This book is dedicated to our families.

GLOBAL CLINICAL TRIALS

Effective Implementation and Management

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ABOUT THE EDITORS

Richard Chin, M.D. is the CEO of Institute for OneWorld Health, the first U.S. nonprofit pharmaceutical company. OneWorld Health, mostly funded by the Bill and Melinda Gates Foundation, develops affordable drugs for neglected patients in the developing world. Dr. Chin has extensive expertise in drug development, including over 45 INDs and 10 drug registrations. Some of the drugs he has overseen include Rituxan, Lucentis, Tysabri, TNKase, Raptiva, Xolair, Cathflo, Prialt, Protropin, Nutropin, Pulmozyme, Azactam, Maxipime, and Bapineuzuma, among others. His previous roles include CEO of a NASDAQ-listed company, Senior Vice President of Global Development at Elan, and Head of Clinical Research for the Biotherapeutics Unit at Genentech. He was named by Businessweek in 2006 as one of the youngest 99 public company CEOs in the United States. Dr. Chin earned an M.D. from Harvard and the equivalent of a J.D. from Oxford, where he studied as a Rhodes Scholar. His previous textbook, Principles and Practice of Clinical Trial Medicine was also published by Elsevier. Dr. Chin serves as Associate Professor at UCSF School of Medicine and was previously on the adjunct faculty at Stanford University School of Medicine. Dr. Chin may be contacted at richardchin@clinicaltrialist.com.

Menghis Bairu, physician, scientist and Sr executive business professional—has more than two decades of international experience in the pharmaceutical/healthcare industry and in working to leverage that experience in the non-profit global health arena. His healthcare expertise spans research and development, commercial, managed care, public health and access sectors of the biopharmaceutical industry, with particular emphasis on the clinical development of important, new therapies. He is currently Executive Vice President and General Manager for Elan Biopharmaceuticals, an internationally renowned neuroscience/biotech company. He was previously the Head of Global Development and Chief Medical Officer for Elan where, on a global basis, Dr. Bairu was responsible for Clinical Development, Biometrics, Regulatory, CMC, Quality/Compliance, Safety and Risk Management, Clinical Operations, and Medical Affairs.

Prior to joining Elan, Dr. Bairu worked for more than five years at Genentech, a period wherein his clinical, commercial and managed care

experience and responsibilities increased exponentially, culminating in his medical marketing role with Rituxan, Genentech's first multibillion dollar product. Dr. Bairu worked as Medical Consulting Director for Fremont Health Corporation/Industrial Indemnity before joining Genentech. He received his undergraduate degree in Business Administration from Instituto VII Tecnico Commerciale in Milan, Italy, attended John Hopkins University (Public Health) and the University of Milan, faculty of medicine & surgery in Milan-Italy where he received his Medical Degree.

Complementing the corporate and philanthropic elements of healthcare advances has always been a focus for Dr. Bairu. In 1999, he co-founded International Medical Foundation, Inc., a 501(c) 3 foundation whose mission is to acquire medical equipment and materials for donation to non-profit institutions and government health care entities in developing and emerging countries.

FOREWORD

Drugs, biologics and medical devices were once local affairs although it wasn't long before these products were shipped from country to country. The consumer protections provided in laws passed in many countries starting around 1900 focused on products in the marketplace which were dangerous or misrepresented and if there were proactive interactions between government regulators and manufacturers it involved inspections and bench testing of vaccines and serum therapies. In 1962 in the United States, in response to the harm caused by thalidomide, sweeping regulatory changes were introduced, the most important being a section of the law which required that prior to marketing a new drug efficacy must be determined by 'adequate and well controlled studies' in humans. While human drug clinical trials had their beginnings in trials of drugs for tuberculosis, high blood pressure and diabetes, the new law made such studies mandatory for all drugs in the US, except those on the market since before 1938. The law also added post-marketing safety reporting requirements, and over the years, along with clinical trials became an international endeavor.

The United States, Japan and many other countries continued to have a strong preference for clinical trials done within their own borders. But as international harmonization efforts and changes in local regulations evolved, medical product development became an international enterprise. Concerns arose that the ethnic and genetic differences between populations would make reliance on foreign trials uncertain. But, in fact, the real challenge is not the genetic differences in drug metabolism, but the wide differences in health care delivery and the practice of medicine from country to country. There are variations in the local practices with respect to informed consent, differences of opinion on the ethical use of placeboes. Logistical challenges persist for the regulators, who have the authority of law at home, but are visiting officials not necessarily able to read or speak the local language when they inspect a foreign trial or manufacturing site. The management of a trial with oversight by multiple in-country regulators can be challenging. But the challenges notwithstanding, the manufacturing, the preclinical investigations, the clinical trials for registration, the post-marketing study requirements, and the safety surveillance is now a global effort, and a better one for it.

This first textbook on global clinical trials that explores the principles and practice of global clinical trials is important and welcome. Just as a multi-center trial differs from a single site trial, global clinical trials differ from a domestic one in many ways, including regulations, ethical issues, and logistics. It is important for those conducting international trials to fully understand the country and region specific differences and requirements. Without a good understanding, many issues including logistic challenges, scientific validity, and privacy violations can ensue. In this book, the authors drawn from a broad range of industry and academia address the critical issues often seen in global clinical trials.

The scope is comprehensive, covering countries from virtually every continent. In each chapter, the authors examine the country and region specific considerations for conducting trials. This book is a landmark publication, and it is likely to stand as the standard reference book for global clinical trials for many years to come.

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