

**March 2007**



**ASAP Newsletter**

**The Philadelphia Chapter of the American Statistical Association**

<http://www.amstatphilly.org/>

**PRESIDENT'S CORNER**

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Our Mid-Winter Gathering January 26 at the Sedgeley Club on Philadelphia's historic Boathouse row was a smashing success! Many thanks to our generous sponsors: Merck, ICON, GSK, Centocor and Wyeth. We had a wide variety of attendees, from an undergraduate English major to weathered career statisticians. Thanks to speakers **Will Fairley** (Analysis & Inference) and **Mary Gray** (American University) for sharing their experiences using statistics in the courtroom. Mary's presentation, entitled "Teaching an Audience of One: The Judicial Reception of Statistical Evidence," has been posted to our website ([www.AmstatPhilly.org](http://www.AmstatPhilly.org)) and has received plenty of positive feedback.

Many thanks also to ASAP Outreach Officer **Cindy Gargano** for coordinating another PASTA (Philadelphia Area Statistics Teachers Association, [www.amstatphilly.org/PASTA/pasta\\_index.htm](http://www.amstatphilly.org/PASTA/pasta_index.htm)) meeting February 27. Be sure to check out their website for meeting minutes and upcoming events. On January 24 Cindy and ASAP Vice President **Bill Pikounis** spent time at Drexel University's career day for students of biostatistics and epidemiology. In order to recruit the next generation of

statisticians it is important to reach out to area primary and secondary school teachers, and these are excellent opportunities to do just that.

We hope you will join us Friday, March 23 at the Fort Washington Hotel and Conference Center (formerly the Holiday Inn, [www.fwholiday.com](http://www.fwholiday.com)) for our annual spring meeting. Two talks by **Simon Zhou** (Wyeth) and **Alan Hartford** (Merck) will focus on interesting aspects of PK/PD issues: Simon will discuss “Graphical Statistics in Population and PK/PD Analysis” and Alan will cover “PK/PD Modeling and Simulation.” Finally, **Winston Richards** (Penn State, Harrisburg) will describe his work on mortality following the Three Mile Island nuclear meltdown on March 28, 1979. Lunch will feature a Mexican buffet, and you will have the pleasure of networking with many area statisticians. Details can be found on pp. 3-6.

We also hope you will join us to judge **Delaware Valley Science Fair** posters Wednesday, April 4. DVSF is one of the nation’s oldest and largest science fairs, and the quality of work continues to impress, particularly in the area of statistics. This year’s fair will take place at the Valley Forge Convention Center; judging begins with continental breakfast at 7:30am and should end around 3:00pm. Please sign up online at [www.dvsf.org](http://www.dvsf.org) by clicking on “Judges” and following the prompts. Note that you are an “ASAP” special awards judge, and leave all subject areas and age groups blank, as we cover all of them. Please email me your cell phone number ([PMJohansen@aol.com](mailto:PMJohansen@aol.com)) to assist our gathering together. Thanks to **SAS/JMP** for again donating prize software.

On the national front, ASA has recently launched a “Webinar Series” for biopharmaceutical statisticians, and nominations for the Gertrude M. Cox scholarship are due April 1. The scholarship, named after the female pioneer in statistics, is designed to encourage women to enter statistically-oriented professions. ASA is also offering travel grants to Portugal in August to attend the 56<sup>th</sup> session of the International Statistical Institute (ISI). See [www.Amstat.org](http://www.Amstat.org) for details.

~Paul Johansen

## CALENDAR OF EVENTS

Sun-Tue, March 18-20	22 <sup>nd</sup> Annual DIA Clinical Data Management Conference and Exhibition, Orlando, FL
Sun-Wed, March 11-14	ENAR, Atlanta, GA ( <a href="http://www.enar.org/meetings.htm">www.enar.org/meetings.htm</a> )
<b>Friday, March 23</b>	<b>ASAP Spring Gathering, Fort Washington, PA</b>
Wed, April 4	Delaware Valley Science Fair judging ( <a href="http://www.dvsf.org">www.dvsf.org</a> )
Sun-Thu, June 17-21	43 <sup>rd</sup> Annual DIA Meeting, Atlanta, GA
<b>Fri, July 13 (tentative)</b>	<b>ASAP Summer Short Course (<a href="http://www.AmstatPhilly.org">www.AmstatPhilly.org</a>)</b>
Sun-Thu, July 29- August 2	Joint Statistical Meetings, Salt Lake City, UT ( <a href="http://www.amstat.org/meetings/jsm/2007">www.amstat.org/meetings/jsm/2007</a> )

# ASAP SPRING MEETING

March 23, 2007

Fort Washington Hotel (formerly the Holiday Inn)

[www.fwholiday.com](http://www.fwholiday.com)

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**Cost:** \$35 including lunch (\$15 for full time students); \$15 without lunch

**Directions:** From the PA Turnpike, take Exit 339 – Fort Washington. After the tollbooth, follow the left-hand lane under the overpass. (DO NOT TAKE THE ROUTE 309 RAMP.) The hotel is 1/8 mile on the left. From Route 309, take the Fort Washington exit. (DO NOT TAKE THE EXIT FOR THE PA TURNPIKE.) Exiting will put you onto Pennsylvania Avenue. Stay in the left-hand lane. The hotel is 1/8 mile on the left. The hotel is close to the Ft. Washington SEPTA stop on the R5 Lansdale/Doylestown line (<http://www.septa.org/service/pdfs/R5LD.pdf>).

Registration: PLEASE REGISTER AND PAY IN ADVANCE by Friday, March 19 to assist with the head-count. Contact Treasurer, Alexandra Hanlon, at [alhanlon@temple.edu](mailto:alhanlon@temple.edu), specifying if you are a student, if you will be eating lunch, if you are an ASA and/or and ASAP member, and your company/institution. Checks should be made payable to “ASAP” and sent to Alexandra Hanlon / 965 Dale Road / Meadowbrook, PA 19046.

## Mortality

Winston A. Richards, PhD

Associate Professor of Mathematics and Statistics

The Pennsylvania State University, Harrisburg

[ugu@psu.edu](mailto:ugu@psu.edu)

### Abstract

This presentation is the product of collaborative work done with Dr. Martin Beibel of the University of Freiburg while we were both visiting scholars at Stanford University Statistics Department during the summer of 2001.

The purpose of this presentation is to call attention to the fact that Dauphin County in South Central Pennsylvania, where Three Mile Island Generating Plant is located, experienced a significant increase (50%) in infant mortality after the accident in March of 1979.

The first approach in the analysis of the infant mortality data was to adapt a method suggested in a paper by Choynowski in which the assumption of uniform risk was taken to be the same for infant mortality for all counties in Pennsylvania. Using this assumption, a pre TMI analysis and a post TMI analysis were carried out to see if the data supported this assumption.

This approach led to another assumption, namely, infant mortality in Dauphin County was similar to that of Pennsylvania before TMI. This assumption was supported by graphical methods as well as analytical statistical methods using chi square methodology.

The CUSUM methodology was then applied to 20 years of time series data to determine when the infant mortality rate of Dauphin County began to deviate from that of Pennsylvania.

Conclusion: Dauphin County experienced a significant jump in infant mortality the year of the TMI accident. CUSUM analysis showed that it took approximately 20 years for infant mortality to return to normal. Also infant mortality rates remained stable in neighboring York County which was used as a control, throughout the similar period for which these data were analyzed.

Key Words: CUSUM chart, Three Mile Island

### **Biosketch**

Present Position: Associate Professor of Mathematics and Statistics, Penn State Harrisburg, 1969-Present. Associate Professor of Health Evaluation Sciences, Penn State College of Medicine, 1999-Present. Visiting Associate Professor, Department of Statistics, Stanford University, summers 1995-Present.

Former Positions: Senior Lecturer, Department of Mathematics, University of the West Indies, Trinidad and Tobago, 1980-82.

Degrees: PhD 1970, MA 1966 Mathematics, University of Western Ontario, London, Canada. MS 1961 Mathematics, BS 1959 Mathematics and Physics, Marquette University, Wisconsin.

Fields of Major Statistical Activities: Trained government statisticians in Trinidad and the English speaking Caribbean under contract to the OAS, Trinidad Government and the UN, summers 1970-80. Surveyed the statistical training needs of Caribbean governments for the United Nations, 1972. Currently an external examiner for the Statistics courses for the Univ. of the West Indies, Trinidad. Peer reviewer for ATSDR, CDC, Atlanta, GA 1993-2000.

Research: health effects of TMI accident, analysis of thyroid data, analysis of burn victim data, exact distribution theory.

Related Professional Activities: Coordinated the 1994 Demonstration Survey Program, Lancaster County, International Statistical Programs Center, US Bureau of the Census 1993, 1994. Coordinated the annual Distinguished Statisticians lecture Series, Penn State Univ. Harrisburg, 1988-Present.

# Graphical Statistics in Population and PK/PD Analysis

**Simon Zhou, PhD**  
Associate Director, Wyeth Research  
[Zhous2@wyeth.com](mailto:Zhous2@wyeth.com)

## Abstract

Traditional hypothesis testing in exploratory drug development requires large clinical trials, offers limited learning, and is inefficient and not sustainable. Rather, studies in early clinical phase should be conducted to learn about the pharmacology and identify the right hypothesis to be tested in late confirmatory trials. A paradigm shift is underway; it is the driver of FDA's Critical Path Initiative promoting model-based drug development. Exposure-response analysis based on population and PK/PD modeling to better define dose response is one of the key aspects of model-based drug development.

Population and PK/PD modeling is a data and computational intensive approach to explore exposure-response. Model building requires experience and skill to drill down many possibilities to arrive at the most plausible and parsimonious solution. The nonlinear nature of PK/PD models makes it tricky to use traditional numerical statistics in evaluating model performance. This presentation aims to introduce fundamental concepts of population and PK/PD modeling with an emphasis on using statistical graphs to address practical and statistical questions arising from the model building process. In addition, use of statistical graphs for better presentation and communication of population and PK/PD modeling will be discussed.

## Biosketch

Simon Zhou holds Bachelor and Master degrees in Chemistry, a Ph.D. in Pharmaceutics and a Graduate Certificate on Modeling of Complex System from the University of Michigan.

Dr. Zhou is currently an associate director in the department of clinical pharmacology at Wyeth Research in Collegeville, PA. Prior to his current position, he has worked in preclinical and clinical drug development functions addressing biopharmaceutical and trial design issues at Pfizer and Bristol-Myers Squibb. He relied heavily in kinetic/dynamic and statistical modeling to integrate and mine voluminous and complex data from clinical trials. He has published manuscripts in biopharmaceutics, drug delivery and pharmacokinetic and pharmacodynamic modeling.

# **PK/PD modeling and simulation**

**Alan Harford**

**Associate Director, Merck Research Laboratories**

## **Abstract**

PK/PD modeling and simulation requires the use of many complex statistical procedures. Many of the advancements in these statistical procedures can be credited to pharmacokineticists who have pain-stakingly frontiered the edge of the limits of statistical knowledge. However, in spite of the adeptness of pharmacokineticists for solving statistical problems, they continue to request and welcome the aid of statistical colleagues; there is still room for statisticians to become more engaged. Several problems could benefit from further statistical research. There are even a few areas well researched that could be more easily applied in practice with the aid of statisticians familiar with these topics. In this talk several of these statistical problems in PK/PD modeling and simulation will be presented.

## **Biosketch**

Alan Hartford is an Associate Director at Merck Research Laboratories leading a group of statisticians supporting Merck's effort in PK/PD modeling and simulation in collaboration with Merck's Drug Metabolism and Clinical Pharmacology departments. He earned a B.S. and an M.S. in mathematics and an M.S. in biometry at the University of Nebraska-Lincoln and also earned a Ph.D. in statistics with a minor in computational engineering at North Carolina State University. His Ph.D. dissertation was Computational Approaches for Maximum Likelihood Estimation for Nonlinear Mixed Models. In addition to his experience at Merck, he previously provided statistical support for PK/PD modeling and simulation at Genentech.

## EMPLOYMENT

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### **Senior Principal Biostatistician, Early Development & Clinical Pharmacology Wyeth Pharmaceuticals, Collegeville, PA**

Maintain productivity and adherence to project target dates with respect to clinical development plans, statistical analysis plan (SAP), protocol development, analysis, and report presentation for assigned projects. Participate in planning, and reporting, of all studies conducted within EDCP, within a given therapeutic area, and at times across several therapeutic areas. This will include providing input on study design, sample size, model building and fitting to diverse data, assay development and validation, and CRF design and methods of analysis.

Clinical biostatistics research experience is required; 3 years with a PhD in Biostatistics, Statistics or Epidemiology, or 7 years with a Masters in one of those majors.

**Please email your resume with “OIAMSTAT-R924252” in the Subject field, plus salary requirements in the email to: [WYETH@TrackCareers.com](mailto:WYETH@TrackCareers.com).**

For more information, visit our website at [www.wyeth.com/careers](http://www.wyeth.com/careers)

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### **Principal Biostatisticians, Clinical Statistics**

#### **Wyeth Pharmaceuticals Collegeville, PA**

The positions provide high-level statistical expertise to projects from Proof-of -Concept through regulatory filings. The position requires active participation in the design of clinical trials, including innovative approaches, analysis and reporting of clinical study data and integrated summaries for evaluation of pharmaceutical drugs.

Selected candidates must possess a Ph.D. in Biostatistics/Statistics and at least 5 years of relevant work experience, a strong command of statistical methods, statistical modeling, design of experiments, statistical computing expertise including SAS, and excellent oral and written communication skills.

Wyeth offers competitive compensation and benefits programs including stock options, child-care subsidies, flex-time, business casual attire, educational assistance and professional development programs.

Please forward your resume with salary requirements, referencing **Source Code: OIAMSTAT-R922882** in the subject line to: [wyeth@trackcareers.com](mailto:wyeth@trackcareers.com).

For more information, visit our website at [www.wyeth.com/careers](http://www.wyeth.com/careers).



[www.nearingzero.net](http://www.nearingzero.net)

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