

**Essential CNS Drug Development**

*Edited by Amir Kalali, MD; Sheldon Preskorn, MD; Joseph Kwentus, MD; and Stephen M. Stahl, MD. Cambridge University Press, 2012, Cambridge, UK, 207 pages, \$99.00 (hardback).*

This compendium on the conduct of modern psychopharmaceutical research programs concisely sets out many important procedures and issues. A wide scope covers rules and problems in drug development for psychiatric illnesses literally from conceptualization to marketing. Chapters are devoted to many interested parties' viewpoints, with the patients' health interests ever present. Regulatory concerns are clearly presented. Nice.

Inconsistencies exemplify diverse interests and goals found in this evolving field. Even as existing drug discovery models are refreshingly challenged, the need for clarity in psychiatric pathophysiology is raised, and wishes for the novel treatment strategies arriving in other medical fields are presented, the editors include a chapter on treating a symptom cluster within a syndromally defined illness (cognitive improvement in schizophrenia). In some measure, this is the state of the art, and the editors are merely the messengers. They point to distances between research populations and real world patients ("... disparity between clinical trial subjects of interest to physicians and payer versus those that sponsors feel best enable delineation of safety and efficacy profiles" [p 93]). They also point to distinctions between rating scale changes and real-life functional milestones (p 182). There is no description, though, of attempts to mine real-world electronic records as an avenue to drug discovery. Instead, the tone simultaneously leaves standing the status quo of pharmaceutical interests and, further, emulates a dying academic, traditional, ivory tower perspective that, after a successful dissemination of the new drug message through marketing, a medication cost-to-consumer problem is not to be addressed by those in drug development. Medical economists might offer a different perspective.

Though the present discovery-to-marketing process is the teaching focus, there are brief mentions of a future move forward from perpetuating the pursuit of a perfect pharmaceutical targeting perfectly profiled, disease-specific binding sites by seeking new biomarkers (p 84). But there is room, in the 21st century, for disease conceptualizations that contemplate highly comorbid families of illnesses (eg, bipolar disorders and diabetes). Might these be found to share physiologic precursors across medical specialties? Further, as we learn more about diet and cultural effects on disease, why are we exporting trial sites globally in a mission to—no, not optimize drugs for all the world's populations—save on drug trial costs?

In fairness, the chapters are authored with considerable expertise and a generally even, finely edited writing style. Most chapters present a historical perspective, teaching how we got into this mess and where we are now and sometimes offer ideas on how to move ahead constructively. New and experienced investigators will find explanations of US Food and Drug Administration (FDA) regulations and corporate sponsorship expectations valuable in comprehending an increasingly complex process of proving new treatment efficacies. It was surprising, though, that contract research organizations (CROs) are barely mentioned, and then only in passing (p 149). Expert views on working with CROs (also known as clinical research organizations)—the intermediaries between the sponsor and the research site—would be valuable.

The experienced authors admirably describe the art and skills of managing the constraints of recruitment criteria, prioritizing participant welfare, and balancing budgetary concerns, but the daunting state of the art is hardly encouraging to a novice. The volume can be recommended for the libraries of senior investigators who are training the next generation as a stimulus in the supervisory process. The text also offers a springboard for discussions among policy makers themselves, hopefully promoting an insight that they are overdue in their effort to overhaul a system nearly imploding under ponderous regulatory, protectionistic, and, unfortunately, often minimally scientific burdens of multiple financial and other interests. The brief format is highly readable, more concise than comprehensive in scope, providing more of an overview of the issues than would be expected from a formal reference text.

Future developments anticipated in the field of commercially sponsored trials are very briefly described, such as instrumented assessments of outcomes that promise a more scientific and precise view of treating mental illnesses. Some of these appendix commentaries (it would be difficult to cite them as chapters) disappoint in comparison to the earlier, better justified and developed sections.

Overall, the editors offer a timely discussion of many strengths and weaknesses of a highly regulated and cumbersome process. An optimistic view is pervasive, expressing hope for a future that will bring new approaches to therapeutics and more efficacious drugs to our patients. May this help optimists of the future find ways to reify all of our hopes!

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