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# Princeton-Trenton Chapter



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

## Spring Seminar

Friday, June 11, 2010

### Holiday Inn

100 Independence Way, Princeton, NJ 08540

### Schedule

10:00 – 11:00 AM	<b>Practical Adaptive Designs for Dose Ranging Phase I/II Clinical Trials</b>	Nuam Khutoryansky, Novo Nordisk
11:00 – 12:00 PM	<b>The Role of Simulation in Clinical Supply Management for Adaptive Design Trials</b>	Weili He, Merck & Co., Inc.
12:00 PM – 1:00 PM	<b>Lunch</b>	
1:00 – 2:00 PM	<b>FDA Draft Guidance on Adaptive Designs: Overview, Key Messages, and Impact</b>	José Pinheiro, Johnson & Johnson PRD
2:00 – 3:00 PM	<b>Information-based sample size adaptation for binomial trials</b>	Keaven Anderson, Merck & Co., Inc.

### Registration Instructions

There is a \$30 charge for this event, including lunch. Full time students and retired statisticians can attend this event for a charge of \$20. A pre-registration is REQUIRED by Thursday, June 3, 2010. The way to register is to reply to the initial email at [weili\\_he@merck.com](mailto:weili_he@merck.com) that contained this attachment with your **Name, Title, and Company/Affiliation**. The payment check should be made out to "Princeton-Trenton Chapter of ASA" and sent to Dr. Weili He, Treasurer PT-ASA, 1129 Boulevard, Westfield, NJ 07090. Payments must be received on or before June 3, 2010.

**Please note that seating is limited to 75 attendees. If you register and are unable to attend please advise us as soon as possible so that others on the wait list can attend.**

## **1. Dr. Nuam Khutoryansky**

### **Abstract: Practical Adaptive Designs for Clinical Trials Phase I-III**

This talk will cover adaptive designs for phase I/II dose ranging clinical trials with objectives either to target the minimum effective dose, or to find the dose response curve and therapeutic range. The following adaptations are under consideration: sample size re-estimation, early stopping due to efficacy or futility, and dropping inferior treatment groups. An escalation / de-escalation approach for dose ranging studies is presented in more detail. Important features of this design are discussed including early detection of the minimum satisfactory dose, increasing sample sizes for more promising doses and mitigating inflation of type 1 error.

**Bio:** Dr. Naum Khutoryansky is a Statistician Fellow at Novo Nordisk Inc. in Princeton. Dr. Khutoryansky has a Ph.D. degree in applied mathematics and a D.Sc. degree in mathematical and statistical modeling. He has over 25 years of research, consulting and teaching experience including more than 10 years of experience in the pharmaceutical industry. His research interests include time dependent processes, longitudinal data modeling, missing data analysis, multiplicity issues in statistical testing, survival analysis and adaptive design methodologies. Dr. Khutoryansky's research results were presented at many conferences and seminars in the USA and abroad, and were published in applied mathematics, statistical and medical journals.

## **2. Dr. Weili He**

### **Abstract: The Role of Simulation in Clinical Supply Management for Adaptive Design Trials**

There are many factors that may have great impacts on drug supply planning and estimates. These may include, but are not limited to, the study design and/or adaptation schemes, the cost of the drug supply, central randomization vs. site- or country-based randomization, acute or chronic treatment of a disease, number of dose levels and dose strengths, sample size and drop out rate, optimal blinding, number of countries/study sites, number of drug supply centers/depots, and optimal packaging configurations. Modeling and simulation (M&S) approach provides a powerful tool to assist with predications of patient recruitment profiles and drug supply requirements. This talk will describe the rationale for M&S in drug supply planning and prediction, propose M&S approaches for drug supply and patient recruitment prediction, illustrate a case study in drug supply estimates, and offer discussions and recommendation for best practices in M&S.

**Bio:** Dr. Weili He is Associate Director of Clinical Biostatistics at Merck & Co., Inc. Dr. He has a Ph.D. degree in biostatistics. She has over 15 years of experience in pharmaceutical industry and close to 20 years of experience conducting clinical trial design and analysis. Her research interests include survival and longitudinal data modeling, cancer phase I & II designs, repeated categorical data modeling, surrogate marker evaluations, and adaptive design methodologies and implementations. She is a core member of the PhRMA Clinical Supply sub-team, collaborating on research looking into clinical supply issues, including modeling and simulation, for adaptive design trials. Dr. He is also an active participant in Merck's adaptive design efforts, focusing on

promoting the use of adaptive design trials in the new Merck environment. Dr He's collaborative experience with colleagues and medical researchers in various disciplines has led to over 30 publications in statistical and medical journals.

### **3. Dr. José Pinheiro**

#### **Abstract: FDA Draft Guidance on Adaptive Designs: Overview, Key Messages, and Impact**

The draft guidance on Adaptive Designs (AD) was recently released by FDA. This guideline document clarifies the FDA position on a wide range of topics related to the planning, execution and analysis of AD, being expected to have a major impact on the future utilization of these methods in clinical drug development. Pharmaceutical companies and the industry trade association, PhRMA, have been actively engaged in reviewing the guidance to provide timely feedback to FDA. This presentation will provide an overview of the guidance, focusing on key regulatory concerns and recommendations on the use of AD in clinical trials, and discussing its potential impact on clinical development, as well as preliminary reactions from the pharma industry to its release.

**Bio:** José Pinheiro has a Ph.D. in Statistics from the University of Wisconsin – Madison, having worked at Bell Labs and Novartis Pharmaceuticals, before his current position as a Senior Director in the Adaptive Designs group at Johnson & Johnson PRD. He has been involved in methodological development in various areas of statistics and drug development, including dose-finding, adaptive designs, and mixed-effects models. A co-leader of the PhRMA working group on Adaptive Dose-Ranging Designs, he is also a co-developer of the NLME software in S-PLUS and R for linear and non-linear mixed-effects models.

### **3. Dr. Keaven Anderson**

#### **Abstract: Information-based sample size adaptation for binomial trials**

We demonstrate methods for information-based sample size re-estimation for binomial trials depending on whether the alternate hypothesis of most interest is stated as a risk difference, odds-ratio or relative risk. Information is computed as a function of the variance of the appropriately scaled treatment difference. Practical considerations are dealt with and routines based on the gsDesign R package will be available to implement the methods. We provide an example for risk-difference and compare an unblinded sample size reassessment scheme. We provide a second example based on relative risk. Each example demonstrates good power over a range of control group response rates.

**Bio:** Keaven Anderson is the head of Biostatistics for late-stage oncology drug development at Merck Research Laboratories where he has worked since 2003. Keaven is the primary author and maintainer of the open source R package gsDesign for designing group sequential trials which will be presented elsewhere at this meeting by his co-author, William Constantine. Keaven has previously worked in many drug, biologic and vaccine development areas at Merck and at Centocor/J&J and on cardiovascular epidemiology at the Framingham Heart Study. He has a B.S. from Iowa State University and a Ph. D. from Stanford University, both in statistics.