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"Can You Handle the Truth?"

"Designing Adaptive Clinical Trials"

FDAnews, 2007, 89 pages, \$335.00

Review by Norman M. Goldfarb

"Designing Adaptive Clinical Trials" clearly explains the uses, benefits and processes for implementing adaptive trials. If you continue to waste millions of dollars on conventional trials because you are not ready to plunge in, this report will give you the confidence to take the leap.

A 22-page essay explains how adaptive trials can save substantial time and money, while reducing the risk of failure in clinical development. For example, to determine the best dosage, start Phase II with a large range of dosages. Use Bayesian statistics to winnow down the choices for Phase III. Start Phase III with a larger-than-conventional range of dosages, and then complete the winnowing process. Because you can stop enrolling subjects midtrial in "losing" study arms, you can reduce the total number of subjects, while collecting more data than normal on the most likely dosages.

Adaptive methods reduce the chance of completely missing the correct dosage. For example, in 2000, Glaxo withdrew Lotronex, an effective treatment for irritable bowel syndrome, from the market because of serious side effects, including deaths. Under pressure from patient advocacy groups, FDA allowed Glaxo to test Lotronex at lower dosages and reintroduce it to the market in 2002. If Glaxo had originally used adaptive methods to test a broader range of dosages, Lotronex may have been marketed originally at a lower, safer dosage.

Adaptive trials require quick access to study data, or the decisions to adapt will be too slow on the draw. An independent statistical center and data monitoring committee minimize the risk of bias. Expanding the study population by about 5% offsets the increased chance of false positives introduced by multiple interim analyses, but the gains are much larger than 5%.

The essay is accompanied by supplemental material, including FDA's draft guidance on the use of Bayesian statistics in medical device clinical trials. Medical devices are particularly well-suited to Bayesian methods because many device trials just test incremental improvements.

The report is available at <http://www.fdanews.com>

Reviewer

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