Dear MRCT Friends,

As we look back on the past year, we are proud and very grateful for your ongoing support to the center. It has been a milestone year for Multi-Regional Clinical Trials Center (MRCT) as we have settled into our new location in the heart of Harvard Square, added new staff and welcomed 10 new sponsors.

Our members, including over 120 of you who actively participated in our initiatives, have worked tirelessly over the last year to help us meet our goals, launch new projects and ensure that the momentum is sustained since our first concept meeting in 2011. This year, we have achieved important milestones: completion of Protocol Ethics Initiative goals; training of new fellows to serve on Data Safety Monitoring Boards; and development of a Harmonized Set of Competencies for Clinical Researchers.

This past January, in response to the shifting regulatory landscape we launched a new initiative in Clinical Trial Data Sharing. We have vigorously advanced this project and developed a robust framework within which responsible data sharing can be enabled. As progress and consensus building is often derived from sharing of ideas across diverse viewpoints, we were delighted to welcome over 150 of you to our Clinical Trial Data Sharing conference in May.

We also continue to grow our global mission of improving the quality of clinical trials through expanded international collaborations, including key players in India, Korea and Japan.

This progress report provides a glimpse into the progress and milestones achieved by our working groups. Their tenacity and hard work has yielded great returns. As our center evolves, and awareness of our mission grows, so too does the number of opportunities. We look forward to 2014 as the year in which we continue at an invigorating pace, forge new collaborations and make even greater strides. We will delve deeper into areas, such as offering guidance in regulatory harmonization, and launching new initiatives including one centered on returning individual results to patients. We also hope to engage those of you who have not yet actively participated. We believe joining would bring new meaning and value to the challenges you face in your own world.

We look forward to working with you in 2014 and beyond. Thanks to you all, we are well positioned to advance our mission in making a difference in how clinical trials are conducted.

Barbara Bierer  
Co-Chair, MRCT

Mark Barnes  
Co-Chair, MRCT

Rebecca Li  
Executive Director, MRCT
To improve the design, conduct, and oversight of multi-regional clinical trials, especially trials sited in or involving the developing world; to simplify research through the use of best practices; and to foster respect for research participants, efficacy, safety and fairness in transnational, trans-cultural human subjects research.
HOW WE WORK

IMPLEMENTATION STRATEGY

Identify Initiatives
Projects selected for launch will be those with demonstrated:
› Impact
› Significance
› Expertise within our stakeholder base
› Actionable within the 6-12 month timeframe

Form Working Groups
Teams will be formed through careful selection and include:
› Global diversity
› World class experts
› Enthusiastic leaders
› Deliverables and clear timeline

Pilot Solutions
Project solutions identified will be:
› Piloted within our sponsor organizations
› Results will be evaluated and published
› If positive, the dissemination strategy will be deployed to ensure widespread adoption

Implement/Adopt
Project solutions implemented through:
› Training programs conducted through our partner organizations
› Deploying MRCT members and stakeholders to disseminate guidelines and practices
› Working with MRCT partner associations to deploy sustainable training
We have five primary focus areas in which we work. Each area was carefully selected to align with the mission and objectives of the Center.

1. **Clinical Trial Data Sharing and Transparency**
   We offer a multi-stakeholder view of how data sharing can be implemented by providing researchers with:
   - A framework for data sharing within which to operate
   - A taxonomy and terms for data sharing
   - Clear criteria and processes for data generators and requestors

2. **Data and Safety Monitoring Boards (DSMBs)**
   This initiative aims to:
   - Build the capacity of DSMBs with a focus on increasing engagement of experts from emerging countries
   - Promote best practice guidelines for DSMBs

3. **Protocol Ethics Guidance**
   Representatives from industry and academia join together to create a practical resource for the ethical design and conduct of multi-regional clinical trials protocols.

4. **Investigator Competence and Training**
   The focus of this initiative is on developing harmonized core competencies for clinical research professionals. This initiative is a collaboration between a dozen like-minded organizations across the clinical trials enterprise.

5. **Global Regulatory Engagement**
   This initiative focuses on engagement of regulators worldwide. We aim to develop authentic substantive partnerships with leaders who live and work in the developing world. The objective of this effort is to bring a more global perspective to MRCT projects and assist in training and implementation of trials in these regions.

Scan for more info on these focus areas or visit: mrct.globalhealth.harvard.edu/pages/focus-areas
Preparing for Responsible Clinical Trial Data Sharing

**Phase 1: Development of a Framework for Sharing**

Against the backdrop of a shift in regulatory policy towards more open sharing of participant-level data, the MRCT Clinical Trial Data Sharing Model Development group was formed in January 2013. This team developed a set of governing principles, models and key criteria to help guide decisions about data sharing.

Four potential models for data sharing emerged. Various subgroups critically analyzed each model, balancing risks and benefits to patient privacy and commercial confidentiality, and evaluating how well the models met the need for transparency and access to data.

**Phase 2: Implementation of Solutions for Data Sharing**

Once a framework, taxonomy and terms for data sharing were established in Phase 1, the Data Sharing Implementation workgroups launched and focused on the following issues: specific criteria for selection and rules of engagement for the requestor, reviewer and data generator; informed consent language; commercially confidential information.
MILESTONES

May 2013
MRCT co-hosted “Issues and Case Studies in Clinical Trial Data Sharing: Lessons and Solutions” with the Petrie-Flom Center at Harvard Law School. One model, employing a “Learned Intermediary” or independent board to evaluate data requests, appealed to many of the stakeholders.

July 2013
MRCT Data Sharing Implementation Initiative Launched and focuses efforts on specific practical solutions to enable participant-level data sharing.

September–October 2013
Major Deliverables Published

› Key publications authored by the Multi-Regional Clinical Trials Center workgroup appear in New England Journal of Medicine and Bloomberg BNA

› Multi-Regional Clinical Trials Center presents framework and criteria at key meetings and conferences including DIA and IOM

› Responses to FDA and EMA policies pertaining to data sharing posted

MEMBERS CONTINUED
Kate Gallin Heffernan, Verrill Dana LLP
Cindy Henderson, Veristat
Paul Hryvniak, MRCT Center at Harvard
Elisa Hurley, PRIM&R
Mercy Imahiyerobo, Harvard School of Public Health
Julie Kaberry, Harvard School of Public Health
Aaron Kesselheim, Brigham and Women’s Hospital
Sarah Larson, Biogen Idec
Marcia Levenstein, Pfizer Inc.
Rebecca Li, MRCT Center at Harvard
Mark Lim, FasterCures
Martin Majchrowicz, Genentech, Roche
Charles Martel, Optum Labs
Justin McCarthy, Pfizer
Jennifer Miller, Harvard University
Jules Mitchell, Target Health Inc.
Sandra Morris, Johnson & Johnson
Patricia O’Rourke, Partners HealthCare
Shawn Pelletier, Bristol Meyers Squibb
David Peloquin, Ropes & Gray LLP
Tom Peppard, Bill & Melinda Gates Foundation
Ben Rain, Harvard Law School
Ben Rotz, Eli Lilly
Don Stanski, Novartis
Caroline Stockwell, Pfizer
Patricia Teden, Teden Consulting LLC
Fabio Thiers, VIS Research Institute
Mary Wacholtz, Johnson and Johnson
Marc Wilenzick, MRCT Center at Harvard
Cris Woolston, Sanofi
FOCUS AREA 2:
DATA & SAFETY MONITORING BOARDS (DSMBs)

Building Capacity in South Korea and Thailand

MRCT recognizes that the countries in which global trials are conducted are often unrepresented in the Data and Safety Monitoring Boards (DSMBs) that oversee safety for these trials. The ultimate goal of our training program is to transform motivated fellows into DSMB champions within their own countries. It is our hope that they would participate, educate and implement DSMBs locally and for global studies.

Maria Im Hee Shin, PhD, a leader in her field of biostatistics, is transforming how South Korea views Safety Monitoring. Dr. Shin, Professor, Chair and Director of the Department of Medical Statistics & Informatics, School of Medicine, Catholic University of Daegu participated in the first class of Harvard MRCT fellows. Traveling from Korea, she realized the importance of DSMBs and how they can be implemented in her country to oversee clinical trials safety.

For additional information on this focus area:
mrct.globalhealth.harvard.edu/pages/data-and-safety-monitoring
Wasana Prasitsuebsai, MD, MPH, one of the fellows trained in Boston, has come full circle in applying her initial training as a leader in her field. Dr. Prasitsuebsai is a pediatric AIDS specialist and since the training has been recruited to serve on an industry Data and Safety Monitoring Board (DSMB) of one of our sponsors. She has also organized a regional MRCT-led DSMB training at the Thai Red Cross – AIDS Research Center conference in January 2014. A new class of Thai fellows has been selected to attend this upcoming training expanding the knowledge base within Thailand. These fellows will also be available to participate on DSMBs for our sponsoring organizations.

**MILESTONES**

September 2012 – April 2013

Curriculum and Mock-DSMB exercises developed for DSMB trainings. Fellows recruited from over 150 applicants.

Workstream produced a concise curriculum focused specifically on preparing Data and Safety Monitoring Board fellows to serve on industry or government trial committees.

May 2013

Training of First class of 11 Fellows

In conjunction with the 34th Society for Clinical Trials Meeting in Boston, Chuck Knirsch (Pfizer), Joe Massaro (Boston University), Susan Ellenberg (U. Penn) and Janet Wittes (Statistics Collaborative) trained 11 MRCT Data and Safety Monitoring Board Fellows. This inaugural class of highly experienced investigators represented Russia, Korea, Brazil, Argentina, Mexico, Tanzania, Thailand, India and South Africa.

October 2013

Training of Korean fellows

In conjunction with the Global Clinical Research Summit - Daegu University, Drs. Barbara Bierer (MRCT Executive Co-Chair) and Joe Massaro (Boston University) trained 20 new fellows at the Global Clinical Research Summit in Daegu City. Six fellows are members of the Korean Ministry of Food and Drug Safety and within their regulatory capacity will serve to champion the concepts of DSMBs in Korea.
Creation of an Ethics Resource Tool for the Protocol Design Process

The MRCT Ethics Essential Elements resource helps ensure that key ethical questions are addressed when navigating the complicated process of designing protocols for multi-regional clinical trials. This resource identifies main decision points and key issues such as country selection, use of placebo, and post-trial access, while incorporating a global perspective, useful examples, references and region-specific considerations.

“We believe that the use of this tool by protocol drafters will help to improve the efficiency of IRB review of research because the drafter will have thought through and addressed in writing the ethical issues prior to submission.”

David Forster
Vice President, Compliance
Western Institutional Review Board
MILESTONES

July 2013

Workgroup completes draft MRCT Ethics Essential Elements including the eleven “essential elements,” elaborated with associated “detailed points to consider” and useful examples. A survey of 100 protocols to verify routine coverage of the Essential survey analysis is launched.

November 2013

The Essential Elements was launched at the PRIM&R conference in Boston and the resource protocol survey project results were presented to provide the rationale for its use.

For additional information on this focus area: mrct.globalhealth.harvard.edu/pages/protocol-ethics-guidance

ETHICS ESSENTIAL ELEMENTS

Addressing Relevant Question  Choice of Control and Standard of Care  Choice of Study Design  Choice of Subject Population  Potential Benefits and Harms  Informed Consent  Community Engagement  Return of Research Results and Management of Incidental Findings  Post-Trial Access  Payment for Participation  Study-Related Injury

Easy to navigate ethics web tool for protocol writers and ethics committees.
FOCUS AREA 4:
INVESTIGATOR COMPETENCE & TRAINING INITIATIVE

Harmonization of Training for Clinical Research Professionals

The MRCT training workgroup is collaborating with a diverse stakeholder group to jointly develop a set of criteria (Domains and Core Competencies) that may be used for the conduct of clinical research. These criteria are harmonized across a number of training content from our collaborators. It is our hope that eventually this harmonized criteria set may be used to support a global effort to increase efficacy and quality in the implementation of clinical research studies.

MILESTONES

May 2013
Launch of the Joint Task Force for Clinical Trial Competency
At the MAGI conference, MRCT helped launch the Joint Task Force for Clinical Trial Competency. This Task Force represents academia, industry and the clinical community and was formed to harmonize individual efforts into a universal set of domains and competencies.

October 2013
Harmonized Competencies Completed
In collaboration with the Consortium of Academic Programs in Clinical Research, MRCT completed harmonizing organizational competencies derived from 8 groups with varying approaches to deriving core competencies for clinical researchers. The output of this work was presented at the MAGI conference, Las Vegas, October 2013 to members of the clinical research enterprise for approval and endorsement.
FOCUS AREA 5:
GLOBAL REGULATORY INITIATIVE

GLOabal Regulatory Mission

Understand
Engage
Act

Understand through discussion with passionate leaders which multi-regional clinical trials issues are most important to our stakeholders.

Engage in critical discussions with our global stakeholders to recognize which regions and issues MRCT’s expertise and skills can add significant value.

Act to build capacity, offer training and develop policy to enable global change in the conduct of multi-regional clinical trials.

Partnering with Global Leaders

The global regulatory initiative focuses on engagement of regulators worldwide to develop authentic substantive partnerships with leaders who live and work in the developing world. The objective of these efforts is to bring a more global perspective to MRCT projects and assist in training and implementation of trials in these regions.

Milestone

Key Relationships Developed
In the last year, MRCT has developed key relationships with regulators and innovative thought leaders in India, Korea, China, Brazil, Russia, the European Union and Canada, and other countries. This global community will work with us to build capacity and produce responsible solutions to shared global problems in the conduct of clinical trials.

Dr. Ock-Joo Kim is an Associate Professor at the Seoul National University College of Medicine. She has been a Global Advisor to MRCT since 2012, offering her perspective from conducting clinical trials in South Korea.

For additional information on this focus area: http://mrct.globalhealth.harvard.edu/pages/global-regulatory-initiative
2013 ACCOMPLISHMENTS

CLINICAL TRIAL DATA SHARING:

**MRCT** publishes in the *New England Journal of Medicine*  
"Preparing for Responsible Data Sharing"  
October 18, 2013

**Informed Consent Subgroup**  
Posts Comments to EMA Draft Policy 0070  
October 18, 2013  
bit.ly/Comments_EMA_Draft_Policy_0070

**MRCT Comments on FDA Docket No. FDA-2013-N-0271**  
Availability of Masked and De-identified Non-Summary Safety and Efficacy Data  
August 2013  
bit.ly/Comments_FDA2013N0271

**MRCT** publishes in Bloomberg BNA  
July 2013  
bit.ly/MRCT_in_Bloomberg_BNA

**MRCT Clinical Trials Data Sharing Conference**  
Co-hosted with Petrie-Flom Center at Harvard Law School  
May 2013  
bit.ly/Data_Sharing_Conference_PPTpresentation  
bit.ly/Data_Sharing_Conference_proceedings

PROTOCOL ETHICS:

**MRCT Ethics Essential Elements and Points to Consider** tool kit and Reference Document  
Launched at 2013 PRIM&R AER Conference  
November 2013  
bit.ly/MRCT_Ethics_Essential_Elements

**MRCT Comments on Declaration of Helsinki**  
Issued for public comment by the Counsel of the WMA  
April 2013  
bit.ly/Comments_Declaration_of_Helsinki

INVESTIGATOR COMPETENCE & TRAINING:

**Measuring PI and Site Qualifications for Conducting Clinical Trials** Proceedings  
Published October 2012  
bit.ly/Harvard_Symposia_proceedings

**Harmonized Core Competencies** for the Clinical Research Professional  
October 29, 2013  
bit.ly/Harmonized_Competencies
Thank you for contributing your expertise to improve the quality standards for global clinical trials and for engaging with other like-minded organizations and stakeholders to address the common challenges associated with globalization. Your contribution ensures that your institution continues to be a leader in its commitment to the ethical conduct of clinical trials and benefits from best practice discussions and MRCT projects.

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The MRCT Team (left to right): Paul Hryvniak, Alla Digilova, Jacquelyn Murphy, Rebecca Li, Helia Morris, and Amish Shah

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