Design, Technology Transfer and First Manufacture, Design and Construction of Facilities, Regulatory Affairs, Validation, Quality Assurance and Control, Plant Operations, Materials Management, and Plant Maintenance.

The chapter ''Process Development'' deals with the bulk drug manufacturing process which is presented as part of a drug development program, mainly based in the context of a large drug company, where all the requisite skills reside in house. Three basic tasks as inseparable parts of the bulk drug process development exist: (i) the preparation of bulk drug supplies, (ii) the definition and achievement of the chemical and physical bulk drug attributes, and (iii) the development of process know-how and data base. The practice of moving a bulk drug process from the development environment to that of first manufacture is one of the issues of the chapter on ''Bulk Drugs: Process Design, Technology Transfer, and First Manufacture''. Questions related to the broad definition of the task and its probable capital cost, venues and timetable help to move the process design without pause as the features of the process take shape. Furthermore, definitions of the various process steps as they might be operated in the most probable venue of choice are given and – with some modification – may be applied to the individual problem of the reader. Although several important questions in that respect are brought up to the attention of the reader, the scope and depth of the book do not allow to present turn-key solutions to all of the questions being brought up to the reader. The chapter on ''Design and Construction of Facilities'' outlines the steps required to design and construct a new API facility or renovate existing capacities including current Good Manufacturing Practices (cGMP) Requirements. A clear execution strategy and the need to understand the scope of the project are reviewed in detail.

It is increasingly necessary for the regulatory area responsible for CMC within a company to develop the expertise needed to successfully register and maintain appropriate information and documentation on the API, and to assure that changing regulations are tracked, understood and properly implemented. The aim of the chapter ''Regulatory Affairs'' as they exist in early 2004 is to guide and assist the CMC scientist in developing such expertise. While it is not the intent to focus only on the regulations published by the US FDA, it is clear that satisfying FDA requirements often ensures that sufficient information and data exist to satisfy other regulatory agencies as well. The main purpose of the investigational application is to demonstrate that the API to be introduced into man is adequately safe and is properly controlled including information on, e.g., key chemical and physical properties, proof of chemical structure, method of manufacture, and discussion of impurities and degradation products, just to name a few. Likewise, similar but not identical contents are described for the marketing applications of the API to the regulatory authorities. Several references to documents of ICH and general references in the www are made. The identification of critical control parameters that impact quality, purity, safety and efficacy of bulk pharmaceutical chemicals and their assembly into a technology transfer document is the key issue of the chapter on ''Validation''. For the sake of insuring completeness in the presentation the authors have included a considerable number of issues which may not yet be embodied in validation protocols within operating companies but which may be subject to inclusion in the future. The quality assurance and control aspects of the API are further elaborated in chapter seven. This chapter contains also an in depth discussion and interpretation on regulations for quality by analyzing the ICH Q7A guidelines section by section.

Finally chapters on plant operations, materials management, maintenance and reliability issues of a typical pharmaceutical plant complete the essential information required to effectively plan and execute manufacturing of quality APIs.

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