

Spring Meeting Workshop

The Spring 2007 will be held on Thursday, October 18, 2007. There will be three speaker sessions covering a variety of topics. The abstracts of the talks to be presented, including the bios of each of the speakers, are provided below.

Continuous Reassessment Method in Phase 1 Dose Finding Studies

Background: Abbott compound ABT-X is being developed for treating selected types of malignancy. The primary objective of a Phase I dose-escalation study is to determine the maximum tolerated dose (MTD) in humans. The conventional rule-based 3+3 design and a continual reassessment methodology (CRM) utilizing either maximum likelihood (ML) or Bayesian approach have been considered. The objective of this research is to evaluate the operating characteristics of the three methods via simulations. MTD is defined as the dose at which 30% of subjects experience a dose-limiting toxicity (DLT).

Methods: In the study, three subjects will be treated per dose level, beginning with the starting dose of 10 mg. For the conventional 3+3 design, if 0/3 subjects experience a DLT, 3 subjects will be enrolled at the next dose level based on a modified Fibonacci sequence. If a DLT is observed in 1/3 subject, an additional cohort of three subjects is enrolled at this same dose level, and if

DLTs are observed in 2/6 subjects, subjects may be enrolled at a lower dose level. The MTD is selected as the highest dose level at which DLT occurs in less than 33% of the subjects. For the proposed CRM, there are two stages. In Stage 1, the study drug dose will be escalated with a doubling of dose not to exceed an increase of 100 mg until the first DLT is observed. Stage 2 will use a dose escalation strategy based on a two-parameter logistic regression model for the relationship between dose and DLT rate. ABT-X dose will be escalated/de-escalated according to the model-estimated MTD, utilizing the maximum likelihood or Bayesian methods. Non-informative priors for the slope and MTD are used for the Bayesian approach.

Results and Conclusions: We assessed 14 dose-toxicity curves, spanning the expected dynamic range of ABT-X doses. The operating characteristics (estimated MTD, true DLT rate associated with the estimated MTD, sample size, and subjects dosed above a dose corresponding to 90% toxicity rate [D90]) are evaluated among the CRM-ML, CRM-Bayesian and the conventional rule-based 3+3 design. Compared with a conventional rule-based 3+3 design, both the ML and Bayesian approaches within the CRM design are expected to estimate the ABT-X MTD more accurately while studying fewer subjects overall and/or at potentially toxic doses. Furthermore, both of the proposed CRM approaches may reduce the number of subjects exposed to non-efficacious doses. Although the Bayesian approach does not provide remarkable savings in the number of subjects over the

ML method, the Bayesian methodology allows for interval estimation of MTD.

Dr. Yi-Lin Chiu, PhD

Dr. Chiu is currently employed as an Associate Director of Statistics at Abbott. She has 10 years of industry experience in the Pharmaceutical Business. She is an Associate Fellow of the Volwiler Society for Exceptional Abbott scientists and researchers. She has experience in a many therapeutic areas including, gastro-intestinal, anti-viral, infectious diseases, cardiovascular, diabetes, and oncology. During her career in the pharmaceutical industry, she has performed a wide variety of analyses, including, analyses of pharmacokinetic and pharmacodynamic data, special population studies (pediatric, hepatic impairment, etc), efficacy/safety, and non-inferiority studies, QT studies, in-vitro dissolution studies, pharmacogenomic studies, animal studies, bridging studies, investigator-initiated studies, and post marketing studies. She has participated in 27 regulatory submissions. Dr. Chiu has PhD and a Master's degree in statistics both from Northwestern University. Before joining Abbot, she also worked as a Biostatistician at the Northwestern University Medical School and Children's Memorial Hospital.

Statistical Considerations and Challenges in Adaptive Designs that Combine Phase II and III - A Case Study

In this discussion, we will focus on the statistical considerations and challenges with regard to seamless study designs that combine Phase II and Phase III studies within the context of adaptive designs. These will be discussed in the context of a case study to illustrate these types of designs and to help illustrate the challenges that one may encounter from a statistical perspective. This study was discussed with FDA and other

agencies and agreed as a single pivotal trial for NDA filing.

Charlie Cao, PhD

Dr. Cao is currently an Associate Director of Statistics at Takeda Global Research & Development Center. Prior to joining Takeda, Dr. Cao worked at Abbott Laboratories and prior to this, he worked for Glaxo. He has over 15 years of Pharmaceutical experience. Dr. Cao has a PhD degree in Statistics from Duke University. He has a wide range of therapeutic work experience within the pharmaceutical industry covering Phase I to IV studies. He has contributed to various scientific publications and conferences and continues to work on independent research in various areas of interest.

Non-Inferiority Testing in Thorough QT/QTc Studies

Evaluation of new drugs for unwanted effects on electrical properties of the heart is receiving heightened attention from pharmaceutical companies and regulatory agencies. This attention arises from recent scientific research that links drug effects in cellular ion channels to changes in electrical characteristics of the electrocardiogram (ECG) that predict clinically important cardiac arrhythmias. An assessment of non-inferiority of the higher dose to placebo is performed in four-period cross-over study as well as four-group parallel study by the union- intersection test within the framework of a linear mixed effects analysis. For the purposes of planning such a study, the joint distribution of the estimate of the difference in means of high dose of investigational drug and the placebo was derived. The power of thorough QT/QTc study evaluated using the joint distribution and the simulation study were quite close.

Balakrishna Hosmane, PhD

Dr. Hosmane is a Statistics Faculty at Northern Illinois University and has been teaching there for the last 23 years. He serves as Director of Consulting Services at NIU. His main research interest is in categorical data, linear and nonlinear mixed models and pharmaceutical statistics. He has been working with statisticians and pharmacokineticists of Abbott Laboratories for the last 18 years as a consultant. He received his PhD from the University of Kentucky and has published over 35 research articles both in applied and theoretical journals.

President's Report

My term as the President of the Northeastern Illinois Chapter of the ASA is almost coming to an end. I would like to take this opportunity to express my sincere gratitude and appreciation to all the members of the Executive Committee for their help in supporting the current Chapter throughout the course of my term of office as president. They include: Anita Ross (President-Elect and Program Chair), Zhen Zhao (Treasurer), Jeffrey Isaacson (Past-President and Chapter Representative), Carolyn Setze (Arrangements), Michele Olds (Webmaster and Arrangements), Carl Slenk (Newsletter Editor), Rick Rode (Workshop Publicity), Coleen Hall (Workshop Publicity and Listserv), and Carole Bernett (Community Activities). I also wanted to extend my thanks to the following team that had helped to put together this year's program of activities: include: Renee Alpern, Joan Chmiel, Joseph Chmiel, Robert Dillard, Coleen Hall, Bala Hosmane, Jeff Isaacson, Donna Kowalski, Domenic Reda, and Rick Rode. Additionally, I would like to thank our workshop speakers for their time and knowledge with the Chapter.

Please keep in mind that the purpose of our chapter is "to foster statistics and its applications and promote the interests of the statistical profession among all groups in the Northeastern Illinois area having an interest in or being concerned with statistical problems." Our Chapter is fortunate in the sense that there has been an excellent history of dedicated volunteers committed to serving our membership and making this Mission a reality. In this regard, I would also like to thank our past officers and committee chairs for their excellent contributions to our chapter and applaud their commitment and efforts to ensure the success of our chapter. Last but not list, I would like to thank all of you the members of the Chapter for your support.

The Executive Committee will have at least one new member next year. Dr. Xuejun Peng who has been nominated as the President-Elect and Program Chair at the next meeting. Anita Ross has done an excellent job as the Program Chair this year and she will transition to President of the Chapter next year. The positions of Secretary and Newsletter Associate Editor are still open. If you are interested in any of these two positions, please contact any of one of the officers listed on the last page of this issue. I am confident that under the leadership of these new officers, NIC-ASA will enjoy another successful year. We are very appreciative of those committee chairs, listed on the last page of the Statfax Newsletter, who have agreed to continue to serve our chapter in 2008. We look forward to seeing you at this meeting on 18th October, 2007.

~ Melvin Munsaka

President-Elect/Program Chair

Xuejun Peng, MD, PhD is currently employed as a Senior Statistician at Takeda Global Research & Development Center,

Inc., (TGRD) in Deerfield, Illinois in the Biometrics and Data Management Department. He has been with Takeda since June 2005. Prior to joining Takeda, Dr. Peng worked as an Assistant Staff in the Department of Quantitative Health Sciences at the Cleveland Clinic Foundation. Prior to that, he worked as Biostatistician and Bioinformatics Consultant at the Microarray Core Facility and also as a Statistical Consultant at Chandler Medical Center at the University of Kentucky. He also worked as a Resident Physician in the Department of Internal Medicine at Hunan Medical University in China. Dr. Peng has a PhD and a Masters Degree in Statistics both from the University of Kentucky. He also holds a MD degree from Hunan Medical University in China. Dr. Peng has published numerous papers in peer reviewed journals and has given many presentations at conferences. He was twice awarded the Charles B. Sampson Award at the Annual Midwest Biopharmaceutical Statistical Workshop and was also a recipient of the Richard L. Anderson Student Paper Award, the Summer Research Conference in Statistics Award from the Southern Regional Council on Statistics and American Statistics Association. He was also the recipient of Biopharmaceutical Student Paper Competition Award at the 2003 Joint Statistical Meeting and he also received the ENAR Junior Researcher Travel Award from the National Cancer Institute. He has been a member of the ASA, International Biometric Society, Eastern North American Region, Drug Information Association, American Society of Human Genetics, American Association for the Advancement of Science, and the American Diabetes Association. Dr. Peng has also served a Regional Advisory Board Member of the International Biometric Society for the Eastern North American Region.

~ Jeffrey Isaacson

Thank You to Volunteers

The Chapter would like to recognize and thank the following meeting registration volunteers:

Dr. Wencan Zhang, TGRD – Spring Workshop

Brian Hobbs, University of Minneapolis/TGRD – Summer Workshop

~ *Melvin Munsaka*

Employment Opportunities

Medical College of Wisconsin

The Medical College of Wisconsin is recruiting for Masters prepared and PhD leveled statisticians in the Section of Quantitative Health Sciences(QHS), Department of Pediatrics. As jointly part of the Children's Research Institute, the section collaborates with investigators in the Children's Hospital of Wisconsin, recently rated one of the top ten hospitals in the United States. It has an exciting program of research which needs the support of a fast growing QHS Section.

PhD Biostatistician:

Appointments will be at the level of assistant, associate or full professor, depending on qualifications and experience. Requirements include: Ph.D. in statistics or biostatistics; working knowledge of the major statistical and database packages; and excellent oral and written communication skills. Experience in the following areas is desirable: research involving data collection and analysis of data from medical practices; formal training or

expertise in the design and analysis of clinical trials and health service research and supervision of programmers and database analysts. Primary responsibilities include collaboration with physicians in the design and analysis of research data. In addition, the successful applicant will be expected to be a collaborating investigator on extramurally funded projects.

For information regarding the PhD Biostatistician please contact: Pippa Simpson, Chief Quantitative Health Sciences Department of Pediatrics, Medical College of Wisconsin 8701 Watertown Plank Road, Milwaukee, WI53226 Email: psimpson@mcw.edu Phone: 414.955.7635 Fax: 414.955.6331

MS Biostatistician: Requirements include: M.S. in statistics/biostatistics or similar; experience in research involving data collection and analysis of data from medical practices is desirable; working knowledge of the major statistical and database packages, especially SAS; ability to work independently; and excellent oral and written communication skills. Primary responsibilities include implementation of statistical analyses and provide data management in support of projects. Secondary responsibilities include collaboration with physicians in the design and analysis of research data. For information regarding the MS Biostatistician: Visit the Medical College of Wisconsin website, www.mcw.edu to learn more about the position or complete an application.

Takeda Global Research & Development Inc

Senior Statistician

Takeda Global Research & Development Inc:
An excellent opportunity for a Senior

Statistician with relevant clinical trials experience. The ideal candidate will provide input in clinical development projects at all phases. Responsibilities include: defining analysis endpoints, sample size estimation, and performing statistical analyses; providing input to protocol development; ensuring accuracy of outputs produced by CROs; providing clinical development documents; and contributing to drug development and submission plans. The Senior Statistician position requires an MS or PhD (preferred) in Statistics or Biostatistics with 5+ years of relevant of experience, ideally within the Pharmaceutical Industry or CRO.

Research Statistician

Takeda Global Research & Development Inc: an excellent opportunity for a Research Statistician with relevant experience. The position will serve as global statistical lead for various therapeutic areas; provide statistical expertise in support of regulatory meetings and submissions; establish and drive program-level functional strategy for methodology, resource allocation, processes and standards to maximize efficiency and global data integration; monitor and influence advances in statistical and clinical trial methodology and serve as an internal expert for the global Statistics organization; lead a team of statisticians supporting global studies and programs; identify and manage external key opinion leaders; monitor and actively contributes (through publication and presentations) to industry advances in statistical methods to optimize study designs and statistical analyses. This position requires a PhD in statistics or biostatistics with 10+ years experience in the pharmaceutical industry supporting clinical trials across multiple therapeutic areas or development phases.

Associate Director, Statistics

Takeda Global Research & Development Inc: an excellent opportunity for an Associate Director of Statistics. The position will serve as global statistical lead for major development programs and therapeutic areas; lead and manage a team of statisticians to provide expertise and capability specialized by therapeutic area or phase of development; oversee all statistics activities for multiple clinical programs to ensure timely and accurate delivery of statistical designs, analyses, and reports ensure achievement of major statistical deliverables and milestones in coordination with other functions including Clinical Research, Safety, Statistical Programming, Data Management, and Medical Writing. This position requires a PhD in statistics or biostatistics with 10+ years experience in the pharmaceutical industry supporting clinical trials across multiple therapeutic areas or development phases plus 5+ years of line management experience.

If you are interested in any of these three positions, please contact Shawn Yu at Takeda Global Research & Development Inc, Deerfield, IL; phone 224-554-6360 or e-mail syu@tgrd.com

Chapter Website

Don't forget to visit our Chapter web page at <http://www.amstat.org/chapters/NortheasternIllinois>. The website has lots of information about our Chapter, including events, program information, and contact information for Chapter officers and committee members. You can also peruse PDF versions of current and past Chapter newsletters. Finally, if the speaker provides them, slides/notes from previous presentations are available to view or download.

Calendar

Midwest SAS® Users Group Conference - The workshop will be held at the Des Moines Marriott Downtown, located in the heart of Iowa's Capital City. Visit the conference web site at www.mwsug.org/dsm2007/ for more details and call for papers. October 28 - 30

PhRMA – Challenges and Opportunities of Multi-Regional Clinical Trials. This workshop will include as one of the topics “Statistical Issues and Challenges in Multi-Regional Trials” with speakers from the FDA (including Robert O’Neill) and Pharma. , October 29-30, 2007. www.phrma.org

BASS - Fourteenth Annual Biopharmaceutical Applied Statistics Symposium, November 5-9, 2007. <http://bass.georgiasouthern.edu/index.html>

BIOCONDUCTOR CHICAGO 2007 - 3-day course on Northwestern University Medical School's downtown Chicago campus will cover advanced topics in genomics and proteomics data analysis using the collection of R packages, October 1-3, 2007. <http://daisy.prevmmed.northwestern.edu/~denise/BiocChicago2007>

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The Chapter's purpose, as stated in its Constitution, is "to foster statistics and its applications and promote the interests of the statistical profession...". Accordingly, diverse views are presented. They do not necessarily reflect the opinions of the officers or the policies of the Chapter

NORTHEASTERN ILLINOIS CHAPTER of the AMERICAN STATISTICAL ASSOCIATION
TREASURER'S REPORT

(September 13, 2007)

4685.69

BALANCE March 1st, 2007

INCOME

Chapter Meeting and Membership

2007 Spring Meeting	3562.00
2007 Summer Workshop	12727.00

Investments

Bank Interest	0.00
	16289.00

TOTAL INCOME

20974.69

TOTAL ASSETS

EXPENSES

Operating Expenses

Spring 2006 Workshop	3711.60
Summer 2006 Workshop	9441.58
Workshop Speaker	
Bank Charge Exp. (check order)	25.16
Student Awards 2006	225.00
Student Awards 2007	250.00

13653.34

TOTAL EXPENSES

7321.35

BALANCE

Respectfully submitted,
Zhen Zhao, Treasurer NIC/ASA 2007