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MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

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Executive Summary

The principal topics discussed at the MRCT Center 2017 Annual Meeting were Real World Evidence, Global Clinical Trial Data Sharing Platform (Vivli), Core Competencies for Clinical Research Professionals, and Return of Individual Results to Participants.

Real World Evidence

First, Dr. Alison Cave (European Medicines Agency) delivered the keynote speech, addressing the challenges of real world data (RWD) for regulatory decision making. RWD was defined as data collected outside the constraints of conventional Randomized Controlled Trials (RCTs). Dr. Cave described the opportunities for utilizing RWD as well as the uncertainties from the regulatory perspective. To address some of the concerns, Dr. Cave emphasized the need for a deeper understanding of the data to define the strengths and limitations and build trust for regulatory decision making. Solutions which may facilitate this include increasing the interoperability and harmonization of RWD via, for example, the use of common data models and minimal standards for data sets, increased transparency around methodologies, detailed documentation of the strengths and limitations of a study to enable robust and consistent validation, measures to address privacy and assure governance, and mechanisms to enable accessibility of the data for the common good.

Dr. Cave concluded by stating that RCTs remain the gold standard for an unbiased estimate of efficacy. However there is increasing interest in the use of RWD, which has been used for some time post authorization. She emphasized that RWD does not necessarily equate to real world evidence (RWE) and that considerations around the acceptability of RWD for regulatory decision making are not necessarily the same pre-and post-authorization: the context of use, unmet need, the weight placed on the evidence and alternative opportunities to capture data should be considered. Further, she highlighted that the question should not be whether RCTs or RWD should prevail, but how the two may complement each other to provide additional insight. Deliberate reflection is needed on the research question, the study design, the quality of the data source, and in particular, the ability to accurately record exposure and outcomes in the patient population of interest. Further, transparency and a clear justification as to what drives the methodological choice will increase confidence and allow external verification.

Invited speakers shared their insights on this topic, including:

- Dr. David Martin (USFDA) offered some background from the FDA's perspective. The 21st Century Cares Act includes a provision that mandates the FDA to provide guidance

in the next five years on how RWE can be utilized. In the US, RWD encompasses the continuum of all data from observational studies to interventional studies that occur outside of the traditional clinical research environment. Since the FDA does not develop drugs, it is looking to industry to bring ideas and concepts for using RWE for moving development programs forward.

- Dr. Cathy Critchlow (Amgen) referred to questions of RWD integrity and utility and the current scarcity of successful use of RWD in regulatory submissions. Dr. Critchlow offered considerations for leveraging RWD across organizations to make the processes more efficient and effective: Incentivizing innovation by gaining commitment from leadership; creating an internal structure that enables cross-functional synergy; and individually and collectively engaging all relevant stakeholders.
- Dr. Sebastian Schneeweiss (Brigham and Women's Hospital) highlighted additional considerations for using RWD: work with databases that are fit for purpose; use of appropriate methods, especially when reproducing a study; and the decision as to when to use RWD to augment regulatory decision making. How closely RWE can replicate RCTs remains an open question.
- Dr. William Crown (OptumLabs) provided an in-depth perspective on one of the key challenges of observational data: confidence in the estimate that is generated. Claims data –where most of the retrospective evidence in the US has been coming from – have limitations around accuracy of diagnostic coding; even though they are very good at capturing the breadth of services. Electronic Health Records (EHR) data have clinical outcome measures that Claims data lack, but EHR sit in provider institutions, often inaccessible to sponsors, external investigators, and regulators. OptumLabs brings together EHR and Claims data.

Discussion between panelists and conference participants focused on whether there can be improvement in the quality of data that go into EHR, whether RWE is going to serve as a complement to or substitute for RCTs, whether there will be improvements in having common standards and interoperability, and who will have access to RWD.

Global Clinical Trial Data Sharing Platform (Vivli)

Second, Dr. Rebecca Li (Vivli) and her team gave an update and live demonstration of the Vivli global clinical trial data sharing platform, an initiative that was launched by the MRCT Center in collaboration with partners:

- Dr. Rebecca Li (Vivli) introduced Vivli as a solution to the current, fragmented landscape in which clinical research data are hosted and shared. Scheduled for public beta launch in March 2018 and formal launch in July 2018, Vivli will be the "complete solution" to present shortcomings. As a 501(c)(3) non-profit entity, Vivli's primary function is to be a neutral convener for stakeholders from biomedical industries and academia. As a platform, Vivli will enable streamlined data submission, data request, data access, and sharing of academic credit.
- Mr. Paul Slater (Microsoft) described how the collaboration between Microsoft, BlueMetal, and Vivli brings together long-standing leaders in technology and digital health to transform how clinical trial data are analyzed and shared. Microsoft's mission—"to empower every person and every organization on the planet to achieve more"—aligns seamlessly with Vivli's—"to promote, coordinate, and facilitate clinical research data sharing through the creation and implementation of a sustainable global data-sharing enterprise." For this reason, Microsoft has committed to build Vivli on the Microsoft Azure platform, which offers flexibility, advanced security capabilities, and global reach.
- Dr. Ida Sim (University of California, San Francisco) led the first public preview of the Vivli platform by demonstrating the technical capabilities of the platform from the perspective of a researcher, an individual who would use Vivli to search for, locate, request, and analyze a set of studies. For a study to be searchable and findable by a researcher on the Vivli platform, Vivli curates study information from final protocols, clinical study reports, and ClinicalTrials.gov. Using the Cochrane vocabulary, Vivli then describes that study using the **P**opulation, **I**ntervention, **C**omparators, and **O**utcomes (PICO) framework. Through Vivli's harmonized data request form, researchers may request access to multiple data sets at once and then analyze approved data sets in a secure analytic environment.
- Mr. Pablo Gazmuri (BlueMetal), principal architect of the Vivli platform, demonstrated the technical capabilities of the Vivli platform from the perspective of a data contributor. Contributors are given the option of performing a sponsor check. In this way, Vivli respects contributors' review processes and data use terms while providing researchers with a centralized mechanism for request.

Discussion between panelists and conference participants focused on how to confront the reality that Vivli is very US centric while standards for data anonymization differ outside of the US, whether there are plans to upload secondary analyses or research outputs onto the Vivli platform, and whether there is concern about the potential of data requestors to confuse the public by generating and publicizing erroneous information.

Core Competencies for Clinical Research Professionals

Third, Dr. Stephen Sonstein (Eastern Michigan University and MRCT Center) gave an overview of the Joint Task Force (JTF) for Clinical Trial Competency that developed a Core Competency Framework for the Clinical Research Professional in 2014. Based on suggestions from those who utilized the framework, the JTF and MRCT Center worked on: (1) creating a website (Clinicaltrialcompetency.org), (2) revising the framework and releasing Version 2.0, and (3) levelling the Version 2.0 framework for each competency into fundamental, skilled, and advanced levels, with examples.

Workgroup members gave examples of how they have used or intend to utilize the competency framework:

- Ms. Rebecca Brouwer (Duke University) has been involved in site-based research and utilized the core competency framework for professional development. Her team completely revised their job descriptions based on the core competency framework and used "tiered positions" as the basis for advancing staff in job categories.
- Mr. H. Robert Kolb (University of Florida) is using levelled competencies for training for clinical research coordinators. He participated in a study that showed that training needs to be targeted to the background and experience of the individual learner. Levelled competencies allow targeting the content for professional development.
- Dr. William Gluck (Durham Technical Community College) has utilized levelled competencies in collaboration with pharmaceutical companies and clinical research organizations (CROs). Evaluating candidates for job openings by competencies can help identify competent and qualified people more quickly, and a certification process could help candidates to determine if they qualify for a position.
- Dr. Carolynn Thomas-Jones (The Ohio State University) is using professional portfolios based upon the core competencies to allow students to demonstrate their skills to potential employers. She is currently using *Portfolium (https://portfolium.com),* a digital portfolio for students to upload their materials such as data management plan, case report forms, consent forms.

Discussion between panelists and conference participants focused on how to standardize the evolving profession of clinical research, how to integrate patients and other researchers into the process, how to handle the situations where the competencies between and among principal investigator may vary, and how to enhance the credibility of observational studies.

Return of Individual Results to Participants

Fourth, Ms. Sandra Prucka (Indiana University) introduced the deliverables of the Return of Individual Results workgroup. During the last year, the work has focused on (1) how investigators and physicians provide information to participants, and (2) how to communicate exploratory results and, in particular, genomic results. Genomics is a complex field of study: technologies are evolving with different technologies generating different types of data, the ability to interpret results and understand their impact changes over time, the results are also generationally impactful and can influence family planning decisions, and there is a lack of global harmonization with respect to laws, regulation, guidance and institutional policy that corresponds to very different access to the output of this research globally. The Recommendations Document and Toolkit provide information on how to return results and who will return results to whom.

Dr. Jessica Scott (GlaxoSmithKline) and Ms. Joan Chambers (CenterWatch, currently SCORR Marketing) introduced a global survey examining the axes of communication between principal investigator, treating physician and participant/patient regarding communicating results from clinical trials. While the response rate was low, 160 completed responses were received. These responses show that while 88-95% of investigators and treating physicians surveyed agree that investigators should receive results, approximately half of investigators never receive these results from sponsors. Furthermore, 69-91% of investigators and treating physicians agree that results should be shared with treating physicians and with patients, while 40-83% have never shared results with treating physicians and 40-71% have never shared results with patients. The main barriers for sharing results with participants are a lack of access to results and a perceived lack of interest by patients in receiving results.

Invited speakers offered their perspectives on the MRCT Center's deliverables for return of individual results:

- Dr. Elizabeth Cahn (Dana-Farber/Harvard Cancer Center Breast Cancer Advocacy Group) raised three points from the perspective of research participants: (1) what may seem like "small data" in research is of great significance and importance to individual participants; (2) study participants have a different relationship to data than researchers; (3) it is important for researchers to be involved with patients and patient advocacy groups.
- Dr. Robert Green (Brigham and Women's Hospital) appreciated the comprehensive and thorough approach that the MRCT Center took, although he cautioned on the use of

terms clinical validity and actionability with regard to genomics. He alluded to three challenges: (1) What to do when people want their own raw data; (2) How to harmonize MRCT Center documents with other contemporaneous reports, and (3) Whether there is a mandate to collect data on the consequences when results are returned?

- Dr. Scott Kennedy (Novartis) appreciated that the documents are instructional but not prescriptive and refer to participants rather than patients, reflecting their central role in this topic. He reminded the audience that there are significant differences in our current understanding of cancer-genetics versus non-cancer genetics and their clinical and medical actionability. Therefore, we should provide substantial genetic counseling support when returning such information to participants and investigators.
- Ms. Carol Weil (National Cancer Institute, National Institutes of Health) highlighted the lack of agreement on what constitutes results that are medically actionable vs. medically significant vs. of personal utility, and that study participants have the right to receive their raw data if they wish to receive it. However, the right not to know should also be respected.

Discussion between panelists and conference participants focused on how to avoid doing unintended harm when returning research results, especially genomic results and other sophisticated medical concepts.

Welcome and Introduction

Barbara Bierer, MRCT Center

MRCT Center Faculty Director, Dr. Barbara Bierer opened the meeting and reviewed the mission of the MRCT Center: 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 aims to be a trusted collaborator and neutral convener with academic credibility. Dr. Bierer acknowledged the MRCT Center Executive Committee and Steering Committee members and introduced changes in leadership as Rebecca Li has left the role of Executive Director at the MRCT Center and became Executive Director at Vivli. Dr. Bierer also introduced the new MRCT Center Senior Advisors: Dr. Rebecca Li, Dr. Stephen Sonstein, and Dr. David Strauss. She gave an overview of the day's agenda and asked all meeting participants to introduce themselves.

Keynote

Alison Cave, European Medicines Agency

Dr. Alison Cave, Principal Scientific Administrator at the European Medicines Agency (EMA), provided the keynote address on The Challenges of Real World Data (RWD) for Regulatory Decision Making. RWD was defined as data collected outside the constraints of conventional Randomized Controlled Trials (RCTs). In terms of regulation, predominant sources include patient disease registries (used extensively in Europe), prescription databases, electronic health records (EHRs) which encompass primary care data and may include hospital records, and claims data (particularly applicable in the US). Dr. Cave highlighted six regulatory challenges to illustrate why it is important to think about Real World Data (RWD):

(1) A fast-moving scientific landscape- illustrated by an increasing number of medicines with genomic mechanism of action and or/genomic biomarkers which are enabling smaller, more focused RCTs but creating regulatory challenges
(2) New innovative medicines and personalized prescribing which creates challenges in understanding long term safety and effectiveness
(3) Rare diseases that may be associated with more limited information at the time of regulatory authorization
(4) The unknown generalizability of RCT results to normal clinical practice increasing the need for new approaches to gather complementary evidence particularly for geriatric and pediatric patients who are usually excluded from trials
(5) The need for additional datasources to better monitor risk/benefit in high risk groups with comorbidities who are often excluded from clinical trials

(6) An increasing interest in combination therapies to treat complex diseases which creates regulatory challenges

Dr. Cave also pointed out that RWE is already routinely used for regulatory decision making; predominantly for marketed products, for safety monitoring and drug utilization. However, pharmacovigilance is not an exact science; it requires balancing multiple sources of evidence, often of varying quality, from different stakeholders to inform decision making and RWD forms part of this jigsaw. For example, nearly a million adverse drug reaction reports were received by the EMA in 2016 for centralized products (products that are authorized across the whole of the EU). However in evaluating these reports only 48 validated signals were identified for further consideration and many still required further evidence to define and understand the information. Thus this example illustrates that which evidence is considered acceptable for decision making depends on the decision being made, the unmet need and the opportunity to capture other data.

Dr. Cave went on to highlight that the challenge facing regulatory decision is to move from the current paradigm of high certainty, illustrated by the controlled environment of randomized clinical trials where structured data of known provenance are generated and analyzed in accordance with strict guidelines, to one of more uncertainty, where unstructured data of unknown provenance need to be processed and analyzed. In considering this, the presentation outlined a number of the uncertainties/challenges which exist around the use of RWE:

(1) The production of RWD is for clinical care delivery and not for research and hence records are subject to systematic and random error
(2) There are unknowns around the consistency, accuracy, completeness, and representativeness of the data, all of which are influenced by the clinical care setting
(3) There is variability in the capture of lifestyle factors among databases
(4) Characterising the patient population, identifying and measuring exposure and outcomes with sufficient sensitivity and specificity is difficult
(5) There are challenges in the integration of data across multiple datasets and across the whole hierarchy of evidence (from RCTs to spontaneous reports)
(6) There are multiple examples where observational studies on the same safety issue produce disparate results

To address some of these concerns Dr. Cave emphasized the need for a deeper understanding of the data to define the strengths and limitations, so that the evidence that is derived from it can be challenged appropriately. Solutions include

(1) Increasing the interoperability to enable harmonization of data which may be delivered by common data models, minimal data sets standards and increased transparency

(2) A detailed documentation of the strengths and limitations of a study to enable robust, consistent validation
(3) Addressing privacy and governance issues at an early stage
(4) Ensuring accessibility of the data for the common good

Dr. Cave concluded by stating that RCTs remain the gold standard for an unbiased estimate of efficacy. However there is increasing interest in the use of RWD, which has been used for some time post authorization. She emphasized that RWD does not necessarily equate to real world evidence (RWE) and that considerations around the acceptability of RWD for regulatory decision making are not necessarily the same pre-and post-authorization: the context of use, unmet need, the weight placed on the evidence and alternative opportunities to capture data should be considered. However, the question should not be whether RCTs or RWD should prevail, but how the two may complement each other to provide additional insights. Deliberate reflection is needed on the research question, the study design, the quality of the data source, and in particular, the ability to accurately record exposure and outcomes in the patient population of interest. Finally, transparency in the methodological choice will increase confidence and allow external verification.

Real World Evidence

David Martin, USFDA

Dr. David Martin offered background on the topic from the FDA's perspective. The 21st Century Cures ACT, signed into law at the end of 2016, has a provision that mandates the FDA to provide guidance within the next five years to industry specifically addressing how RWE may be utilized for both supplemental New Drug Applications (NDAs) and Biologic Licensed Applications (BLAs). The Prescription Drug User Fee Act (PDUFA VI) commitments are aligned with the 21st Century Cures ACT. While generally the FDA and EMA are in alignment in the approaches to assessing RWE, one slight difference is that, in the US, RWD encompasses the continuum of all data from observational studies to interventional studies that occur outside of the traditional clinical research environment. The FDA is currently working on a framework for evaluation of RWD, and sponsors who are considering making RWE submissions to the FDA are encouraged to connect with relevant reviewing divisions working in the specific therapeutic area. RWE has been used both in the rare disease area and in certain conditions of unmet medical need, in which the absence of treatment leads to a predictable disease course and therefore a concurrent control may not be needed. Since the FDA does not develop drugs, it is looking to industry to bring ideas and concepts in how RWE may help advance development programs. As part of the review process, the FDA is evaluating the use cases and coordinating internally to

share knowledge. The FDA is also engaged in specific demonstration projects that are addressing fundamental questions and core challenges, including determining when an interventional study is necessary and. when RWE is sufficient. Often these answers depend on the therapeutic area as well as the outcomes that are assessed.

Cathy Critchlow, Amgen

Dr. Cathy Critchlow offered her personal opinions on the issue of RWE. Industry recognizes the potential in RWE but, as a relatively risk-averse culture, wishes to ensure that RWE is implemented correctly. However, lack of organizational familiarity with RWE and questions of RWD integrity and utility renders implementation difficult. Often, observational research is done as a complement to RCTs or when no other information is available. Currently, there are a limited number of examples of the successful use of RWD in regulatory submissions. Thus to leverage RWD, the processes that are efficient and effective should be developed. Additional suggestions include:

- Incentivizing innovation by gaining commitment from leadership
- Setting up an internal structure that enables cross-functional synergy
- Individually and collectively engaging all the relevant stakeholders

Sebastian Schneeweiss, Brigham and Women's Hospital

Dr. Sebastian Schneeweiss begun by highlighting the key difference between experimental and non-experimental studies. By definition, non-experimental studies are used to study how the health care system is recording and surveilling outcomes through RWD. Investigators are not in control of the measurements. Pragmatic approaches to working with RWD/RWE is essential. In this regard, a database that is fit for purpose, i.e. able to answer a specific question, is necessary. A second consideration is the use of appropriate methods to derive results. A significant regulatory challenge is determining the validity of a study. An important first step is sufficient transparency (e.g. data sources, methods, statistical analysis) to permit subsequent reproducibility of the study. A joint task force between the International Society for Pharmacoeconomic and Outcomes Research (ISPOR) and International Society for Pharmaceutical Engineering (ISPE) detailed recommendations to define the parameters of good procedural practice when conducting these studies to ensure reproducibility (see: https://www.ispor.org/RWE-Data-treatment-comparative-effectiveness-guideline.pdf and https://www.ispor.org/RWE-reproducibility-validity-assessment-healthcare-databases-guideline.pdf). Once Reproducibility advances the assessment of validity. Evolving confidence in RWD studies will help to determine when these approaches can be used to augment

regulatory decision making. Notably, outcomes are not often systematically measured in the real-world. Even though progress on analytic methods has been made, the need to demonstrate the RWE can replicate RCTs is nevertheless needed and there are several ongoing initiatives to demonstrate replication. In replication, the selection of the RCTs is important, since not all outcomes or measures are coded in claims data--and sometimes not in EHR data. A final consideration for regulators is determining what replication threshold is sufficient (e.g. 90%, 95% or 99% of selected clinical trials.)

William Crown, OptumLabs

Dr. Bill Crown provided a perspective on one of the key challenges of observational data: confidence in the estimates that are generated. Often with observational data, the accuracy of the measurements of important variables must be evaluated. Claims data –from which most of the retrospective evidence in the US – have known limitations including the accuracy of diagnostic coding, despite the ability of claims data to capture the breadth of services delivered. There is, however, now more widespread availability of EHR, maintained in provider institutions, that appear to contain clinical outcome measures absent from Claims data contained in payer organizations. OptumLabs currently has 130 million lives of commercial Claims data, seven years of Medicare fee-for-service claims data and about 85 million lives of EHR. All data link at the individual level that have all been previously de-identified. In partnership with the MRCT Center, OptumLabs has launched the OPERAND initiative that aims to replicate RCTs that were used for product approval. One of the primary objectives is to develop empirical data to understand data quality – and the limitations of RWD – from various data sources as well as the assumptions necessary to use such data for replication.

Panel Discussion

EHRs contain parsimonious data. Is there any hope that there can be an improvement in the quality of EHR data that will lead to better usability for RWE?

Incentive structures for providers to encourage accurate data capture in EHRs must be developed or encouraged. One mechanism would be to introduce "feedback loops" to illuminate practice patterns, such that the recording physician relatively immediately benefits from insights from the data that was regenerated. There may be "messiness" in the data due to clinical practice, but there may be methodologic approaches to address that. The technology community can also help create software that is visual, easy to use with an embedded data collection system at the point of care, and research-ready. Nevertheless, data quality is expected to improve over time.

Data are not evidence – how can we push that terminology consistently? Additionally, is there consensus that RWE is going to serve as a complement to RCTs rather than a substitute?

It is imperative to distinguish between RWD and RWE. The application of valid analytics to RWD render RWE. The conduct of clinical trials will evolve. At this time, RWE is particularly useful in settings wherein it is difficult to conduct RCTs (e.g. rare diseases), but RWE also provides complemental evidence for RCTs. RWE is not replacing but rather complementing the clinical trial paradigm.

There has been a paradigm shift in the utility of clinical data for regulatory decision-making. How should sponsors approach regulators to exchange ideas and reasonable proposals for stimulating innovation and to develop a path forward?

Early engagement with regulators is important. There are different, non-binding means of engaging with regulators that do not influence future considerations. At the EMA these include business pipeline meetings, scientific advice, and protocol assistance mechanisms. At the EMA these predominantly center around scientific advice but other opportunities exist including business pipeline meetings and the Innovation task force. At the FDA there is heterogeneity on engagement processes across divisions, but there is a formal mechanism for consideration of RWE through the Office of Medical Policy.

There has not been much progress in terms of having common standards and interoperability of date. Will this become a reality in the near term?

The challenge of interoperability has been a focus of technology companies and progress is being made. The FDA's Sentinel Initiative has also been working on common data models. In Europe, the heterogeneity of data remains a challenge but a topic that the EMA is actively discussing.

Who will have access to RWD? Will RWD be transparent? Will "citizen scientists" also have access to these data?

OptumLabs makes data open to collaborators but at a cost, to reimburse for to cost of database infrastructure. The Brigham and Women's Hospital has obtained longitudinal data for about 350 million lives. These data were, however, licensed from various organizations and data use agreements do not allow for data to be shared with others. One approach to circumvent this restriction has been to share the analytics of the data for people who wish to view it, through a transparent and dynamic database system with an analytical interface.

Vivli: Global Clinical Trial Data Sharing Platform

Rebecca Li, Vivli

Dr. Rebecca Li, Executive Director of Vivli, Inc., introduced Vivli as a solution to the current, fragmented landscape in which clinical research data are hosted and shared. At present, there are over sixty sites that offer data hosting and sharing services; however, there is variation in these sites' standards, policies, security mechanisms, and accessibility, creating a data sharing environment in which there are both duplications of effort and gaps of capacity. What is missing from the current landscape is a global, neutral data sharing platform that could create economies of scale by introducing sustainability to the data sharing enterprise. Scheduled for public beta launch in March 2018 and formal launch in July 2018, Vivli is envisioned to be the complete solution to present shortcomings. As a 501(c)(3) non-profit entity, Vivli's primary function is to be a neutral convener for all stakeholders—including pharmaceutical, biological, and biomedical device companies, academia, non-profit funders and foundations, government funders and regulators, patients, and patient advocates. Vivli will address governance and policy challenges of data sharing by developing harmonized language and agreements. As a platform, Vivli will also enable streamlined data submission, data request, data access, and sharing of academic credit by offering the following features:

- User-friendly interface
- Data hosting for data contributors, as needed
- Secure, full-featured analytic environments and tools in which researchers may perform analyses
- Aggregation of data from multiple contributors
- Harmonized, transparent governance

Vivli is excited to be working with Microsoft and BlueMetal on the creation of the Vivli platform; the partnership was made possible by the support of the Doris Duke Charitable Foundation, the Helmsley Charitable Trust, the Laura and John Arnold Foundation, Lyda Hill, PhRMA, and Ropes & Gray LLP.

Paul Slater, Microsoft

Mr. Paul Slater, Chief Technology Officer Life Sciences at Microsoft, described how the collaboration between Microsoft, BlueMetal, and Vivli brings together long-standing leaders in technology and digital health to transform how clinical trial data are analyzed and shared. Microsoft's mission—to empower every person and every organization on the planet to achieve more—aligns seamlessly with Vivli's—to promote, coordinate, and facilitate clinical research data sharing through the creation and implementation of a sustainable global data-sharing enterprise. Microsoft seeks to enable innovation, to increase efficiency of drug development, to

demonstrate treatment effectiveness, to enhance regulatory compliance, and—ultimately—to democratize data sharing. Vivli's commitment to promoting the ethical and transparent use of data, making individual participant-level data more widely available, and bringing data sharing into the public sphere therefore embodies the Microsoft spirit. For this reason, Microsoft has committed to build Vivli on the Microsoft Azure platform, offering flexibility, advanced security capabilities, and global reach. Vivli is one of five Microsoft-supported initiatives chosen across a variety of industries to demonstrate how cloud services can support the contextual usage of data while preserving data provenance. Microsoft is providing a platform that allows parties with shared and competing interests to collaborate effectively, which will be key to Vivli's success as a neutral third party to industry and academic stakeholders.

Ida Sim, UCSF

The first public preview of the Vivli platform was led by Dr. Ida Sim, Vivli's Technical Lead and a professor of medicine at the University of California, San Francisco. The Vivli platform was constructed as part of the Vivli Pilot by BlueMetal, an Insight Company that specializes in digitally transforming healthcare and life sciences companies into continuously learning health systems. The Vivli Pilot, which begins in March 2018, will test a number of Vivli's technical features, including the provision of individual participant-level data in a research environment, metadata ingestion, the data contributor interface, and the analysis environment. Once the Vivli platform is publicly launched in July 2018, its search-and-request interface will be available for all listed studies, and its research environment will allow for data integration with powerful statistical tools. During her presentation, Dr. Sim demonstrated the technical capabilities of the Vivli platform from the perspective of a researcher, who would use Vivli to search for, locate, request, and analyze a set of studies. For a study to be searchable and findable by a researcher on the Vivli platform, Vivli will curate study information from final protocols, clinical study reports, and ClinicalTrials.gov. Using the Cochrane vocabulary, it then describes that study using the **P**opulation, **I**ntervention, **C**omparators, and **O**utcomes (PICO) framework. This enables precise searching of description-rich source data, which allows researchers to target and request studies that are most useful to them. Through Vivli's harmonized data request form, researchers may request access to multiple data sets at once. If the data request is approved, the holders of the requested studies will provide either a basic or a full individual participant-level data package ("IPD Data Package") to a secure analytic environment, wherein researchers can combine data across studies and perform analyses. To link to the broader ecosystem of data sharing, Vivli will mint digital object identifiers (DOIs) for metadata records of Vivli-listed studies, submitted data requests, primary IPD data sets, and datasets underlying secondary analyses. Having DOIs for these objects allows for future citation of researchers' datasets, which is critical for establishing academic credit.

Pablo Gazmuri, BlueMetal

Pablo Gazmuri, BlueMetal's principal architect of the Vivli platform, demonstrated the technical capabilities of the Vivli platform from the perspective of a data contributor. When a researcher requests access to a dataset through Vivli's harmonized data request form, the contributor of that dataset is given the option of performing a sponsor check prior to review by an independent review panel. In this way, Vivli respects contributors' review processes and data use terms while providing researchers with a centralized mechanism for request.

Panel Discussion

The Vivli Pilot is very U.S. centric, but standards for anonymization of datasets differ outside of the United States. How will Vivli confront this reality?

The eventual goal of the data sharing enterprise is to harmonize anonymization processes across the globe. However, Vivli is one piece of a larger puzzle and cannot change the culture of data sharing singlehandedly. That being said, Vivli will encourage users to embrace a harmonized approach to anonymization, and will actively work to protect against the formation of artificial boundaries around datasets.

Are there any plans to upload the secondary analyses or research outputs onto the Vivli platform?

Vivli will assign each secondary dataset its own DOI, which enables that output to be searchable and discoverable on the Vivli platform. Assigning a DOI to each secondary dataset promotes accountability and transparency in secondary research, which Vivli fully endorses.

Is Vivli worried about the potential of data requestors to confuse the public by generating and publicizing erroneous information?

Microsoft, BlueMetal, and Vivli agree that the problem of "junk science" is not solved by making data less available. Vivli is committed to highlighting instances in which data are misused, but it will do so in pursuit of promoting transparency in the data sharing process.

Core Competencies for Clinical Research Professionals

Stephen Sonstein, Eastern Michigan University and MRCT Center

Dr. Stephen Sonstein explained that the Joint Task Force (JTF) for Clinical Trial Competency was established in 2013 since there were few standards or educational requirements for clinical research professionals. Subsequently, the JTF compiled and harmonized competency statements available from various professional organizations and created a harmonized core competency framework for the clinical research professional, first published in 2014.

In October 2016, individuals from organizations around the world who had utilized the framework convened at Harvard to present case studies and to make suggestions for the revision of the framework. Since that time, many suggestions have been addressed, namely: (1) a website has been created (Clinicaltrialcompetency.org) which enables the clinical research community to review JTF activities, provide input into future iterations of the Framework and post how their own organizations have utilized the JTF contributions to enhance workforce development efforts, (2) the framework has been revised based on suggestions received and Version 2.0 has been released, (3) a workgroup is currently expressing the competency statements within the Framework to reflect entry level, mid-level and advanced level knowledge, skills and attitudes.

Workgroup members gave examples of how they have used or intend to utilize the competency framework:

Rebecca Brouwer, Duke University

Ms. Rebecca Brouwer has been involved in site-based research and utilized the core competency framework to facilitate professional development. Her team revised the organization's clinical research role descriptions and reduced the number from 81 to 10, based on the core competency framework. Competencies for professional development were levelled in tiers for the majority of their research professionals: Fundamental (needs coaching), skilled (works independently), advanced (is the go-to expert, provides training). These "tiered positions" are used as a basis for advancing staff in job categories, e.g., coordinators, regulatory coordinators, program leaders. Based on objective assessment of applied knowledge--preferably through direct observation, but also self-report, case studies, knowledge assessments, review of documents--individuals move to higher levels of competency if they reach the requirements defined for the next tier of the levelled competency. About 10% of their workforce is currently going through assessment. Version 2 will be streamlined since assessment is laborious, especially for experienced positions who have to be tested on all

competencies. More information can be found on the Duke CRPWG website (https://medschool.duke.edu/research/clinical-and-translational-research/duke-office-clinical-research/about-clinical-research-and-navigating-research-duke/staffing-clinical-research).

H. Robert Kolb, University of Florida

Mr. Robert Kolb is using levelled competencies for the training of clinical research coordinators. He emphasized that having a competent workforce is important for safer clinical trials, protecting people in studies, and for better data integrity. He has collaborated in a study, published this week in *The Qualitative Report*[1] about a 2-day standardized training based on the competencies for a group of novice and experienced coordinators, showing that" one size of training does not fit all." The authors found that there is a need to target training – not just for novice and experienced coordinators, but according to the requirements of the specific study. While the concept of targeting training is important, the levelled competencies create tools to target content for professional development.

William Gluck, Durham Technical Community College

Dr. William Gluck has utilized levelled competencies in collaboration with pharmaceutical companies and clinical research organizations (CROs). They assessed that there were over 14,000 different role descriptions for clinical research professionals and that a large number were very similar but used different names. In the absence of understanding the specific demands of the job, unnecessary time and effort is expended to find appropriately qualified individuals. Dr. Gluck recommends that candidates for the job be evaluated by competencies not expertise. In addition, he suggested candidates be encouraged to become professionally certified and that the certification process be based on the core competencies.

Carolynn Thomas-Jones, The Ohio State University

Dr. Thomas-Jones is using competencies to have students create professional portfolios in her work as a trainer and academic educator. When utilizing objective assessment of competencies to create portfolios students can demonstrate their skills and show what they have achieved in their academic course work. Initially, Dr. Thomas-Jones used portfolios in low-resource countries in South America when teaching clinical research in order to give students a means to share via PowerPoint presentations of what they learned. Then, *WordPress* became available for e-portfolios in academic courses; however, this software lacked connectivity and had other issues. The current system that Dr. Thomas-Jones is using is called *Portfolium,* a digital portfolio that allows students to upload materials (e.g. data management plan, case report forms,

[1] Behar-Horenstein LS, Potter JE, Prikhidko A, Swords S, Sonstein S, Kolb HR. Training Impact on Novice and Experienced Research Coordinators. The Qualitative Report. 2017 Dec 1;22(12):3118-38.

consent forms.) Students manage portfolios according to core competency domains. Some students have appended the portfolio URL for job applications as one means of assessment for core competencies.

Panel Discussion

The profession of clinical research is evolving. What are efforts to standardize the evolving profession?

Dr. Sonstein acknowledged that the profession of clinical research became an academic discipline about 20 years ago. While about 100 academic programs exist that educate clinical research professionals, each evolved independently and similar content is taught in entry and advanced degree programs. Utilizing the levelled core competencies will enable the process of academic program standardization. Dr. Sonstein is chairing a committee on accreditation which functions under CAAHEP (Commission on Accreditation of Allied Health Education Programs) that offers the first academic program accreditation process for the clinical research profession. The next step is to follow the standard health professional model and link academic education, hands-on experience (internship, preceptorship) and professional certification.

We see an increasing demand for patients as study participants. How can patients be integrated into the core competency framework?

People from across the community participate in a community engagement board at the University of Florida to advise on development of protocols. This is an example of bringing participants in as team members. Additional efforts should be made.

How should one deal with a profession in which the Principal Investigator may not meet the entry level competencies?

Since there is virtually no clinical research related content in the medical school curriculum, mentoring has been the standard method whereby investigators learn about delegated responsibilities and to "know what you don't know." In many cases study coordinators are responsible for caring for clinical trial participants. It is time to raise the issue of core professional responsibilities, professional development, delegation of authority, and collaboration for clinical investigators.

How to give more credibility to observational studies?

While interventional clinical trials are the ones most often utilized for the approval of new medicines, a very large number of investigator initiated studies are observational in nature.

They should also be functioning within the competency framework. As concerns the competencies, there should be very little distinction between interventional and observational studies.

Return of Individual Results: Genomics and Axes of Communication in Results Return

Sandra Prucka, Indiana University

Ms. Prucka explained the objectives of the workgroup: (1) determine principles that can guide the return of individual research results, (2) determine methods to facilitate the return of individual results, and (3) develop best practices and a framework for communicating the results. The output of this workgroup can be seen in the deliverables: Principles Document, Recommendations Document, and Toolkit for the Return of Individual Results to Participants.

Ms. Prucka highlighted the data types diagram (included in Recommendations Document and Toolkit) that illustrates the types of data that are generated during a clinical trial. The diagram indicates what the workgroup recommended as most appropriate for returning to participants. During the last year, the work has focused on (1) how investigators and physicians provide information to participants, and (2) how to communicate exploratory results, in particular, genomic results.

The overall principles from the Recommendations Document for returning individual results are applicable to genomics. In addition, there are further considerations—including evolving knowledge and technologies, results which may not be actionable but useful for family planning, complexities involved with delivering results which impact a family and not just the individual, , right to refuse results, and international laws and regulations—which led to discussion in the workgroup. For example, large data sets may include information that is relevant for an individual but may not be related to the research question. These data may also be generated only years after a clinical trial concludes and scientific understanding of the results implications for healthcare management may only be understood years after the result was generated. What is the threshold for returning results? Is there responsibility to "hunt" for medically actionable data? Where is the comfort level for not returning medically actionable data if the participant refused to receive results? To whom can one release genetic information after the trial finished and still maintain privacy? The Recommendations Document provides a deeper understanding of these complexities while the Toolkit provides additional resources to aid in addressing some of these complexities when putting together a data return plan.

Once a plan for data return is in place it becomes essential to effectively communicate this plan to research participants. The Toolkit includes special considerations for informed consent documents such as how to address privacy, access to genetic information, the impact the results may have, and the impact of withdrawing from the study. The Recommendations Document and the Genomics section also address how to return and who will return results. For Genomics, it is essential to communicate that results are probabilistic, not deterministic. It is also important to communicate the results to appropriate individuals and to make sure they know with whom to follow up for questions. National laws, regulations and ethics guidance govern which information we are able to share. In some countries, research participants are allowed to request any information generated about them in a clinical trial, no matter how preliminary. The Toolkit provides resources to better understand current laws and regulations, and recommends using the informed consent process to communicate to research participants how the regulatory landscape can impact their ability to request and receive this information.

Joan Chambers, CenterWatch (currently SCORR Marketing) and Jessica Scott, GlaxoSmithKline

Dr. Scott introduced a survey about at the axes of communication between principal investigator, treating physician and participant/patient in regard to communicating results from clinical trials. This survey was conducted in order to understand current practice and preferences with regard to what might be an "ideal" practice as to whom and how to communicate study results to participants.

Ms. Chambers gave an overview of the study design. The survey built on results from telephone interviews conducted in the Fall of 2016. An online survey was sent to a list of 20,000 global investigators and some practicing physicians and was available for responses from June to September 2017. The largest group of respondents (48%) were those who serve as both principal investigators and treating physicians. 43% respondents were from Europe, and 35% of respondents had 21 years or more experience in clinical research. The sample size of 160 was small in part because it was a complex survey. The most frequently represented therapeutic areas were neurology, oncology, and cardiology.

Dr. Scott highlighted the results that the survey had a response rate of only 1%. Nevertheless, the 160 responses demonstrated that while 88-95% of investigators and treating physicians agreed that investigators should receive results, approximately half of investigators never receive these results from sponsors. Furthermore, 69-91% of investigators and treating physicians agree that results should be shared with treating physicians and with patients, while 40-83% have never shared results with treating physicians and 40-71% have never shared results with patients. This was consistent across the five types of results that the survey asked about (aggregate results, study group assignment, individual primary endpoint result, routine

results, and urgent results). When asked who should share the results with study participants, approximately half think investigators should share results while about a third think either investigator or treating physician should share results. The main barriers for sharing results with participants are perceived to be both lack of access to results and apparent lack of interest by the patient in receiving results. Approximately half of the respondents suggested tools to help in returning results: the exchange of contact information between investigator and treating physician at the beginning of the trial, patient consent for the investigator to contact treating physician, and investigator sharing of periodic updates with treating physicians. Thus, potential pragmatic solutions were identified. Feedback from MRCT Center sponsors and from a future Bioethics Collaborative meeting were encouraged.

Elizabeth Cahn, Dana-Farber/Harvard Cancer Center Breast Cancer Advocacy Group

Dr. Cahn raised three points from the perspective of research participants: (1) what seems "small data" in research is of "big data" and of central importance to individual participants as participants make decisions about what to do with each data point; (2) study participants have a different relationship to their data than researchers since participants have to cope with a series of data points over a period of time, even after the researcher is no longer involved, and participants also have highly disparate levels of health literacy; (3) it is important for researchers to be involved with patients and patient advocacy groups who are affected by their research. The closer the researchers can remain to the people who are affected by the research, the better outcomes they may be able to get.

Robert Green, Brigham and Women's Hospital

As an opening statement, Dr. Green said, "something makes people crazy about genomic data" and he argued to "de-exceptionalize" genomic information. He also stated that there is no standard of care for how to handle unanticipated findings.

Dr. Green appreciated the organized, comprehensive, thorough and thoughtful approach that the MRCT Center workgroup had taken in developing their documents, although he cautioned on the use of some terminology. Clinical validity in genomics needs contextualization in terms of family history, symptoms, age, and how much one may care. Actionability needs to be used carefully since there is no agreement on its definition between clinicians and patients. Dr. Green appreciated the focus on involving treating physicians in returning of study results in the MRCT Center materials.

Dr. Green addressed three challenges: (1) What should we do when people want raw data? (2) What can be done to harmonize the MRCT documents with similar reports from the National Academy, Global Alliance for Genomic Health, Susan Wolf and other groups so as to harmonize for worldwide consensus? (3) Is there a mandate to collect data on what happens when results

are returned? If not, we are making decisions without data. The return of genomic information is an intervention, and we need rigorous data to understand its implications.

Moderator Mark Barnes mentioned that he is part of the Susan Wolf project and SACHRP committee and that reports and information have been exchanged with the National Institutes of Health and the National Academy of Sciences. Thus, the various initiatives have communicated.

Scott Kennedy, Novartis

Dr. Kennedy also appreciated the comprehensive, yet intertwined, nature of the Recommendations Document and Toolkit that have been developed by a diverse group of individuals. He commended the fact that the materials are written as instructional but not prescriptive documents, containing significant guidance in the form of a 61-step checklist of points to consider, 19 regulatory guidance references and an ICF prototype for patients to express their wishes. He appreciated the reference to participants rather than patients and acknowledged the voluntary nature of their participation and therefore the responsibility to share results if participants want to have them. It is important to ensure that participants understand the decisions they are making, not simply signing a long or overly complicated form.

Sponsors rely on principal investigators to enroll and interact with trial participants. Therefore, Dr. Kennedy found the survey quite informative. He was surprised that such a low percentage of investigators and physicians receive information from sponsors and this represents an opportunity for improvement.

Dr. Kennedy reminded the audience that in complex, common diseases such as Alzheimer's disease, asthma, and obesity there are no or extremely limited validated genomic variants suggesting causation, but largely variants of unknown significance. Thus, the concept of clinical validity and medical actionability can differ greatly between cancer-genetics and non-cancer diagnoses and genetic associations. We need to be cognizant of the intent to do good versus harm by returning too much or too little information and do so with the appropriate genetic counseling expertise. Finally, we need to be aware and diligent given that our understanding of genetic variation is rapidly evolving. A cautionary example is a company that is currently being sued for not classifying a variant as pathogenic some years ago when the test results were generated; i.e. non-medically actionable when it subsequently turned out to be the cause of a rare disease and a person's death.

Carol Weil, National Cancer Institute/Institutes of Health

Ms. Weil discussed clinical validity and actionability: there is no single answer as to clinically actionable. Further, returning information is important for participants not only for medical actionability but for family planning, estate planning, and other personal decisions.

Respect for autonomy demands that participants are entitled to their genetic information including the raw data if they wish to receive it, despite its complexity and potential misunderstanding and/or distress. Fundamentally, individuals have the right to their data and we should be cautious to guard against "creeping paternalism."

There is also a right not to know and thus, we should present research results in such a way that it offers recipients the opportunity to decline and the opportunity to understand what the risks are to receiving the information.

Moderator Mark Barnes mentioned that in the EU, people have a clear right to get data that are traceable to them, particularly after May 2018, and this may extend to the US in time.

Panel Discussion

How to avoid doing unintended harm when returning research results, especially genomic results and other sophisticated medical concepts, realizing that we need to communicate in a manner and a health literacy and numeracy level that is accessible?

Fifteen years of research have thus far found no evidence of catastrophic psychological distress in people who have been apprised of their choice to receive genetic information of any type. A second type of potential harm is false reassurance that appears to confirm the absence of a genetic predisposition but wherein certain mutations may not have been tested. A third type of potential harm is societal harm if tests identify an apparent risk that leads to unnecessary tests, x-rays, preemptive surgery, and other procedures that may not be needed.

We should consider the unique context in which people receive this information in a clinical trial. Most clinical trials do not prepare participants sufficiently to receive genetic results. People volunteer to enroll in clinical trials for various reasons and may be surprised to learn they will be asked to participate in exploratory genomic research and even more surprised to learn they may have the option to receive genomic information that they did not anticipate.

All communication should be in plain language, whether in health care or research. The MRCT Center will initiate a project on plain language communication tools. One notably complex concept is an understanding of risk.

The issue of contextualization is pertinent to the issue of communication. Both the principal investigator and the treating physician should give contextualization to the results when communicating to patients. To date there has been a chasm between study physicians and treating physician that can be improved upon. The involvement of treating physicians who are not investigators in the clinical trial ecosystem is important.

Different communication skills will be required with different patient populations. As young professionals are trained, skills to communicate results with different cultural groups is essential. Different skill sets are required to communicate with these patients as different skill sets are required to recruit them.

An online web portal could give access to every participant and connect him or her with a genetic counselor: https://www.genomemedical.com/ could potentially be helpful.

Closing Remarks

Mark Barnes and Barbara Bierer, MRCT Center

Mr. Barnes thanked the participants for coming and for all the work they have done throughout the year, including contributing to discussions and reviewing documents. He pointed out that the MRCT Center has a small core staff and producing the reports that we have issued would not have been possible without this voluntarism.

Dr. Bierer added her thanks and assured participants that the MRCT Center is open to suggestions, thoughts and comments as people think of them, at this meeting and throughout the year. She added her appreciation for all the work and commitment of this "community of dedicated souls" who aim to make this world a better place.

Appendix 1: Meeting Participants

First Name:	Last Name:	Institution/Affiliation:	Job Title:
Hayat	Ahmed	MRCT Center	Project Coordinator
Carmen	Aldinger	MRCT Center	Events and Training Manager
Salvatore	Alesci	Takeda Pharmaceuticals U.S.A.	Head R&D Global Science & Biomedical Policy
Sarah	Alummootil	Early Access Care	Expanded Access Coordinator
Maria	Apostolaros	PhRMA	Sr. Director, SRA
Andre	Araujo	Eli Lilly and Company	Director, Biomedicines Research, US Health Outcome
Sylvia	Baedorf Kassis	MRCT Center	Program Manager
Jessica	Baker	Center for Bioethics - Harvard Medical School	Masters Student
Mark	Barnes	MRCT Center / Ropes & Gray, LLP	Faculty Co-Director
Karina	Bienfait	Merck & Co, Inc.	Principal Scientist
Barbara	Bierer	MRCT Center	Faculty Director
Paul	Bleicher	OptumLabs	CEO
David	Bobbitt	CDISC	President and CEO
Rebecca	Brouwer	Duke University	Director, Research Initiatives
Erin	Brower	New England IRB, WIRB-Copernicus Group	IRB Chair
Elizabeth	Cahn	Dana-Farber/Harvard Cancer Center Breast Cancer Advocacy Group	Patient and Research Advocate
Elaine	Call	Sunovion Pharmaceuticals	Senior Privacy Counsel
Alison	Cave	European Medicines Agency	Principal Scientific Administrator
Joan	Chambers	Scorr Marketing	Senior Strategic Advisor
Dominic	Chiarelli	Quorum Review	Manager, Legal & Regulatory Affairs

Karla	Childers	Johnson & Johnson	Senior Director, Strategic Projects
Luther	Clark	Merck	Global Executive Director, SMPP
Cathryn	Clary	Novartis Pharmaceuticals	Global Head Patient Affairs and Policy
Theodora	Cohen	Baim Institute for Clinical Research	Executive Director, Biostatistics and ARO Services
Elizabeth	Connolly	BlueMetal	Senior Software Engineer
Cathy	Critchlow	Observational Research	Vice President
Anne	Cropp	Early Access Care	Chief Scientific Officer
William	Crown	OptumLabs	Chief Scientific Officer
Patrick	Cullinan	Takeda Pharmaceuticals	Head of Scientific Advocacy and Transparency Policy
Gina	Daniels	Boston University School of Medicine	Human Research Quality Manager
John	Dornan	Project Data Sphere, LLC	Chief Operating Officer
Peter	Dull	Bill & Melinda Gates Foundation	Deputy Director, Global Health Program
Rebecca	English	National Academies of Sciences, Engineering, and Medicine	Program Officer
Cristin	Freeman	Merck	Assoc. Principal Scientist, GpGx
Pablo	Gazmuri	BlueMetal	Principal Architect
Luke	Gelinas	Petrie-Flom Center	Senior Researcher
William	Gluck	Durham Technical Community College	Program Director - Clinical Trials Research
Robert	Green	Brigham and Women's Hospital, Broad Institute and Harvard Medical School	Professor of Medicine (Genetics)
Anya	Harry	GlaxoSmithKline	Director, Clinical Development
Cindy	Henderson	Veristat	Executive Vice President, Strategic Development
Spencer	Hey	Harvard Center for Bioethics	Faculty

Nina	Hill	Pfizer	VP, Science Policy and Advocacy
David	Hosford	Kowa Research Institute	Chief Medical Officer
Elisa	Hurley	PRIM&R	Executive Director
Carolynn	Jones	The Ohio State University, College of Nursing	Associate Professor- Clinical Nursing
Ariella	Kelman	Genentech, a member of the Roche Group	Global Head of Bioethics
Scott	Kennedy	NVS Institutes for Biomedical Research	VP, Global Head of Biomarker Development
Joanna	Koft	Biogen	Director, Data Standards and Governance
H Robert	Kolb	University of Florida	Assistant Director Clinical Research
Janet	Krause	Biogen	Principal Analyst
Sang Gyu	Kwak	Daegu Catholic Univ. Medical Center (DCUMC) / CIMI	Assistant Professor
Sarah	Larson	Biogen	Director, Clinical Trial Transparency
Marcia	Levenstein	Retired , Pfizer	Statistician
Rebecca	Li	Vivli	Exec director
David	Martin	FDA CDER	Associate Director for RWE Analytics, OMP
Kevin	McCourt	Association of Clinical Research Professionals	Senior Director of Operations
Linda	McMaster	MRCT Center	Administrative Assistant
David	Miller	UCB Biosciences	Head of RWE Methods, Analytics, and Health Econ
Allison	Moriarty	Brigham and Women's Hospital	VP, Research Administration and Compliance
Richard	Moscicki	PhRMA	Chief Medical Officer
Stan	Neumann	BlueMetal Architects	Senior Project Manager
P. Pearl	O'Rourke	Partners HealthCare	Director, Human Research Affairs
Sharon	Pan	Pfizer	Senior Director of Biostatistics

Jeannette	Potts	Takeda Pharmaceuticals	Vice President, Legal
Sandra	Prucka	Indiana University School of Med/Dept. of Medical and Molecular Genetics	Director of Genetic Counseling Clinical Services
Parthena	Psyllos	Pfizer Inc	Senior Corporate Counsel
Joseph	Rhatigan	Brigham and Women's Hospital	Associate Professor
Stephen	Rosenfeld	Quorum Review IRB	Executive Board Chair
Andrew	Sabo	Shire	Associate Director, Clinical Quality & Compliance
Wendy	Sanhai	Deloitte Consulting	Specialist Leader
Rick	Sax	QuintilesIMS	Senior Vice-President, Design & Delivery Innovation
Sebastian	Schneeweiss	Harvard Medical School, Brigham and Women's Hospital	Professor
Jessica	Scott	GSK	Medical Governance
Lewis	Seton	Brigham and Women's Hospital	Senior Grants Administrator
Carmel	Shachar	Petrie-Flom Center	Executive Director
J. Jina	Shah	Roche/Genentech	Bioethics Leader
Im Hee	Shin	Daegu Catholic Univ. Medical Center (DCUMC) / CIMI	Professor
Ida	Sim	UCSF	Professor of Medicine
Paul	Slater	Microsoft	CTO Healthcare
Stephen	Sonstein	MRCT Center	Senior Advisor
Emily	Statham	MRCT Center	Project Coordinator
Walter	Straus	Merck	Assoc Vice President, Clinical Safety & Risk Mgmt
Elyse	Summers	AAHRPP	President and CEO
Magdalena	Taber	Independent Consultant	Independent Consultant

Carol	Weil	National Cancer Institute, National Institutes of Health	Program Director
Sarah	White	Partners Healthcare	Director, Quality Improvement Program
Julie	Wood	Vivli	Director of External Affairs
Crispin	Woolston	Sanofi	Deputy Head, Science Policy

Appendix 2: Meeting Agenda

MRCT Center 2017 Annual Meeting: AGENDA

Wednesday, December 6, 2017

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

7:30 – 8:00	Breakfast & Registration
8:00 – 8:15	**Welcome & Introductions** Moderator: Barbara Bierer and Mark Barnes
8:15 – 8:45	**Keynote** **Alison Cave (European Medicines Agency):** EMA's Perspective on Real World Evidence and Regulatory Decision-Making Moderator: Barbara Bierer
8:45 – 9:45	**Real World Evidence** Panel Discussion: • William Crown (OptumLabs) • Sebastian Schneeweiss (Brigham and Women's Hospital) • Cathy Critchlow (Amgen) • David Martin (USFDA) Moderator: Barbara Bierer Followed by group discussion and Q&A
9:45 – 10:45	**Vivli: Global Clinical Trial Data Sharing Platform** **Vivli – Current progress, opportunities and timeline to launch** **Vivli public preview – Live Demonstration** **Panel Discussion** • Rebecca Li (Vivli) • Paul Slater (Microsoft) • Ida Sim (UCSF) • Pablo Gazmuri (BlueMetal) • Julie Wood (Vivli)

	Moderator: Rebecca Li Followed by group discussion and Q&A
10:45 – 11:00	**Break**
11:00 – 11:45	**Core Competencies for Clinical Research Professionals** Framework Version 2.0 and expectations of professional competencies for advancement • Steve Sonstein (Eastern Michigan University and MRCT Center Senior Advisor) Panel Discussion: • Rebecca Brouwer (Duke University) • William Gluck (Durham Technical Community College) • H. Robert Kolb (University of Florida) • Carolynn Thomas-Jones (The Ohio State University) Moderator: Steve Sonstein Followed by group discussion and Q&A
11:45 – 12:45	**Return of Individual Results: Genomics and Axes of Communication in Results Return** Presentation: • Sandra Prucka (Indiana University) • Joan Chambers (CenterWatch, currently SCORR Marketing) • Jessica Scott (GSK) Panel Discussion: • Elizabeth Cahn (Cancer Connection) • Robert Green (Brigham and Women's Hospital) • Scott Kennedy (Novartis) • Carol Weil (National Institutes of Health) Moderator: Mark Barnes Followed by group discussion and Q&A
12:45 – 1:00	**Closing Remarks** Moderators: Barbara Bierer & Mark Barnes

Appendix 3: Speaker Biographies

Rebecca Namenek Brouwer, MS is the Director of the Duke Office of Research Initiatives. In this role, she is responsible for providing strategic and operational leadership of special research initiatives and engagement activities for Duke researchers. Previously she was the Associate Director of Clinical Research Operations in Duke's School of Medicine, responsible for Training, Communication and Outreach for the clinical research community at Duke. Through both of these activities, she has supported staff and faculty in the conduct of clinical research, which led to a strong understanding of the skills and expertise needed to function successfully in clinical research in an Academic Medical Center. Rebecca has served on the Clinical Research Professionals Working Group (CRPWG) at Duke since its inception in 2013. The CRPWG aimed first to simplify the number of job classifications and use a competency-based approach to professionalize the clinical research professionals working environment. The group successfully mapped all incumbent staff into the new positions, and has developed and implemented a competency-based approach to professional advancement.

Ms. Brouwer joined Duke in 2000. Prior to this, she received a B.S. from the College of William & Mary, and an M.S. from Eastern Michigan University.

Elizabeth Cahn, PhD, is a member of the Dana-Farber/Harvard Cancer Center Breast Cancer Advocacy Group and the Rays of Hope Center for Breast Cancer Research Advocacy Council (Springfield, MA). She is a breast cancer survivor and BRCA1 mutation carrier, and has been involved in cancer research advocacy since 2007. She also has extensive experience as a caregiver for family members with cancer and traumatic brain injury.

Elizabeth is employed as Program Coordinator at Cancer Connection, a community-based non-profit in Northampton, MA, that provides support services for individuals with all types of cancer as well as their caregivers and families. Prior to this, she worked in the fields of architecture and planning, in higher education, and in community outreach related to women's health and public safety.

Elizabeth has undergraduate degrees in Fine Arts and Architecture and master's degrees in Architectural History, Theory, and Criticism and Art Therapy. She earned a PhD in Regional Planning from the University of Massachusetts Amherst, where she also completed the Certificate in Advanced Feminist Studies. She lives in Amherst, MA, where she is a member of the Human Rights Commission.

Dr. Alison Cave joined the European Medicines Agency in January 2016 as a Principal Scientific Administrator in the Pharmacovigilance and Epidemiology Department where she leads on developing mechanisms to increase capacity in the use of real world data in medicines regulation. She also co-chairs the Joint HMA-EMA Big Data taskforce which is exploring the regulatory challenges presented by Big Data. She holds a BA Honours degree and PhD from the University of London and has over 20 years of academic research experience in the cardiovascular field. Prior to joining the EMA she was Head of Cellular, Developmental and Physiological Sciences at the Welcome Trust and, prior to this, an Expert Scientific Assessor at the UK Medicines and HealthCare products Regulatory Agency

Joan A. Chambers, Senior Strategic Advisor, SCORR Marketing. With more than 20 years of experience in the clinical trials industry, Joan is a health science executive who brings a unique blend of strategy, leadership and competitive intelligence skills to SCORR's clients. She designs and executes collaborative solutions that drive brand awareness and improve market share and profitability.

As a published author and presenter at many industry conferences, Joan synthesizes her understanding of critical issues and business challenges into viable client solutions. She advises on thought leadership opportunities that maximize SCORR's clients' visibility and impact.

Prior to joining SCORR, Joan was the chief operating officer at CenterWatch, where she set the strategic direction and financial goals for the organization and managed all departments. Her career also included roles at Cambridge Healthtech Institute, the Tufts Center for the Study of Drug Development and PAREXEL.

Cathy W. Critchlow, PhD, Vice President, Center for Observational Research, Amgen, Inc. As Head of the Center for Observational Research (CfOR), Dr. Critchlow provides operational and strategic leadership for the design and conduct of observational research within Amgen. The CfOR Real World Data (RWD) Platform provides widespread access to patient health data and visualization and analytic tools based on innovative technologies to aid teams in the generation of real world evidence in support of drug development and commercialization of Amgen products.

Dr. Critchlow joined Amgen in 2004 where she led a number of Therapeutic Areas within Global Epidemiology prior to her being named Head of CfOR in 2012. Prior to joining Amgen, Dr. Critchlow was a faculty member in Epidemiology at the University of Washington. Dr. Critchlow was a member of the Endocrinologic and Metabolic Advisory Committee of the Food and Drug Administration and has served on a number of research review committees for the National Institutes of Health.

Dr. Critchlow earned her bachelor's degree from Stanford University, and both her master's degree in biomathematics and her doctorate degree in epidemiology from the University of Washington. Dr. Critchlow is an Affiliate Professor of Epidemiology at the University of Washington and a Fellow of the American College of Epidemiology.

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.

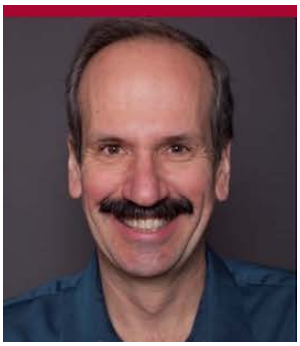
Dr. Crown is currently affiliate faculty, Mongon Institute for Health Policy, at Harvard University.

Pablo Gazmuri, Principal Architect, BlueMetal. As an IT leader with 20 years of experience in the field, Pablo has participated and led numerous web-based and rich client software development projects using a diverse range of technologies. These include custom .NET applications, portals (intranets and extranets including search and social features), custom search implementations, mobile apps, public facing websites, and cloud-first applications. Through client engagements, Pablo has gained experience in legal, medical, pharmaceutical, consumer products, retail, manufacturing, energy, financial, and other industries.

William Gluck: Dr. Bill Gluck serves as the Program Director for the Clinical Trials Research and Medical Product Safety/Pharmacovigilance programs at Durham Technical Community College in Durham North Carolina. He is also the President of the Consortium of Academic Programs in Clinical Research and a Commissioner on the Commission on Accreditation of Allied Health Education Programs. Bill began his career in academia at the community college and university levels in 1980. Prior to returning to academia in 2014, Dr. Gluck spent more than 32 years in various management roles in sponsor companies, CRO's, and technology development organizations. He is recognized for his expertise in clinical data management and has been an invited international speaker on EDC, eSource, RBM, and the critical importance of process adaptation as a critical component in optimizing technology. Dr. Gluck has a Bachelor of Science degree from the University of Scranton and Master and Ph.D. degrees from North Dakota State University.

Robert C Green, MD, MPH is Professor of Medicine at Harvard Medical School, and directs the Genomes2People Research Program in translational genomics at Brigham and Women's Hospital and Broad Institute. He conducts empirical research on the medical, behavioral and economic outcomes around the implementation of genomic medicine. Dr. Green currently leads and co-leads the first randomized trials to explore the implementation of medical sequencing in adults (MedSeq Project) and newborns (BabySeq Project). With support from the Air Force, and in collaboration with military medicine colleagues, he is developing an exome sequencing implementation study to be conducted in active duty military personnel (MilSeq Project). Scientific contributions include publication of the first randomized trials to assess the impact of common complex genetic risk markers, empirically measuring the outcomes of DTC genetic testing, design of a variant interpretation pipeline and single page summary for reporting clinical results of whole genome sequencing. Dr. Green was lead author on the original recommendations for managing incidental findings in clinical sequencing from the American College of

Medical Genetics and Genomics and led the first study of aggregate penetrance of genomic variants in an unselected population. He recently published the first randomized trial to assess whole genome sequencing in primary care.



Dr. Scott Kennedy is Vice President and Global Head of Biomarker Development, Translational Medicine, for Novartis Institutes for Biomedical Research.

Scott leads a global group of scientists who work in partnership with Novartis and external translational biologists, physicians and companies to develop stratified medicines for all stages of clinical development. His group applies state of the art imaging, proteomic, genetic, genomic, cellular and computational approaches to address clinical and biological biomarker questions. In addition, Scott leads a cross divisional team ensuring access and appropriate use of human tissue for translational research.

After completing a post-doctoral fellowship at Yale University School of Medicine Department of Pathology, Scott joined Alexion Pharmaceuticals, a biotechnology start-up company focusing on treatments for transplant rejection and inflammatory diseases. He moved to Pfizer Global Research and Development where he assumed increasing levels of responsibility, including Head of Biology Research, Vice President of Development in Drug Safety Research and Development, and Head of Pfizer's External Research Network. Prior to joining NIBR in 2010, Scott served as Chief Scientific Officer for RainDance Technologies, a biotechnology start-up company focusing on microdroplet technology applications in next generation sequencing and single cell analysis.

Scott received his B.S. Biochemistry from Trinity College and Ph.D. Immunology from the University of Connecticut Health Center.

H. Robert Kolb, RN, MS, CCRC, is Director of Clinical Research Coordinator programs with the University of Florida Clinical Translational Science Institute's (UF CTSI) Workforce Development Directorate and Assistant Director of UF CTSI's Regulatory Knowledge and Support services. In addition he designated as Research Participant Advocate as well as Chair of UF CTSI's Research Professionals Advisory Council. With over 30 years of direct clinical and administrative experience Robert's back ground includes experience as Research Programs Coordinator, Coordinator Clinical Programs, Assistant Director Clinical Research and Research Consultant, as well as Utilization Review, Pediatrics, Critical Care, Emergency Medicine, Physical Rehabilitation, Cardiology, Oncology, and Communications. He has worked in a variety of relevant settings ranging through industry and the academic sectors, as well as Veterans Affairs Research Service. He has worked on NIH funded, Industry

Sponsored, and VA Cooperative studies and conducted, managed or consulted on hundreds of protocols, from international multi-center trials to investigator initiated studies, and from Phase 1 through 4, including Genetics and Pharmacogenetics. A board certified Registered Nurse since 1977, he is also a longstanding member of the Association of Clinical Research Professionals (ACRP) and has held a Certification as a Clinical Research Coordinator (CCRC) for over 20 years. With degrees in Technical and Health Communication his broad academic exposure includes relevant areas of focus such as Health Care Marketing and Management, Health Education, Nursing and Psychology, with work in Project Management, Research Administration, Nursing Research, Nursing Informatics and Drug Development Informatics.

David Martin, MD, MPH is the Associate Director for Real World Evidence Analytics in the Office of Medical Policy at the US FDA Center for Drug Evaluation and Research. He provides oversight for the FDA Catalyst program, the Effectiveness Research with Real World Data to support FDA's Regulatory Decision Making program, and other demonstration projects intended to support the agency's evaluation of real world evidence which is mandated by the 21st Century Cures Act. He is a member of the Medical Policy Subcommittee which will review real world evidence included in submissions to CDER and contribute to policy development. He is also involved in opening Sentinel resources to the public through the IMEDS program, and he is the principal investigator for the first study to capture patient-provided data through a mobile device application, store it in a secure repository, and link it to electronic data in Sentinel and PCORnet.

As a former Branch Chief, Division Director, and Acting Deputy Office Director in the Center for Biologics Evaluation and Research, 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, Dr. Martin practiced flight and occupational medicine in the U.S. Air Force. He received his M.D. and M.P.H. from the Johns Hopkins University, and he is a Fellow of the American College of Occupational and Environmental Medicine.

Sandra Prucka, M.S., LCGC, is the Director of Genetic Counseling Clinical Services and Asst. Professor of Medical and Molecular Genetics at Indiana University School of Medicine. She currently co-chairs the MRCT Individual Research Results Working Group.

Sandy joined the Dept. of Medical and Molecular Genetics in August of 2017. Her primary role is to lead the vision and strategic plan for the provision of genetic counseling services and expansion of these services into new areas. This will include the development of leadership, research,

and outreach capabilities and promotion of educational efforts for the genetic counselors she supervises within the department to ensure continued delivery of excellence in clinical care.

After completing her Masters in Genetic Counseling at the University of Pittsburgh School of Public Health, Sandy joined the University of Alabama at Birmingham (UAB) where she provided genetic counseling in the areas pf pediatric, prenatal, cardiovascular, and cancer genetics and assumed the role of Director of Genetic Counseling Services for UAB. In 2009 Sandy joined Eli Lilly and Company working for the next 8 years primarily in the area of Tailored Therapeutics. In this role she supported pharmacogenomics and biomarker sample collection efforts from global clinical trials with specific expertise in the areas of bioethics, global laws/regulations affecting biomarker research, informed consent and genetic education. Due to her expertise in these areas Sandy served as the co-chair (2015-17) of the Industry Pharmacogenomics Working Group (I-PWG), is the current I-PWG Education and Communication Task Force Leader (2013 – present), and was a member of the Innovative Medicines Initiative Coordination and Support Action for Data Privacy (2015-17).

Sandy received her B.S. in Cellular and Molecular Biology from the University of Michigan and her M.S. in Genetic Counseling from the University of Pittsburgh School of Public Health.

Sebastian Schneeweiss, M.D., Sc.D., is Professor of Medicine and Epidemiology at Harvard Medical School and Vice Chief of the Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, a world-leading research and training center. His NIH, PCORI, and FDA-funded research focuses on the comparative effectiveness and safety of biopharmaceuticals. He has developed analytic methods to improve the scientific validity of epidemiologic analyses using complex longitudinal healthcare databases for newly marketed medical products. The overarching theme of his research is applying advanced real world data analytics for regulatory decision making transparently and in rapid cycles in the US and EU. His work is published in >350 articles.

Dr. Schneeweiss is Director of the Harvard-Brigham Drug Safety Research Center funded by FDA/CDER and Co-Chair of the Methods Core of the FDA Sentinel Initiative. He is voting consultant to the FDA Drug Safety and Risk Management Advisory Committee. He was President of the International Society for Pharmacoepidemiology, inaugural member of the PCORI Methods Committee and is Fellow of the American College of Epidemiology, the American College of Clinical Pharmacology, and the International Society for Pharmacoepidemiology.

At Harvard he teaches courses on *Database Analytics for Pharmacoepidemiology* and on *Effectiveness Research in Longitudinal Healthcare Databases* among others.He received his medical training at the Ludwig-Maximilians University of Munich and his doctoral degree in pharmacoepidemiology from Harvard.

Jessica Scott, MD, JD: Director, North America Medical Policy and Advocacy. Jessica received her M.D. from Tufts University School of Medicine in Boston, Massachusetts (1993), completing her residency in Family Medicine with the University of Virginia. She practiced Family Medicine in North Carolina for more than a decade, leaving her medical practice in 2012 to join GlaxoSmithKline. Jessica also attended Campbell University School of Law, graduating with honors with admittance to the NC Bar in 2010, where she is currently licensed. Jessica has served on the NC Bar Association Health Law Section Council and the Ethics Committee. She is a certified mediator with advanced certification having mediated over 60 cases. She has instructed both mediation and collaborative law training courses and has worked in law firms on issues related to health care and medical errors. In 2011, Jessica pioneered and led the development and implementation of an innovative program for improving patient outcomes through early dispute resolution in her role as Director, Healthcare ADR Innovation at Carolina Dispute Settlement Services. Entitled the Integrated Accountability & Collaborative Transparency (IACT) Program, this initiative is well underway in NC and is currently before the NC General Assembly for consideration as a state-wide pilot program with multi-stakeholder support as it couples increased disclosure, dispute resolution and the patient safety movement.

In her role at GSK, Jessica sits within the Global Medical Organization, leading efforts related to clinical trial transparency, the development of plain language summaries, and patient partnership efforts, engaging extensively with external entities and workgroups including Harvard Multi-Regional Clinical Trial Center, TransCelerate BioPharma, the Health Research Authority's Layperson Summary Task Force, PhRMA and the National Academies of Science, Engineering and Medicine.

Ida Sim, MD, PhD is Professor of Medicine at the University of California, San Francisco, and Co-Director of Biomedical Informatics at UCSF's Clinical and Translational Sciences Institute. Her research focuses on computational methods for data sharing and decision making for clinical research and mobile health. She is Co-Founder and Technical Lead for Vivli, a global data sharing platform for participant-level trial data. In 2005-6, she led the World Health Organization's International Clinical Trials Registry Platform which established the first global policy on clinical trial registration and defined the common Trial Registration Data Set.

Dr. Sim is also co-founder of Open mHealth, a non-profit organization building open APIs and tools for integrating mobile health data. Dr. Sim has served on multiple national advisory committees on health information infrastructure for clinical care and research. She is a recipient of the United States

Presidential Early Career Award for Scientists and Engineers (PECASE), a Fellow of the American College of Medical Informatics, and a member of the American Society for Clinical Investigation. She is also a practicing primary care physician.

Paul Slater: Director, and Worldwide Industry Strategist, Pharmaceuticals, Microsoft Corporation.

Paul Slater is the Worldwide Industry Strategist for Pharmaceuticals in the Microsoft Health Industry team. In this role, he is responsible for defining Microsoft's life sciences strategy, developing strategic relationships and partnerships with key life sciences customers and partners, building industry-leading solutions that showcase Microsoft technologies, and educating the Microsoft internal community on the needs of the industry. Under Paul's leadership, Microsoft is working with partners to develop innovative platforms and solutions that span the life sciences value chain from discovery and development, through manufacturing and distribution to commercialization.

Paul has been at Microsoft for 6 years. Prior to his current role he worked as a Director of Enterprise Architecture, focused on developing incubation solutions in the life sciences industry and multiple other industries, including energy production, discrete manufacturing, energy, education and information technology.

Before joining Microsoft, Paul was a Senior Enterprise Architect at Weyerhaeuser – a global forest products company. As such he was responsible for the overall technology architecture of the organization. He developed Weyerhaeuser's virtualization, cloud and security strategies, and defined a target architecture for shared services across multiple lines of business.

He is the author of multiple Microsoft position papers on hybrid, private and public cloud, platform modernization and IT Portfolio Management and has authored or co-authored several books on solution and enterprise architecture issues. He has spoken at multiple conferences in the United States and Europe, including Microsoft Tech Ed, the Global Data Center conference, and Data Center World. He holds a Bachelor's of Science (Hons) in Mathematics from King's College. London.

Carolynn Thomas Jones, DNP, MSPH, RN is Associate Professor of Clinical Nursing and Faculty Lead for the Master of Clinical and Preclinical Research program. She was formerly faculty at UAB School of Nursing. She has over 30 years of experience working in clinical research roles ranging from coordinator, director, educator to PI. She was Director of the NIAID-funded Mycoses Study Group Coordinating Center located at UAB from 1990-2000. She has developed and taught online courses on Clinical Research since 2005, including an NIH Fogarty Challenge Grant, "Promoting Enhanced Research Capacity for Global Health" (PERC) which was offered to 150 coordinators in 39 countries. Ms. Jones has a DNP in nursing with a concentration on clinical research nurse role delineation and an MSPH in Epidemiology. She is PI of the NCATS-sponsored DIAMOND grant and other clinical research workforce development grants. Her faculty practice also includes working with the Mycoses Study Group Education and Research Consortium, an independent 501c3, where she assists in multi-center protocol and CRF development, data review committees, and continuing education. She is Past-President of the Consortium of Academic Programs in Clinical Research (CoAPCR) and is a member of: Commission on Accreditation (CoA) for CoAPCR, the Joint Task Force for Clinical Research Competency, International Association of Clinical Research Nurses Research Committee; ACRP, DIA and SoCRA. She has published widely on subjects related to clinical research management, education and role delineation; including the recently released ANA Scopes and Standards for Clinical Research Nurses. Jones.5342@osu.edu

Carol Juliet Weil, JD, is a member of the MRCT's Return of Individual Results project team and its working subgroup on genomics. She is a program director for ethical and regulatory affairs at the National Cancer Institute (NCI) and an expert in research protections pertaining to the collection, storage, and downstream uses of biological samples and genomic and clinical data. In her job at the NCI, Ms. Weil navigates the ethical, legal, and social implications of cancer research including policies on consent, data sharing, biobank governance, community engagement, and disclosure of research results and incidental findings. She facilitates the development of embedded bioethics protocols in NCI's precision medicine oncology trials, including surveys about tissue donation and genetic counseling pilots for returning genomic findings. She has served as a non-scientist member of the NCI institutional review board since 2012.

Ms. Weil came to the NCI in July 2010. She obtained her law degree from the University of California at Berkeley which was followed by a fellowship in medical ethics at the University of California, San Francisco Medical School. Ms. Weil has served the U.S. Department of Health and Human Services since

1987, first with the Inspector General's Office, where she prosecuted Medicare/Medicaid fraud and abuse cases, and from 1999 to 2010 with the Office for Human Research Protections (formerly, the Office for Protection from Research Risks at NIH), where she handled compliance cases and developed policies and educational guidance for institutional review boards and clinical investigators.

Julie Wood is currently responsible for External Relations at Vivli. Julie was previously at the Cochrane Collaboration, where she was the Head of Communications and External Affairs for the past three years.

During her time at Cochrane, she developed the team that focused on communications, media, dissemination, translations, strategic partnerships, branding and events, and fundraising. Wood was instrumental in the delivery of Cochrane's re-brand, where she coordinated and launched the first-ever Global Evidence Summit.

Prior to joining Vivli, she spent a year working for a Microsoft partner and more than 12 years at Oxfam Great Britain, the development agency. Her final role at Oxfam GB was as the Director of Corporate Communications.

MRCT Center Leadership

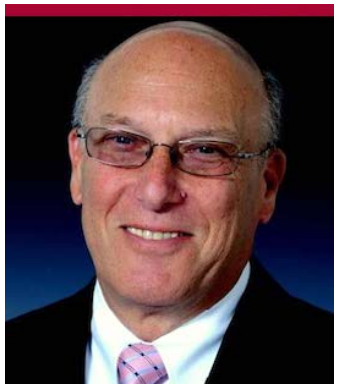
Mark Barnes JD, LLM, MRCT Faculty Co-Director & Co-Chair**,** Partner, Ropes & Gray LLP, and Lecturer, Yale School of Medicine; Visiting Lecturer, Yale Law School. Mark's law practice and his teaching at Yale focus on health care law and finance, human and animal research, stem cell and genetic research, research grants and contracts, research misconduct, and international research. Mark formerly served at Harvard as the Senior Associate Provost and University Senior Research Officer and started and directed Harvard's HIV/AIDS treatment programs in Nigeria, Tanzania and Botswana. He serves on the Ethics Working Group of the NIH's HIV Prevention Trials Network (HPTN) and is the ethics advisor to HPTN Trial 071 in South Africa and Zambia. Mark has held senior appointed positions in the New York City and State departments of health.

Barbara E. Bierer, M.D., is the Faculty Director of the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center), a Professor of Medicine, Harvard Medical School and Brigham and Women's Hospital, Boston and a hematologist/oncologist. She is the Director of the Regulatory Foundations, Ethics and the Law Program of the Harvard clinical and translational sciences center. Previously she served as senior vice president, research at the Brigham and Women's Hospital for 11 years, and was the institutional official for human subjects and animal research, for biosafety and for research integrity. She initiated the Brigham Research Institute and the Innovation Hub (iHub), a focus for entrepreneurship and innovation. In addition, she was the Founding Director of the Center for Faculty Development and Diversity at the BWH.

In addition to her academic responsibilities, she serves on the Board of Directors of Public Responsibility in Medicine and Research (PRIM&R), dedicated to promoting the ethical conduct of biomedical and behavioral research; Management Sciences for Health (MSH), an international organization working in partnership globally to strengthen health care, local capability, and access; and the Edward P Evans Foundation, a foundation supporting biomedical research. Previously she has served as the chair of the Board of Directors of the Association for Accreditation of Human Research Protection Programs (AAHRPP) and as chair of the Secretary's Advisory Committee on Human Research Protections, HHS. She has authored or co-authored over 180 publications and is on the editorial boards of a number of journals including *Current Protocols of Immunology.*

Dr. Bierer received a B.S. from Yale University and an M.D. from Harvard Medical School

Rebecca Li, Ph.D., is a Senior Advisor to the MRCT Center and the Executive Director of Vivli. Previous to her current role she was the Executive Director of the MRCT Center of Brigham and Women's Hospital and Harvard for over 5 years and remains a Senior Advisor at the Center. The MRCT Center is a neutral convening organization that works to define actionable policy solutions for the clinical trial enterprise. The Center was chartered to improve the integrity, safety and rigor of global clinical trials. Dr. Li has over 20 years of experience spanning the entire drug development process with experience in Biotech, Pharma and CRO environments. She currently is an Instructor in Medicine in the Division of Global Health Equity, Department of Medicine in the Harvard Medical School and teaches Research Ethics at the Center for Bioethics. She completed a Fellowship in 2013 in the Division of Medical Ethics at Harvard Medical School. Prior to joining Harvard, Dr. Li served as the VP of Clinical Research at the New England Research Institutes for 6 years. She was also previously employed at Wyeth Research as the Associate Director in Translational Clinical Research. She earned her PhD in Chemical and Biomolecular Engineering from Johns Hopkins University.



Stephen A. Sonstein, PhD, Senior Advisor, MRCT Center, Professor Emeritus, Eastern Michigan University. In addition to his current role as Senior Advisor, Dr. Sonstein is Chair of the Committee on Accreditation of Academic Programs in Clinical Research. Previously, he was founder and director of the academic programs in Clinical Research at Eastern Michigan University, one of the first programs to offer academic credit for content in clinical research. During his academic career, he served as faculty member, program director, department head and assistant dean at Eastern Michigan University, University of Wisconsin-Milwaukee, University of Dayton and Columbus College. He earned a BS from Rutgers Universitiy and a PhD in Microbiology and Biochemistry from Hahnemann Medical College, has conducted basic, preclinical and clinical research in the area of antibiotic mechanism of action and antibiotic resistance, and is a Fellow of the American Academy of Microbiology. He is Co-chair of the Joint Task Force for Clinical Trial Competency, is a Commissioner on the Commission for Accreditation of Allied Health Education Programs and serves on the Certification Board of the Regulatory Affairs Professions Society. He was a founding member of the Consortium of Academic Programs in Clinical Research and served on the Board of Directors of the Drug Information Association and the Advisory Board of the Inter-American Foundation for Clinical Research.

David H. Strauss, MD is a Senior Advisor to the MRCT Center and Director of Research Operations and Compliance at the Columbia University Department of Psychiatry and the NYS Psychiatric Institute (NYSPI) where he oversees human and animal research ethics, regulatory affairs, and core research facilities. Dr. Strauss co-chairs Columbia University's Standing Committee on the Conduct of Research.

From 2010 to 2016, Dr. Strauss served as Vice Chair for Research Administration, Ethics and Policy for the Columbia University Department of Psychiatry and Director of Research at NYSPI. From 2000 until 2010, he chaired the NYSPI IRB and directed its Office of Humans Subjects Research. He co-directed the Ethics, Public Policy, and Human Rights Core of the HIV Center for Clinical and Behavioral Studies.

Dr. Strauss is past recipient of two NIH grants on research ethics training and the enhancement of human subjects oversight for psychiatric research. He is a former member of the HHS Secretary's Advisory Committee on Human Research Protections and co-chaired its Subcommittee on the Inclusion of Individuals with Impaired Decision-making in Research. He currently serves on a SACHRP subcommittee charged with developing recommendations to enhance Subpart A or the "Common Rule."

Dr. Strauss is a member executive committee of the Board of Directors of PRIM&R, and chairs its Public Policy Committee. He is a member of the Bioethics Advisory Group at Takeda Pharmaceuticals

Dr. Strauss practices psychotherapy and psychopharmacology and teaches, lectures, and consults on matters of human subjects protections and applied research and professional ethics.

MRCT Center Staff

Hayat Ahmed joined the MRCT Center as Project Coordinator in August 2017. Prior to joining the MRCT Team, Hayat has worked with the John Snow Research & Training Institute and Harvard T.H. Chan School of Public Health on Global Health projects. She has also worked as a Technical Research Assistant in an HIV/AIDS research laboratory in the Department of Infectious Disease at Brigham and Women's hospital.

Hayat obtained her Master of Science degree in Global Health and Population from Harvard T.H. Chan School of Public Health. She earned a Bachelor of Arts in Biochemistry from Mount Holyoke College.

Carmen Aldinger, Ph.D., MPH, is Administrative and Training Manager at the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center). She joined the MRCT Center in October 2014 as Program Manager and assumed the role of Administrative and Training Manager in July 2017. She provides managerial oversight for the MRCT Center training initiatives and for several workgroups, including return of individual results and return of aggregate results, post-trial responsibilities, and core competencies for clinical researchers. She also manages events and conferences, the MRCT Center website and newsletter and other operational and procedural aspects of the MRCT Center.

Dr. Aldinger has 20 years of experience in global health, including project management and leadership, materials development and capacity building, monitoring and evaluation, collaboration and coordination. Prior to coming to the MRCT Center, she has worked as a Project Director and Associate Center Director at Education Development Center's Health and Human Development Division, Global Programs, co-directed the World Health Organization Collaborating Center to Promote Health through Schools and Communities, and subsequently worked as an independent consultant for United Nations agencies and non-profit organizations. Dr. Aldinger has a Ph.D. in Educational Studies from Lesley University, a Master of Public Health in international health from Yale University, and a Bachelor's degree in health education from Towson University.

Emily Statham joined the MRCT Center of Brigham and Women's Hospital and Harvard as Project Coordinator in June 2017. Before joining the MRCT Team, Emily worked with the Baylor College of Medicine Center for Medical Ethics and Health Policy, Medivation Biopharmaceuticals, Inc., and The University of Texas MD Anderson Cancer Center's Department of Integrated Ethics.

Emily received her Master of Bioethics from Harvard Medical School, where she concentrated on Health Law, Policy, and Research Ethics. She holds a Bachelor of Arts in both Biomedical Ethics and Spanish & Portuguese from Rice University.

Linda McMaster joined the MRCT Center in July 2017. Since 1999, Linda has been working in local non-profits as a case manager, trainer, and program manager. Her areas of expertise include trauma-informed care, domestic violence, and the intersection of poverty and mental illness in the lives of women.

Linda has a Bachelor of Arts in English and Political Science; she is currently pursuing a Master of Social Work degree at Simmons College.