
Princeton-Trenton Chapter



The Princeton-Trenton Chapter of the American Statistical Association is pleased to present :

Fall Seminar

Wednesday, November 8, 2006

Holiday Inn

100 Independence Way, Princeton, NJ 08540

Schedule (see abstracts on next page)

9:00 – 9:30 AM	BREAKFAST	
9:30 – 10:15 AM	Cross-Trial Estimation Of Control Effect And False Positive Issues In Active-Control Trials	Abdul Sankoh, Ph.D. Associate Director/Acting Deputy Therapeutic Head - Neurology Sanofi-Aventis
10:15 – 10:30 AM	BREAK	
10:30 AM – 12:15 PM	Flexible Adaptive Trial Design: Improving the Return on Clinical Trial	Cyrus R. Mehta, Ph.D. Co-Founder and President, Cytel Inc.
12:15 – 1:00 PM	LUNCH	

Registration Instructions

There is a \$35 charge for this event, including breakfast and lunch. Full-time students can attend this event for a charge of \$20. A pre-registration is **REQUIRED** by Friday, November 3. To register, reply to the initial email that contained this attachment with your **Name, Title, and Company/Affiliation**. The payment check should be made payable to "Princeton-Trenton Chapter of ASA" and sent to Dr. Isaac Nuamah, Treasurer PT-ASA, 5 ORLY WAY, BURLINGTON, NJ 08016 (Email: INuamah@PRDUS.JNJ.com). Payments must be postmarked by November 2, 2006. Payment at the door will be \$40. **Please note that seating is limited to 75 attendees. If you register and unable to attend, please advise Dr. Nuamah as soon as possible so that others on the wait list can attend.** For more information, please contact any one of the PT-ASA officers:
<http://www.amstat.org/Chapters/princetontrenton/officerlist.html>

Flexible Adaptive Trial Design: Improving the Return on Clinical Trials

Cyrus R. Mehta, Ph.D.
Co-Founder and President, Cytel Inc.

Abstract:

An adaptive trial is one in which interim data from the trial itself is used to modify and improve the study design, without undermining its validity or integrity. Trial sponsors and regulators have expressed a great deal of interest in designing such trials because of their potential benefit for Phase II and Phase III programs. In the Phase II setting an adaptive trial can assign a larger proportion of the enrolled subjects to the treatment arms that are performing well, drop arms that are performing poorly, and investigate a wider range of doses so as to better identify the nature of the dose-response relationship and select doses that are most likely to succeed at Phase III. When the trial proceeds to Phase III an adaptive design can facilitate early identification of efficacious treatments, determine if the trial could be terminated for futility, and make sample size adjustments at interim looks so as to ensure that the trial is adequately powered. In some cases it might even be possible to enrich the patient population by altering the eligibility criteria at an interim look. Thus, adaptive trials have the potential to translate into more ethical treatment of patients within trials, more efficient drug development, and better focusing of available resources. On the other hand, such trials require tremendous up-front planning and simulation to verify their operating characteristics, precisely because they are so flexible. In this seminar we give an overview of adaptive clinical trials, pointing out their advantages as well as their limitations. Many different types of adaptive trials will be discussed including Phase II dose ranging trials, seamless phase II/III trials, Phase III group sequential trials and Phase III trials with sample size re-estimation. The presentation will be conceptual rather than technical and will be illustrated by several examples of actual trials, some of them drawn from our own consulting experience. Logistical and regulatory issues will be discussed.

Cross-Trial Estimation Of Control Effect And False Positive Issues In Active-Control Trials

Abdul Sankoh, Ph.D.

Sanofi-Aventis

Abstract

The interpretation of efficacy results from active-control clinical trials requires a cautious approach. This is because efficacy results from active-control trials cannot be reliably interpreted without a thorough understanding of the historical efficacy evidence that formed the basis for the approval of the active-control. The difficulty in interpreting efficacy results from such trials is compounded when drug efficacy is to be established on the basis of clinical evidence from the traditional two-arm active-control clinical equivalence studies. This is because in addition to over reliance on the quantification of a clinically irrelevant acceptable margin of inferiority from historical data, such interpretation also depends on cross-trial inference for demonstration of experimental drug effect. We review in this presentation some of the design issues and discuss regulators' concern regarding false positive findings in cross-trial demonstration of experimental drug effect when point estimate (PE) method is used to quantify the non-inferiority margin. We present limited simulation results that show, when combined with percent preservation of control effect, adequate control of the type I error rate is achieved with $\geq 75\%$ retention of control effect but that the regulators' preferred confidence interval (CI) approach is ultra-conservative. A couple of plausible alternative approaches for establishing non-inferiority are discussed via a numerical example from real clinical trial data.