International Initiatives Subcommittee
Proposal for JSM 2016

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(Ed. note: this is the latest in a series of reports from the Biopharmaceutical Section International Initiatives Subcommittee, with perspectives spanning the different regions represented by the members)

The globalization of medical product development has largely been motivated by the need to access the best science and molecules, to stimulate innovation and to accelerate the delivery of new medicines that target unmet patient needs. Global collaboration and harmonization among relevant stakeholders around the world, including academia, governments, industry, scientific organizations and patient groups, is key to achieve these needs in an efficient way. However, technical standards as well as ethical and legal frameworks may often be different in different regions of the world. In addition, societies may have different experiences and expectations because of differences in legal requirements for drug approval, biological medical devices and diagnostics, or simply because of cultural differences. It is therefore necessary to overcome these differences through global collaborations in order to produce effective and productive collaborative work.

In medical product development, a new medicine or medical device must pass several hurdles and exami-
nations in a multi-step evaluation process, by controlling costs with time and risk as primary indexes. Statisticians, who are involved in such a process as key players, should have the necessary statistical and clinical knowledge for the execution of the professional and associated technical/strategic duties. However, in a new era for global medical product development, a naturally arising question in my mind involves what additional skills/techniques and knowledge are required beyond the traditional ones, especially when educating the next generation of statisticians, being sensitive to cultural differences and having a collaborative mind.

In late March 2015, I hosted the Austria-Japan Joint Statistics Workshop on “Innovative Clinical Trial Designs and Personalized Medicine for Accelerating Medical Product Development” in Osaka, Japan, which was co-organized with Professor Martin Posch and Professor Franz König from the Medical University of Vienna. This workshop was sponsored by the Bilateral Joint Research Seminars of the Japan Society for the Promotion of Science (JSPS) and the Austrian Science Fund (FWF). This was a good opportunity for exchanging the current state of research on clinical trial methodology, getting a better mutual understanding of the region-specific perspectives on innovative statistical methodology and clinical trial designs of sponsors, academia and regulatory agencies between these two countries, and beyond. It helped to identify current gaps in the available knowledge on innovative clinical trials that constitute an obstacle for their application in both countries, and to define research topics addressing the identified challenges from the perspectives of different regions, stakeholders and academic disciplines. In addition, this was an opportunity for young Japanese researchers to learn about adaptive clinical trials design and analysis and be inspired by distinguished researchers including Professor Peter Bauer from the Medical University of Vienna, Dr. Frank Bretz from Novartis, Dr. Alex Dmitrienko from Quintiles, and Dr. James Hung from US Food and Drug Administration. Although this was a small event, we had more than 100 participants from academia, governments and industry, representing 9 different countries in total. Based on the output from the workshop, Japanese and Austrian researchers are now seeking further future opportunities for collaborative research in innovative clinical trials designs. This harmonized work between the two countries could be an example for collaborations among other countries.

As Dr. Brian Wiens reported in the previous Biopharmaceutical Report (Winter 2015), the Executive Committee of the Biopharmaceutical Section has chartered the International Initiatives Subcommittee to find a way to a long and fruitful global collaboration and community platform which can bring new information to Section members and provide service to statisticians around the globe. One of the initial activities of the subcommittee is to propose an Invited or Topic Contributed session tentatively entitled “Global Challenges, Global Collaboration in Biopharmaceutical Statistics” at JSM 2016 in Chicago. The objective of the proposal is to discuss global communications and education for interaction and integration among statisticians working in biopharmaceutical sectors to cover problems in biopharmaceutical and statistical science in the world. This proposed session will focus on the opportunity for educating the next generation of biostatisticians working in the biopharmaceutical industry or biostatisticians who are considering a career in biostatistics. It will also discuss opportunities for professional global collaborations, i.e., research group for innovative clinical trials and statistical methodology, to share experiences with various regulatory agencies. However, these are still early ideas. Any proposal or suggestion is very welcome, as we have some time before needing to propose the details of such a session for JSM 2016.
Statistical issues in generalized linear models in clinical trials

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Department of Biometrics, Eli Lilly and Company

Introduction
Categorical data, including binary, count, and ordinal or non-ordinal multicategory data, are quite common in randomized clinical trials. For instance, in diabetes studies, researchers are looking for better therapies which can achieve the treatment target of HbA1c \( \leq 7.0\% \) established by the American Diabetes Association and reduce hypoglycemic events. The status of a patient reaching the HbA1c treatment target is a binary variable. Hypoglycemic events are captured as recurrent events through patients’ self-reporting diary and considered as count data in statistical analyses. For this type of data, a generalized linear model (GLM) (McCullagh and Nelder, 1989) is widely used (e.g., logistic regression for binary data, and Poisson or negative binomial (NB) regression for count data). Generally, a GLM extends the traditional linear model via a link function to allow the linear relationship between the mean response and predictors:

\[
g(\mu_i) = X_i \beta
\]

where \( \mu_i \) is the expectation of the response variable \( y_i \) for subject \( i \), which follows a distribution in the exponential family; \( X_i \) denote covariates usually including baseline characteristics and treatment, \( \beta \) denotes coefficients of covariates, and \( g(\cdot) \) is the link function. Parameters in GLM can be estimated by methods of maximum likelihood, generalized estimating equations or pseudo-likelihood estimation.

A GLM is powerful since it allows an arbitrary distribution for the response variable. However, the model complexity may cause issues in real-data analyses due to these attributes:

1. The magnitude of the variance is a function of its predicted value. The function varies with the distribution of the response variable. To relax the relationship between the variance and the predicted value, an over-dispersion parameter may be considered in the model estimation.
2. The relationship between the response and predicted value is established via a link function, which often is a non-linear function.

This paper will focus on the following issues and solutions identified in GLM:

1. GLM estimation by adjusting for covariates for count data
2. Piecewise negative binomial regression (PWNB) for longitudinal count data
3. Group mean versus least-squares mean (LSM) in GLM
GLM estimation by adjusting for covariates for count data

As a member of GLM, NB regression is emerging as a standard model to analyze aforementioned hypoglycemia events in diabetes clinical trials. The main reason for choosing NB regression is that the number of hypoglycemic events generally has a skewed distribution. NB regression can be considered as an extension of Poisson regression by introducing a dispersion parameter in the modeling: \( \text{var}(y) = \mu + k\mu^2 \). Here \( \mu \) denotes the mean, \( k \) is the dispersion parameter. The NB model reduces to Poisson regression when \( k = 0 \).

In clinical data analyses, adjusting for baseline covariates can correct potential baseline imbalance between treatments and potentially increase the estimation efficiency. For NB regression, let’s assume that the condition \( \text{var}(y) = \mu + k\mu^2 \) holds. However, in a model with baseline covariate adjustment, the relationship \( \text{var}(y|X) = \mu(X) + k\mu(X)^2 \) may be violated. Further, we cannot guarantee the condition that response \( y|X \) is NB distributed. Luo and Qu (2013) investigated this problem, and showed through simulations that Type I error was not controlled well when adjusting for baseline hypoglycemic event rate in the basic NB regression, even though \( y \) follows a NB distribution. The Type I error was inflated to more than 10% for a moderate correlation (e.g., \( \rho=0.5 \)) between baseline and post-baseline hypoglycemia event rates.

One way to solve this problem is to introduce over-dispersion to ease the strict assumption by \( \text{var}(y|X) = \varphi[\mu(X) + k\mu(X)^2] \), where \( \varphi \) denotes the over-dispersion and explains additional dispersion. In the GLM framework, the over-dispersion can be estimated through Deviance or Pearson Chi-square statistic \( x^2 = \sum_i \frac{(y_i-\hat{\mu}_i)^2}{\hat{\mu}_i+k\hat{\mu}_i^2} \) of a fitted model (McCullagh and Nelder, 1989). Considering that the introduction of the over-dispersion alone may not be able to control Type I error, a more relaxed estimation for the variance-covariance structure can be considered. Generally, the empirical or sandwich estimator for the variance-covariance of coefficients \( \beta \) is not sensitive to the choice of the covariance model

\[
\text{cov}(\beta) = \left( \sum_{i=1}^n D_i' \Sigma_i^{-1} D_i \right)^{-1} \left( \sum_{i=1}^n D_i' \Sigma_i^{-1} e_i e_i' \Sigma_i^{-1} D_i \right) \left( \sum_{i=1}^n D_i' \Sigma_i^{-1} D_i \right)^{-1}
\]

where residual \( e_i = y_i - \hat{\mu}_i \), \( \Sigma_i \) is the variance of \( y_i \), and \( D_i \) is the matrix of first derivatives of \( \mu_i \).

A NB regression which combines the sandwich estimator for the covariance and over-dispersion was proposed and compared to other NB models such as a basic model, models with only over-dispersion, zero-inflated NB model, etc. Simulations and real-data permutations showed that the Negative Binomial regression with Sandwich estimator for the covariance together with Pearson chi-square statistic for over-dispersion (denoted by NBSP) is more robust than others for analyzing the hypoglycemia data, even when the data were very skewed or not generated from a NB distribution. Type I error was well controlled and statistical power was increased when adjusting for baseline covariates compared to no covariate adjustment. The SAS procedure GLIMMIX (SAS 9.2, 2009) provides options to perform NBSP easily. In subsequent research, Luo et al. (2013) systematically analyzed 15 clinical trials in diabetes and demonstrated that adjusting for baseline hypoglycemic event rate in the NB regression analysis generally resulted in smaller standard errors and improved power.
PNWB for longitudinal count data

In clinical trials, missing data are a challenge for longitudinal data analysis, no matter whether for continuous or categorical outcomes. According to Little and Rubin (2002), missing data can be classified into 3 categories: missing completely at random (MCAR); missing at random (MAR); and missing not at random (MNAR). The generalized estimating equations (GEE) method (Liang and Zeger, 1986) has been widely used for longitudinal categorical data, since it only requires marginal distributions specified for the longitudinal or cluster outcomes. The correlation between outcomes within a cluster or subject is indicated through a “working” correlation matrix. GEE works well when data are complete or MCAR. However, when data are MAR, GEE estimation may be biased. To solve this issue, an alternative method, weighted GEE (WGEE) (Robins et al., 1995; Troxel et al., 1997), was proposed by combining GEE and a drop-out model. WGEE is valid under MAR when the drop-out model is specified correctly; however, it is worse than GEE when the dropout model is misspecified (Preisser, et al., 2002). Liu and Zhao (2011) compared GEE, logistic regression with multiple imputations, and generalized linear mixed model (GLMM) for analyzing longitudinal binary outcome under MCAR and MAR, and concluded GLMM with pseudo-likelihood estimation performed better in controlling Type I error and bias.

Regarding the hypoglycemic events in diabetes trials, patients may discontinue the study early, resulting in incomplete data. In a NB regression model without considering repeated measures, one implicitly assumes either the unobserved time period has a similar event rate compared to the observed time period or the unobserved time period has a similar event rate compared to the same period for those patients who do not drop out, which implies MCAR. This assumption is too strong, however, and may introduce bias in estimates and/or inflate Type I error, when the missing mechanism is MAR, which is often a more reasonable assumption than MCAR in clinical trials. In addition, researchers may be interested in comparing event rates at different time periods (e.g., first 3 months of treatment, 3-6 months of treatment, etc.). Fitting a NB regression model for each individual time period separately may not be optimal since the information outside of the specific time period is totally ignored.

Alternatively, Wang et al. (2014) proposed to analyze recurrent hypoglycemia data through a PWNB

\[
\log(\mu_{ipg}) = \beta_{pg} + \gamma_i
\]

where \( \mu_{ipg} \) is the event rate for subject \( i \) in treatment \( g \) (\( g = 0 \) for the control group and \( g = 1 \) for the treatment group) at time interval \( p \), and \( \beta_{pg} \) is a scalar coefficient indicating the event rate in treatment \( g \) at time interval \( p \). The random effect \( \gamma_i \sim \mathcal{N}(0, \sigma^2) \) was introduced in the model to account for within-subject variability.

As aforementioned, GLMM with pseudo-likelihood estimation was demonstrated to be better than GEE by Liu and Zhao (2011) and therefore was used to conduct the PWNB model. Similarly as with the NBSP model, the sandwich method was used for variance estimation to obtain more robust estimation.

This research showed that NB regression may inflate Type I error even though it adjusts for exposure for the count data when missing data exist due to patient dropouts. PWNB regression with GLMM to incorporate the within-subject correlation provides an estimator with little bias and preserves Type I error. This finding is consistent with the expectation that likelihood-based estimation can preserve Type I error. In addition, the PWNB model can estimate the relative rate at various time periods within one model.
Through simulations, it was shown that PWNB performance is improved and robust when combining 3 techniques in the SAS GLIMMIX procedure: 1) estimation based on maximization of subject-specific residual likelihood through pseudo-likelihood technique with Taylor linearization; 2) Newton-Raphson ridge optimization; 3) covariance structure of estimates calculated by sandwich estimation. The authors also proposed 3 methods to calculate the overall relative rate covering all time periods: 1) unweighted overall relative rate, based on the average difference in coefficients between treatments without considering the possible different length of various time periods; 2) exposure-weighted relative rate, considering the length of various time periods as weights; 3) the relative rate based on the ratio of overall number of expected events between treatments during the entire period. For the third method, a delta method was used to estimate the standard error of the overall relative rate. One can select the quantity of interest based on the nature of the real data and parameter of interest. For hypoglycemic events, this article suggested the third method to estimate the overall relative rate.

**Group mean versus LSM in GLM**

As the model-predicted population margin, LSM estimates the marginal means over a balanced population. In clinical trials, we usually present LSM for treatment groups and compare LSM between treatments to make statistical inference. In statistical software, such as SAS and R, LSM in the GLM framework is denoted for treatment \( z \)

\[
\mu^*_z = g^{-1}(\beta_0 + X'_i\beta_x + z'\beta_z)
\]

where \( g^{-1} \) is the inverse of the link function and \( \bar{X} = n^{-1}\sum_{i=1}^n X_i \) is the mean of covariates for the overall population (e.g., mean baseline covariates in the model). This LSM is the response at the mean value of the baseline covariates for the overall population, which is generally not equal to the group mean response for the overall population, defined as

\[
\mu_z = n^{-1}\sum_{i=1}^n g^{-1}(\beta_0 + X'_i\beta_x + z'\beta_z)
\]

If the link function \( g(.) \) reduces to the identity function for data with Gaussian distribution, \( \mu_z^* \) will be equivalent to \( \mu_z \). If \( g^{-1} \) is a convex function such as an exponential function for count data analysis, then it is easy to show \( \mu_z^* \leq \mu_z \) based on Jenssen’s Inequality.

Sometimes, clinicians may be interested more in \( \mu_z \) than \( \mu_z^* \). However, the current available statistical software only provides LSM. Qu and Luo (2014) estimated the group mean and utilized the delta method to obtain the standard error of the group mean:

\[
\operatorname{Var}[\hat{\mu}_z] = \left[ \frac{1}{n} \sum_{i=1}^n \frac{\partial g^{-1}(\beta_0 + X'_i\beta_x + z'\beta_z)}{\partial \beta} \right]' \tilde{\Omega}_\beta \left[ \frac{1}{n} \sum_{i=1}^n \frac{\partial g^{-1}(\beta_0 + X'_i\beta_x + z'\beta_z)}{\partial \beta} \right]
\]

The authors investigated the performance of the group mean estimate in scenarios of longitudinal logistic regression for repeated binary outcome and a PWNB model for repeated count data with baseline covariate adjustment. Both MCAR and MAR missing mechanisms were included in the simulations. The coverage of the proposed group mean was preserved at nominal level in all scenarios.
Discussion and remarks

The purpose of this article is not to provide a comprehensive review of the GLM. Instead, we focus on summarizing some common issues and our recent research in GLM for categorical data analyses in clinical trials. With the complex attributes in categorical analyses, there are still some practical questions yet to be addressed:

- If there are missing baseline values for some subjects with post-baseline responses, how can we adjust for baseline and still include these subjects in the model? The multiple imputation method can be applied before applying the categorical analysis model. Alternatively, similar to the linear constrained longitudinal data analysis model treating baseline as part of response (Liu et al., 2009), a constrained longitudinal categorical model may be applied. Research is ongoing to understand this problem.
- Qu and Luo (2014) derived the standard error for the group mean estimator for longitudinal categorical models without random effects. The standard error for the group mean estimator in the presence of random effects will need to be derived.
- Convergence is often difficult for longitudinal logistic or negative binomial regressions using PROC GLIMMIX (SAS 9.2, Cary, NC 2009) when the number of events is small. Sometimes, model estimates are questionable, but the procedure provides no warning message. It deserves software developers’ attention to build a more robust computation method for categorical data analysis models.
- Logistic regression is in general questionable for binary data with a separation or semi-separation issue. This situation is quite common in clinical trials; when sample size is small, the incidence of event is rare or highly prevalent, or the data are unbalanced and have highly predictive risk factors. To handle this issue, we can utilize exact logistic regression which is appropriate for studies with small sample size, or alternatively conduct a logistic regression with Firth bias–reduced penalized likelihood estimation (Firth, 1993; Heinze and Schenper, 2002). Firth logistic regression can be easily conducted with SAS logistic procedure (SAS 9.2, Cary, NC 2009). However, its extension to longitudinal binary data is still a gap and may deserve further research in the area of GLM.
References


Announcing the New Pharmacometrics ASA Interest Group

Alan Hartford
Abbvie

The ASA Council of Sections Governing Board recently approved the formation of a new ASA Interest Group focusing on Pharmacometrics, the science concerned with mathematical and statistical models of biological processes, particularly those relating pharmacology, disease, and physiology. Pharmacometrics is widely used in drug development so this new interest group has a natural alignment within the Biopharmaceutical Section.

The founders of this interest group hope for an increased sharing of knowledge in both directions between statisticians and pharmacometricians. Differences of opinion have emerged among some in each group. For example, a common difference pits the inferential advantage of preplanned analyses against the flexibility advantage of exploratory modeling.

Pharmacometricians historically were primarily trained in a variety of backgrounds with statistics as a supportive discipline. This path, in regard to training in statistics, starts with learning basic summary statistics, t-tests, simple linear regression, and ANOVA and then skips over some core statistics courses needed for statistics degrees to proceed directly to the advanced area of nonlinear mixed effects models. This expert knowledge in nonlinear mixed effects models without other statistical preparatory coursework can make it difficult for pharmacometricians and statisticians to quickly find common ground for discussing modeling approaches and interpretation; most statisticians do not have more than superficial training in nonlinear mixed effects models nor do they understand many pharmacometric principles, e.g., mechanistic models, pharmacology, or physiology. This has resulted in many scientists from both fields performing their own methodological research in a vacuum and using different terminology for similar procedures. However, some pharmacometricians dive deeply into statistical methodology and have provided advancements in the literature, including in topics of model selection, numerical integration, and Bayesian statistics which is accessible to both pharmacometricians and statisticians. Although both pharmacometricians and statisticians have separately achieved success in disease modeling, greater gains in drug development are being attained where the two work together closely.

In recent years, many statisticians have chosen careers in pharmacometrics, learning principles of pharmacokinetics and physiological modeling on the job. This new ASA interest group can assist with familiarizing statisticians with this career option and provide training opportunities for statisticians to learn both the concepts and language of pharmacometrics. This new ASA interest group will also promote the use of statistics within the pharmacometrics fields and will work to increase the collaboration between these two related disciplines. Increasing shared knowledge and improving collaboration will enhance the rigor of quantitative science-based decision making and ultimately benefit patients through the development of better medicines.

We are currently in the planning stage for refining our goals but you can still join this interest group now by contacting Alan Hartford at alan.hartford@abbvie.com. ASA membership is not required for interest group membership so please also invite your pharmacometrician colleagues to join.

Stay tuned as we move forward with our interest group activities!
Your Thoughts About the Biopharmaceutical Section Mentoring Program?

By Amarjot Kaur, Jennifer Gauvin, Yue Shentu

You may have seen from previous communications that the Biopharmaceutical Section initiated a Mentoring Program last year for the benefit of its members. This program is ongoing with several mentor-mentee pairs enrolled.

If you participated in this program, we hope you found your mentee-mentor interaction stimulating and are beginning to experience some of the rewards of these interactions. You may also have identified areas for further improvement of this program.

Your feedback on this program is very important!

A survey was recently mailed to the current participants in this program and we would appreciate your candid input and participation in this survey. As statisticians we all understand the importance of quality data in decision making so we are looking for your full participation. This will help us refine the mentoring program as we move forward.

In case you missed the deadline to fill out the survey, please feel free to send informal feedback at any time to the mentoring committee members at biopharmmentoring@gmail.com.

Announcements for the next round of the mentoring program for 2015-16 will be coming out soon, in the May-June 2015 timeframe. We would look forward to hearing from you if you are interested in joining the program as a mentee or a mentor, or can nominate a statistician who may be looking to participate in a mentorship program. This information will also be made available via the Biopharm website: http://community.amstat.org/biop/aboutus/subcom/mentoring.

You may also contact us anytime if you are interested in participating or need any additional information or clarification related to this program.

Calling All Volunteers!

Want to get involved in Biopharm Section activities, but not sure how? The Section is always looking for volunteers, so drop us an e-mail at volunteer.asabiopharm@gmail.com.

Let’s Hear from You!

If you have any comments or contributions, please contact the Editors: Jerry Wang, email jerry.wang@merckgroup.com; Ugochi Emeribe, email ugochi.emeribe@astraZeneca.com; or Paul Gallo, email paul.gallo@novartis.com. We are looking for volunteers to write articles or suggest topics that will be of interest to our members. The topics can be technical, but non-technical articles related to biopharmaceuticals are welcome. Please send us an email.

The Biopharmaceutical Report is a publication of the Biopharmaceutical Section of the American Statistical Association.
71st Annual Deming Conference on Applied Statistics

American Society for Quality: NY/NJ Metropolitan Section & Statistics Division
American Statistican Association: Biopharmaceutical Section
December 7 – 11, 2015: Tropicana Casino and Resort, Havana Tower, Atlantic City, NJ

Reduced Registration Fee for Students and Retirees; One Day Registration Also Possible
Registrants May Submit Poster Abstracts for Approval by Conference Committee
Register Online at www.demingconference.com after August 15.

Three hour conference tutorials, Monday - Wednesday

- **Doing Bayesian Analysis Using PROC MCMC**
  Fang Chen; SAS Institute
  
- **Multiple Testing for Correlated Multiple Endpoints in Clinical Trials**
  Changchun Xie; University of Cincinnati
  Din Chen; University of Rochester

- **Design Issues in Biomarker-Based Clinical Trials in Oncology**
  Daniel J Sargent; Mayo Clinic

- **Graphical Approaches to Multiple Testing**
  Dong Xi; Novartis

- **Applying Bayesian Evidence Synthesis In Comparative Effectiveness Research**
  David Ohlssen; Novartis

- **Statistical Methods for Tailored Therapies In Pharmaceutical Drug Development**
  Lei Shen; Eli Lilly

- **Sensitivity Analysis for Missing Data Using Bayesian and Imputation Approaches - Case Studies**

- **Studies from DIA Bayesian Working Group**
  Frank Liu; Merck & Neal Thomas; Pfizer

- **Statistical Methods for Medical Product Safety Evaluation**
  Jie Chen; Novartis & Mei-Chiung Shih;
  VA Cooperative Studies Program & Stanford University

- **Propensity Score Methods for Estimating Causal Effects In Non-Experimental Studies: The Why, When, and How**
  Elizabeth Stuart; Johns Hopkins

- **Advanced Statistical Concepts and Methodologies For Development of Personalized Medicines**
  Cong Chen; Merck

- **Design and Analysis of Non-Inferiority Trials**
  Brian Wiens; Portola Pharmaceuticals

- **Network Based Analysis of Big Data**
  Shuangge Ma; Yale University

Courses, Thursday – Friday

- **Quantitative Evaluation of Safety and Benefit Risk In Drug Development**
  Larry Gould, William Wang & Weili He; Merck
  Qi Jiang; Amgen Inc.

- **Matched Analysis for Observational Studies Using R and the Rubin Causal Model**
  Ben Hansen & Ed Rothman; University of Michigan

* Session is based on a text that will be sold at a substantial discount at the conference.
Biopharm-Deming Student Scholar Award

In an effort to increase the visibility of applied statistics and encourage student participation in scientific conferences, the ASA Biopharmaceutical Section and the Deming Conference have jointly established the Biopharm-Deming Student Scholar Award. This award will provide travel support to 2-3 students, currently enrolled in a Ph.D. degree program in Statistics or Biostatistics in the United States, to attend the 3-day tutorial sessions at the Deming Conference and deliver a poster presentation.

The 2015 Deming conference will be held in Atlantic City, NJ from December 7 to 11, 2015, with the first 3 days devoted to 12 half-day tutorials and the last 2 days devoted to two short courses. For more details about the conference please visit [http://demingconference.com](http://demingconference.com).

Eligibility Criteria
Ph.D. students in Biostatistics or Statistics programs in the United States

Application Materials
- Personal statement (<500 words)
- Abstract for the potential poster presentation
- 2 letters of recommendation
- Resume

Timeline
- Application deadline: August 31, 2015
- Decision notification: September 15, 2015
- Deming Conference: December 7-11, 2015, Atlantic City, NJ

How to Apply
An application form is available on the Deming Conference website [http://demingconference.com](http://demingconference.com)
Please email the complete application to the Chair of the Student Award Selection Committee:

Ivan S.F. Chan, Ph.D.
Executive Director, Late Development Statistics
Merck Research Laboratories
ivan_chan@merck.com
ASA Biopharmaceutical Section
FDA-Industry Statistics Workshop

The ASA Biopharmaceutical Section FDA-Industry Statistics Workshop is sponsored by the Biopharmaceutical Section in cooperation with the FDA Statistical Association. Each year, approximately 800 regulatory, academic and industry colleagues gather together to share insights into key trends in statistical topics relevant to pharmaceutical and medical device development. The 2015 Workshop will take place September 16-18 in Washington D.C. at the Marriott Wardman Park Hotel. The plenary program includes presentations and panel discussion on The Future of Precision Medicine. As part of the plenary program, Susan A. Murphy, Professor of Statistics and Professor of Psychiatry at the University of Michigan, will discuss the use of mobile devices in micro-randomized trials. Tentatively, Lisa LaVange of CDER/FDA will also speak in this plenary session, and panel discussion to address prepared and audience questions will include Murphy and LaVange, Greg Campbell of CDRH/FDA, Cong Chen of Merck, Estelle Russek-Cohen of CBER/FDA, Richard Simon of the National Cancer Institute.

Further, the two-day program will include 42 parallel sessions of invited talks and 50 roundtable discussion topics which include, but are not limited to, Bayesian methods, biomarkers, cardiovascular safety in type II diabetes, CMC, data standards and transparency, estimands and sensitivity analysis for missing data, generics and biosimilars, incorporating patient perspectives, patient enrichment, statistical leadership, subgroups, and methodologies for vaccine and veterinary development.

Eight half-day pre-workshop short courses will provide advanced training from subject-matter experts:

- An Overview of Statistical Considerations in Personalized Medicine: Concept and Methodology (with emphasis on companion diagnostics) - Meijuan Li, FDA
- Handling Missing Data in Clinical Trials - Sonia Davis, University of North Carolina at Chapel Hill; Michael O’Kelly, Quintiles
- Equivalence and Similarity Testing - Shein-Chung Chow, Duke University; Yi Tsong, FDA/CDER
- Introduction to PK/PD Modeling for Statisticians - Yaming Hang, Biogen Idec; Alan Hartford, AbbVie
- Dose-Finding in Drug Development: Methods and Implementation, with Focus on MCP-Mod - Frank Bretz, Novartis; Jose Pinheiro, Johnson & Johnson
- Statistical Strategies for Clinical Development of Personalized Medicines (with emphasis on adaptive enrichment strategies) - Cong Chen, Merck
- Bayesian Adaptive Phase I Oncology Trials: Methodology and Implementation - Beat Neuenschwander, Novartis Pharmaceuticals AG; Satrajit Roychoudhury, Novartis Pharmaceuticals
- Designing Observational Comparative Studies Using Propensity Score Methodology in Regulatory Settings - Donald Rubin, Harvard University; Lilly Yue, FDA/CDRH

Registration is open June 3 to September 7. Space is limited, so be sure to register early!
**ASA Biopharmaceutical Section Executive Committee**  
**Meeting Minutes, March 11, 2015 at ENAR, Miami, Florida**  
**Ed Luo, Secretary**

**Dionne Price**, Biopharmaceutical (BIOP) Section Chair, welcomed committee members and called the meeting to order. Seven committee members were present, and 22 attended the meeting via phone.

**Heather Thomas**, Treasurer, summarized the 2014 year-end financial report. The balance as of December 31, 2014 was $388,349.48, representing a surplus of $20,859.55.

**Christie Clark**, Chair-Elect, announced the appointment of Ed Luo as the industry co-chair of the 2016 FDA-Industry Statistics Workshop.

**Matilde Sanchez**, Past Chair, announced the slate of candidates for the 2016 election:

- **Chair-elect**: Alex Dmitrienko, Veronica Taylor
- **Program Chair**: Jennifer Gauvin, Satrajit Roychoudhury
- **Publication/Communication Officer**: Ugochi Emeribe, Richard Zink
- **CoS Representative**: Rima Izem, Aparna Raychaudhuri

**Matilde Sanchez** alerted the EC of two conference funding requests. Following discussion, the EC voted to approve a request of $1,000 from ASA Health Policy Statistics Section (HPSS) for two student travel awards ($500 each) at an upcoming conference, and a request of $5,000 from the 2015 Nonclinical Biostatistics Conference to sponsor a conference in October. Another request of $1,000 from HPSS to sponsor a conference in October was rejected by the EC.

**Alan Hartford** informed the EC that the Section on Statistics in Genomics and Genetics has been approved.

**Olga Marchenko** confirmed that the Working Group for Safety Analysis information is available at BIOP Section website. The working group plans to add at least one more workstream/sub-group, and is seeking volunteers. The group also plans to establish a library on safety methods for the ASA BIOP members.

**Richard Zink and Wei Zhang** announced that theme of the 2015 FDA-Industry Statistics Workshop is Personalized Medicine. The Workshop will occur September 16–18 at the Marriott Wardman Park Hotel in Washington, DC.

**Gary Aras** reported that BIOP will sponsor 242 talks in 31 sessions in the 2015 JSM. There will be 20 Topic Contributed Sessions. **Olga Marchenko** reported that BIOP will sponsor 7 roundtables.

**Ted Lystig** announced the winners of the Best Contributed Paper Award for JSM 2014. The winners include Devan Mehrotra, Scott Evans, and Sharon Murray. Richard Forshee, Michael Hale, and Jesse Berlin received honorable mentions.

**Richard McNally** reported that three winners and two honorable mentions in the 2015 BIOP Student Paper Competition have been selected. The awards will be given during the BIOP Business Meeting at the 2015 JSM.

Following a number of additional committee reports, **Dionne Price** thanked the EC for the thoughtful discussion and adjourned the meeting.
2015 Nonclinical Biostatistics Conference
October 13 – 15, 2015, Villanova, PA

Nonclinical Statistics – building continuity from discovery through manufacturing

The fourth U.S. conference dedicated entirely to nonclinical biostatistics topics will take place in Driscoll Hall on the campus of Villanova University. Members of the nonclinical/preclinical Statistics community are invited to submit proposals for presentations and posters discussing significant scientific and regulatory issues. Attendees will have ample opportunity to network, share experiences and discuss current scientific issues with colleagues and leaders in the field.

Abstract submission and registration is through the conference website [www.ncb2015.net](http://www.ncb2015.net). Contributed presentation abstract/poster submission cutoff date is June 26, 2015. Nominations for Outstanding Nonclinical Paper Award being accepted.

Keynote speakers on Tuesday October 13:
- **David Morgenstein**, ASA President 2015
- **Lisa Lavange**, Director of the Office of Biostatistics, FDA

Choice of half-day short course:
- Statistical Methods in Drug Combination Studies (Harry Yang, MedImmune)
- Applied Bayesian Statistics for Nonclinical (David LeBlond, Consultant)

21 Invited or contributed presentations covering:
- Discovery/Biomarkers – John Peterson, Matthew Nelson, Michael Wu
- Safety/Pharmacology – Dan Holder, Steve Bailey, Dhammika Amaratunga
- CM&C/Manufacturing – Yi Tsong, Helen Strickland, Celia Cruz, Lori Pfahler, Kim Vukovinsky

Special emphasis on student involvement: Growing the Future
Wednesday evening Wine and Cheese Mixer with Poster Presentations

The Biopharm section of the ASA is a contributing sponsor of the conference.