ISoP News

Sept 2017

IN THIS ISSUE

Message from the President

By **Rene Bruno**

Dear ISoP members,

ISoP has been amazingly successful since its inception in 2012 as a continuation of ASoP (2011) with around 600-800 members since its start (754 members in 2016 from 27 countries, incl. 485 dual members with ASCPT). Members have been very active in Committees, Special Interest Groups (SIG) as well as in Local Events and educational initiatives. Two new SIGs were created this year: The Mathematical and Computational Sciences SIG and the Clinical Pharmacometrics SIG. In addition, the ISoP student community was also launched this year with participation from students all over the world; so great momentum.

However, despite our membership being spread across 27 countries, most members (85%) are from the US. As such, it has become a focus of the Board of Directors to internationalize the ISoP footprint. In May, ISoP organized the first out-of-US local event in Paris and will have partnered with several scientific organizations for conferences or trainings around the world with specific emphasis in sponsoring students. These include Population Approach Group of Australia and New Zealand (PAGANZ, January 2017), Population Approach Group in Europe (PAGE, June 2017), the Society for the Study of Xenobiotics - India (October 2017), Iberoamerican Pharmacometrics Group, Uruguay (November 2017), and the International Symposium in Quantitative Pharmacology - China (ISQP, December 2017). The board is also committed to developing ISoP activities, maintaining a high level of membership engagement through ACoP programming (fully coming from the members with a record 58 proposals this year), and developing our partnership with ASCPT through activities such as co-sponsored scientific programs, as well as to increase out-of-US membership with initiatives in Asia and Europe. The elections of four new Board members will bring additional diversity to ISoP Leadership.

Beyond the Board commitments, the Society does not exist without involvement of its members. Please engage in one of ISoP's activities through committees, SIGs, discussion forum, conferences, local events, and webinars. Get a chance to promote the science and education of Pharmacometrics (e.g. by contributing to white papers, tutorials, webinars…) and expand your network within our community (e.g., through Local Events), as well as with sister disciplines like Clinical Pharmacology (ASCPT) or

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Registration for ACoP8 filled fast this year reaching the limit of attendees before the early bird deadline. We are still taking registration for the preconference, pre- and post-conference workshops and tutorial. The conference is shaping up to be the most comprehensive ACoP to date with more than 20 symposia and 300 posters being showcased over the course of the conference! The ACoP8 program will feature talks on a wide-range of topics, including Clinical utility of Pharmacometrics, Advances in model building approaches, Physiological-based modeling, PKPD modeling, Quantitative Systems Pharmacology, all focusing on applications in drug development and informing decision making across multiple therapy areas. Please review the update at http://www.acop8.org/conference-program

This year's preconference , entitled "Systems Pharmacology: From Innovation to Impact," will kick-off bright and early on Sunday, October 15th co-chaired by Drs Cynthia J. Musante and Saroja Ramanujan. The preconference commences with a sunrise session by Valeriu Damian (QSP SIG Chair-Elect) for attendees interested in an introduction to the systems pharmacology field. The main preconference session features keynote lectures by Andrew McCullough (UCSD) and Richard Gray (FDA) describing exciting advances in medicine through the application of physiologically-realistic 3D beating heart models. The rest of the day is jam-packed with talks highlighting innovative and impactful examples of QSP and related approaches, a panel discussion with audience participation, and a lunchtime poster session to facilitate interactions and discussions.

Don't forget to join in some fun at Mondays night social event. The theme is "Barbecue, Sand, and a Drink in your Hand." Wear your favorite tropical outfit as we roll out a steel drum band and beach games. Tuesday late afternoon highlights an innovation and communication session. Please join us to see who will be voted the ACOP8 innovative communicator.

This year's meeting is BYOB (Bring Your Own Bag). Please feel free to bring your own favorite bag to facilitate your meeting experience.

We look forward to seeing everyone in Fort Lauderdale.

ISoP First EU Local Event in Paris

ISoP has held its first out-of-US local event hosted by the Université Paris Diderot and the French National Institute of Health and Medical Research (INSERM) in Paris on May 19, 2017. The event was fully booked with more than 70 attendees and the ISoP Board members. The audience covered the full spectrum of pharmacometric research in France from Universities (Marseille, Paris, Toulouse, Poitiers), National Institutes (INSERM, INRA), Industry (Servier, Sanofi) as well as a few participants from other EU countries (The Netherlands, Spain). Cynthia J. Musante (Pfizer) introduced the audience to "the role of quantitative system pharmacology in drug discovery & development" while Emmanuelle Comets (INSERM) summarized the recently published tutorial on "model evaluation of continuous data pharmacometric models" (Nguyen et al, CPT:PSP. 2017, 6(2):87-109) that was developed by a working group from the ISoP Best Practice Committee. Five short communications were then given on topics covering the diversity of expertise in France, from population pharmacokinetics to model-based drug development and mechanistic modeling. France Mentré (Université Paris Diderot/INSERM) gave the final presentation on "Bridging the Gap Between Pharmacometricians and Statisticians in Clinical Pharmacology and Therapeutics" from her featured presentation at ASCPT earlier this year. In closing after a few ISoP Updates, Mirjam Trame (University of Florida) presented the ISoP Student Community to the many students attending the meeting. Everybody convened for a networking session sharing drinks, snacks but also science with featured posters !

The event was very well received from the participants and it was agreed to redo it next year… Stay tuned.

On behalf of the organizing committee: Jérémie Guedj, Emmanuelle Comets, France Mentré (Université Paris Diderot/INSERM, Site Bichat), Sylvie Retout (Roche), Laurent Nguyen (Sanofi), Marylore Chenel (Servier), René Bruno (Roche/Genentech, ISoP).

Interview with Stacey Tannenbaum

by Peter Bonate

Tell us about yourself?

I received my BSE in Biomedical Engineering from Duke and my PhD in Pharmaceutical Sciences and Applied Math at the University of Arizona. After a postdoc at the Center for Drug Development Science with Carl Peck, I joined the Modeling and Simulation department at Novartis where I spent the first 8.5 years of my industry career. I joined Astellas in Jan 2012 starting as a project modeler; in April of this year I was promoted to Sr. Director and the global lead of the M&S group. I'm a co-founder, Fellow, Past President, and Former Board member of ISoP, co-founder of ACoP, co-founder of MoSAiC, Member-at-Large for AAPS, previous M&S Focus Group chair for AAPS, and Executive Committee Chair for WCoP 2020. Giving back to the Pharmacometrics community is definitely a passion of mine!

What drew you to pharmacometrics?

My college professor Jim Jacobs had done some work with the anesthesiology group at Stanford (Don Stanski and Steve Shafer) on "computer assisted continuous infusion" (CACI), and he was interested in engineering applications towards pharmaceutical sciences. He offered an elective course in the subject, which I took solely because it fit in my schedule and I liked Dr. Jacobs- I really had no specific interest in the topic. Until this time, I had planned to have a career in orthotics and prosthetics, but that class changed the course of my life- we really only got through the one and two compartment PK model, but that was all I needed. I fell in love with PK and have been smitten ever since!!

What is your favorite part of the job? Of pharmacometrics in general?

In my new role as M&S lead for Astellas, I have the opportunity to set the strategy for the department, and am working with colleagues from stats and medical to embed model informed drug development into our processes, which is very exciting! As for Pharmacometrics, I still find it endlessly fascinating. I love that I can apply my skills in math, computers, and engineering to help make people's lives healthier and better. I enjoy working with the project team to understand their needs, and help translate the model that is developed into real answers that can support decision making. I think it's wonderful that PMX has expanded beyond PKPD into so many different areas: biostatistics, QSP, PBPK, decision analysis, health outcomes, programming… I still learn something new at every conference. And the pharmacometrics community may be relatively small, but it's full of great and smart people who I consider friends- going to conferences like ACoP and PAGE feel like family reunions!

Any advice for students?

Join Toastmasters! Seriously. The ability to communicate clearly, succinctly, and to audiences with various levels of technical ability is key. Training programs focus so much on technical skills, but if you can't explain the best model in the world to the consumer (the project team, for example), they won't use it, and all your hard work is for naught. Toastmasters will help you develop good communication skills as well as leadership tools that will take you far in your career. I've been a member since 2003 and I still learn new things. And make sure you understand drug development, and where the task you are working on fits in- you need to know what question you are trying to answer! Most of us (myself included!) want to jump in as soon as we get the data and get our hands dirty, but a perfectly fitting model that is not predictive or doesn't help to inform the appropriate decision is a waste of everyone's time. And lastly, in the same vein- know when to say when and to stop modeling. It's not comfortable to stop when it's not a perfect fit, but you'll learn with time when it's good enough.

What is the biggest challenge facing pharmacometricians today?

I think the challenge for not just pharmacometrics but every specialty scientific discipline is the ability to work in an interdisciplinary environment. Pharmaceutical science is a team sport, but every player speaks their own language and uses their own tools, techniques, and standards. Skills like communication, collaboration, healthy conflict, and building relationships with team members may seem "soft" and non-scientific, but without those skills you can't do your job effectively. Learning these competencies will make you a better scientist and pharmacometrician, because they will help you make your team members understand, value and use your models, and build your credibility for a future collaboration.

How has ISoP benefitted your career?

I can't even count the ways! Being the face of ACoP for the first years gave me visibility, recognition, and credibility in the pharmacometrics community that few people have so early in their career. While I had professional leadership experience going in (through AAPS and MoSAiC), being intimately involved with every aspect of planning a conference flexes leadership muscles you don't even realize you have – I gained skills in project management, time management, delegation, volunteer management, budgeting, customer service, conflict resolution, problem solving…. and so much more. Establishing ISoP added even more to my resume with respect to organizational development, and leading in a way that is all about the members that we serve. Time and project management are critical for a modeler on a development project, and all of the leadership skills I gained have set me up for success in my current role as the global M&S group lead at Astellas. Plus, ACoP and ISoP have given me the opportunity to interact and mentor so many students and young scientists, something I really love.

NEW EMA GUIDANCE

In July, the European Medicines Agency (EMA) revised its **Guideline on Strategies to Identify and Mitigate Risks for First-in-Human and Early Clinical Trials with Investigational Medicinal Products**. The new guideline will go into effect February 2018.

News from the Standards and Best Practices Committee

by Justin Wilkins

The Standards & Best Practices Committee provides best practices and recommendations for standard pharmacometric analyses (e.g. population PK/PD, exposure-response, disease models) to increase the consistency, productivity, quality, communication, and impact of pharmacometrics on decision making. In the future, we anticipate expanding to cover quantitative systems pharmacology as well.

Our two main workstreams have been very busy in 2017.

The Model Evaluation Working Group ("MoEv"), led by France Mentré, is tasked with producing a series of model evaluation tutorials for publication in the peer-reviewed literature. This year, the first of these was published (on diagnostics for continuous-data models, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5321813/), and the second, on time-to-event model diagnostics, is undergoing internal review. A third, dealing with categorical data models, is in the early stages of preparation.

The Data Standards Working Group, led by Andrijana Radivojevic, is developing a set of standards for population PK datasets, which we ultimately hope will be folded into the CDISC standard, and investigating ways to improve the provenance of source data. High-level results for a data standards survey conducted in 2016 have been published on the ISoP website (http://www.go-ISoP.org/assets/docs/Data_Standards/ISoP%20data%20standards%20-%20survey.pdf), and a position paper describing our strategy is currently in revision. The first version of the standard is nearing completion, and we hope to publish it before the end of the year.

We're always looking for feedback and volunteers! Come and visit us at http://www.go-ISoP.org/standards-best-practices-committee, or contact Justin directly at justin.wilkins@go-ISoP.org.

News from the Student Community

by Mirjam Trame

The ISoP student community seeks to foster the interest in pharmacometrics by promoting communication among trainees from various disciplines aiming for efficient drug development and rational drug treatment in patients. The main focus of this community is to create a dynamic platform for educational and scientific events that allows trainees to exchange and broaden their knowledge in this field. Furthermore, peers from all over the world now have the opportunity to interact and support each other's professional development. The ISoP student community is composed of trainee members from academic institutes across the globe, and whoever is interested is encouraged to join by becoming a member.

To find out more, feel free to contact the leadership team or the respective representative from your University/country/region on the steering committee. Please go to http://www.go-ISoP.org/ISoP-student-community to find your peers and learn about upcoming events.

Student Community Leadership Team

Chair:
Kayla (Yi Ting) Lien (University of Florida), Email: yitinglien@ufl.edu

Co-chair:
Vijay Siripuram (University of Otago), Email: vijay.siripuram@otago.ac.nz

Vice-chair:
Sinziana Cristea (Leiden University), Email: s.cristea@lacdr.leidenuniv.nl

Mathematical and Computational Sciences Special Interest Group

The Mathematical and Computational Sciences (MCS) Special Interest Group (SIG) was approved in 2017 as an official ISoP SIG. The objectives of the MCS SIG are to promote advanced mathematical and computational techniques in pharmacometrics and to serve as forum for mathematical modelers. Activities have mostly focused on setting up the structure of the MCS SIG, and some planning for future events. The original organizing committee consisted of 31 ISoP volunteers who helped with the wording of a charter that was written from scratch, and decisions about the governing structure. The organizing committee also elected officers (chair, vice chair, and secretary) for one-year terms, and selected a subset of 8 individuals to serve as a steering committee (with an ex officio ISoP Board Member). The officers created a web page, planned content for the ACoP 2018 Meet the SIG event, and advertised the MCS SIG in relevant sessions at two July 2017 conferences: the Society for Industrial and Applied Mathematics (SIAM) and the Society for Mathematical Biology (SMB). The steering committee submitted two proposals for ACoP 2018 sessions with mathematical/computational content, one of which was accepted. Recruitment of ISoP members to join the MCS SIG has begun. Our hope is to attract both those with mathematical or computational backgrounds, and those who are interested in learning more and supporting such approaches. The leadership team of the MCS Sig is Wojciech Krzyzanski of SUNY Buffalo, Helen Moore of BMS, and Gilbert Koch of the University Children's Hospital in Basel, Switzerland. If you are interested in joining the MCG Sig, contact Wojciech Krzyzanski (wk@buffalo.edu) or Helen Moore (dr.helen.moore@gmail.com).

Message From the President

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Biostatistics (ASA). In line with the ISoP mission to maximize the promotion, advancement and impact of the discipline of pharmacometrics, it is also critical for ISoP and its members to reach out outside of our community and collaborate with regulatory agencies and therapeutic areas focused organizations and meetings. We hope ISoP can become a crucial component for your scientific advancement and career development as we grow together! Please reach out to any of the Board members, to Committee or SIGs leadership (http://www.go-ISoP.org/home) to get involved and offer new ideas. See you at ACoP8.

René Bruno, ISoP President, rene.bruno@go-ISoP.org

Interesting Papers

by The ISoP Publications Committee
(Angela Birnbaum, Peter Bonate, David D'Argenio, Ashwin Karanam, Shaun Kumar, Jin Niu, Ana Ruiz, & Catherine Sherwin)

Yates FE. Good manners in good modeling: mathematical models and computer simulations of physiological systems. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, 234(5): R159-R160, 1978 (suggested by David D'Argenio).

The evolution in the discipline we now call pharmacometrics has benefitted greatly from concepts, methods and tools borrowed from other fields of study. For my first reading recommendation in this forum, I suggest an editorial on the use of modeling in systems physiology (the precursor of systems pharmacology) written in 1978 by Gene Yates, the editor of the then new journal in which the article appears.

Yates's editorial goes beyond oft repeated aphorisms regarding mathematical modeling. He provides a succinct summary of both the advantages and limitations of the modeling process, as well as "welcome characteristics" in a paper on modeling, all of which remain remarkably pertinent and insightful some 40 years later. For example, Yates recalls the intellectual debates in the 1960's and 70's surrounding the use of mathematical modeling in some fields of science, including biology, that should provide guard rails for current day efforts in quantitative systems pharmacology. In addition, he reminds us that models in science are hypotheses, and, as such, "models are logically strongest when they fail". Of course, in pharmacometrics we not only use models as scientists use them, but we also use models as engineers use them: to predict system performance under new conditions, and to estimate values of experimentally inaccessible variables and system properties (numbers 5 and 6 from Yates's list of "Advantages"). Yates ends the editorial by noting that his observations and recommendations are not at all new ("after all, … the rules of good modeling are just the rules for good thinking") and directs the reader to the "first sermon on the subject, from which all others derive". He cites aphorism 95 from the 1620 Novum Organum of Francis Bacon, suggesting that in systems modeling we take the path of the bee.

Bartelkink IH, Zhang N, Keizer RJ, Converse PJ, Dooley KE, Nuermberger EL, & Savic RM. New paradigm for translational modeling to predict long term tuberculosis treatment response. Clin Trans Sci 2017 May 31 (epub ahead of print) (suggested by Catherine Sherwin).

This manuscript describes a translational PK/PD model from mouse to human that can potentially be used to predict long-term tuberculosis (TB) response. The manuscript shows an innovative approach and demonstrates the proposed paradigm in a carefully designed framework.

Investigating TB therapy and accounting for the progress of the disease has provided challenges when evaluating the results from clinical trials. Results from these trials have been disappointing especially those related to extrapolating the data from mice to humans, where there are concerns related to the predictions of clinical efficacy. The investigators in this manuscript have recognized these limitations and have outlined the development of a new paradigm, which has begun to address these disparities.

Using information related to pre-clinical exposure-response, TB disease pathology and the body's immune response, the authors have linked the mouse-to-human translational PK/PD to build a model that can be used to inform and improve clinical trial outcomes and predications. The developed model can be used as a base to inform dosing regimen optimization and predict outcomes of ongoing trials where there is drug development for TB therapies.

Liu C, Yu J, Li H, Liu J, Xu Y, Song P, Liu Q, Zhao H, Xu J, Maher VE, Booth BP, Kim G, Rahman G, & Wang Y. Association of time-varying clearance of nivolumab with disease dynamics and its implications on exposure-response. Clin Pharmacol Ther 27 May 2017 (ePub ahead of print) (suggested by Ana Ruiz) .

The impact of longitudinal disease status on drug exposure (clearance) of some therapeutic monoclonal antibodies is discussed. This could significantly impact the E-R analysis as the predicted exposure metrics based on population pharmacokinetic analysis could be biased.

Paglialunga S, Offman E, Ichpurani N, Marbury TC, Morimoto BH. Update and trends on pharmacokinetic studies in patients with impaired renal function: practical insight into application of the FDA and EMA guidelines. Expert Rev Clin Pharmacol 2017 Mar; 10(3), 273-283 (suggested by Ana Ruiz).

This paper describes how population pharmacokinetic analysis could avoid the need for a renal impairment study. This is critical in oncology drug development where many drugs cannot be given to healthy volunteers. Further, enrolling otherwise healthy volunteers with renal impairment function or cancer patients with several degrees of renal impairment is challenging and may have a profound effect on timelines.

How FDA Plans to Help Consumers Capitalize on Advances in Sciences

by Scott Gottlieb, M.D., Commissioner of the Food and Drug Administration

Dr. Gottlieb was sworn in as Commissioner of the Food and Drug Administration on 11 May 2017. On 7 July 2017 in the FDA Voice, Dr. Gottlieb published this blog on this opinions about the future of the FDA. Many of his comments are relevant to the pharmacometrics world and we thought it would be of interest to reprint his blog here. We've highlighted particular passages of importance.

We're at a point in science where new medical technologies hold out the promise of better treatments for a widening number of vexing conditions. Over the last few decades, science has enabled fundamental advances in our understanding of the genetic and protein bases of human disease. These developments are already being translated into new medicines. In more cases, these treatments target the underlying mechanisms that drive different diseases. These advances hold out the promise of arresting and even curing a growing number of diseases.

To build upon such opportunities, FDA will soon unveil a comprehensive Innovation Initiative. It will be aimed at making sure our regulatory processes are modern and efficient, so that safe and effective new technologies can reach patients in a timely fashion. We need to make sure that our regulatory principles are efficient and informed by the most up to date science. We don't want to present regulatory barriers to beneficial new medical innovations that add to the time, cost, and uncertainty of bringing these technologies forward if they don't add to our understanding of the product's safety and benefits.

This imperative is driven by our mandate to promote the public health. It includes a responsibility to make sure that we're taking steps, within the scope of our existing responsibilities, to also help facilitate access to new innovations once FDA approves them. Access to advances in medical care is a critical component of public health. And the price of new technology affects the ability of people to access these new treatments. We therefore need to be mindful of the costs of our regulatory processes, to the degree that these costs also affect the availability of new innovations, and the way that they are ultimately priced.

New medical innovations are ultimately priced to a measure of the cost of the capital it takes to develop these technologies. This is true not only when it comes to the direct costs of research and development. Cost is also a function of the time and uncertainty of these endeavors.

For these reasons, as part of our public health mandate, we need to make sure that we're taking a risk-based approach in everything we do. The 21st Century Cures Act gave FDA many new authorities and resources to accomplish this mission. "Cures" provides FDA with tools aimed at modernizing our regulatory programs. The goal of many of these efforts is to make sure that we're taking every appropriate step to facilitate access to safe and effective new innovation.

Today we announced our detailed work plan for the steps we're taking to implement different aspects of Cures. I want to highlight one example of these steps, which we're investing in, and will be expanding on, as part of our broader Innovation Initiative. It's the use of in silico tools in clinical trials for improving drug development and making regulation more efficient.

In silico clinical trials use computer models and simulations to develop and evaluate devices and drugs. Modeling and simulation play a critical role in organizing diverse data sets and exploring alternate study designs. This enables safe and effective new therapeutics to advance more efficiently through the different stages of clinical trials. FDA's efforts in modeling and simulation are enabled through multiple collaborations with external parties that provide additional expertise and infrastructure to advance the development of these state-of-the-art technologies.

FDA's Center for Drug Evaluation and Research (CDER) is currently using modeling and simulation to predict clinical outcomes, inform clinical trial designs, support evidence of effectiveness, optimize dosing, predict product safety, and evaluate potential adverse event mechanisms. We'll be putting out additional, updated guidance on how aspects of these in silico tools can be advanced and incorporated into different aspects of drug development.

A variety of drug development, regulatory, and therapeutic questions are addressed by CDER through modeling and simulation strategies. CDER's Office of Translational Sciences (OTS) uses these same strategies in the review of Investigational New Drugs Applications (INDs) and New Drug Applications (NDAs). To take just one example of the benefits of these approaches, as we enter an era of drug individualization, modeling and simulation that incorporates aspects of individual physiology and genetics in drug metabolizing enzymes is being used to identify patient subgroups that need dose adjustments. These approaches are incorporated to assess the combined effect of drug interactions, renal impairment, and hepatic insufficiency in patients, with clinical management strategies described in drug labeling where appropriate.

Another example is the use of modeling and simulation to assist in the creation of natural history databases to support model-based drug development. This could make clinical trials more efficient—for example, by enabling FDA to model some aspects of the behavior of the placebo arm in clinical trials. Right now, FDA is collaborating with scientists to develop such natural history models in Parkinson's disease, Huntington's disease, Alzheimer's disease, and muscular dystrophy. An important objective of modeling and simulation is to better evaluate the behavior of new treatments in rare disease populations that are inherently hard to study due to their small size.

To advance these opportunities, we need to continue to invest in high performance computing. These computing capabilities are becoming a key requirement to the ability of our review staff to manipulate the large data sets that are now a common feature of drug applications. FDA is actively working to expand the agency's capabilities in high performance computing, and to explore modeling approaches and enhance their regulatory impact, through an effort enabled by the work of the agency's Scientific Computing Board.

FDA's device center is also an integral part of this work. The Center for Devices and Radiological Health (CDRH) is also building in silico regulatory models for product design and evaluation, including the development of a digital library of models and a family of "virtual patients" for device testing. An important goal is consistency. We need to make sure that the adoption of these strategies is consistent across different medical products and across the agency.

FDA is working hard to maximize the authorities and resources Congress granted us to advance medical innovation for patients. To ensure smooth coordination and communication across the agency, we established an intra-agency Cures Steering Committee. Since enactment of the nearly 1,000-page law on December 13, 2016, the team has conducted a detailed analysis of the law's provisions, compiled a list of all of its FDA-related requirements, and is helping to advance the work teams that will enable FDA to deliver on the law's opportunities. Today, we're posting an initial list of our Cures deliverables. It will eventually become a tracking tool to help the public follow our progress.

As you can see from the list, we've already implemented several important Cures provisions. Section 1002 of Cures authorized $500 million in new funding over 9 years to help FDA cover the cost of implementing certain parts of the law. Consistent with the law's requirements, we developed a draft work plan demonstrating how FDA would use that funding, subject to annual appropriations. We submitted the draft work plan to FDA's Science Board for its consideration at a public meeting in May. Today we're posting the final work plan that we delivered to Congress on June 9th. It includes the recommendations from FDA's Science Board.

Among some of the other noteworthy actions that we're pursuing under Cures:

- Our Center for Biologics Evaluation and Research (CBER) is implementing the Regenerative Medicine Advanced Therapy, or RMAT designation. This new process provides another pathway to access FDA's existing expedited programs, and is available for certain cell therapies, therapeutic tissue engineering products, and certain combination products. The goal of these efforts is to help foster the development and approval of these novel products. We've already received almost two dozen requests for RMAT designation and granted four such designations to date. To continue to advance these opportunities, we'll be announcing this September a comprehensive framework for the development and proper FDA oversight of regenerative medicine. This new policy effort will comprise a series of new guidance documents covering many aspects of the regulation of regenerative medicine products. It will be announced as part of our Innovation Initiative. It will delineate our policies for appropriate and efficient regulatory oversight of regenerative medicine products, in order to demonstrate their safety and effectiveness. It will also create an accessible framework that will enable providers to more easily collaborate on proving these principles for regenerative products that are advanced within local medical institutions. We want to help facilitate these scientific advances, which hold out tremendous potential for treating and even curing diseases. To achieve these goals, we need to make sure that we have a modern regulatory framework in place that can allow innovators to meet the statutory requirements for demonstrating safety and effectiveness.
- The newly established Oncology Center of Excellence is the first inter-center institute at FDA that focuses on a specific disease area rather than type of product. It's designed to take advantage of the synergies that can be achieved by coordinating the clinical review of products across FDA's drug, device, and biologic centers to make the development of oncology and hematology medical products more efficient. This new center will allow our expert review staff to work together and take a life-cycle approach to the development and post-market regulation of new cancer treatment options.
- Under provisions of Cures, CDRH exempted more than 70 Class I device types from the requirement to submit to FDA a 510(k) submission. CDRH also proposed exempting another 1,000+ Class II device types from having to submit a 510(k) submission based on an initial determination that premarket review is not necessary to provide a reasonable assurance of safety and effectiveness. This action will decrease regulatory burdens on the device industry and eliminate private costs and expenditures.
- To further align our regulatory requirements with the provisions of Cures, CDRH also amended its current regulations to allow more devices to qualify for a humanitarian device exemption for small patient populations. We'll allow researchers to seek approval for device clinical trials through a central institutional review board rather than mandating the use of local review boards. Under the provisions of Cures, CDRH has also published the list of reusable device types for which FDA will require validated instructions for use and validation data regarding cleaning, disinfection, and sterilization in 510(k)s. These new requirements go into effect on August 8, 2017.
- Finally, last month CDER, working with CBER, issued a plan for the development and issuance of patient-focused drug development guidances. The workshops and the new guidance will set forth our plan to facilitate a more systematic approach to gathering and using patient perspectives to inform FDA's regulatory decision-making.

We're at the beginning of a transformative era in science and medical technology. Through our implementation of Cures, and our efforts to build on its provisions through a new Innovation Initiative, we hope that our collective efforts will help consumers benefit from this new progress. FDA's headway in pursuing the opportunities enabled by Cures illustrates the agency's enthusiasm and commitment to the law—both its letter and its spirit. Please bookmark the Cures web page and our tracker to follow our progress as we work to vigorously advance these shared goals.

Communication Corner

by Peter Bonate

Give Yourself Enough Time For Preparation

Earlier this year I did a webinar with Stacey Tannenbaum for Certara on giving virtual presentations (1). Afterwards, Certara started a blog about the presentation and a question came in, *"…what might be a typical time it takes to prepare a well delivered presentation. This is from when you start making presentation slides, adding different features to engage the audience, practicing and editing/fine-tuning the finished slide deck."* (2) That's a good question, one that is rarely addressed, and one that is quite timely because as I am writing this I have hanging over my head a presentation I am giving next week at the 13th Basel Modeling & Simulation Seminar for which I haven't even started preparing yet.

And here's the answer: it depends. There isn't a hard and fast rule here because it depends on many factors like how well you know the material, how much of the material for the presentation is already made, and how much time you need to practice. Working backwards, I personally plan for 5 to 7× the length of the presentation for practice. If the presentation is for an hour I will practice 5 to 7 hours. For important presentations I will practice more, a lot more. But this is me. You may require more time, or less time, depending on how comfortable you are with your talk. Practicing your talk should take as much, if not probably more, of your time compared to any other task.

You should practice until you feel relaxed presenting the material from any point in your presentation. Most people practice starting from the beginning of their talk. Towards the end they may be tired or not as focused as when they started, particularly for longer presentations. Hence, the closing of a talk tends to not be a strong as the opening. Instead, try practicing another way. Once you have practiced from the beginning a few times, try starting from the middle or any random place in your slide deck. Things happen during a presentation. Questions may arise. Technical problems may ensue. These may stop the flow of your presentation and when you restart you may be bit flummoxed about where you left off and what you meant to say. Practicing from random spots not only helps you stave off these hiccups, but gives you an added level of confidence that you can conquer anything during your talk. That's the feeling you want when you walk out on that stage or start talking. There's a phrase for this, and that's knowing it *cold*. You want to know your material cold, no matter how long that takes you to achieve.

A more difficult estimate is the amount of time it takes to create a polished slide deck. This starts with planning. What do you want to say? What is the point of your talk? If the audience leaves with remembering just one thing from your talk, what is that one thing you want them to remember? Planning your talk will help you save time later when you put your slide deck together. I would say that you should plan at least as long as your talk for what you will say and what you will show.

Someone, I forget who, said it takes 20 to 30 min to create a "good" slide. That's probably about right on-average for a complicated slide with graphics, but is on the high side for textual slides. For a 1-hour talk, where you have ~1 slide per minute, then I would say it should take about 10 to 20 hours to prepare those slides. For a 10 min talk to a core team for a project-related talk then about an hour or two is needed.

The original question asked about prep time from conception to presentation, but they forgot one important part, and that is afterwards. You should always get feedback afterwards from your audience

on how you did. I'm not talking about platitudes about how great you were. I'm talking about constructive feedback to help you prepare for next time. Good feedback is a gift (if your ego can take it and listen because sometimes feedback can be brutal). Maybe you like to create certain graphs that you think look cool, but in reality, don't help the audience understand what you are trying to convey. Getting that as feedback will help the audience during your next presentation.

So, what do all these numbers add up to? For a 1-hour talk of high importance it should take about 30 to 35 hours of preparation starting from scratch. However, the exact numbers are not that important. What matters is that you give yourself enough time to prepare, however long that is. This means that you should not procrastinate and wait till the last minute. I can't tell you how many horrible presentations I've sat through that seemed as though they were slapped together at the last minute by the speaker. Don't be that person. Be the polished speaker. Be the speaker that when your name is introduced, the audience knows that they are in for a treat. They know that you will have put the time in to give them a quality presentation and that you won't be wasting their time.

(1) https://www.certara.com/webinar-archive/
(2) https://www.certara.com/2017/08/18/speaking-into-the-ether-challenges-of-the-virtual-pharma-workplace/