Note from the editors
Welcome to the first issue of the Biopharmaceutical (BIOP) Report for 2017! 2016 was an exciting year for the Biopharmaceutical Section, with a number of key accomplishments and initiatives that are continuing into 2017. These are described in the transition report of this issue from Sections chairs B. Christine Clark (2016) and Alex Dmitrienko (2017). For this issue’s featured article, we are pleased to present a great topic on using data visualization to assess the sensitivity of clinical trial design assumptions by Richard Zink and Xiaotong Jiang.

This issue also presents updates on some other section activities; in particular, a summary of the Section Executive Committee Transition Meeting held on 07 October 2016, by Ugochi Emeribe, an update from the Publication Officer, Richard Zink, and an announcement about the 2017 Regulatory-Industry Statistics Workshop from the Workshop Co-chairs Martin Ho and Weili He. In 2016, two new working groups were established within the BIOP Section: namely, the Nonclinical Biostatistics Working Group and the Clinical Trial Designs with Re-Randomization Working Group. In this issue, Anastasia Ivanova wrote an introduction about the Clinical Trial Designs with Re-Randomization Working Group, and Steven Novick provided information about an upcoming Nonclinical Biostatistics Conference at Rutgers University. The BIOP Section is excited to support an Online Training Program that will provide convenient and inexpensive training options for the Section’s members. In this issue, Alex Dmitrienko provided some background about this Online Training Program, and we also included an enthusiastic note from Abie Ekangaki.

Finally, we would like to thank the outgoing Editor, Paul Gallo for his great service to the Biopharmaceutical Section and the Biopharmaceutical Report in the past few years. For 2017, Junyuan Wang slides into the role of “Past Editor” and Amy Xia takes over as Editor. We also warmly welcome Jeff Maca as the incoming Associate Editor. We the editors are privileged to continue to help disseminate information for our members in 2017, and we also welcome feedback and suggestions to help improve the BIOP Report. We hope you enjoy reading this issue, and we look forward to a wonderful 2017!
LOOKING BACKWARD AND FORWARD:
BIOPHARMACEUTICAL SECTION 2016 AND 2017

B. Christine Clark (BIOP Chair 2016) and Alex Dmitrienko (BIOP Chair 2017)

First of all, we would like to thank Dionne Price, Past Chair 2016 for her help and guidance during last year. In addition the BIOP Executive Committee, committee chairs and members, and many other volunteers have dedicated countless hours to make BIOP not only the largest of ASA’s Sections, but one of the strongest and, in our opinion, the best. Thank you to all.

In looking back to BIOP in 2016 and at our work in 2017, the words that come to mind are, “good things come in 3s.” The Latin version, omne trium perfectum, sounds a bit more elegant but with the same meaning as the English version.

We will begin with three notable results during 2016 that resulted from the efforts of many BIOP members. Of course there were more than three, but only three will be highlighted here.

**ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop**

The ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop was held on 28-30 Sep 2016 in Washington, DC. This was the 20th anniversary of the 1st of these Workshops and was attended by nearly 900 individuals.

The Workshop co-chairs of Freda Cooner and Ed Luo did an outstanding job along with many volunteers who served on the Steering Committee. The Workshop theme was Statistical Innovation: Better Decisions through Better Methods.” The packed program consisted of eight short courses on Day 1; three plenary speakers, one panel discussion, seven parallel sessions, 28 roundtable luncheons, and an evening mixer in celebration of the 20th anniversary on Day 2; and new for 2016, 20 posters on Day 3. Congratulations to the many whose efforts in planning and participation contributed to the success not only of the 2016 Workshop but the success of the previous Workshops, culminating in a strong legacy of educational, collaborative, and networking service to the profession.

**Nonclinical Biostatistics Working Group**

As of Oct 2016, the Nonclinical Biostatistics Working Group (NBWG) is now a formal Working Group within BIOP. For the previous 13 years an informal group of statisticians working in various nonclinical areas of the pharmaceutical industry—discovery, safety, development, and manufacturing, actively and successful promoted communication and discussion of important statistical and regulatory topics within the biopharmaceutical community. The leadership group organized and held a Nonclinical Biostatistics Conference every two years starting in 2009. The 5th US conference is scheduled to occur 12-14 Jun 2017, on the Piscataway, NJ campus of Rutgers University. Registration is now open at [http://community.amstat.org/biop/events/ncb/index](http://community.amstat.org/biop/events/ncb/index) and discounted fees are available through 31 Mar. Because attendance will be capped at 175, early registration is encouraged. Now that the Nonclinical Biostatistics Working Group is part of BIOP, we anticipate increased ease of collaboration between nonclinical and clinical statisticians with the ultimate goal of enhancing “the application of statistics to the development and use of therapeutic drugs, biologics, and devices in humans and animals,” namely, the key activities of BIOP’s charter. Co-chairs of the 2017 Conference are Steve Novick and John Kolassa. Current Chair of the NBWG is Mandy Bergquist.

**New Working Group**

Consistent with emphasis in recent years by the BIOP Executive Committee on the importance of establishing and promoting various working groups to pursue specific topics of interest in our field (a BIOP Safety WG was established several years ago), Bruce Binkwitz (Chair) and the BIOP Working Group Committee vetted and recommended establishment of a WG to investigate “Clinical Trial Designs with Enrichment by Response.” This new WG will be co-chaired by Anastasia Ivanova and Gheorghe Doros. For those unfamiliar with the topic, the goal of designs with enrichment by response is to detect the treatment effect in a more
efficient way than is often available using current, routine methodology. The goal of the WG is to increase the understanding of and familiarity with these designs with a result of hastening their acceptance in planning of future trials, with the ultimate intent of increased and earlier patient benefit.

These activities happen only with the efforts of many dedicated individuals who volunteer their time. BIOP continues efforts to increase participation of additional volunteers and welcomes contact from anyone who is interested in contributing to existing initiatives and/or has a new proposal for a Scientific Working Group or other idea to implement within the scope of BIOP.

The Year Ahead

Now that we are already well into 2017, the baton has been passed to Alex Dmitrienko and the following is a brief summary of 3 main topics we are going to focus on this year.

In addition to our successful webinar series that was started exactly 10 years ago in March 2007, we are excited to launch an Online Training Program that will provide convenient and inexpensive training options for the Section’s members. The Online Training Program will include short courses on key topics in biopharmaceutical statistics. The courses can be accessed 24/7 on a computer or even a smartphone. The cost of online training will be quite low compared to traditional training options and can be further reduced by using a group-training format. For example, up to 25 people can view an online training course with a single registration. Back in January, we launched a pilot program with three online training courses that are based on popular short courses offered at numerous conferences around the world. This pilot has already attracted attention across the biopharmaceutical industry and will help us gauge the overall level of interest in online training.

We will be starting new initiatives or expanding existing initiatives to provide service to the profession in general and BIOP members in particular. To give two quick examples, we recognize the fact that

“BIOP continues efforts to increase participation of additional volunteers and welcomes contact from anyone who is interested in contributing to existing initiatives and/or has a new proposal for a Scientific Working Group or other idea to implement within the scope of BIOP.”

the Regulatory-Industry Statistics Workshop has been attracting increasing attention across the industry. To address numerous challenges faced by the steering and organizing committees and improve the participants’ experiences, we are creating a task force that will identify solutions to these challenges and present them to the Executive Committee. Secondly, we have been discussing options for creating awards for students based on their research in biopharmaceutical statistics, leadership and service to the profession. This initiative is aimed at encouraging students to be actively involved with the Section and to cultivate a new generation of BIOP leaders.

And finally we have started spending more time on organizing the Section’s information and improving internal processes. We are, after all, the largest ASA section with multiple committees and numerous projects on our plate. Although most of this work has been going on behind the scenes, we are beginning to see how the new focus on “operational excellence” is helping us improve our collaboration and support seamless transitions for Executive Committee members. This work will help us provide better service to our membership. And we will all continue the long tradition of BIOP service to a field with the ultimate goal of improving lives of patients throughout the world.
Using Data Visualization to Assess the Sensitivity of Clinical Trial Design Assumptions

Richard C. Zink, SAS Institute Inc and University of North Carolina at Chapel Hill
and Xiaotong Jiang, University of North Carolina at Chapel Hill

Introduction
Sample size calculations are an important part of the design of any clinical trial. On the one hand, these calculations ensure a sufficient number of patients to detect clinically-meaningful differences for primary endpoints between two treatments with high probability (i.e., power). On the other hand, and perhaps less-often discussed, the sample size exercise is important so that resources are not wasted studying too many observations to test a particular hypothesis. Since patients may be randomized to doses of a novel treatment with a limitedly known safety profile, or a placebo which provides no therapeutic benefit, sample size calculations in clinical trials come with an ethical burden not experienced in many subject-matter areas. Studying too many or too few patients exposes these individuals to unnecessary risk. Unlike textbooks that perform a single calculation to design an experiment, the sample size of a clinical trial should be determined using a wide range of assumptions, with as much data as is available, and with input from clinical colleagues. The recommendation to assess the sensitivity of sample size is included in Section 3.5 of the statistical guidelines of the International Conference of Harmonisation (ICH) E9. This guidance proposes other best practices—stating the hypotheses on which sample size is based, the study population used to evaluate the primary endpoint, the probability of type I and type II errors, margins for non-inferiority or equivalence trials, as well as the rules for sample size adjustments for trials that include adaptations. Details on sample size calculations are reported in study protocols, statistical analysis plans, and final clinical study reports.

Formulas for sample size calculations are numerous, and vary due to the type of endpoint, the particular test statistic used for analysis, the summary statistics available for calculation, the form of the null and alternative hypotheses, and other assumptions such as the duration of patient accrual and follow-up time (for time-to-event endpoints). Entire texts have been devoted to the subject; a thorough summary is not possible with the space available here. Despite their variety, all formulas for sample size involve a few common elements. These include the specified probabilities for type I and type II error rates, which are the likelihood of false positive or false negative results, respectively; a clinically-relevant difference to detect; and the variability of the outcome. While type I and type II error rates are easily fixed by the study team, often at 0.05 and 0.10-0.20, respectively, the difference to detect and the variability of the outcome are based on our best guesses of how the treatments will (or will not) affect patient response. There may be data to suggest appropriate values for treatment response and variability but, in general, these quantities are unknown.

Important relationships between sample size and the above elements are implied by the formulas. For example, as type I and type II error rates decrease, sample size increases. As variability increases, sample size increases. As the size of the difference to detect increases, sample size decreases. Note that power, the probability of rejecting the null hypothesis when the null hypothesis is false, is equal to one minus the type II error rate, often 0.80-0.90 in practice. This means that power and sample size are inextricably linked—as sample size goes up, power goes up; as sample size goes down, power goes down.

When we say a clinical trial is powered at 90%, this power is specific to a particular set of study assumptions, i.e. a single set of treatment responses and estimate of variability. If the treatment responses or variability are different from planned values, then the trial power varies according to the rules specified in the preceding paragraph. One sensitivity analysis that is often employed during the design phase of a clinical trial is to assess how the power for the primary endpoints change...
for differing values of treatment response and variability when the trial sample size is fixed. The goal of these analyses is to show that for our final selected sample size, the study is reasonably powered over a wide range of possible alternatives. The results of these sensitivity analyses are often presented in tables, or using straightforward graphics such as line plots.

Numerous data visualizations have been proposed to efficiently summarize and communicate the results of data obtained from clinical trials; their usage in various aspects of trial design have received less attention. Here, we propose the use of contour plots to better assess, report and communicate the sensitivity of clinical trial design assumptions. For example, contour plots can provide a more complete sensitivity analysis for power. A contour plot is a two-dimensional plot that can be used to summarize three variables by using either color or reference lines to describe the third dimension. Contour plots are often used to summarize changes in elevation or depth in geographic maps. For example, green to brown shows increasing elevation for mountainous areas; light to dark blue often signifies greater depths for bodies of water. When the use of color is limited, contour lines are drawn at a subset of values of the third dimension to communicate meaningful changes across the X-Y plane.

**Power Contours**

Gordon and co-authors described a randomized, double-blind, placebo-controlled, active-comparator trial comparing multiple doses of guselkumab to adalimumab in 293 patients with moderate-to-severe plaque psoriasis [2]. The primary endpoint was the proportion of patients with scores of 0 or 1 based upon a physician’s global assessment at Week 16. For this particular example, focus lies on 2 of the 7 treatment arms available, patients taking either 100 mg of guselkumab (= 42) or adalimumab using the standard regimen for psoriasis (= 43). Results showed 36 (86%) and 25 (58%) of patients met the primary endpoint for guselkumab and adalimumab, respectively. For the purposes of this example, assume that the minimally clinically important difference (MCID, guselkumab minus adalimumab) is 15%; that is, 15% is the smallest treatment difference that would be considered meaningful to continue development with a goal to achieve superiority of guselkumab 100 mg compared to adalimumab. Based on this information, how can

![Figure 1. Power contour for all possible responses for guselkumab and adalimumab for the plaque psoriasis example](image)
the study team appropriately power a new study?

Though the results look promising – an observed treatment effect of 28% - the study team needs to consider the variability of the results from this particular trial or sample. A 95% confidence interval of the treatment difference is denoted by,

\[ \hat{p}_g - \hat{p}_a \pm 1.96 \sqrt{\frac{\hat{p}_g(1-\hat{p}_g)}{n_g} + \frac{\hat{p}_a(1-\hat{p}_a)}{n_a}} \]

and this confidence interval represents the plausible values of the true unknown treatment difference. In this example, this interval is (9.9%, 46.1%). While this interval does not contain 0, it does suggest that the unknown treatment difference can be as small as 9.9%. However, the study team may decide that these results warrant performing an additional trial. Using 86% and 58% as estimates of the unknown treatment responses, a two-sided Pearson chi-square test at \( \alpha = 0.05 \) and at least 90% power will require 52 patients per arm. Note that the statement “the trial is powered at 90%” is only true for the specific values used for the guselkumab and control response (86% and 58%, respectively). But what if these values are not accurate? If the sponsor proceeds with this trial of 104 patients, how would the power change if 86% and 58% do not reflect the unknown treatment responses?

For this clinical trial example, the sponsor can take an extreme approach and use a contour plot to summarize the power for all possible combinations of response for the two trial arms (Figure 1). The location of a particular guselkumab-adalimumab pair communicates the power for a two-sided Pearson chi-square test at \( \alpha = 0.05 \) and at least 90% power will require 52 patients per arm within the contour lines. For example, coordinates between the 0.900 and 0.990 contour lines indicate guselkumab and adalimumab response combinations that result in a statistical test with power between 90 and 99 percent. Further, the power beyond either of the 0.990 contour lines is at least 99%; the contour lines signify where 99% power first occurs. In Figure 1, the diagonal solid black line denotes where the treatment arm responses are identical. The diagonal dashed black line indicates the MCID between the treatments—everything at or above this line meets the criteria for the MCID. Reference lines to help communicate treatment response are presented every 10% for each axis. It is not surprising that areas where the treatment arms are or nearly equal to each other provide almost no power to test for a significant difference (within the 0.100 bands). Also apparent is the curvilinear nature for the individual contour lines – this is due to the fact that as the treatment response approaches 50% for a binary outcome, the variance for the response is maximized. The reader should note how quickly the power can change for our original comparison for even minor deviations in guselkumab or adalimumab response.

While Figure 1 is informative, the guselkumab and adalimumab axes can be limited to a range that most likely contains the true unknown responses. For each axis, the following confidence interval formula can be used:

\[ \hat{p} \pm 1.96 \sqrt{\frac{\hat{p}(1-\hat{p})}{n}} \]

In this example, the 95% confidence interval is (75.5%, 96.5%) and (43.2%, 72.8%) for the guselkumab and adalimumab arms, respectively. Based on this information, the study team produces Figure 2. Though the confidence interval for the treatment effect (9.9%, 46.1%) should communicate that a non-clinically-significant result may be possible, this fact may be more apparent and more easily communicated with Figure 2. For the area where a clinically-significant treatment effect is possible, the power is at least 40% save for where adalimumab response is between 57 and 65%, likely due to the increased variance in the treatment difference. In situations where an adaptive clinical trial is not possible, such as when the study enrollment occurs too quickly, it may be of interest to increase the sample size so that the MCID has a power of at least 80% in all cases. Alternatively, if the sample size is already too high, or too much of the area of Figure 2 does not represent a clinically-meaningful effect, then it may be more appropriate to consider an adaptive design. Possible adaptations could allow for early stopping for futility and/or a potential sample size increase to maintain high power when interim results appear promising. This approach avoids committing too many resources up front when the trial outcome is still so uncertain. Given the modest sample size requirements for this trial, it may be worthwhile to consider adding an additional arm for guselkumab. This contingency can protect against a single guselkumab dose that has either disappointing efficacy (too low) or
tolerability issues (too high). In reality, however, unless adalimumab is considered the standard of care by regulators, the development program would likely proceed with comparisons of guselkumab against placebo.

**Sample Size Contours**

Our primary focus thus far has been to generate an effective sensitivity analysis of trial power for the final selected sample size. We began with power contours for two reasons: first, to illustrate that a “well-powered” trial is only well-powered under a very narrow range of assumptions, and second, to encourage greater transparency by including a more complete sensitivity analysis of power within study documents. However, the presentation of power contours assumes that the trial sponsor has arrived at a sample size with which they are comfortable. To generate the power contours in the examples above, the “final” sample size was based upon a single calculation assuming that the observed treatment response reflected the truth. This approach to sample size calculations is inadequate and entirely inappropriate in practice! Our time has not been wasted, however. Though the sensitivity of power for a fixed sample size was explored, the problem can easily be inverted to assess changes in sample size for a fixed level of power. For example, Figure 3 presents a contour plot of total sample size for a fixed power of 90% for the plaque psoriasis example discussed above. Similar to Figure 2, the y- and x-axes are the responses for the guselkumab and adalimumab arms, respectively. Unlike Figure 2, the various contour lines represent sample sizes for a fixed power, and not power for a fixed sample size. The data set and figure communicate that a sample size of 312 patients (156 per arm) will provide at least 90% power for an MCID of 15%. This sample size is 3 times the sample size used to generate Figures 1-2! Here, the study team must consider (and potentially include in the analysis) other sources of evidence, the availability of sufficient funds and/or patients in order to arrive at a final trial sample size. To aid in this decision, power contours can be used to select a final sample size from a set of potential candidates.
Conclusions

Data visualization has an important role in the design of clinical trials; our focus here was to illustrate the effectiveness of contour plots for communicating power and sample size. While these figures can be a useful tool for the study team in designing the trial and choosing a final sample size, contour plots can be included in study protocols and other study documents to better communicate the rationale for sample size for clinicians and regulators, while providing some assessment of the sensitivity of power for the final selected sample size. Further, contour plots provide greater transparency as to the uncertainty of the currently available information, and can be useful in deciding whether to consider an adaptive design. In an adaptive design, contour plots can be used to summarize expected sample size, stopping probabilities, or other quantities across the planned interim looks. Though this paper examines the design of a single new clinical trial in isolation, contour plots for power and sample size are useful graphical techniques for assessing alternate development strategies in clinical scenario evaluation.

For more information, including examples for continuous and time-to-event endpoints, applications for adaptive clinical trials and meta-analysis, and sample code, please see [3].

Reference


Christie Clark, Biopharmaceutical (BIOP) Section Chair, welcomed the Executive Committee (EC) and other committee members, and called the meeting to order. Six committee members attended in-person while twenty-four attended the meeting via telephone.

Christie informed EC that there was a proposal to combine transition meeting with ASA BIOP Regulatory-Industry Statistics Workshop, and that the incoming Chair, Alex, will take up the proposal.

Dionne Price, Past Chair, announced that the newly elected officers for 2017 will be as follows:

- **Chair-Elect**: Heather Thomas
- **Program Chair-Elect**: Qi Jiang
- **Treasurer**: Alan Hartford
- **Council of Sections**: Erik Pulkstenis

Alex Dmitrienko, Chair-Elect, announced two appointments for ad hoc members of EC, and they are:

- **Sandeep Menon** sandeep.m.menon@pfizer.com
  - Vice President, Head of Statistical Consulting group at Pfizer
- **Abie Ekangaki** abie.ekangaki@ucb.com
  - Senior Director, Head of US Statistics at UCB

Also, Alex announced that planned initiatives for 2017 will include the following:

- BIOP on-line training on the usage of Google for communication and document repository
- Monthly meeting of core EC members to discuss topics such as funding requests from other organizations and collaborations

Heather Thomas, Treasurer, notified meeting participants that the Year-To-Date (09/22/2016) balance is $403,350.14, change from previous year is $4,051.00, and revenue received is $20,985.58. Revenue was generated from membership dues and webinar registration. Expenses included awards, meeting support, and contributions to other organizations. Also, participants were informed that the Council of Sections had indicated that there is large cash on-hand. So, it was decided at the JSM EC meeting that membership fees for the BIOP Section would be reduced by $1 and provide free membership for the first 5 years for recent graduates. The changes to membership fees will be implemented in 2017.

Olga Marchenko, informed participants that the Safety Working Group has formed two work streams with two teams within each work stream, and they are as follows:

**WORKSTREAM 1**

- **Safety Strategies and Analysis**, is co-chaired by Qi Jiang and Olga Marchenko
  - **Team 1**: Strategies and Statistical Considerations in CVOT
  - **Team 2**: Sources of Safety Data and Statistical Strategies

**WORKSTREAM 2**

- **Safety Monitoring**, is chaired by Bill Wang
  - **Team 1**: Regulatory Guidance Review and Industry Survey
  - **Team 2**: Statistical Methods on Safety Monitoring

Christie Clark, requested that EC vote on Non-Clinical Biostatistics group application to become part of BIOP Section. Based on previous discussions, EC voted unanimously to create a Nonclinical Statistics Scientific Working Group (NSWG) within BIOP, and to appoint a maximum of two persons, the chair (or co-chairs, if applicable) of the Nonclinical Statistics Conference to BIOP EC for an appointment period of two years.

Jennifer Gauvin, Program Chair, reported that the BIOP Section had received 19 proposals for invited
sessions and a small group has been formed to review the proposals. Also, participants were informed that volunteers are needed to chair sessions.

Bruce Binkowitz, Scientific Working Group committee co-chair, notified participants that one proposal on “Enrichment by Response Design” which has been reviewed by the committee was recommended for approval by EC. The EC approved the proposal, and the SWG committee plans to use the format as a pilot for future proposals.

Willie He and Martin Ho, ASA BIOP Regulatory-Industry Statistics Workshop, informed attendees that the kick-off meeting for the 2017 workshop has taken place. There will be no structural changes to the workshop. However, there are proposals to increase visibility and attendance, and the co-chairs will further discuss the proposals.

Ted Lystig, Best Contributed Paper Award, informed EC that counted/tallied results will be presented at ENAR 2017.

Zhiwei Zhang, Best Student Paper Award, announcement of student paper award will be updated on the website.

Yue Shentu and Amarjot Kaur, Mentoring Committee continues its efforts to match mentors and mentees, and they are encouraged to meet at JSM.

Richard Zink, Publications Officer, notified EC that BIOP website is up-to-date except for past information that is still located on old website. Also, EC was informed that 7 webinars were conducted in 2016, and all webinars are in a re-organized location on the website. There are 3 podcasts for the remainder of the year, and they include a podcast on Patient Preferences in Medical Product Evaluation, EFSPI Benefit-Risk Working Group, and Statistical Leadership. A couple of podcasts have been scheduled for early 2017 and they include Estimands and ICH E9R1; and ICH E17 and Multiregional clinical trials.

Matilde Sanchez-Kam, Funding Committee has no new funding request, and participants were reminded to fill out forms for only new request for funding. The manual of operation will be updated with information on process, eligibility, and requirements for funding.

Following a few other updates, Christie thanked EC members for their support throughout her tenure as Chair of ASA BIOP section, and the meeting was adjourned.

ASA BIOPHARMACEUTICAL SECTION
REGULATORY-INDUSTRY STATISTICS WORKSHOP
SEPTEMBER 25–27, 2017 | WASHINGTON, DC

WORKSHOP UPDATE
Martin Ho and Weili He, Workshop Co-chairs

The 2017 Workshop will take place September 25-27 (Monday – Wednesday) at the Marriott Wardman Park Hotel in Washington D.C. The theme for the 2017 Workshop is “Value to Patients: Benefits, Risks, and Costs.” This year’s program includes two plenary sessions, 42 parallel sessions, eight short courses, 48 roundtable discussions, and 20 posters. There will be a mixer on the late afternoon of September 26. Housing and workshop registration will be open on June 1, 2017. www2.amstat.org/meetings/biopharmworkshop/2017
NEW ASA BIOPHARMACEUTICAL WORKING GROUP: CLINICAL TRIAL DESIGNS WITH RE-RANDOMIZATION

Anastasia Ivanova, University of North Carolina at Chapel Hill

The ASA Biopharmaceutical Section Executive Committee has recently approved a new working group, the Clinical Trial Designs with Re-Randomization working group.

Designs with re-randomization are designs where subjects are randomized between experimental treatment(s) and a control in the first period and then all or some subjects are re-randomized in the second period. In each period subjects are followed long enough to observe the primary endpoint.

Designs with re-randomization might result in more efficient clinical trials because some subjects contribute more than one observation to the primary analysis set. Crossover design, Sequential Parallel Comparison Design (SPCD) and Two-way Enriched Design (TED) are examples of designs with re-randomization. The goal of a crossover design, SPCD and TED is to efficiently compare a new intervention with a control. Another example of a trial with re-randomization is Sequential, Multiple Assignment, Randomized Trial (SMART).

The goal of this design is to determine the best sequence of decision rules. The first task of the new working group is to evaluate the existing data analysis strategies and strategies for handling missing data in SPCD and TED trials and apply these strategies to datasets from completed SPCD trials. Currently the new working group includes 15 members with about equal representation from academia, FDA and industry. Anastasia Ivanova (UNC Chapel Hill) and Gheorghe Doros (Boston University) serve as co-chairs of the group.

The new working group is the second working group under the ASA Biopharmaceutical Section. The Safety working was established in 2013, and has two workstreams, first led by Qi Jiang (Amgen) and Olga Marchenko (QuintilesIMS), and the second led by Bill Wang (Merck).
The Nonclinical Biostatistics Conference is sponsored by the ASA Biopharmaceutical Section in cooperation with the Rutgers University Statistics Department. The biennial conference lasts three days with invited and contributed talks on nonclinical biostatistics topics with speakers from industry, regulatory, and academia. Two short courses are offered on the morning of the first conference day. Registration opens on February 1, 2017. The conference takes place at the Fiber Optics Building on the Piscataway, New Jersey campus of Rutgers University from June 12 – 14, 2017.

Members of the nonclinical statistics and academic communities are encouraged to submit abstracts for contributed talks and posters. Submission deadline is March 1, 2017 for talks and May 15, 2017 for posters. To submit your abstract, visit the website (http://community.amstat.org/biop/events/ncb) and click on the abstracts tab. Manuscripts from the NCB presentation are eligible to be submitted to a special edition of the Statistics in Biopharmaceutical Research journal.

We are excited to announce the ASA Presidential speaker this year is Lisa LaVange (ASA President-elect, FDA) and the NCB Keynote speaker is John Storey (Princeton University). Attendees are welcome to their choice of two half-day courses on Monday morning: “Practical Bayesian Calculations in Proc MCMC” with Dr. Fang Chen, SAS and “Topics of Advanced Experimental Design” with Dr. Steve Buyske, Rutgers Statistics Department. Two and a half days will be filled with a distinguished set of invited and contributed speakers representing all areas of nonclinical biostatistics. After-presentation receptions round out Monday and Tuesday evenings, allowing for extra time to network and socialize.

Special programs are available for graduate students, including a panel discussion with industry experts as well as a student poster competition. The best student poster will be awarded a prize of $250. To submit your student poster abstract, send your abstract directly to Katja.S.Remlinger@gsk.com. Student registration is $100 (early bird) with limited scholarships available to offset travel costs. Preference is given to students who present posters.
ONLINE TRAINING PROGRAM CREATED

Alex Dmitrienko, Mediana

The Biopharmaceutical Section is excited to support an Online Training Program that will provide convenient and inexpensive training options for the Section’s members. This program serves as a natural extension of the Section’s Webinar Program that started 10 years ago.

The Online Training Program includes short courses based on professionally recorded videos using a format similar to that used in YouTube videos. The videos can be accessed 24/7 on a computer or even a smartphone. The cost of online training is quite low compared to traditional in-person training, and it can be further reduced by using a group-training format.

While the Webinar Program is aimed at shorter two-hour seminars, the Online Training Program supports longer courses that provide in-depth overview of key topics in biopharmaceutical statistics. At the same time, the online training format is quite flexible. Each participant has a seven-day period to watch the videos included in each course at their convenience and select the topics that would be of most interest to them.

Earlier this year, we launched a pilot program with three online training courses based on popular short courses offered at numerous conferences around the world:

**ANALYSIS OF LONGITUDINAL AND INCOMPLETE DATA (FULL-DAY COURSE)**
Instructors: Geert Verbeke (Katholieke Universiteit Leuven and Universiteit Hasselt, Belgium), Geert Molenberghts (Universiteit Hasselt and Katholieke Universiteit Leuven, Belgium).

**KEY MULTIPLICITY ISSUES IN CLINICAL TRIALS (FULL-DAY COURSE)**
Instructor: Alex Dmitrienko (Mediana).

**STATISTICAL EVALUATION OF SURROGATE ENDPOINTS IN CLINICAL TRIALS (HALF-DAY COURSE)**
Instructor: Geert Molenberghts (Universiteit Hasselt and Katholieke Universiteit Leuven, Belgium).

For more information about the Online Training Program and to sign up for the individual online courses, visit [http://sprmm.com/asa-biopharmaceutical-section](http://sprmm.com/asa-biopharmaceutical-section).

Abie Ekangaki, UCB

On learning about the Biopharmaceutical Section’s online training program, I was energized to see that the Section was proactively offering its members an easily accessible online avenue to help refresh their methodological prowess in key areas of applied statistics. In today’s environment where statisticians often find themselves juggling multiple projects with tight timelines, there is an innate acquiescence to prioritize strategic needs of the business over individual professional development.

Many biopharmaceutical companies urge statistical innovation in-house and they support their statisticians in publicly disseminating their creative methodological applications at key conferences. Companies also encourage continued statistics education by authorizing staff attendance at short courses, usually tied to conferences, or through occasional internal or external statistics seminars. While these avenues remain essential, they offer only a one-off instructional session that covers a range of ideas which may not always be easily digestible in the moment.

For industry statisticians who seek balance between their obligation to fulfill the compendium of critical project responsibilities and their desire to refresh or further develop their knowledge of statistical methods, there is value in having extended access to pre-recorded online short courses in statistics that cover important analytic methods and are of equal caliber as courses offered at major statistics conferences. For biopharmaceutical companies in particular, the ability to grant such online access to a team of statisticians could veritably trigger collaborative group learning among peers and thus, enrich the passion for statistics methodology within a department. At UCB BioPharma we are embarking down this avenue.

It is promising when individuals with expertise in specific areas of statistical methodology contribute to the growth of statistics by developing pre-recorded short courses, accessible via online training outlets for extended periods of time.

Perhaps this medium in general and the Section’s online training program in particular, can yet serve an important future role in helping strengthen the knowledge base among statisticians and thus extend the broader impact of our statistics discipline.
UPDATE FROM THE PUBLICATIONS OFFICER

Richard C. Zink, SAS Institute Inc and University of North Carolina at Chapel Hill

Hi, folks! Here is an update on Publication Team activities. See what is new at the BIOP Website!

Check out new members of the Executive Committee. 
http://community.amstat.org/biop/aboutus/executivecommittee

Award winners! Poster and paper winners for the Joint Statistical Meetings (JSM) are listed, as well as the poster winner for the 2016 Regulatory-Industry Statistics Workshop. Check out the winners and explore the winning posters. 
http://community.amstat.org/biop/awards/pastwinners

Interested in a conference or training opportunity? We have you covered! Check out the calendar of events! 
http://community.amstat.org/biop/events/recentcommunityeventsdashboard

Have an idea for a scientific working group (SWG)? Check out the SWG Proposal Committee page for guidelines and to submit a proposal. For 2017, the Pub Team will be developing a new section of the website to better highlight the efforts of the Safety SWG, the Nonclinical SWG, and other newly formed groups. 
http://community.amstat.org/biop/aboutus/subcom/swg

Want to get involved with the Section but don’t know how? Go to the homepage and click the Volunteer link at the top of the page. Be sure to tell us your interests. 
http://community.amstat.org/biop

New full- and half-day online training! As a starting point, we are launching a pilot with three online training courses based on popular short courses offered at numerous conferences around the world. If there is sufficient interest, further courses will be added in the future. http://sprmm.com/asa-biopharmaceutical-section

• Analysis of Longitudinal and Incomplete Data (Full-Day Course)  
  Instructors: Geert Verbeke (Katholieke Universiteit Leuven and Universiteit Hasselt, Belgium), Geert Molenberghs (Universiteit Hasselt and Katholieke Universiteit Leuven, Belgium).

• Key Multiplicity Issues in Clinical Trials (Full-Day Course)  
  Instructor: Alex Dmitrienko (Mediana Inc).
• **Statistical Evaluation of Surrogate Endpoints in Clinical Trials** (Half-Day Course)  
  **Instructor:** Geert Molenberghs (Universiteit Hasselt and Katholieke Universiteit Leuven, Belgium).

**Check out the webinar archive** and explore slides for all 62 webinars from 2008-2016 (you must be logged in). Speaking of BIOP webinars, below is a list of upcoming training! Webinars are free for BIOP Section members! [http://community.amstat.org/biop/events/webinar-archive](http://community.amstat.org/biop/events/webinar-archive)

• **Introduction to Bayesian Nonparametric Methods for Causal Inference**  
  **Jason Roy**, University of Pennsylvania, Date and Time: 23 Feb 2017, 12-2pm EST

• **Bayesian Biopharmaceutical Applications Using SAS®**  
  **Fang Chen**, SAS Institute, Date and Time: 11 Apr 2017, 12-2pm EST

• **Sequential and Adaptive Analysis with Time-to-Event Endpoints**  
  **Scott Emerson**, University of Washington, Date and Time: 18 Apr 2017, 12-2pm EST

**Take a look at the website** for the 2017 Nonclinical Biostatistics Conference (NCB) or the 2017 Regulatory-Industry Statistics Workshop (RISW). Abstracts for speaking (NCB) or posters and roundtables (RISW) are currently being accepted.  
[http://community.amstat.org/biop/events/ncb/index](http://community.amstat.org/biop/events/ncb/index)  

Finally, want a brief introduction to a topic that you can enjoy while driving to work? Fill up that time with a podcast ([http://community.amstat.org/biop/podcast](http://community.amstat.org/biop/podcast)). Recent episodes feature the EFSPi Benefit-Risk Working Group, and discussions of multiregional clinical trials and statistical leadership. A future episode will include a sit-down with BIOP chair Alex Dmitrienko. Don’t forget, you can subscribe via iTunes ([https://itunes.apple.com/us/podcast/asa-biopharms-podcast/id700715344?mt=2](https://itunes.apple.com/us/podcast/asa-biopharms-podcast/id700715344?mt=2)). Have an idea for a future podcast? Send me an email ([richard.zink@jmp.com](mailto:richard.zink@jmp.com))!

**Interested in mentoring?** JSM and the Regulatory-Industry Statistics Workshop are just around the corner and provide an opportunity for mentors and mentees to meet face-to-face. Why not volunteer? [http://community.amstat.org/biop/aboutus/new-item/mentoring](http://community.amstat.org/biop/aboutus/new-item/mentoring)