Proceedings
Multi-Regional Clinical Trials Center (MRCT Center) of Brigham and Women's Hospital and Harvard
2018 Annual Meeting

5th December, 2018 • 8:00 AM – 1:00 PM

Loeb House at Harvard University • Cambridge, MA

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

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Executive Summary

The MRCT Center's 2018 Annual Meeting convened a diverse group of approximately 80 stakeholders focusing on global clinical trials. The principal topics discussed at the MRCT Center 2018 Annual Meeting were: (1) European Union General Data Protection Regulation (GDPR), (2) Representation of Diverse Populations, (3) Advancing the Study of Clinical Trials, (4) Capacity Building, and (5) Health Literacy in Clinical Research.

European Union General Data Protection Regulation (GDPR)

Professor Guido Rasi (EMA) discussed the digital revolution and its impact on the regulatory environment. He spoke specifically about the challenge related to the growing web of potential data sources. Such increased access to digital information, including electronic health data, allows tremendous potential for scientific discovery but are as yet largely unstructured, multi-dimensional and not standardized. The use of these data in regulatory decision-making will depend upon the creation of systems that enable fast and reliable determinations of product safety and causality. Professor Rasi shared his thoughts regarding the critical nature of responsible data sharing and discussed actions that the EMA has taken to facilitate the responsible sharing of clinical trial data, including passing Policy 0070 and adopting the European Union General Data Protection Regulation (GDPR).

Representation of Diverse Populations

Dr. Bierer (MRCT Center) moderated the panel, opening with a brief description of the diversity clinical trials project and its scope of work, timeline, members, and challenges.

- Dr. David Strauss (Austen Riggs Center, MRCT Center Senior Advisor) discussed the growing public consciousness around the importance of diversity and inclusion with respect to age, sex, gender, race, and ethnicity over the last few decades. He explained that the MRCT Center project, Representation of Diverse Populations, is structured into two workstreams that (1) addresses the knowledge gaps and make the case for diversity and (2) Identifies challenges and provides a means to move things forward for target audiences.
- CAPT Richardae Araojo (USFDA) shared the efforts that have been undertaken by the FDA in advancing diverse participation in clinical trials. CAPT Araojo described the mission and activities of the FDA's Office of Minority Health and provided commentary on opportunities to advance minority participation in clinical trials.
- Dr. Luther Clark (Merck) discussed various considerations around race, ethnicity and genomics. He noted that ethnic minorities are still underrepresented in genomic studies,

leading to significant gaps in knowledge with regards to potential health care disparities in genomic medicine and precision health. The MRCT Center workgroup is exploring the evolving role of genomics and the future of drug development.

- Dr. Barbara Bierer discussed the current organizational and operational challenges that hinder diversity in clinical trials and identified potential directions and deliverables for the project. The MRCT Center is working on developing comprehensive recommendations and resources comprising approaches and toolkits to enhance diversity across the clinical trial landscape.

Advancing the Study of the Clinical Trial

Dr. Deborah Zarin, who joined the MRCT Center in January 2019 as Program Director, *Advancing the Clinical Trial Enterprise*, provided the second keynote. The keynote highlighted the challenges with many clinical trials including inadequate study design, insufficient power to answer the study question, lack of specificity and/or fidelity to the trial protocol, and incomplete reporting of outcomes and adverse events. Dr. Zarin proposed devoting more effort to improving the quality of the clinical trial enterprise. Dr. Zarin stressed the need to evaluate trials prior to initiation, with a specific focus on design, analysis, reporting, and feasibility. She suggested three steps to help advance these goals: (1) Conduct landscape analyses to determine how any new study would fit into the world of ongoing/existing studies, (2) ensure independent third-party scientific review, and (3) ensure complete trial registration and results reporting.

Capacity Building

Ms. Sarah White (MRCT Center) gave an update on MRCT Center's capacity building efforts. Recent efforts have focused on training regulators on International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines for Good Clinical Practice (GCP) and Multi-Regional Clinical Trials (MRCT). The MRCT Center has been endorsed as Training Partner by ICH and as Training Center of Excellence by the Asia-Pacific Economic Cooperation (APEC). Starting in 2019, the MRCT Center will begin conducting in-country training, the first of which will be held in collaboration with Health Canada in Ottawa Canada in February of 2019. In addition, at the invitation of ICH, the MRCT Center is currently developing an introductory online training on ICH E6(R2) GCP.

- Dr. Murray Lumpkin (Bill & Melinda Gates Foundation) discussed the challenges for clinical trials in low income countries (LICs). He highlighted the work of the African Vaccines Regulatory Forum (AVAREF) to develop an expanded strategy to address these challenges including determining resources needed to create adequate infrastructure

and increased capacity building. A treaty to create an African Medicines Agency (AMA) will be submitted for final approval by African Union member state heads of government in February 2019.

- Dr. Michelle Limoli (USFDA) explained that training is an important focus for the ICH. Dr. Limoli reviewed ICH's training priorities and recent training efforts. Dr. Limoli is also the US representative to the APEC Regulatory Harmonization Steering Committee (RHSC), a committee whose main goal is capacity building and training.

Health Literacy in Clinical Research

Ms. Sylvia Baedorf Kassis (MRCT Center) introduced the background of the Health Literacy in Clinical Research project and the progress that has been made thus far. The Health Literacy workgroup was initiated in April 2018 and is working on developing tools and resources along the clinical trial lifecycle for clinical research stakeholders to access. This project will address different facets of health literacy in addition to plain language and including reading and writing, interpretation of risk, numeracy, visualization, and in-person communication.

- Dr. Marilyn Neault (Parkinson's Foundation) provided foundational insights into the clinical trial participant experience and reminded the audience of the importance of the patient perspective and voice. Further, for the patient voice to be heard and to conquer, it must first be procured. Dr. Neault discussed key needs of participants that are often overlooked by researchers and offered suggestions to increase researcher/participant understanding.
- Associate Professor Christopher Trudeau, JD (University of Arkansas for Medical Sciences (UAMS)) provided a case study about integrating health literacy into an academic medical center at his own institution. He emphasized the importance of building awareness at an organizational level, engaging key stakeholders to secure buy-in for health literacy, and assessing the current state of communications received by research participants. The steps that UAMS took can be summarized: (1) Raise internal awareness, (2) provide education on health literacy best practices, (3) assess current practices, (4) develop health-literate research materials (e.g. a health-literate consent template), and (5) user test those materials to better ensure they resonate with the intended audience.
- Ms. Laurie Myers (Merck) provided a case study on the experience Merck has had integrating health literacy into their company. Health literacy is essential because patients benefit most from medical innovation when they understand their diagnosis, why their doctors recommend certain treatments, and how to take their medicines correctly. Merck has worked to integrate health literacy principles into patient

materials, including patient labeling for new molecules, and some clinical trial materials, packaging, and patient education. A key learning has been that everyone, even those with proficient health literacy, prefers health literate materials. Great progress has been made over the last decade, with much opportunity remaining. Work today focuses on improving awareness of the importance of health literacy in different regions around the world, understanding how to improve comprehension across all levels of health literacy, and developing standardized processes to integrate health literacy principles into patient materials.

- Ms. Sarah White (MRCT Center) provided a preview of the online delivery platform for the resources and tools that are under development. This platform will be a dedicated site for health literacy in clinical research, with easily accessible and easy-to-use resources for all stakeholders within the clinical trial lifecycle. The beta launch for this site is scheduled for mid-2019.

Welcome and Introduction

Mark Barnes and Barbara Bierer, MRCT Center

MRCT Center Faculty Co-Director, Mark Barnes, opened the meeting and welcomed the participants. MRCT Center Faculty Director, Barbara Bierer, called for a moment of silence on the occasion of the national day of mourning for the late President George H.W. Bush. Then she asked all meeting participants to introduce themselves.

Dr. Bierer briefly reviewed the mission of the MRCT Center: to bring together diverse stakeholders to address emerging issues of global clinical trials, including ethics, conduct and regulatory environment, and to develop practical solutions. The MRCT Center aims to be a trusted collaborator and an independent convener with academic credibility.

Dr. Bierer announced that Dr. Deborah Zarin will join the MRCT Center as Program Director, *Advancing the Clinical Trial Enterprise*, in January 2019. Dr. Bierer also welcomed the Senior Advisors who have joined the MRCT Center during 2018: Luke Gelinas, who currently serves as Chairperson at Advarra IRB, and Elizabeth Cahn, a patient advocate, and former patient who currently serves as the Program Coordinator at Cancer Connection.

Dr. Bierer gave an overview of the day's agenda and clarified that the projects presented this year are in flight and encouraged participants to provide constructive feedback. She also announced next year's Annual Meeting: December 4, 2019.

Mark Barnes explained why the following two projects were not on the agenda at this meeting:

- Vivli was spun off successfully as its own non-profit entity, with its own staff and funding. The official launch of Vivli was in July 2018.
- In India, regulations for the clinical trial infrastructure are under revision and the process for public comments is ongoing. The MRCT Center published a comprehensive history from 2013 to the present. This topic will be revisited next year if the regulations are finalized.

Keynote: Digital Revolution and Regulatory Environment – Are These Compatible?

Guido Rasi, European Medicines Agency

Professor Guido Rasi, Executive Director at the European Medicines Agency (EMA), delivered the first keynote address titled *Digital Revolution and the Regulatory Environment—Are These Compatible?* Professor Rasi described how the digital revolution has expedited the processes by which electronic health data are generated and stored. With the surfeit of data has come tremendous potential for scientific discovery; the inherent variability, complexity, and heterogeneity of the data, however, have created complex challenges for the conduct and oversight of clinical research.

One such challenge is related to the growing number of potential data sources. Unlike randomized controlled trials (RCTs) of the past, wherein data of high fidelity were primarily collected as a consequence of the trial itself, RCTs of today must grapple with whether and how to integrate data from the real world. Such data are accumulating rapidly, but are unstructured, multi-dimensional and not standardized. The use of these data in regulatory decision-making will therefore depend upon the creation of systems that enable fast and reliable determinations of product safety and causality.

According to Professor Rasi, clinical trial data sharing is vital to the success of these systems. Responsible data sharing should be guided by the following foundational principles:

1. Potential research participants should be made aware of the benefits and risks of data sharing.
2. Data should be anonymized in a manner that both protects participants' privacy and preserves scientific utility.

EMA has taken a number of actions to facilitate the responsible sharing of clinical trial data, including implementing Policy 0070 and adopting the European Union General Data Protection Regulation (GDPR). The GDPR intends to enhance trust in the clinical research enterprise by safeguarding citizens' right to protect their personal data.

Despite uncertainty regarding international data transfer and secondary use of research data under the GDPR, Professor Rasi concluded by acknowledging that the GDPR is not intended to inhibit the conduct of clinical research. As such, the EMA is committed to developing resources that are responsive to the needs of the clinical research community. The European Data Protection Board (EDPB), for example, has been tasked with clarifying stakeholder obligations

and promoting consistency in the GDPR's application. In addition, several large research consortia are developing Codes of Conduct for the GDPR in order to clarify present ambiguities.

Discussion

Attendees responded to Professor Rasi's remarks with a number of comments, including the observation that because EMA intends to use Big Data to learn additional information about the safety and efficacy of approved medications, robust post-market surveillance may lead to the development of mechanisms for bringing drugs to market sooner.

Representation of Diverse Populations

Dr. Bierer opened by giving the context by which the MRCT Center project Representation of Diverse Populations began. The overview provided the scope of the work, timeline of the project, and members of the workgroup. Achieving the enrollment of a diverse participant population in trials will require a multi-stakeholder, multi-factorial approach that is iterative and continuous.

David Strauss, Austen Riggs Center

Dr. David Strauss, Director of Research at Austen Riggs Center and Senior Advisor at the MRCT Center, began by discussing the growing public consciousness around diversity and inclusion with respect to age, sex, gender, race, and ethnicity over the last few decades. Nonetheless, despite the intention to recruit diverse and representative study populations in trials to detect differences in drug metabolism, safety, or treatment outcome, many trials fail to enroll traditionally underrepresented subgroups in proportion to the prevalence of the illness in these populations. This raises questions about the generalizability of scientific results as they pertain to these groups and has important implications for their healthcare; further, this failure challenges basic notions of fairness and justice in access to the benefits of research, and raises consideration of the institutional, cultural, logistical and cultural barriers that are responsible—motivation/incentives/ownership of the goal of diversity, expectations/accountability related to that goal, and knowledge/tools/infrastructure to achieve it. The project is structured into two workstreams in such a way that

1) Addresses the knowledge gaps and makes the case for the importance of diversity
2) Identifies challenges and provides a means to move things forward with specific target audiences in mind.

This group is divided into eight sprint teams that each address specific topics that required more substantive discussion and analysis.

CAPT Richardae Araojo, USFDA

CAPT Richardae Araojo, Associate Commissioner for Minority Health, described FDA efforts to advance diverse participation in clinical trials. The mission of FDA's Office of Minority Health is to promote and protect the health of diverse populations through research and communication that address health disparities. Multiple reasons for the low minority participation in clinical trials were discussed including history, mistrust and distrust of the medical system, inadequate recruitment and retention efforts, lack of minority participant awareness, an insufficient minority research workforce (physicians, researchers and clinical investigators), and misunderstanding of minorities' values that contribute to their decision-making process, among others.

The FDA's Safety and Innovation Act (FDASIA) Section 907 of 2012 directed the FDA to examine how well demographic subgroups (sex, age, race, and ethnicity) are included in clinical trials in applications for medical products submitted to the agency for marketing approval. Additionally, the Act also required the assessment of the availability of data that focused upon subgroup-specific safety and effectiveness. To address this directive the FDA set forth three priorities and strategies:

1) **Quality:** Improve the completeness and quality of demographic subgroup data collection, reporting and analysis. The FDA has developed two guidance documents with this objective.
2) **Participation:** Identify barriers to subgroup enrollment in clinical trials and employ strategies to encourage greater participation. The FDA hosts public meetings and develops tools to support diverse clinical participation.
3) **Transparency:** Make demographic subgroup data more available and transparent. The FDA has created the Drug Trials Snapshots to provide consumers information about who participated in the clinical trials that supported an FDA approval of a new drug.

The FDA has also initiated the Minorities in Clinical Trials Campaign and generated resources to encourage participation across all levels.

The presentation also highlighted understanding the Socio-Ecological Model as one mechanism to enhance participation in clinical trials. It underscored the need for multi-faceted efforts to engage patients in all aspects of trial design – protocol development, outcomes and endpoint determinations, feedback on study materials, recruitment and retention strategies, and consistent engagement for future trials.

Luther Clark, Merck

Dr. Luther Clark, Deputy Chief Patient Officer, Global Director, Scientific Medical and Patient Perspective at Merck, discussed various considerations around race, ethnicity, and genomics in

clinical trials. It is estimated that the U.S. will be majority non-white by 2045. While racial categories are social and political constructs, there are examples of diseases that dispro-portionately affect racial and ethnic minorities. Dr. Clark cited a study which revealed that between 2008 and 2013, 21% of the new molecular entities approved by the FDA had racial or ethnic (or both) differences in safety, efficacy, pharmacokinetics, or pharmacogenomics. There is also a lack of ethnic diversity in genomics research, consequently affecting the understanding of the relationship between genes and diseases in understudied populations. The result is significant gaps in knowledge with regards to potential health care disparities in genomic medicine and precision health. At present, self-identified race continues to have utility as it can correlate with geographic ancestry – a determinant of genomic variation that can influence response to drugs. Furthermore, it may serve as a proxy for other difficult-to-measure factors such as social determinants of disease (environment, health behaviors, effects of chronic bias, comorbidities etc.) that may impact treatment. The MRCT Center workgroup is discussing the role of genomics and the future of drug development – beyond products specifically targeted at genomic variation¬– in order to understand variability in drug response.

Barbara Bierer, MRCT Center

Dr. Barbara Bierer discussed the current organizational and operational challenges that hinder diversity in clinical trials and identified potential directions and deliverables for the project. Perceived challenges range from factors related to time and cost of participation in the trial, to logistical issues during trial conduct, to inconsistencies and variability around data collection and analysis. Potential solutions were suggested prior to the start of the trial, including making the business case for diversity and highlighting the corporate responsibility and commitment to diversity and inclusion of under-represented groups in clinical trial populations. Additionally, collating successful educational and community engagement strategies and being attentive to necessary logistical changes during study conduct were raised. Health literate communication strategies as well as returning results to participants were proposed. Finally, innovative methodologies and standard agreements for the collection, analysis, reporting and sharing of data were put forth.

The MRCT Center is working on developing comprehensive recommendations and resources comprising approaches and toolkits to enhance diversity across the clinical trial landscape.

Panel Discussion

Dr. John Whyte from WebMD, formerly of the FDA, provided commentary on the importance of always asking how to best determine if there is variability of drug response and, if so, how to approach its analysis *a priori* and as a component of trial design. This is particularly useful when thinking about subgroups and subpopulations globally. The importance of capacity building and

training was mentioned in areas where the clinical trial infrastructure is not robust. The question was raised as to the metrics of success: what is the measure of 'good' or 'successful' diversity in a clinical trial. A quota system is not the answer to these issues.

Keynote 2: Advancing the Study of the Clinical Trial

Deborah Zarin, MRCT Center

Dr. Deborah Zarin, who joined the MRCT Center in January as Program Director, *Advancing the Clinical Trial Enterprise*, provided the second keynote.

In her presentation, Dr. Zarin noted that traditionally, researchers and sponsors decided whether, when, and where to publish their research, resulting in three main problems:

1) Publication bias – suppression of data
2) Lack of fidelity to trial protocol in terms of outcome reporting
3) Incomplete reporting of adverse events

In an effort to address these issues, trial registration and aggregate results reporting were introduced by the journal editors, Federal law (FDAAA), and some funding bodies. Despite this, some challenges remain, such as

- 1/3 of clinical trials are registered after the first enrollee
- Some trials are never registered
- 50% of initial registrations are rejected for poor outcome measure specification and lack of understanding of basic concepts
- Compliance with aggregate results reporting is generally low

Dr Zarin described that study design is often inadequate and results are insufficiently powered. Further findings include lack of specificity in the initial trial protocol, lack of adherence to the protocol, and incomplete reporting of outcomes and of adverse events.

As a result, Dr. Zarin proposed devoting more effort to improving the quality of the clinical trial enterprise. She highlighted the importance of trial worthiness and whether the bar is set too low for research on human subjects, especially in academia, where academic medical centers often take credit for research at their sites but do not take adequate responsibility for the ongoing research. In addition, the web of incentives for academic investigators to conduct research is skewed towards more trials, more funding, and more publications rather than high quality trials that advance the field. Non-informative trials absorb research participants and

resources, and from a patient perspective, it can be difficult for participants to identify a study that is right for them and that would provide scientific value.

Dr Zarin concluded by reiterating the need to evaluate trials prior to initiation with a focus on design, analysis, reporting, and feasibility and suggested the following three steps to help advance the clinical trial enterprise:

1) Conduct landscape analyses utilizing PubMed, ClinicalTrials.gov and other registries to determine how the new study fits into the world of ongoing and completed studies
2) Ensure an independent third-party scientific review of all trials
3) Ensure complete, timely and accurate trial registration and aggregate results reporting

Discussion

The audience responded to Dr. Zarin's remarks with the following comments:

- Phase 1 and preclinical studies are not always registered on www.ClinicalTrials.gov so it is difficult to see the breadth of that type of research that is happening.
- The IRB is not staffed to review the literature so determining who is responsible for the landscape analysis would be helpful.
- NCI Cancer Center Grants require a Scientific Review Committee that appears to help improve investigator-initiated studies.
- Industry sponsor protocols see challenges when a scientific committee at one academic medical center raises an issue that stops a study that is primed to begin enrollment globally.
- There may be a role for patient advocacy groups and others to download data and curate it.
- Many registries that exist globally do not have consistent or sufficient funding which is critical to the accuracy and reliability of the information.
- From a health literacy perspective, information on ClinicalTrials.gov is intended to reflect what is in the protocol and is not easily translated to communications for a broader audience. Developing health literate language based on ClinicalTrials.gov data would help all applicable stakeholders better understand the protocol.

Capacity Building Update

Sarah White, MRCT Center

Ms. Sarah White, MRCT Center Executive Director, gave an update on the MRCT Center's capacity building efforts. She noted that training and capacity building have been a

longstanding commitment of the center, which has trained regulators, data management committee members, institutional review board members, principal investigators, and others around the world on a variety of topics. Recent efforts have focused on training regulators on International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines for Good Clinical Practice (GCP) and Multi-Regional Clinical Trials (MRCT). The MRCT Center has been endorsed as training partner by ICH and as Training Center of Excellence by the Asia-Pacific Economic Cooperation (APEC).

In April 2018, the MRCT Center conducted a successful APEC Pilot Center of Excellence training, training 22 participants from 12 countries on ICH Good Clinical Practice Multi-Regional Clinical Trial Guidelines. Ms. White explained that the training was a success, while noting that the MRCT Center is moving to a new model of conducting in-country (not Boston-based) training. The first in-country training is scheduled to take place in collaboration with Health Canada in late February 2019 in Ottawa, Canada.

In addition, the MRCT Center is currently developing an introductory online training on ICH E6(R2) GCP, that will be offered free of charge. This 10-module online training includes dynamic training slides, voice-over audio, embedded case studies, and quiz questions. The modules will be loaded into a Learning Management System that allows tracking and issuance of a certificate of completion.

The MRCT Center is in the early stages of exploring capacity building in Africa.

Murray Lumpkin, Bill & Melinda Gates Foundation

Dr. Murray Lumpkin, Deputy Director – Integrated Delivery and Lead for Global Regulatory Systems Initiatives at the Bill & Melinda Gates Foundation, explained the Foundation's recent experience in Africa. The Gates Foundation focuses on products for neglected diseases in low-income countries and has engaged with African regions and various partners over the past several years to optimize the regulatory systems through which these products are procured and used legally in LICs.

There are many challenges for clinical trials in LICs, and particularly in Africa, a continent of 55 countries. While South Africa has a large number of clinical trials and thus infrastructure to support those trials, other countries have very few trials, lack training and resources, and in some cases have only one person in a regulatory capacity focused on research oversight. The African Vaccines Regulatory Forum (AVAREF), launched by the World Health Organization (WHO) in 2006, has recently turned its focus to developing an expanded strategy to address this lack of clinical research oversight infrastructure and capacity across Africa. Challenges and considerations include determining what capacity and abilities are needed. The WHO has

recognized the University of Ghana and the Ghana FDA as a Center of Excellence for clinical trials oversight and hopes to utilize the Ghana experience as a model. A treaty to create an African Medicines Agency (AMA) will be submitted for final approval by the heads of government in February 2019. After approval, 15 member state parliaments must ratify the treaty before the AMA will be operationalized. When the AMA is operationalized, the AVAREF initiative will become the platform for a continental approach to clinical trial governance and policies that will then be instituted by the member states at local and regional levels.

Michelle Limoli, USFDA

Dr. Michelle Limoli, Senior International Health Science Advisor, Center for Biologics Evaluation and Research (CBER), at the U.S. Food and Drug Administration (USFDA) expressed her thanks to the MRCT Center on behalf of ICH and APEC. She explained that training has become an important issue since the ICH governance structure has changed. Dr. Limoli currently chairs the ICH Management Training Subcommittee. A recent needs assessment identified five priorities for training needs: (1) Q1 Series Stability Testing, (2) E6(R2) Good Clinical Practices, (3) Q7 GMPs for APIs, (4) E2B(R3) Clinical Safety Data Management & others E2 series, (5) M4(R3) Organization of the Common Technical Document. The MRCT Center has provided training in the area of Good Clinical Practice since 2017. In 2018, the ICH Training Subcommittee continued to work with the MRCT Center to develop online training on ICH E6(R2).

Dr. Limoli also discussed the APEC Regulatory Harmonization Steering Committee (RHSC). APEC consists of 21 economies of great diversity, bordering the Pacific Ocean. The RHSC does not create standards but promotes implementation of harmonized guidelines. Its main goal is capacity building and training. To increase the global footprint, APEC also invites participants from non-APEC economies to join its trainings, if space allows. APEC's work is focused on seven Priority Work Areas (PWAs) of which Multi-Regional Clinical Trials and Good Clinical Practice Inspections is one PWA. Since 2017, APEC has formally established Training Centers of Excellence (CoE) of which the MRCT Center is the latest to be approved as a CoE.

Health Literacy in Clinical Research

Sylvia Baedorf Kassis, MRCT Center

Ms. Sylvia Baedorf Kassis, MRCT Center Program Manager, introduced the background of the Health Literacy in Clinical Research project at the MRCT Center, and the progress that has been made thus far. The need for health literacy in clinical research was identified by members of the MRCT Center Return of Results project in 2013. Members of this group noted the necessity of clear communication throughout the entire trial, not just in results reporting. The Health Literacy workgroup was initiated in 2018 and has identified five key times during a clinical trial

of particular importance for health literate communication: discovery, recruitment, consent, on-study, and end of study. The group is working to develop tools and resources for clinical research stakeholders to support communication throughout this clinical trial lifecycle.

The workgroup aims for these resources to address the two-sided nature of health literacy -– rather than focus on the "deficits" of the listener, there must be equal or greater focus on the ways the communicator can facilitate better understanding. Ms. Baedorf Kassis noted this project will address many different facets of health literacy, including reading and writing, interpretation of risk, numeracy, visualization, and in-person communication. To aid clinical research stakeholders, there are also resources one can use to advocate for health literacy at their institution. The incentives to health literacy in clinical research were also highlighted, and include the ethical imperatives, cost savings, increased data validity, improved compliance, and generalizability of study findings.

Lastly, this project will generate health literate resources for participants and to which researchers can refer.

Marilyn Neault, Parkinson's Foundation

Dr. Marilyn Neault, Research Advocate at the Parkinson's Foundation, provided foundational insights into the clinical trial participant experience, and reminded the audience of the importance of the patient perspective and voice. Further, for the patient voice to be heard and to conquer, it must first be procured. There are key needs of participants that are often overlooked by researchers, such as how the trial fits into their life and their schedule and how participants can be most helpful or connected with others going through a similar experience. Dr. Neault noted there is still much improvement to be made in terms of health literacy – researchers and clinicians can and should talk more clearly and more audibly; font sizes on medications and on instructions can and should be larger, easier to interpret, and follow; and diagrams and pictures can and should be included to highlight the key points that participants need to know. Researchers (and their trials) could benefit from visits being paid to research participants to understand their day-to-day life, their motivators, and their needs. Greater synergy between researchers and participants as to why a trial matters will results in greater protocol adherence.

Christopher Trudeau, University of Arkansas (UAMS)

Christopher Trudeau, JD, Associate Professor at the University of Arkansas, provided a case study about integrating health literacy throughout his own academic medical center. At an organizational level, Trudeau noted that building awareness is critical. Health literacy is limited across the US and can lead to fundamental problems and disparities in quality of life and health outcomes. Despite this, many are not aware of the need for health literate communications,

and even fewer are aware of the need for increased health literacy in the clinical research enterprise. Engaging Institutional Review Boards (IRBs) and CTSAs, such as UAMS's Translational Research Institute, is an important first step in securing buy-in for health literacy, as is assessing the current state of communications received by research participants. He noted that informed consent forms (ICFs) can be a good place to start and readability assessments (though limited) can be used to gauge the difficulty of understanding the material. At UAMS, a retrospective readability assessment of its past investigator-initiated consent forms (most in the 10-12th grade reading level) found that ICFs were at too high a reading level for the average participant.

Since UAMS began focusing on health literacy through its Center for Health Literacy (CHL), led by Trudeau's colleague, Dr. Kristie Hadden, there has been incremental but certain progress at integrating health literacy throughout UAMS. CHL has helped lead changes that better inform patients and participants in both the clinical and research enterprises at UAMS. In fact, CHL now offers document creation and review services for all areas of UAMS. Through these services, CHL has worked extensively with UAMS's IRB to create a health-literate, user-tested ICF template that has helped lower the reading level of UAMS's investigator-initiated consent forms to below the 8th grade level. These offerings have been met with support and encouragement from UAMS leadership. Because of this support, CHL has also amplified and broadened its services to include widespread user testing of patient- or participant-facing material, health literacy training for all incoming students, and more care and attention to health literacy in the development and pre-development of communications and materials.

To summarize, the steps UAMS took to get to this place in the research enterprise included:

1. Raising internal awareness and support for health literacy
2. Providing education on health literacy best practices
3. Assessing current institutional practices
4. Developing health-literate research materials (e.g. a health-literate consent template)
5. User testing those materials to better ensure that the meet the needs of the intended audience.

Laurie Myers, Merck

Ms. Laurie Myers, Global Health Literacy Director at Merck, provided a case study on the experience Merck has had integrating health literacy into their company. Health literacy aligns with the company's long-standing mission of patients first. Communication must be viewed alongside medical innovation as part of the cure: people do not fully reap the intended benefits

unless they first understand their diagnosis, why their doctors recommend certain treatments, and how to take their medicines correctly.

Merck has established a center of excellence in health literacy that educates, supports and embeds health literacy into different functional units across the organization. One important objective is the development of health-literate patient labeling for new molecules, which includes several rounds of patient input from people across a range of health literacy levels, including those with low health literacy. Health literacy improvements acknowledge that everyone, not just those with low literacy, can benefit from simple, clear communication, and, in fact, prefers it. Patients have responded positively to the improved materials. Anecdotally, people with low health literacy seem to prefer clear materials because they feel informed and empowered; people with proficient health literacy appreciate being able to quickly and easily find the information they need.

Merck has conducted health literacy trainings to over 1,000 employees to spread knowledge and awareness about the importance of incorporating health literacy principles into patient-facing materials. Care and attention are being paid to health literacy in many aspects of bringing a drug to market. Looking ahead, the focus is on identifying global opportunities and developing standardized processes to integrate health literacy into patient materials. External work continues, through publications and presentations, to help increase understanding of the importance of health literacy, including among regulators.

Sarah White, MRCT Center

Ms. Sarah White, Executive Director of the MRCT Center, concluded the Health Literacy presentation with a preview of the online delivery platform for the resources and tools that are under development. This platform will be a dedicated site for health literacy in clinical research, with easily accessible and easy-to-use resources for all stakeholders within the clinical trial lifecycle. The site itself will also serve as a model of health literate communication best practices. The beta launch for this site is scheduled for mid-2019, after content finalization and user-testing.

Closing Remarks

Mark Barnes and Barbara Bierer, MRCT Center

Mr. Barnes thanked attendees for their attention and participation. He explained that the topics covered in the morning session represented only a part of the MRCT Center's work and encouraged participants to engage with the MRCT Center throughout the year.

Dr. Bierer added her thanks and reminded participants of upcoming meetings in 2019. Dr. Bierer thanked participants for their commitment, support, and engagement.

Appendix 1: Meeting Participants

First Name:	Last Name:	Job Title:	Institution/Affiliation:
Albert J. "A. J. "	Allen	Senior Medical Fellow	Eli Lilly and Company
Carol	Ames	Sr Director, Development Administration	Sunovion Pharmaceuticals
Maria	Apostolaros	Sr. Director, SRA	PhRMA
Richardae	Araojo	Associate Commissioner For Minority Health	FDA
Behtash	Bahador	Senior Manager, Quality and Compliance	CISCRP
Kristen	Buck	SVP, Chief of Clinical Development	Optum
Elizabeth	Cahn	Program Coordinator	Cancer Connection
Susan	Chin	Staff	Harvard Law School
Luther	Clark	Deputy Chief Patient Officer	Merck
Cathryn	Clary	Global Head Patient Affairs and Policy	Novartis
Patrick	Cullinan	Head Science Advocacy	Takeda
Theresa	Devins	Sr. Associate Director	Boehringer Ingelheim
Michael	DiMaio	Associate	Ropes & Gray
Jacquelyn-My	Do	Regulatory Affairs Operations Officer	Harvard Catalyst - Harvard Medical School
Luke	Gelinas	Chairperson	Advarra IRB
Jennifer	Goldsmith	Director of Administration, Global Health Equity	Brigham and Women's Hospital
Bridget	Gonzales	Director, Training and Professional Development	ACRP
Elisa	Hurley	Executive Director	PRIM&R
Yoichiro	Inagaki	Vice President	Kowa Pharma Development Co.
Tesheia	Johnson	Dir Clinical Research Yale School of Medicine	Yale School of Medicine
Ariella	Kelman	Global Head of Bioethics	Genentech
Aaron	Kirby	Director of Regulatory Affairs and Operations	Harvard Catalyst
Sidney	Klawansky	Instructor	Harvard Chan School of Public Health
Barbara	Kress	Executive Director	Merck
Sabrina	Kurtz-Rossi	Assistant Professor	Tufts University School of Medicine
Sarah	Larson	Director, Global Clinical Engagement	Biogen
Joaquina	Lazaro	Assistant General Counsel	Pfizer Inc.
Marcia	Levenstein	Senior Advisor	Vivli

Rebecca	Li	Executive Director	Vivli
Michelle	Limoli	Senior Int'l Health Science Advisor	CBER, US FDA
Murray	Lumpkin	Deputy Director - Integrated Development	Bill & Melinda Gates Foundation
Jules	Mitchel	President	Target Health Inc.
Sandra	Morris	VP Strategy Realization	Johnson & Johnson
Laurie	Myers	Global Health Literacy Director	Merck & Co., Inc.
Marilyn	Neault	Research Patient Advocate	Parkinson's Foundation
Norm	Neault	Spouse/Caregiver	retired
Maxine	Nogard	Director, Ethics and Compliance	Alnylam Pharmaceuticals
Ellie	Okada	Senior Fellow	Boston Cancer Policy Institute
Mitchell	Parrish	EVP & General Counsel	Quorum Review IRB
Jenny	Petersen	Associate Director, Clinical Trial Transparency	Alnylam Pharmaceuticals
Guido	Rasi	Executive Director	European Medicines Agency
Maria	Rocha	Sr. Manager, Clinical Trial Disclosure	Sunovion Pharmaceuticals
Stephen	Rosenfeld	Executive Board Chair	Quorum Review IRB
Angie	Sanchez	Research Fellow	MGH CARE Research Center
Jennifer	Scanlon	Director Pharma Ventures	Northwell Health
Jessica	Scott	Head of R&D Patient Engagement	Takeda
Patricia	Seymour	Director of IRB Operations	New England IRB
Im Hee	Shin	Professor, School of Medicine	DCUMC/CIMI(Daegu Catholic Univ. Medical Center/Comprehensive and Integrative Medicine Institute)
Paul	Slater	Co-Founder, Life Sciences Innovation	Microsoft
Michael	Steel	Senior Advisor, Chief Medical Office	Novartis Pharma AG
Anna	Suojanen	Regulatory Affairs Operations Officer	Harvard Medical School
Magdalena	Taber	Consultant	Independent Consultant
Christopher	Trudeau	Associate Professor	University of Arkansas for Medical Sciences
Robert	Truog	Director, Center for Bioethics	Harvard Medical School
Jennifer	Van Ekelenburg	Head Human Subject Research Gov & Disclosure	GSK
Ainhoa	Vilarrubias	Staff Administration	MGH CARE Research Center
Peter	Wahl	Senior Director Clinical Research	Optum
Jonathan	Walland	Pfizer Inc.	Senior Corporate Counsel
Junyang	Wang	Clinical Analyst	US FDA
John	Whyte	Chief Medical Officer	WebMD

Thomas	Wicks	CSO	TrialScope, Inc.
Brad	Wilken	Deputy Director Product Development Operations	Bill and Melinda Gates Foundation
Rebecca	Williams	Assistant Director, ClinicalTrials.gov	NIH
Delia	Wolf	Associate Dean	Harvard T. H. Chan School of Public Health
Julie	Wood	Director of Strategy and Operations	Vivli
Crispin	Woolston	Deputy Head, Science Policy	Sanofi
Zheng	Yang	Head of Technology and Data Innovation	Boehringer Ingelheim
Ming	Zhao	CSO	Hormometer Hub
MRCT Center Faculty and Staff			
Hayat	Ahmed	Project Coordinator	MRCT Center
Carmen	Aldinger	Administrative and Training Manager	MRCT Center
Sylvia	Baedorf Kassis	Program Manager	MRCT Center
Mark	Barnes	Faculty Co-Director	MRCT Center
Barbara	Bierer	Faculty Director	MRCT Center
Linda	McMaster	Administrative Assistant	MRCT Center
Lisa	Murray	Student Researcher	MRCT Center
Emily	Statham	Project Manager	MRCT Center
David	Strauss	Senior Advisor	MRCT Center
Sarah	White	Executive Director	MRCT Center
Deborah	Zarin	Program Director, Advancing Clinical Trial Enterprise	MRCT Center

Appendix 2: Meeting Agenda

MRCT Center 2018 Annual Meeting

Agenda

Wednesday, December 5, 2018

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

Time	Topics/Speakers
7:45 – 8:15 AM	**Breakfast & Registration**
8:15 – 8:30 AM	**Welcome and Introductions** Mark Barnes and Barbara Bierer
8:30 – 9:15 AM	**Keynote** **Topic: GDPR** **Introduction: Mark Barnes** **Professor Guido Rasi, Executive Director, European Medicines Agency (EMA), United Kingdom** **Moderator: Mark Barnes**
9:15 – 10:00 AM	**Representation of Diverse Populations – Panel** • **David Strauss** (Austin Riggs Center): Introduction to the project, scope of work, and how we can affect change • **CAPT Richardae Araojo** (USFDA): Diverse patient engagement in clinical trials and current states (FDA Perspective) • **Luther Clark** (Merck): Diversity in the genomic era • **Barbara Bierer** (MRCT Center)**:** Current operational barriers and potential solutions **Moderator: Barbara Bierer**
10:00 – 10:45 AM	**Keynote 2:** **Topic: Advancing the study of the clinical trials** **Deborah Zarin, Program Director, *Advancing the Clinical Trial Enterprise*, MRCT Center** **Moderator: Sarah White**

10:45 – 11:15 AM	**Break**
11:15 – 11:45 AM	**Capacity Building** Update / Training • **Sarah White** (MRCT Center) • **Murray Lumpkin** (Bill & Melinda Gates Foundation) • **Michelle Limoli** (USFDA) **Moderator: Sarah White**

11:45 AM – 12:30 PM	**Health Literacy in Clinical Research – Panel**
	• **Sylvia Baedorf Kassis** (MRCT Center): The Health Literacy Need
	• **Marilyn Neault** (Research Patient Advocate): Call to Action: The Participant Experience
	• Health Literacy Case Studies
	  ○ **Christopher Trudeau** (University of Arkansas): Academic Center
	  ○ **Laurie Myers** (Merck): Pharmaceutical Company
	• **Sarah White** (MRCT Center)**:** The future of health literacy at the MRCT Center: Introduction of interactive website
	Moderator: Sarah White

12:30 – 12:45 PM	**Closing Remarks** Mark Barnes and Barbara Bierer
12:45-1:00 PM	**Lunch**

1:00-5:00 PM	**Executive Committee & Steering Committee Meeting** *For MRCT Center sponsors only*

Appendix 3: Speaker Biographies

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

CAPT Richardae Araojo serves as the Associate Commissioner for Minority Health and Director of the Office of Minority Health in the Office of the Commissioner at the U.S. Food and Drug Administration (FDA). In this role, CAPT Araojo provides leadership, oversight, and direction on minority health and health disparity matters for the Agency. The Office of Minority Health aims to promote and protect the health of diverse populations through research and communication that addresses health disparities.

CAPT Araojo previously served as the Director of the Office of Medical Policy Initiatives (OMPI) in FDA's Center for Drug Evaluation and Research (CDER), where she managed the OMPI immediate office and three divisions. She led a variety of broad-based medical and clinical policy initiatives to improve the science and efficiency of clinical al trials and enhance professional and patient labeling. CAPT Araojo worked collaboratively with other FDA disciplines, program areas, and FDA centers to foster an interdisciplinary approach to policy development and to enhance the integration of the continuingly evolving science and policy into FDA's drug development and regulatory review processes. She provided oversight and direction for cross-cutting center and Agency working groups, as well as collaborations with external constituents, to advance medical policy development.

CAPT Araojo joined FDA in 2003, where she held several positions in CDER's Office of New Drugs, first serving in the Division of Psychiatry Drug Products (formerly the Division of Neuropharmacological Drug Products) and then with the Pediatric and Maternal Health Staff (currently the Division of Pediatric and Maternal Health). She then transitioned to the Office of Medical Policy in 2010, where she served as Acting Director of the Division of Medical Policy Programs, Deputy Director of OMPI, and finally Director of OMPI.

CAPT Araojo received her Doctor of Pharmacy Degree from Virginia Commonwealth University, completed a Pharmacy Practice Residency with Emphasis in Community Ambulatory Care at the University of Maryland, and later earned a Master's degree in Pharmacy Regulation and Policy from the University of Florida.

Luther Clark, M.D., is Deputy Chief Patient Officer, Global Director, Scientific Medical and Patient Perspective (SMPP), and leader of the Patient Insights team in Merck's Patient Innovation and Engagement group. His responsibilities include (1) oversight responsibility for expanding Merck's capacity and competency in assuring that patients' perspectives remain central to all work; and collaboration with partners inside and outside of Merck to develop patient insights relevant to scientific, commercial, and manufacturing efforts.

Dr. Clark is also co-leader of the team that champions health care equities (including clinical research diversity and promotion of health literacy) and chairs Merck's Investigator Initiated Studies Research Committee on Patient Engagement, Health Literacy and

Diversity. Prior to joining Merck, Dr. Clark was Chief of Cardiovascular Medicine and Director of the National Institutes of Health (NIH) funded Brooklyn Health Disparities Research Center at the State University of New York Downstate Medical Center (Brooklyn, NY).

Dr. Clark earned his Bachelor of Arts degree from Harvard College and his Medical degree from Harvard Medical School. He is a Fellow of the American College of Cardiology (FACC) and the American College of Physicians (FACP), and a member of the Board of Directors of the Founders Affiliate of the American Heart Association. He is a nationally and internationally recognized leader in cardiovascular education, clinical investigation, cardiovascular disease prevention, and health equity. He has authored more than 100 publications and edited and was principal contributor to the textbook Cardiovascular Disease and Diabetes (McGraw-Hill). Dr. Clark has received numerous awards and honors, including the Harvard University Alumni Lifetime Achievement Award for Excellence in Medicine.

C. Michelle Limoli, Pharm.D., Senior International Health Science Advisor, Center for Biologics Evaluation and Research (CBER), U.S. Food and Drug Administration.

Michelle Limoli is with the International Programs Office in U.S. Food and Drug Administration's Center for Biologics (CBER). She is responsible for coordinating and collaborating on activities and strategic programs with various international organizations and governments, as well as within the CBER.

During her career at FDA, she has coordinated activities in various harmonization, multilateral and trade initiatives such as ICH (International Council on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use) currently serving as the Chair of the ICH Training Subcommittee, VICH (ICH for Veterinary Medicinal Products), APEC Regulatory Harmonization Steering Committee as current Co-Chair, ICCR (International Cooperation on Cosmetics Regulation), GHTF (Global Harmonization Task Force on Medical Devices), IMDRF (International Medical Device Regulators Forum), IPRP (International Pharmaceutical Regulators Program), the OECD, and WHO.

Michelle joined CBER after having worked in the Center for Drug's international programs, and the Office of the Commissioner, where Michelle served as the Director of FDA's Europe Office. She has also worked on various cross-cutting initiatives such as international medical product anti-counterfeiting, nanotechnology, IRB and ethical issues, and exporting of pharmaceuticals for international clinical trials.

Michelle is a clinical pharmacist with both hospital and community pharmacy experience. She earned a B.S. Pharm and Pharm.D. from the University of Georgia.

Murray M. Lumpkin, M.D., M.Sc. is the Deputy Director – Integrated Delivery and Lead for Global Regulatory Systems Initiatives (except pharmacovigilance) at the Bill and Melinda Gates Foundation from January 2014 to the present. These initiatives are focused on working with partners such as WHO, PAHO, AFRO, regulatory regionalization initiatives, and NRAs (in all parts of the world) to make more efficient and effective (without sacrificing product quality, efficacy, or safety) the regulatory processes through which medical and vector control products must pass to be developed, be eligible for procurement, and be legally marketed *in low- and middle-income countries*.

Prior to joining the Gates Foundation, Dr. Lumpkin had a 24-year career with the US FDA, including Director - Division of CDER's Anti-infective Drug Products (1989-1993), Deputy Center Director for Review Management at US FDA's CDER (1993-2000), Associate, then Deputy Commissioner for International and Special Programs (2005-2011), and Commissioner's Senior Advisor & Representative for Global Issues (2011-2013).

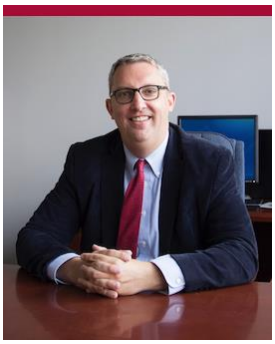
Dr. Lumpkin holds a M.D. (board certified in pediatrics), served a post-graduate fellowship in pediatrics and pediatric infectious diseases at the Mayo Clinic, Rochester, Minnesota and as Fulbright Scholar - M.Sc. in medical parasitology – University of London. He holds a Diploma in Tropical Medicine & Hygiene at the London School of Hygiene and Tropical Medicine and served for 3 years as pediatric hospitalist and lead for infectious diseases at East Tennessee Children's Hospital. He has also worked in refugee camp in Bangladesh.

Laurie Myers, MBA, Global Health Literacy Director, Merck & Co., Inc. For the past 8 years, Laurie has led Merck's health literacy efforts in support of improved patient communications, including medication labeling, packaging, clinical trial materials, lay summaries, and patient education. Laurie has worked to include respondents with low health literacy into patient labeling research, which earned her and her team an IHA national health literacy award. She works and speaks internationally, aiming to increase awareness of the importance of health literacy especially in policy. She has co-chaired two US working groups on lay summaries and health literacy in clinical trials, at the MRCT (Multi-Regional Clinical Trials Center of Brigham and Women's and Harvard). She served as an invited member of the EMA lay summaries working group, where she helped to influence final EU guidance to reflect principles of health literacy, numeracy, and readability. She did a plenary session at the 2017 Asia Health Literacy Conference and recently at an EU labeling conference, highlighting global best practices in patient labeling. She was an invited speaker by the FDA at a 2017 labeling conference, with an international audience of over 2000 people in 42 countries. She has co-authored six publications, and serves on the US National Academies Health Literacy Roundtable. She has a Bachelor's degree from Yale and an MBA from Wharton.

Marilyn Neault, PhD, Research Advocate, Parkinson's Foundation**.** Dr. Neault retired in March 2017 from 45 years in pediatric audiology, the last 35 years at Boston Children's Hospital, where she directed audiology programs in the Department of Otolaryngology and Communication Enhancement and served as Assistant Professor of Otolaryngology at Harvard Medical School. She maintains an association with Boston Children's Hospital for the purposes of advocacy, special projects, and ties to consumer organizations. Prior to her retirement, she chaired the Cochlear Implant Specialty Certification committee for the American Board of Audiology. She served as program chair biennially over 20 years for the Northeast Cochlear Implant Convention, a unique convention of consumers and clinicians teaching and learning together. She served for 10 years on the audiology advisory panel for a cochlear implant manufacturer. She chaired the task force that spearheaded the Massachusetts law which provides for universal newborn hearing screening. She worked with a parent coalition to support the passage of the Massachusetts law which mandates health insurance coverage for hearing aids for children. Her clinical research interests centered on hearing loss in special pediatric subgroups and on optimization of pediatric cochlear implant outcomes. Her symptoms of Parkinson's Disease (PD) began in 2004, and PD was diagnosed in 2009. She now participates in Parkinson's activities for dance exercise, choral singing, fundraising, and legislative advocacy. She recently participated as a subject in a Phase 3 clinical trial for a new drug for Parkinson's. She serves on a Parkinson's patient advisory board for a pharmaceutical company. She has attended a Parkinson's Foundation Learning Institute at Emory University to develop skills in research advocacy from the patient's viewpoint. She enjoys her new-found, accidentally-discovered ability to compose piano music. Marilyn was born in Wisconsin and lives in Westwood, MA with her husband Norm. They have two grown daughters and three grandchildren.

Professor Guido Rasi, began his second term as Executive Director of EMA on 16 November 2015. From November 2014 to mid-November 2015, Professor Guido Rasi served as EMA's Principal Adviser in Charge of Strategy. From November 2011 to November 2014 he was the Executive Director of the European Medicines Agency and a member of its Management Board in the three years prior to this. He was Director-General of the Italian Medicines Agency from 2008 to 2011 and member of the Management Board from 2004 and 2008. He was made full professor of microbiology at the University of Rome 'Tor Vergata' in 2008. From 2005 to 2008 he was Director of Research at the Institute of Neurobiology and Molecular Medicine of the National Research Council (CNR) in Rome. From 1990 to 2005 Professor Rasi worked at the Institute for Experimental Medicine of the National Research Council, Italy. He had a teaching and research experience at the University of California, Berkeley in 1999.

Professor Rasi holds a degree in medicine and surgery, with specialisations in internal medicine, allergology and clinical immunology, from the University of Rome. From 1978 to 1990, he worked as a physician in hospital, research and private practice. He is author of more than 100 scientific publications. Prof Rasi was born in Padova, Italy and is married with two children.



Christopher Trudeau, JD is an Associate Professor at the University of Arkansas for Medical Sciences' Center for Health Literacy. He holds a dual appointment with the Faculty of Law at the University of Arkansas Little Rock, Bowen School of Law. In this dual role, he teaches health literacy courses for all of UAMS's health programs, he teaches law & medicine for medical students, and he teaches clear legal writing for law students.

Professor Trudeau is an internationally recognized expert on health literacy, plain language, and the law, who is a member of the National Academies of Science, Engineering, and Medicine's Roundtable on Health Literacy. He frequently speaks on improving informed consent practices, creating clear legal documents that people can understand, and on novel ways to improve health equity and health outcomes while reducing organizational risks and increasing legal compliance.

Deborah Zarin, MD was the Director of ClinicalTrials.gov between 2005 and 2018. In that capacity, she oversaw the world's largest clinical trials registry, as well as the development and implementation of the first public database for summary clinical trial results. She also played a major role in the development and implementation of key legal and policy mandates for clinical trial reporting, including regulations under FDAAA (42 CFR Part 11) and the NIH trial reporting policy. Dr Zarin's recent research has been on the quality of trial reporting, as well as issues in the design and analysis of clinical trials. Dr. Zarin will be joining the MRCT Center, where she will be Program Director, *Advancing the Clinical Trial Enterprise*, and Member of the Faculty, Harvard Medical School.

Previous positions held by Dr. Zarin include the Director, Technology Assessment Program, at the Agency for Healthcare Research and Quality, and the Director of the Practice Guidelines program at the American Psychiatric Association. In these positions, Dr. Zarin conducted systematic reviews and related analyses in support of evidence based clinical and policy recommendations.

Dr. Zarin graduated from Stanford University and received her doctorate in medicine from Harvard Medical School. She completed a clinical decision making fellowship and a pediatric internship, and is board certified in general psychiatry as well as in child and adolescent psychiatry.