

Pfizer La Jolla Laboratories
and the
San Diego Chapter of the ASA



Present

Flexible Adaptive Trial Design: Improving the Return on Clinical Trials

by Cyrus R. Mehta, PhD
Co-Founder and President, Cytel Inc. and
Adjunct Professor of Biostatistics, Harvard School of Public Health

Date: June 7, 2006
Time: Reception: 5-6pm
Talk: 6-7pm
Location: Pfizer La Jolla Labs
Science Center Drive Bldg CB4
Rm 2250 (Sea Training Room)
San Diego, CA 92121

Please RSVP to Patricia English (858-526-4288 or patricia.english@pfizer.com) by 3:00PM on Tuesday, June 6, for Pfizer security purposes. Driving directions are on the last page.

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.

Biographical Sketch

Cyrus R. Mehta, Ph.D is the Co-founder and President of Cytel Software Corporation, and Adjunct Professor of Biostatistics at the Harvard School of Public Health. He received his Ph.D. from the Massachusetts Institute of Technology. For the past 15 years, Dr. Mehta has concentrated his research activities on developing permutational algorithms which can be applied to categorical data analysis, nonparametric tests, power and sample size calculations, the analysis of contingency tables and, more generally, to inference concerning the more generally, to inference concerning the parameters of regression models for categorical data. These algorithms have made it computationally feasible to obtain accurate p-values, confidence intervals, and sample-size designs for small or unbalanced data sets and for sparse contingency tables. Thus they are a useful supplement to large-sample theory. The ideas underlying this research span three disciplines: statistics, computer science, and operations research. A second major research interest is in field of group sequential inference for clinical trials. Dr. Mehta collaborates with his colleagues in the department of biostatistics by developing software packages based on their research.

Dr. Mehta is co-founder and President of Cytel Software Corporation, Cambridge, Massachusetts (<http://www.cytel.com>). Cytel's mission is to pursue advanced research in the fields of computational statistics, group sequential inference, toxicological risk assessment, missing data problems and longitudinal data problems, and to convert the fruits of that research into user-friendly software. So far Cytel has developed six statistical packages; StatXact, LogXact, EaSt, Egret, ToxTools and StaTable. These software packages have been favorably reviewed by the Royal Statistical Society and the American Statistical Association. They are installed world-wide, with sites at numerous universities, pharmaceutical corporations, medical research centers, and government agencies like the FDA and the CDC. In 1998 Cytel received an award from the Massachusetts Technology Development Council for outstanding technology development funded by the Small Business Innovation Research program.

Dr. Mehta has published over 65 papers in journals like JASA, Biometrika and Biometrics. He and his co-authors, Dr. Nitin Patel and Dr. Karim Hirji received the 1987 George W. Snedecor Award from the American Statistical Association. In 1995 Dr. Mehta was elected a Fellow of the American Statistical Association.

He has been a member of the faculty in the [Department of Biostatistics](#), Harvard School of Public Health since 1979. Previously he taught at the University of Pittsburgh. He gives numerous short-courses and workshops at pharmaceutical companies, universities and government agencies both in the USA and overseas. Dr. Mehta is also the Zoroastrian representative on Harvard University's Board of Ministry.

Directions to Pfizer La Jolla Laboratories

CB2 Visitors Center: 10770 Science Center Drive, San Diego, CA 92121

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- You will be escorted at all times while on site
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