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Executive Summary

The MRCT Center's 2019 Annual Meeting convened a diverse group of stakeholders focusing on global clinical trials. The principal topics discussed were: (1) Life Sciences Regulation and Policy in Today's China, (2) Health Literacy in Clinical Research, (3) Real World Evidence and the OPERAND project, (4) Representation and Inclusion of Diverse Populations in Clinical Research, and (5) European Union General Data Protection Regulation (EU GDPR).

Keynote: Life Sciences Regulation and Policy in Today's China

Professor Chenguang Wang (Tsinghua University) gave an overview of China's evolving pharmaceutical regulations, China's recent efforts to unify and advance pharmaceutical innovation, revisions to the Drug Administration Law (DAL), and establishment of the National Medical Products Administration (NMPA, formerly the China Food and Drug Administration or CFDA) to oversee drug regulation. The revised DAL aims to position China as a global pharmaceutical leader by (1) decreasing the drug time lag for new active substances being introduced into the market, (2) extinguishing data inaccuracy and fraud in research, (3) increasing the quality of generic drugs, (4) increasing China's capacity for pharmaceutical innovation, (5) strengthening administrative and regulatory controls, and (6) mitigating popularly-criticized high drug prices. Professor Wang concluded by highlighting how the evolving Chinese regulatory system has been modeled after the United States' Food and Drug Administration (FDA) and that both nations have significant motivation and opportunity to cooperate in pharmaceutical innovation.

Katherine Wang (Ropes & Gray, Shanghai) surveyed several regulatory developments in China, and began by highlighting the regulatory ambiguity concerning how the NMPA will handle drugs developed internationally. Furthermore, new medical device regulation in China emphasizes regulatory compliance across the product's entire life cycle. This includes holding individuals personally liable for their institution's actions. Moreover, China's Human Genetic Resource (HGR) regulation creates stringent restrictions on the collection and processing of biospecimens from Chinese citizens. Evolving data privacy legislation is similarly positioning health data as a Chinese national security priority.

Mark Barnes (MRCT Center, Ropes & Gray) summarized the ongoing National Institutes of Health (NIH) and Department of Defense (DoD) investigations into foreign influence on American research. The investigations identify scientists in the United States that have received and not properly disclosed foreign appointments and remuneration. The NIH has named 180 scientists at 71 institutions and asked the respective institutions to investigate them. The investigations have primarily affected academia, but their impact may spread to industry if scientists that hold academic appointments in addition to conducting clinical trials are penalized for wrongdoing.

Panel Discussion: Health Literacy in Clinical Research

Sylvia Baedorf Kassis (MRCT Center) gave a brief overview of the trajectory of the MRCT Center's Health Literacy in Clinical Research project, an overview of project updates, and the recent launch of the MRCT Center's [Health Literacy website](#). She detailed how health literacy is critical to the research process and applicable to all phases of a clinical trial (Discovery, Recruitment, Consent, On-study, and End of Study); and that bilateral communication is mutually beneficial at each step of the participant's journey. Ms. Baedorf Kassis previewed and demonstrated features of the Health Literacy website (see <https://mrctcenter.org/blog/projects/health-literacy-clinical-research/>) before moderating a panel discussion with experts in the field of human research participant protections.

Elyse Summers (AAHRPP) described the ways in which this project goes above and beyond legal requirements for health literacy. She then outlined the ways the website aligns with the three domains covered by AAHRPP for accreditation: (1) organization, (2) IRB or ethics committee, and (3) researchers and research staff.

Martha Jones (Partners HealthCare) noted that each role of the clinical research ecosystem is represented within the comprehensive Health Literacy website. She highlighted aspects of the website that particularly resonated with her, including the call to action, clear direction to users, the implementation examples such as the teach-back concept, and the holistic approach to the study life cycle.

Project Update: Real World Evidence – OPERAND project

William Crown (OptumLabs) gave an overview of the regulatory imperatives that are driving interest in real-world evidence (RWE) and highlighted the central question researchers want to answer, including whether or not one can infer causality from observational data. Dr. Crown reported about a high-profile case where an observational study and a randomized clinical trial (RCT) reached similar conclusions after an issue with study design was addressed. The OPERAND (Observational Patient Evidence for Regulatory Approval and uNderstanding Disease) Project, conceptualized by the MRCT Center and Optum Labs, was designed to understand the sources of variation in design, approach, methodology, statistical measures, and decision making. In the Spring of 2019 two institutions— Brown University and Harvard Pilgrim Health Institute—were selected to replicate two trials: the ROCKET study for atrial fibrillation and the Lead-2 study for Type 2 diabetes control. The preliminary results from the ROCKET AF Trial and replication study showed a distribution of estimates that fell within the 95% CI of the trial, with all ten methods that were used to derive the estimates.

David Martin (USFDA) discussed ways of thinking about RWE for regulatory purposes more broadly. At the end of 2016, the U.S. Congress asked the FDA to evaluate the potential use of RWE but not that the FDA should modify its threshold of “substantial evidence” for regulatory decision making regarding the effectiveness of drugs and biologics. The imperative now is to

retain the substantial evidence standard while examining the potential utility of RWE for effectiveness, comparative effectiveness, and comparative safety studies. The OPERAND project is important and interesting because it helps illuminate how different data, methods, and approaches to decision making modulate conclusions, and it will be of interest to the FDA.

Panel Discussion: Representation and Inclusion of Diverse Populations in Clinical Research

Barbara Bierer (MRCT Center) explained that the MRCT Center continues to work on Diversity and inclusion in Clinical Research and is finalizing the first draft of the Guidance Document. That document aims to balance scientific purposes and social justice components of the case for diversity, as well as provide practical tools to help stakeholders adopt and implement research respective to diverse inclusion.

Maria DeLeon (Parkinson's Foundation) shared her approach on the topic of diversity in clinical research from the perspectives of a physician, a patient, and a patient advocate. There is empirical evidence that a gap remains for fair and proportional representation of Hispanics and women in research, and this is especially seen in Parkinson's Disease. It is critical to continue to improve diversity in clinical research in order to address scientific understanding and social justice of treatment.

Matthew Rotelli (Eli Lilly and Company) complimented the MRCT Center for its work on the guidance document and the thorough and comprehensive approach to diversity in clinical research. In addition to suggesting that the document would be better digested if it is subdivided, Dr. Rotelli distilled the document's objectives into four approaches and offered ways to strengthen each: (1) clarify the goals of diverse representation, (2) substantiate the value of diversity, (3) explain why diverse representation has not improved, despite increased focus on the issue, and (4) develop and offer resources to stakeholders that will improve diversity.

William Tap (Memorial Sloan Kettering Cancer Center and American Society of Clinical Oncology) complimented the document as being the most comprehensive effort to address the issue of diversity within the clinical research enterprise. Dr. Tap advised that the MRCT Center review the overall tone and language of the document and to take a more definitive declaration on the need to improve diversity in clinical research and to emphasize that appropriate diversity is achievable. He also suggested the document clearly define what is meant by 'clinical research' (versus clinical trials) and offered additional suggestions and ideas, including defining and identifying all stakeholders, highlighting adolescents and young adults (AYA), addressing bias and oversight, encouraging community immersion, providing guidance on workforce diversity, and justifying eligibility criteria through clinical rationale tailored to each trial.

Project Update: EU General Data Protection Regulation (GDPR)

David Peloquin (Ropes & Gray) remarked that the MRCT Center has published many articles and convened several meetings to discuss the GDPR beginning with the issuance of the proposed text of the regulation in 2013 and leading up to and following the regulation's May 2018 implementation. The European Data Protection Board (EDPB) released in November 2019 GDPR guidelines on the territorial scope of the GDPR that address certain of the issues in MRCT Center's comments submitted in January 2019 on the EDPB's draft territorial scope guidelines. The MRCT Center recently co-sponsored a seminar in Brussels, Belgium, to discuss the research challenges posed by the GDPR and potential solutions. Prior to the Brussels seminar, the MRCT Center co-authored an input paper that addressed challenges and solutions through specific case studies. The MRCT Center is collecting feedback on this paper and working with sponsors of the Brussels meeting to plan for future meetings on this topic.

Welcome and Introduction

Mark Barnes and Barbara Bierer, MRCT Center

MRCT Center Faculty Co-Director, Mark Barnes, JD, and MRCT Center Faculty Director, Dr. Barbara Bierer, opened the meeting and welcomed the participants. Dr. Bierer asked all meeting participants to introduce themselves.

Dr. Bierer briefly reviewed the vision of the MRCT Center: to improve the integrity, safety, and rigor of global clinical trials, and its mission: to engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions. The MRCT Center brings together a variety of people, organizations, and communities to accomplish its goals. Two presentations at this meeting represent the deliverables of project-focused workgroups: (a) Health Literacy in Clinical Research and (b) Representation and Inclusion of Diverse Populations in Clinical Research.

The MRCT Center team has grown. David Peloquin (Ropes & Gray) joined as Senior Advisor in 2019. Dr. Bierer acknowledged and appreciated the diverse group of organizations and individuals that constitute the Executive Committee and Steering Committee of the MRCT Center. In 2019, Alexion Pharmaceuticals and Microsoft Life Sciences Innovation joined the Executive Committee, and AstraZeneca will join in early 2020. BIO and Boehringer Ingelheim joined the Steering Committee in late 2019, and PanAmerican Clinical Research will join in early 2020.

Dr. Bierer introduced the agenda of today's Annual Meeting and announced that next year's Annual Meeting will be at a different location at Harvard University with greater meeting space.

Keynote: Life Sciences Regulation and Policy in Today's China

Professor Chenguang Wang, Tsinghua University

Professor Chenguang Wang commenced the keynote session with an overview of China's evolving pharmaceutical regulations. China's recent efforts to unify and advance pharmaceutical innovation include revisions to the Drug Administration Law (DAL) and establishment of the National Medical Products Administration (NMPA, formerly the **China** Food and Drug Administration or CFDA) to oversee drug regulation. The revised DAL aims to position China as a global pharmaceutical leader by (1) decreasing the drug time lag for new active substances being introduced into the market, (2) extinguishing data inaccuracy and fraud in research, (3) increasing the quality of generic drugs, (4) increasing China's capacity for pharmaceutical innovation, (5) strengthening administrative and regulatory controls, and (6) mitigating popularly-criticized high drug prices. Specific measures to achieve these goals include:

- Mandating review of 1,622 pending pharmaceutical applications by requiring pharmaceutical applicants to self-review clinical trial data prior to applying for drug approval
- Introducing the Market Authorization Holder (MAH) system that allows Chinese pharmaceutical developers (companies, academic institutions, individual scientists, etc.) to retain or outsource manufacturing responsibilities
- Re-classifying “new drugs” into Category (1) new compounds that have never been marketed in the world and Category (2) new drugs that are derived from known therapeutic compounds but have never been marketed in the world
 - Previous “new drug” classification only examined if the drug had been marketed in China
- Allowing qualified institutions to conduct equivalence studies and promoting only those generic drugs that pass equivalence studies
- Establishing the NMPA’s authority to inspect and review research across the entire pharmaceutical life cycle
- Prohibiting additional hospital charges on drugs
- Setting up a drug distribution model market that is partially under governmental control
- Simplifying the drug application process
- Increasing penalties for pharmaceutical fraud

Several questions remain as China’s new regulations are implemented. For example:

- How will the DAL regulations be enforced at the local level since the NMPA only oversees national-level operations?
- Does the NMPA have the experience necessary to regulate and be respected by the Chinese pharmaceutical enterprise?

Professor Wang concluded by highlighting how the evolving Chinese regulatory system has been modeled after the United States Food and Drug Administration (FDA). Furthermore, both countries are leaders in cell therapy development. The United States is a large pharmaceutical exporter whereas China is a large pharmaceutical importer. Thus, the two states have significant motivation and opportunity to cooperate in pharmaceutical innovation.

[Katherine Wang, Ropes & Gray, Shanghai](#)

Katherine Wang surveyed several regulatory developments in China, beginning by highlighting the regulatory ambiguity concerning how the NMPA will handle drugs developed internationally. Internationally developed drugs have historically been regulated by a separate pathway compared to domestic drugs in China. However, the NMPA could integrate the separate systems into one pathway and in turn increase the opportunity for cross-border interactions in pharmaceutical innovation while simplifying drug management.

New medical device regulation in China emphasizes regulatory compliance across the product's entire life cycle. This includes holding individuals personally liable for their institution's actions, and many medical device leaders are wary of taking the blame for others' wrongdoing. The aforementioned MAH system will also impact medical device innovation by allowing companies to outsource device manufacturing. This will continue to generate opportunities for international companies to participate in China's medtech economy and should thus quell concerns about the 2025 "Made-In-China" initiative that might otherwise have inhibited international cooperation on drug development.

China's Human Genetic Resource (HGR) regulation creates stringent restrictions on the collection and processing of biospecimens and their derived data from Chinese citizens. Whereas previous regulations only addressed the collection and processing of genetic data, the new regulation institutes stricter approval requirements for research involving genetic information, imaging data, and lab test results among other forms of data. The HGR also includes harsher fines for violations. Overall, the policy positions data as a national security priority for China. Uncertainty remains around how the HGR impacts basic discovery projects as companies are unsure of what data can be exported from China. Additionally, the HGR does not distinguish research and development from other activities that may involve data collection and processing. This is particularly a concern for Chinese hospitals that now must submit approval requests for every project involving foreign influence and/or collaboration, even trainings that are funded by foreign organizations.

Evolving data privacy legislation is similarly positioning health data as a Chinese national security priority. Cybersecurity investigations are increasing in frequency, and companies should be prepared to cooperate with Chinese investigations in cybersecurity on their online platforms. Preparation may include categorizing systems containing sensitive IP and creating Standard Operating Procedures (SOPs) for complying with investigations.

[Mark Barnes, MRCT Center and Ropes & Gray](#)

Mark Barnes concluded the keynote session by summarizing the ongoing National Institutes of Health (NIH) and Department of Defense (DoD) investigations into foreign influence on research funded by U.S. government agencies. The investigations identify scientists in the United States who have received – but not properly disclosed or received pre-clearance for – foreign academic appointments, remuneration and research funds. The transactions themselves do not necessarily constitute wrongdoing, but researchers who receive federal funding must disclose foreign financial interests, research support and time commitments, and receive pre-approval for portions of U.S. government-funded grants performed in whole or part outside the U.S.. The United States government may disapprove federal research funding if the research involves sensitive technology and a foreign component. The NIH has named over 180 scientists at about 70 institutions and asked the respective institutions to investigate the foreign ties and research of those scientists. Implicated foreign countries include Russia, Iran, Germany, and Italy, but the largest actor appears to be China, with many connections being established with researchers in the United States through the Thousand Talents program. The

Chinese program consists of research support for China-based projects and a separate personal financial award.

The NIH's ultimate plan is unclear, but the American government may be concerned that foreign influence on scientific research is allowing the transfer of intellectual property (as well as pre-clinical hypotheses) to foreign countries without being subject to export regulations set forth by the Department of Commerce. While research has historically been exempted from export regulations, a new law under the DoD Authorization Act has expanded the definition of intellectual property to include research that may be related to national security. The investigations have primarily affected academia, but their impact may spread to industry if scientists that hold academic appointments in addition to conducting industry-sponsored clinical trials and pre-clinical research are found to have violated federal regulations. Ultimately, the investigations may be more harmful than helpful for the United States in some cases, as they potentially sour international research collaboration and might prevent valuable intellectual property from being imported into the United States through these foreign collaborations.

Discussion

Keynote discussion focused on clarifying the Market Authorization Holder (MAH) system. The keynote speakers first noted that previous Chinese regulations required pharmaceutical developers to conduct manufacturing operations themselves. The new MAH system allows pharmaceutical developers to outsource pharmaceutical manufacturing operations to outside contractors if they desire. Regardless of whether manufacturing responsibility is retained or outsourced, the MAH remains legally liable for the pharmaceutical. The MAH system may require foreign-owned companies that conduct pharmaceutical operations in China to apply to be an MAH through their Chinese colleagues. The MAH system has many pending issues, and it is currently being tested in 10 provinces.

Panel Discussion: Health Literacy in Clinical Research

Sylvia Baedorf Kassis, MRCT Center

Sylvia Baedorf Kassis (MRCT Center), Program Manager of the Health Literacy project, gave a brief overview of the MRCT Center's Health Literacy in Clinical Research project trajectory, a description of health literacy as applicable to clinical research, and an overview of project updates, including the recent launch of the MRCT Center's [Health Literacy website](#). She reminded members that the project idea originated from the MRCT Center's previous work in Return of Aggregate Results and Return of Individual Results. The project workgroup, which commenced monthly meetings in April of 2018, was always committed to representing and engaging patients and participants as a critical aspect to overall stakeholder engagement throughout all project phases.

She detailed how health literacy is critical to the research process and applicable to all phases of a clinical trial (Discovery, Recruitment, Consent, On-study, and End of Study); and that bilateral communication is mutually beneficial at each step of the participant's journey. She underscored that the vast majority of individuals in the US—9 out of 10—require assistance with health literacy at some point in their lives. Ms. Baedorf Kassis previewed and demonstrated features of the [Health Literacy Website](#) including case studies, tools and materials, and best practices — the first ever focusing on health literacy in clinical research—that went live in October 2019.

[Elyse Summers, AAHRPP](#)

Ms. Elyse I. Summers, JD, is President and CEO of AAHRPP, an organization that accredits human research protection programs (HRPPs). She described the ways in which the MRCT Center project goes above and beyond legal requirements in promoting and supporting health literacy. She then outlined the ways the website aligns nicely with the three domains covered by AAHRPP for accreditation. The first domain is the organizational domain that describes overarching organizational responsibilities and includes responsibilities related to research participants and the community, involvement of patients at each step in the process, and standards that include constant evaluation and improvement, all of which are very much central to the health literacy website. The second domain is the IRB where issues and components such as risk/benefit analysis, data safety management, the protection of vulnerable populations and additional safeguards beyond consent are included. The third domain includes researchers and staff who are implementing multiple aspects of a study. Ms. Summers discussed the ways the AAHRPP process tracks with the various tenants of health literacy in including clear communication, transparency, and accessibility.

[Martha Jones, Partners HealthCare](#)

Ms. Martha Jones, MA, CIP, Vice President, Human Research Affairs at Partners Healthcare, discussed how the use of plain language benefits research participants and supports the overall conduct of research. Ms. Jones noted the many roles in clinical research she has filled over her career and observed that each role is represented within the comprehensive Health Literacy website. She talked about the critical need for clear communication, use of a common language, plain language tools and resources, and the need to be mindful of the participant experience. She highlighted aspects of the website that particularly resonated with her, including the call to action, clear direction to users, the implementation examples such as the teach-back concept, and the holistic approach to the study life cycle.

[Discussion](#)

The panel closed with a brief discussion on details of current and upcoming dissemination efforts, including a published National Academies of Medicine perspective, various blogs, select presentations, and speaking opportunities. Further discussion about present and potential applicability of health literacy to better understanding data use and data sharing ended the panel.

Project Update: Real World Evidence – OPERAND

William Crown, OptumLabs

William Crown began with an overview of the regulatory imperatives that are driving interest in real-world evidence (RWE). These include the Prescription Drug User Fee Act (PDUFA) VI that mandates that the FDA publish guidance for RWE applications by the end of fiscal year 2021. PDUFA VI is coupled with the 21st Century Cures Act (section 3022) that mandates that the FDA propose a framework and enact a program to evaluate RWE to support approval of new indications and to satisfy post-approval requirements. There is current yet limited literature that suggests that observational studies yield results similar to randomized clinical trials (RCTs). The Cochrane Collaborative examined 14 prior reviews comparing RCTs to observational studies, and concluded that on average, there is little difference between the results obtained for RCTs and observational studies.

Dr. Crown highlighted the central question researchers want to answer, which is whether or not one can conclude causal inference with observational data. There are many methods for causal modeling with healthcare data with a growing interest in using machine learning to reach causal inference with observational data. However, causal frameworks with a thoughtful research design are needed to actually replicate RCTs.

Dr. Crown explained a high-profile case in which an observational study and an randomized clinical trial (RCT) initially differed in their conclusion. The Nurses' Health Study (an observational study) found that hormone replacement therapy (HRT) was protective against cardiovascular events whereas the Women's Health Initiative (an RCT) did not find that HRT protected against heart disease. Later, reanalysis found that the conflict was due to differences in study design of the observational study; once addressed, the conclusions were the same. Since then, significant work has been done to elucidate how to compare RCTs with observational data. Further, there are also a limited but growing number of observational studies that are replicating RCTs: prospectively, concurrently, and retrospectively.

The Observational Patient Evidence for Regulatory Approval and uNderstanding Disease (OPERAND) Project was conceptualized by the MRCT Center and OptumLabs and was designed collectively by convening a technical expert panel. OPERAND was devised to understand the sources of variation in design, approach, methodologies, statistical analyses, and decision making. Since its launch, two institutions—Brown University and Harvard Pilgrim Health Institute—were selected to replicate two trials: the ROCKET for atrial fibrillation and Lead-2 for Type 2 Diabetes control. Separation between the two groups has been maintained, and the blind will not be broken until all work is completed. Using the OptumLabs data warehouse, both claims data and electronic health records are accessed. The teams were asked to document assumptions and choices made when emulating the published RCTs. Further, to ensure compatibility, the teams were given a common clinical question, the study RCT protocol, and a

defined set of anticipated methods, but had the flexibility to use their own methods in certain areas.

There are two measures of replication. First, a regulatory agreement is defined as a statistically significant result with directional equivalence between the RCT and observational study. The second is an estimate agreement, defined as the point estimate of the observational study falling within the 95% confidence interval of the Average Treatment Effect (ATE) from the RCT using the reported errors of the RCT to define the confidence interval. The preliminary results from the ROCKET AF Trial and replication study showed a distribution of estimates that fell within the 95% confidence interval (CI) of the trial, with all ten methods that were used to derive the estimates. The results from the Lead 2 trial are still in progress and expected to be completed by the end of December 2019.

[David Martin, USFDA](#)

Dr. Martin discussed ways of thinking about RWE for regulatory purposes more broadly. He underscored that end users of medical evidence appreciate RCTs because they are the gold-standard since there are minimal a priori assumptions, rigorous controls against bias, and structured prospective data collection and analytic methods. At the end of 2016, however, the U.S. Congress asked the FDA to evaluate the potential use of RWE, but the language used retained the evidentiary standard ("substantial evidence") for FDA regulatory decision making regarding drug and biologic effectiveness. To reconcile these expectations, one must understand that the nature and quality of real-world data will need to improve and will likely look different ten years from now. The capacity to do randomized and non-randomized trials using RWE will continue to grow. The imperative now is to bring real-world data (RWD) and RWE up to par to keep the standard for regulatory decision making while leveraging more RWD improved RWE methods over time. As such there is a significant need to understand the landscape.

The OPERAND project is important and interesting because it helps illuminate how different data, methods, and approaches to decision making modulate what conclusions are reached. It is also using linked claims and electronic health record data. This will be of interest to the FDA. The FDA is also pursuing parallel projects to build the evidence base. One of those projects is the RCT DUPLICATE project which aims to examine differences across different therapeutic areas. The project identified 40 trials to replicate, but those trials are only able to use claims data for replication; the hope is to find 75% of trials that are feasible to analyze. There are also other groups such as the Observational Health Data Sciences and Informatics (or OHDSI, pronounced "Odyssey") and Yale University and Mayo Clinic Center of Excellence for Regulatory Science that are engaged in trial replication. A related project with the University of North Carolina will also evaluate the performance of sensitivity analyses in observational studies. Thus, there are a number of empirical experiments in process; we are moving towards consensus to find areas where non-interventional methods work and do not work, and how to quantify residual uncertainty in a way that illuminates the benefits and limitations for regulatory review.

Discussion

An audience member inquired about the data sources for the OPERAND project and wondered if the same patients appeared in both the EHR and claims data, and if there were ways to link them. Dr. Crown explained that OptumLabs has a very large data set containing over 120 million lives in claims and over 80 million lives in EHR data. EHR data that lives in provider settings is not typically linkable to claims data. However, OptumLabs has methods to encrypt the data using unique but coded identifiers so that there is linkage between the two types of data. Dr. Bierer added that both Brown University and Harvard Pilgrim Health Care had access to the same data but that their choices of analytical methods and ways of approaching replication differs.

Another audience member asked about the issue of studying the use of medical marijuana, the difficulty in designing an observational study due to federal regulations, and apparent problems with products in the market that do not have standardized dosing. Dr. Martin responded by emphasizing that although this issue is not his area of focus, it is something that he has seen come up in major international regulatory conferences. One of the major challenges is exposure assessment: if one is unable to understand the dose, it would be difficult to study anything. He advised that in Italy, the regulator recently reported that the dosage is controlled, and there are some relevant studies performed there. Thus, it might be beneficial to look internationally to advance this work.

Panel Discussion: Representation and Inclusion of Diverse Populations in Clinical Research

Barbara Bierer, MRCT Center

Dr. Barbara Bierer provided an overview of this project, initiated in February of 2018, before introducing session panelists Dr. Maria DeLeon, (Parkinson's Foundation) Dr. Matthew Rotelli (Eli Lilly and Company), and Dr. William Tap (Memorial Sloan Kettering Cancer Center, American Society of Clinical Oncology [ASCO]). Dr. Bierer shared the following high-level updates before seeking comments and feedback from the panelists:

1. The Diversity Leadership team includes CAPT. Richardae Araojo (FDA), Barbara E. Bierer (MRCT Center, Harvard), Luther T. Clark (Merck), Milena Lolic (FDA), David H. Strauss (Columbia University), and Sarah White (MRCT Center).
2. There is continuous and active participation from the Diversity Workgroup, including over 40 representatives from more than 30 institutions/organizations. Workgroup members participate in monthly calls as well as on subteams.
3. The Diversity Leadership developed and refined a set of 'diversity principles' based on feedback from the Workgroup. The 'principles' are broad, universally agreeable, and approved by the Workgroup.
4. The Diversity Leadership team and MRCT Center provided a draft guidance document to the Diversity Workgroup and convened a meeting to review the document in November

2019. The guidance document is undergoing revisions based on the feedback received from the Diversity Workgroup and from the panelists at this meeting. It is not final, but a work in progress.

5. It is important to remember that no single trial is determinative; rather each trial provides an important contribution that is collectively regarded as the knowledge base.

Dr. Bierer explained that the MRCT Center continues to work on the “Diversity and inclusion in clinical research” guidance document that aims to balance the scientific and social justice components of the case for diversity, as well as provide practical tools to help stakeholders adopt and implement research respective to diverse inclusion. She then gave an overview of the sections of and high-level content in the guidance document.

[Maria DeLeon, Parkinson’s Foundation](#)

Maria DeLeon, MD, and research advocate for Parkinson’s Foundation shared her approach on the topic of diversity in clinical research from the perspectives of a physician, a patient, and a patient advocate. There is empirical evidence that a gap remains for fair and proportional representation of Hispanics and women in research, and this is especially true in Parkinson’s Disease (PD). For example, nearly 61% of women with PD are misdiagnosed initially. Further, while the diagnosis of the disease takes approximately three years in men, it often takes more than five years in women. The underrepresentation of women and Hispanics in clinical trials results in lack of data and worsens the discrepancy in the management of the disease. Tools are being developed and Centers for Excellence are increasing in availability (e.g. Mohammed Ali Parkinson Center), but it is critical to continue to improve diversity in clinical research to address scientific understanding and social justice.

[Matthew Rotelli, Eli Lilly and Company](#)

Matthew Rotelli, Senior Advisor for the Bioethics Program at Eli Lilly, complimented the MRCT Center for their work on the guidance document and its thorough and comprehensive approach to diversity in clinical research. In addition to suggesting that the document would be better digested if it is divided up into smaller sections, Dr. Rotelli distilled the document’s objectives into four approaches and offered ways to strengthen each:

- 1) Clarify the goals of diverse representation**
 - a. Define diversity clearly and clarify the goals to achieve diversity.
 - b. Present the tensions between scientific and social goals.
 - c. Explain that the approach to diverse inclusion and design of the trial may need to change if there are anticipated differences between populations versus when there is not.
 - d. Explain when it is appropriate to invest in further research and perhaps delay the benefit to some in order to understand the risk in other populations.

- 2) Substantiate the value of diversity
 - a. It is clear that there is a challenge in making the value case for what is the right thing to do; present the argument for the value of diversity as reaching beyond clinical trials into building real world evidence.
 - b. It is a long-term commitment and while we will not likely be able to justify the value to an individual trial or even clinical development program, the value in shifting the overall enterprise is to build trust in research to find answers that the public needs. It will build value in the medicines we provide.
- 3) Explain why diverse representation has not improved, despite increased efforts
 - a. Include what has been attempted and where it has and has not worked – for example, CDISC attempted to standardize data collection, but in what situations do those answers not work?
 - b. How do efforts to increase diversity apply with regard to patient engagement and workforce diversity – what has worked and what hasn't?
- 4) Develop and offer resources to stakeholders that will improve diversity
 - a. Clearly break down advice by the intended audience and make suggestions accessible and actionable.
 - b. Create a website similar to Health Literacy that is easily navigable by stakeholder, presents examples and provides resources.

[William Tap, Memorial Sloan Kettering Cancer Center, and ASCO](#)

Dr. William Tap, bioethicist and physician at Memorial Sloan Kettering Cancer Center and past Chair of Health Equity at the American Society of Clinical Oncology (ASCO), complimented the MRCT Center on its document as being the most comprehensive resource tackling the issue of diversity within the clinical research enterprise. Dr. Tap underscored the importance of the topic and explained that long-term and sustained commitment from stakeholders is the solution to address this issue, one that is so deeply entrenched in our culture. In this light, Dr. Tap advised that the MRCT Center review the overall tone and language of the document and to take a more definitive, forceful stance on the need to improve diversity in clinical research and the fact that it *is* achievable.

First, Dr. Tap suggested the document clearly define what is meant by 'clinical research' and that the document looks beyond clinical trials to also encourage the approach of promoting equity in population-based and outcomes research, and especially the sharing and use of real-world data. Additional suggestions and overarching ideas from Dr. Tap included:

- 1) Define and identify all stakeholders and offer manageable, well-focused mandates for each. Create metrics to monitor steps involved in improvement, metrics that may be required in order to hold stakeholders accountable for the privilege of conducting clinical research.
- 2) Highlight the adolescent and young adults (AYA) population as an area of distinct need. The guidance document mentions pediatric and elderly populations but fails to address the dynamic issues involved in AYA populations.

- 3) Address that bias and oversight are on a continuum and need to be accounted for from the outset and continuously reviewed throughout the research process.
- 4) Mention and encourage that in order to broaden engagement, a *continual presence* in the community is a requirement. Community immersion enables bidirectional flow of information between the community, the study sites and the sponsors.
- 5) Provide guidance on how to address workforce diversity; it is a deeply rooted and intricate cultural change issue that requires organizations and leadership to be trained and supported.
- 6) Suggest that eligibility criteria be justified through clinical rationale and tailored to each trial, not duplicated from past trials. In addition to this and of similar rationale, bring transparency back into feasibility assessments and site selection to move the clinical research enterprise toward a more holistic, meaningful, well-balanced representative process.

Dr. Tap encouraged the MRCT Center to further investigate the concept of a Bayesian hierarchy model to study rare population subsets. He concluded by mentioning that inclusion of real-world evidence is key, although controversial, and should be further explored.

Discussion

The panel was opened to the audience for questions. The first question asked about current efforts to address the workforce issue in clinical research and noted that in Boston, clinical research coordinators (CRCs) are often white, affluent individuals. How are organizations engaging more people of color or conducting their community-based research? Dr. Tap responded that having a diverse workforce is critical and that entry into academic research or medicine has its own impediments. ASCO has a designated task force addressing how to improve workforce diversity and have taken several approaches, including partnering with local institutions, employing grassroots efforts to bring academic questions into the community and then actively working to bring people from the community back into the workforce.

The second question asked how organizations, sponsors, and other stakeholders can make trials more accessible to people who cannot access them. Dr. Tap replied that if it is difficult to get people to a facility, it may be possible to decentralize the trial and bring the trial to the patients. There are ways to develop infrastructure in the community, reduce financial constraints, hire local physicians/clinicians, work with research organizations that have mobile clinics, and travel to different sites or rural areas. It is about understanding the population and helping them overcome the limitations to participation.

A question arose about the problem with responding to race, ethnicity, sex and gender. Sometimes a form offers a 'wish not to say' option and if so, do we want to rely on this data if the question is unanswered? Dr. Bierer responded that these are difficult standards and that some countries do not allow the question to be asked, and the document does address the need for the data and how to report the data if some fields are not answered. Furthermore, it

requires research to recognize that data definitions in one place may be different in another (i.e. race in the USA may be defined differently than other parts of the world).

Project Update: EU General Data Protection Regulation (GDPR)

David Peloquin, Ropes & Gray

Mr. David Peloquin remarked that the MRCT Center has published many articles and convened several meetings to discuss the GDPR beginning with the issuance of the proposed text of the regulation in 2013 and leading up to and following the regulation's May 2018 implementation:

- Publications
 - **November 2013:** Publication of article in *Bloomberg BNA* discussing challenges that draft GDPR poses to secondary use of clinical trials data
 - **August 2014:** Publication of article in *Bloomberg BNA* discussing interaction of draft GDPR and EMA Policy 0070 on clinical trials data transparency
 - **February 2016:** Publication of article in *Bloomberg BNA* discussing potential impact of final GDPR text on scientific research and secondary uses of data
 - **2017-2018:** Publication of several articles on the basis for processing personal data under GDPR, the extraterritorial effect of GDPR and implications on U.S. academic medical centers, and consent under GDPR
- Convened Meetings
 - **July 2018:** MRCT Center holds meeting of life sciences, government and academic medical center/university stakeholders in Boston to outline challenges of GDPR for research
 - **November 2018:** MRCT Center, through the Research, Regulatory and Development Roundtable (R3), organizes meeting in New York to continue discussion from July 2018 meeting
 - **January 2019:** MRCT Center submits comments on European Data Protection Board guidelines on territorial scope of GDPR
 - **May 2019:** MRCT Center representatives meet in Dublin with Irish Data Protection Authority along with representatives of the National Institutes of Health and University College Dublin to discuss GDPR challenges for research

The European Data Protection Board recently released GDPR guidelines, and they are seemingly influenced by the MRCT Center's comments submitted in January. One example is that the guidelines explicitly address the GDPR's applicability in the situation in which a United States research participant travels to Europe whilst a mobile application continues to collect data for the research. The MRCT Center also recently co-sponsored a seminar in Brussels to discuss the research challenges posed by the GDPR and potential solutions. The meeting, which took place on November 17, 2019, was structured around four topical panels: (1) scientific research and safeguards, (2) secondary research, (3) transnational transfers of personal data for research,

and (4) challenges for international collaboration and Horizon Europe. The panels included two members of the European commission, and 70% of the attendees were from EU member states.

Prior to the Brussels seminar, the MRCT Center co-authored an input paper that addressed challenges and solutions through specific case studies. The topics discussed include:

- Difficulties in identifying clear legal basis for processing data in both prospective and secondary research
- Providing notice to data subjects for secondary research
- Treatment of pseudonymized data as anonymized data
- Role of institutions and sites as controller vs. processor in relation to research data
- Transfers of personal data outside of the European Union (EU)
- EU-based vendors as processors for non-EU controllers

The MRCT Center will collect feedback on the Brussels seminar as well as the input paper and continue to collaborate with the Intelligence in Science (ISC), National Institutes of Health, and University College Dublin as the research enterprise continues to navigate the GDPR.

Closing Remarks

[Sarah White, MRCT Center](#)

Ms. Sarah White, MRCT Center Executive Director, gave a big thank you to all the speakers. She reviewed the date for next year's Annual Meeting, for the upcoming Bioethics Collaborative meetings and Research, Development & Regulatory Roundtable (R3) meetings in 2020, as well as for Executive & Steering Committee Meetings 2020.

Appendix 1: Meeting Participants

First Name:	Last Name:	Job Title:	Institution/Affiliation:
Maria	Apostolaros	Sr Director, SRA	PhRMA
Behtash	Bahador	Associate Director	CISCRP - Center for Information and Study on Clinical Research Participation
Ginny	Beakes Read	Executive Director, GRR&D Policy	Amgen
Poorvi	Chablani	Senior Manager, Clinical Trial Transparency	Biogen
Susan	Chin	Staff	Harvard Law School
Luther	Clark	Deputy Chief Patient Officer	Merck & Co., Inc.
Cathy	Critchlow	Vice President Center for Observational Research	Amgen
Merce	Crosas	University Research Data Officer	Harvard University
William	Crown	Chief Scientific Officer	OptumLabs
Patrick	Cullinan	Sr Director, Medical Writing	Bluebird Bio
Emily	Dayalji	Associate Director, Business Operations	OptumLabs
Maria	De Leon	MD/ Research Advocate	Parkinson's Foundation
Lucas	DiLeo	President	Broadland Advisors
Jackie	Do	Reg Affairs Operations Officer	Harvard Medical School Harvard Catalyst
Rhonda	Facile	VP, Development Opportunities	CDISC
Jamie	Flaherty	Senior Research Counsel	Boston Medical Center
Hassan	Ghanny	Project Coordinator	Research Apprenticeship Multicultural Partnership at the Urban College of Boston
Jennifer	Goldsmith	Brigham and Women's Hospital	Brigham and Women's Hospital
Polly	Goodman	Associate Director of Regulatory Affairs Operation	Harvard Medical School Harvard Catalyst
Sharareh	Hosseinzadeh	Global Head Clinical Patient Engagement	Novartis Pharmaceutical
Martha	Jones	Vice President, Human Research Affairs	Partners HealthCare
Kraig	Keeter	Vice President, Clinical Operations	PanAmerican Clinical Research
Aaron	Kirby	Director of Regulatory Affairs and Operations	Harvard Medical School Harvard Catalyst

Sidney	Klawansky	Instructor	Harvard Chan School of Public Health
Thomas	Kosloff	Director for clinical policy	Optum/UnitedHealth Group
Mayumi	Kusunose	Senior technical scientist	RIKEN
Katherine	Laessig	Vice President, Therapeutic Strategy	IQVIA
Vivian	Larsen	Associate Director - R&D Patient Engagement	Takeda Pharmaceuticals
Kathy	Lenhard	CEO PanAmerican Clinical Research	PanAmerican Clinical Research LLC
Marcia	Levenstein	Senior Advisor	Vivli
Suzan	Levin	AGC	Pfizer
Rebecca	Li*	Exec Director	Vivli
Huimin	Lu	Collaborator	Brigham and Women's Hospital
Priya	Mannan	Associate General Counsel	Novartis
David	Martin	Associate Director Real World Evidence Analytics	U.S. Food and Drug Administration
Jules	Mitchel	CEO	Target Health LLC
Trupen	Modi	Digital Health Advisor	Microsoft, Lifesciences Innovation
Lisa	Murray	Epidemiologist	MA Department of Public Health
Marilyn	Neault	Patient Research Advocate	Parkinson's Foundation
Lauren	Neighbours	Senior Director, Regulatory Affairs	Optum
Mitchell	Parrish	President	PanAmerican Clinical Research
Catherine	Pearcy	Children's National Hospital	Children's National Hospital
David	Peloquin*	Attorney	Ropes & Gray LLP
Claude	Petit	VP Biostatistics and Data Sciences	Boehringer Ingelheim
Maria	Rocha	Assoc. Director, Disclosure and Transparency	Sunovion Pharmaceuticals
Matt	Rotelli	Senior Advisor, Bioethics	Eli Lilly and Company
Jessica	Scott	Head of R&D Patient Engagement	Takeda
Jessica	Seyfried	Director	National Minority Cardiovascular Alliance
Moke	Sharma	Senior Vice President	Alexion
Im Hee	Shin	Professor	DCUMC / CIMI
Sharon	Shriver	Director of Programs	Public Responsibility in Medicine and Research (PRIM&R)
Paul	Slater	Co-Founder, Clinical Research Innovation Hub	Microsoft, Lifesciences Innovation

Evan	Sohn	Regulatory Affairs and Education Coordinator	Harvard Medical School Harvard Catalyst
Michael	Steel	Senior Advisor, Chief Medical Office	Novartis Pharma AG
David	Strauss*	Special Lecturer	Columbia University
Elyse	Summers	President and CEO	AAHRPP
Magdalena	Taber	Independent Consultant	Campanaro Clinical Trial Consulting
William	Tap	Medical Oncologist	Memorial Sloan Kettering Cancer Center
Michael	Thomas	Human Subject Research Medical Governance	GlaxoSmithKline Pharmaceuticals
Amanda	Truesdale	Vice President, Biometrics	Veristat
Ryan	Tubbs	Clinical Research Innovation Hub	Microsoft, Lifesciences Innovation
Tianna	Umann	Solution Architect	Microsoft, Lifesciences Innovation
Chenguang	Wang	Professor	Tsinghua University
Katherine	Wang	Partner	ROPES & GRAY LLP
Brad	Wilken	Deputy Director Product Development Operations	Bill and Melinda Gates Foundation
Lina	Williamson	President & Chief Innovation Officer	TMAccelerator LLC
Ji	Zhao	Program Director	Brigham and Women's Hospital
Ming	Zhao	Scientific Director	Hormometer AI
Hayat	Ahmed	Project Manager	MRCT Center
Carmen	Aldinger	Administrative and Training Manager	MRCT Center
Sylvia	Baedorf Kassis	Program Manager	MRCT Center
Mark	Barnes	Faculty Co-Director	MRCT Center
Barbara	Bierer	Faculty Director	MRCT Center
Jennifer	Ewing	Senior Communications Specialist	MRCT Center
Lisa	Koppelman	Program Manager	MRCT Center
Linda	McMaster	Administrative Assistant	MRCT Center
Laura	Meloney	Program Manager	MRCT Center
Walker	Morrell	Project Manager	MRCT Center
Joshua	Smith-Sreen	Graduate Student Researcher	MRCT Center
Sarah	White	Executive Director	MRCT Center
Deborah	Zarin	Director, Advancing Clinical Trials Enterprise	MRCT Center

*MRCT Center Senior Advisor

Appendix 2: Meeting Agenda

MRCT Center 2019 Annual Meeting Agenda Wednesday, December 4, 2019

Loeb House at Harvard University, 17 Quincy Street, Cambridge, MA

Time	Topics/Speakers
7:30 – 8:00 AM	Breakfast & Registration
8:00 – 8:15 AM	Welcome and Introductions <ul style="list-style-type: none"> Mark Barnes and Barbara Bierer
8:15 – 9:55 AM	Keynote: Life sciences Regulation and Policy in Today's China Introduction & Moderator: Mark Barnes (MRCT Center, Ropes & Gray) <ul style="list-style-type: none"> Life Science Cooperation Between China and the US Professor Chenguang Wang, PhD, LLM Tsinghua University Law School, P.R. China Overview of China Regulatory Updates Katherine Wang, LLM, LLB Ropes & Gray LLP, Shanghai "Foreign Influence" and Implications for China/U.S. Collaborative Research Mark Barnes, JD, LLM MRCT Center; Ropes & Gray
9:55 – 10:45 AM	Panel Discussion: Health Literacy in Clinical Research Introduction & Health Literacy website: Sylvia Baedorf Kassis (MRCT Center) Moderator: Sylvia Baedorf Kassis Panel: <ul style="list-style-type: none"> Martha Jones (Partners HealthCare) Elyse Summers (AAHRPP)

	<p>Unable to attend due to weather-related difficulties: Panelist: Alicia Staley (Medidata) General Discussion Moderators: Laurie Myers (Merck), Christopher Trudeau (University of Arkansas)</p>
10:45 – 11:00 –AM	Break
11:00 – 11:45 AM	<p><i>Project Update:</i> Real World Evidence – OPERAND</p> <p>Moderator: Barbara Bierer</p> <p>Presentation of Results: William Crown (Optum)</p> <ul style="list-style-type: none"> • Response: David Martin (FDA)
11:45 AM – 12:45 PM	<p><i>Panel Discussion:</i> Representation and Inclusion of Diverse Populations in Clinical Research</p> <p>Introduction/Moderator: Barbara Bierer</p> <p>Panel:</p> <ul style="list-style-type: none"> • Maria DeLeon (Parkinson’s Foundation) • Matthew Rotelli (Eli Lilly and Company) • William Tap (Memorial Sloan Kettering Cancer Center, ASCO)
12:45 – 12:55 PM	<p><i>Project Update:</i> EU General Data Protection Regulation (GDPR)</p> <ul style="list-style-type: none"> • David Peloquin (Ropes & Gray)
12:55 – 1:00 PM	<p>Closing Remarks</p> <ul style="list-style-type: none"> • Mark Barnes and Sarah White
1:00 PM	Lunch
1:30-5:00 PM	<p>Executive Committee & Steering Committee Meeting <i>For MRCT Center sponsors only</i></p>

Appendix 3: Speaker Biographies

Information and Biographies for MRCT Center Leadership, Senior Advisors and Staff are available on our website: <https://mrctcenter.org/about-mrct/people/>



William Crown, PhD, is chief scientific officer of OptumLabs. Prior to his current role, Dr. Crown held a number of leadership roles at Optum. Most recently, he served as President of the Health Economics, Late Phase Research Business Unit at Optum Life Sciences.

From 1994 to 2004, Dr. Crown was Vice President of Outcomes Research and Econometrics at Thomson Reuters Medstat. He has also taught graduate courses in statistics and conducted research on the economics of aging and long-term care policy at Brandeis University.

Dr. Crown received his doctorate degree in urban and regional studies from MIT, and an MA in economics from Boston University. The author of two books, and co-author of two others, he has published over 165 journal articles, book chapters and other scholarly papers.

Dr. Crown is currently affiliate faculty, Mongon Institute for Health Policy, at Harvard University.



María L. De León M.D. is a fellowship trained movement disorder specialist as well as an avid research advocate. Over the last decade, she has spent most of her time championing women's issues and setting ground for understanding of gender differences in neurological diseases particularly that of Parkinson's Disease (PD); while attempting to decrease the disparity in healthcare treatment among minorities through her work as part of PAIR (Parkinson's Advocates in Research) program. She served as a member of PPAC (People with Parkinson's Advisory Committee) for 4 years for *Parkinson's Disease Foundation* (now known as *Parkinson's Foundation*) and has been instrumental in developing the 'Women & PD initiative.' As such she wrote the first book for women with PD addressing the gender differences. She has also authored 2 other books and several other publications— "*Viviendo mas alla...*" (*Living beyond...*) takes into account the cultural barriers that exist for Hispanics to obtain diagnosis and treatment for PD along with the obstacles that preclude them from participating in clinical research. This has led to an extensive collaboration with the Hispanic Outreach program through MACP (Muhammad Ali Center of Parkinson's). She currently serves as a public policy advocate for Michael J Fox Foundation working closely with the DOD in helping secure grant money for Parkinson's research. She also is a blogger for Brain and Life magazine, health union and her personal blogs defeatparkinsons.com and parkinsonsdiva.org the latter concentrating on women's issues in living with chronic illness and PD.

Since her diagnosis with YOPD, her commitment to helping improve research disparity has solidified. Dr. De León received her B.A from the University of Pennsylvania and her M.D. from Hahnemann Medical School.



Martha F. Jones is the Vice President of Human Research Affairs at Partners HealthCare in Boston, MA. For the past ten years, she has served as the Executive Director of the Human Research Protection Office at Washington University in St. Louis. Martha is a strategic-thinker, thought-leader, mentor, and service-oriented leader. In addition to previously serving as an IRB Chair and IRB Executive Director, she has a strong background across diverse areas including conducting both clinical and non-clinical research, leading a data management and statistical center for human research studies, and initiating a center for public health statistics research. Martha is a leader at the national level currently serving as a member of the Board for the Public Responsibility in Medicine and Research (PRIM&R) and as Council Vice-Chair for the Association for the Accreditation of Human Research Protection Programs (AAHRPP).



David Martin is the Associate Director for Real World Evidence Analytics Office of Medical Policy, FDA Center for Drug Evaluation and Research. David Martin leads the Real-World Evidence Staff in the Office of Medical Policy. He oversees demonstration projects intended to support the agency's evaluation of real-world evidence, reviews real world evidence submissions, and contributes to medical policy development mandated by the 21st Century Cures Act. He is also the architect of the open source FDA MyStudies mobile app system.

As a former Branch Chief, Division Director, and Acting Deputy Office Director, he led analyses of spontaneous reports, formalized risk management planning, and helped develop the Sentinel system. He also served on detail as the FDA Liaison to the European Medicines Agency. Before joining the FDA, he practiced flight and occupational medicine in the U.S. Air Force. He completed his undergraduate degree at the Citadel and his M.D. and M.P.H. at the Johns Hopkins University. He is board certified in occupational medicine and clinical informatics.



Matthew D. Rotelli, PhD, is currently the Senior Advisor for the Bioethics Program at Eli Lilly and Company in Indianapolis, Indiana. He leads the company's evaluation of bioethical considerations across the continuum of its research, development, and commercialization activities. Dr. Rotelli has over 20 year of pharmaceutical development experience at Eli Lilly and Company. He has led multiple quantitative disciplines to bring medicines to patients in oncology, immunology, cardiovascular, endocrine, and neuroscience indications. He is passionate about making the drug development process more reliable, efficient, and trustworthy. Dr. Rotelli was formerly a Director of Pharmacokinetics, Pharmacodynamics (PK/PD), and Pharmacometrics and also a Director of Statistics. Previously, he was a Research Advisor in the Advanced Analytics Hub

focusing on Data Mining and Bayesian applications. Throughout his career, he has performed or directed statistical and PK/PD work in all phases of clinical development, including commercialization, pharmacovigilance, and Health Outcomes.

Dr. Rotelli earned his B.A. in Mathematics from Cornell University and his M.S. and Ph.D. degrees in Statistics from Virginia Tech. He is a graduate of the Lilly Bioethics Leadership Academy (BELA) and a member of the American Statistical Association (ASA), the American Society for Bioethics and Humanities (ASBH), and Public Responsibility in Medicine and Research (PRIM&R). He is a former chair of the DIA Comparative Effectiveness Scientific Working Group and of the joint ASA and ISoP Statistics and

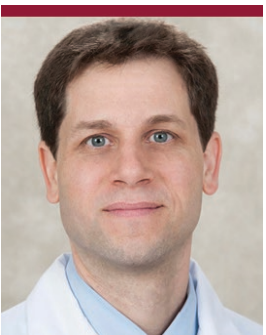
Pharmacometrics Scientific Interest Group. Dr. Rotelli is currently on the Executive and Steering Committees of the MRCT Center and a member of the Biopharmaceutical Industry Bioethics Forum.



Elyse I. Summers, JD, is President and CEO of the **Association for the Accreditation of Human Research Protection Programs, Inc.® (AAHRPP)**. Ms. Summers has been AAHRPP's President and CEO since October 2013. She provides strategic and substantive leadership and oversight on all aspects of AAHRPP's operations and is looking forward to leading AAHRPP well into the 21st century as the indispensable global organization for the accreditation of human research protection programs.

Prior to AAHRPP, Ms. Summers was the Director of the Division of Education and Development at the US Department of Health and Human Services' Office for Human Research Protections (OHRP), a position she held from 2008-2013. Ms. Summers first began working for OHRP's predecessor organization (the Office for Protection Research Risks [OPRR]), in 1998, first in the Division of Compliance Oversight and then in the Division of Education. Prior to joining OPRR/OHRP, Ms. Summers practiced law pertaining to food, drugs, and other medical products (Buc & Beardsley). Included in her practice was the provision of guidance and counseling on Federal and State law, regulations, and ethical issues related to the conduct of biomedical research. Prior to that, Ms. Summers spent five years in the Office of the Commissioner at FDA, as Special Assistant to the Deputy Commissioner for External Affairs, and later as an original staff member of FDA's Office of Women's Health.

Ms. Summers has spoken extensively and published several articles and book chapters on biomedical and behavioral research and human research protections. She has also practiced the law of tax-exempt organizations (with, respectively, Baker and Hostetler, and, Steptoe and Johnson), and has spoken and written on that topic as well. Ms. Summers began her career at the Association of American Universities, representing research universities. She earned her J.D. from the George Washington University National Law Center and her B.A. from the University of Michigan. She is a member of the Bar of the District of Columbia and of the Commonwealth of Pennsylvania.



William D. Tap, MD is the Chief of the Sarcoma Medical Oncology Service at Memorial Sloan Kettering Cancer Center in New York. Bill has extensive experience in translational medicine and is currently in charge of the clinical, basic science, and translational aspects of the Sarcoma Medical Oncology Program at MSKCC. Bill received his Medical Degree from Jefferson Medical College in Philadelphia, PA and performed his residency in Internal Medicine at the Vanderbilt University Medical Center in Nashville, TN and his fellowship in Hematology and Medical Oncology at the UCLA Medical Center in Los Angeles, CA. Bill also has a tremendous interest in Global Health Care initiatives, specifically in effecting health disparity in underserved areas of the world.



Professor Chenguang Wang is a Professor of Law at Tsinghua University. He holds a B.A., LL.M., Ph.D. from Peking University; and LL.M. from Harvard Law School. He taught at Peking University Law School, City University of Hong Kong; and is currently Professor of Law teaching at Tsinghua University Law School, Director of Health Law and Pharmaceutical Product Law Research Center; and was Dean from 2002 to 2008. Professor Wang was Legal Advisor of former CFDA, and General Administration of Quality Supervision, Inspection and Quarantine; Deputy Chair of China Association of Legal Theory, Deputy Chair of China Health Law Association, and Deputy Chair of China Association of Legal Education. He participated in drafting Basic Healthcare and Health Promotion Law, Vaccine Management Law and revising Drug Administration Law. Professor Wang is a Visiting Scholar at Yale Law School, Visiting Professor of University de Navarra (Spain), NYU Law School, Cornell Law School and University of Pennsylvania Law School. His research areas include: Jurisprudence, Comparative Law, Sociology of Law, and Health Law.



Katherine Wang is a partner in Ropes & Gray life sciences group. Widely regarded as a leading life sciences regulatory lawyer in China, Katherine assists pharmaceutical, biotechnology, and medical device companies on a wide range of matters, including early-stage discovery, product registration, regulatory/GxP compliance, pricing, reimbursement, clinical studies, promotional practices, and product safety issues. Katherine provides day-to-day counseling on issues that life sciences companies face in relation to their interaction with agencies including the National Medical Products Administration (NMPA, formerly the CFDA), the National Health Commission (NHC) and the State Administration of Market Regulation (SAMR), among others. She also assists institutional investors and corporate clients in structuring transactions and conducting regulatory due diligence, including good laboratory practice (GLP), good clinical practice (GCP), good manufacturing practice (GMP) and pharmacovigilance, on investment targets and prospective business partners in China.

Before entering into private practice, Katherine served as the head of AstraZeneca's legal department in the Asia-Pacific region. In this role, she advised on critical strategic and operational initiatives to ensure legal compliance and realization of business objectives. She was also responsible for cross-functional intellectual property enforcement and anti-counterfeiting efforts.

Katherine received LLM from Harvard Law School and National Taiwan University respectively.