

The Agile Approach to Adaptive Research: Optimizing Efficiency in Clinical Development

By Michael J. Rosenberg

Adaptive clinical research is one of the 'hot topics' of the day. As a relatively new field, it certainly has its challenges, but it also has the potential for considerable improvements in drug development efficiency. Dr Rosenberg's new book *The Agile Approach to Adaptive Research* first outlines the current state of the pharmaceutical and biotechnology industries, where considerably increased research and development expenditures have not led to a greater number of investigational drugs reaching marketing approval. He then captures the current excitement surrounding adaptive clinical research (also called adaptive design), and provides a very readable introduction to the methodologies involved in implementing such research.

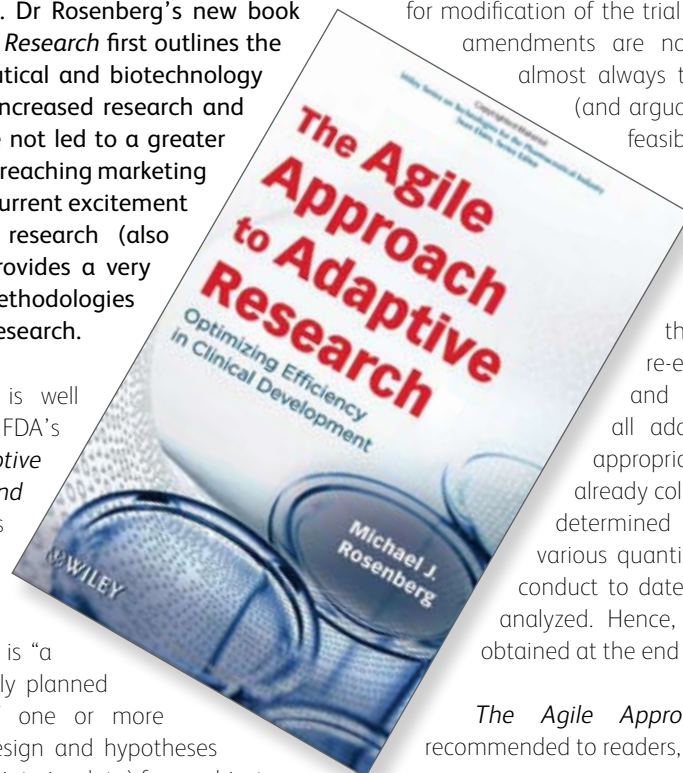
The timeliness of this text is well reflected by the release of the FDA's draft Guidance for Industry, *Adaptive Design Clinical Trials for Drugs and Biologics*, in the same month as the book's publication, February 2010. The FDA's definition of an adaptive design clinical trial in the context of its draft guidance is "a study that includes a prospectively planned opportunity for modification of one or more specified aspects of the study design and hypotheses based on analysis of data (usually interim data) from subjects in the study." An adaptive trial therefore contrasts with the traditional fixed-design trial, in which a study proceeds from start to finish as described in the study protocol without modification.

There are some individuals who would comment that we have long conducted 'adaptive research' via the writing of protocol amendments--these documents alter the nature of the remainder of the trial once implemented. However, there is one fundamental

and critical difference between true adaptive research and the use of protocol amendments, a difference captured in the FDA's definition. A true adaptive design provides *prospectively* planned opportunity for modification of the trial's remaining stage(s), while protocol amendments are not prospectively planned, and are almost always the result of a problem that could (and arguably should) have been addressed in feasibility studies conducted before writing the original study protocol.

Rosenberg's book provides information on many aspects of adaptive design, including these three key considerations: sample-size re-estimation, adaptive enrollment, and adaptive monitoring. Any and all adaptations made are the result of appropriately analyzing clinical trial data already collected in the context of prospectively determined decision-making algorithms and various quantitative metrics concerning the trial's conduct to date that have also been collected and analyzed. Hence, the validity and legitimacy of results obtained at the end of the trial are maintained.

The Agile Approach to Adaptive Research is recommended to readers, and receives the JCS Library Award.



John Wiley & Sons
February 2010,
Hardcover
274 pages
February 2010
£53.50 (€66.70, US \$79.95)
ISBN: 978-0-470-24751-8



J. Rick Turner, PhD, Editor-in-Chief, joined the journal's Editorial Board this January. He is Senior Scientific Director, Cardiac Safety Services at Quintiles, and also an accomplished author and editor who has a real passion for books. We are pleased to announce that Rick has agreed to become Editor-in-Chief of a new addition to our journal, the JCS Book Corner. He will be reviewing books of interest to our readership, and giving JCS Library Awards to outstanding books that should be in your company's library, or perhaps even in your personal collection. On occasion, he will be inviting other Editors to review books too.

Rick's first book was written while he was actively involved in research in the field of Cardiovascular Behavioral Medicine. Entitled *Cardiovascular Reactivity and Stress: Patterns of Physiological Response* (1994, New York: Plenum Press) it was the first student textbook examining the putative role of psychological and behavioral stress in the development of high blood pressure, and potentially other cardiovascular sequelae. The journal *Psychophysiology* commented that "Cardiovascular Reactivity and Stress is an extremely readable and well organized text... As an introduction to the field, Turner's book is a superb resource." Rick edited four other books in the field of Behavioral Medicine before moving into the pharmaceutical industry in 1996.

Since being in this industry, Rick has published three books discussing various issues within new drug development. The first, *New Drug Development* (2007, Hoboken, NJ: John Wiley & Sons) was a general overview of this topic. The *Journal of Applied Statistics* commented that "The book gives a refreshing run through of the drug discovery and development process and it is probably the book you need to have to learn about this fascinating field." An updated, expanded, and less technical second edition will be published later this year by Springer Science (New York). His other books, both co-authored with Todd Durham, are *Introduction to Statistics in Pharmaceutical Trials* (2008, London: Pharmaceutical Press) and *Integrated Cardiac Safety: Assessment Methodologies for Noncardiac Drugs in Discovery, Development, and Postmarketing Surveillance* (2009, Hoboken, NJ: John Wiley & Sons).

We are delighted that Rick is bringing his publishing experience and his love of books to the journal, and we particularly look forward to featuring books written by our readers. If you would like to submit your book to the JCS Book Corner for review, please ask your publisher to send a copy to: **Pharma Publications, Building K Unit 104, Tower Bridge Business Complex, Tower Point, London, SE16 4DG**