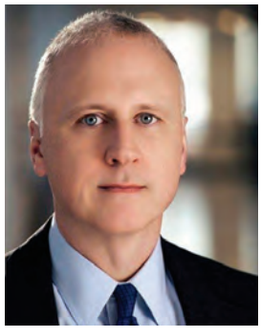
2013 PROGRESS REPORT

GLOBAL FOCUS

MRCT Multi-Regional Clinical Trials

The MRCT Center at Harvard


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

OUR MISSION »

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.

OUR OBJECTIVES

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

FOCUS AREAS »

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

FOCUS AREA 1:

CLINICAL TRIAL DATA SHARING & TRANSPARENCY »

PHASE 1

Four Models of Data Sharing and Framework

CONFERENCE AT HARVARD

"Consensus Building of the Issues and Case Studies in Clinical Trial Data Sharing Conference" May 17, 2013

PHASE 2

Implementation of Solutions for Data Sharing

PHASE 1 CO-CHAIRS

Salvatore Alesci, *PhRMA*

Michelle Mello, *Harvard School of Public Health*

PHASE 2 CO-CHAIRS

Barbara Bierer, *Brigham and Women's Hospital, MRCT*

Jessica Scott, *GlaxoSmithKline*

MEMBERS

Albert J. Allen, *Eli Lilly*
Mark Barnes, *Ropes & Gray LLP*
Martine Benoit, *Department of Justice, Canada*
Melissa Binz, *Novartis*
Theodora Cohen, *Harvard Clinical Research Institute*
Karen Craun, *Sanofi*
Amy Davis, *PRIM&R*
Alla Digilova, *MRCT Center at Harvard*
David Dorsey, *Janssen Research & Development*
Denise Edmonds, *Chiltern*
Yaniv Erlich, *Whitehead Institute for Biomedical Research*
Susan Forda, *Eli Lilly*
David Forster, *Western IRB*
Jeffrey Francer, *PhRMA*
Zach Hallinan, *CISCRP*

For additional information on this focus area:

mrct.globalhealth.harvard.edu/pages/clinical-trial-data-sharing-and-transparency

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.

Expert panels debate the MRCT team recommendations.

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

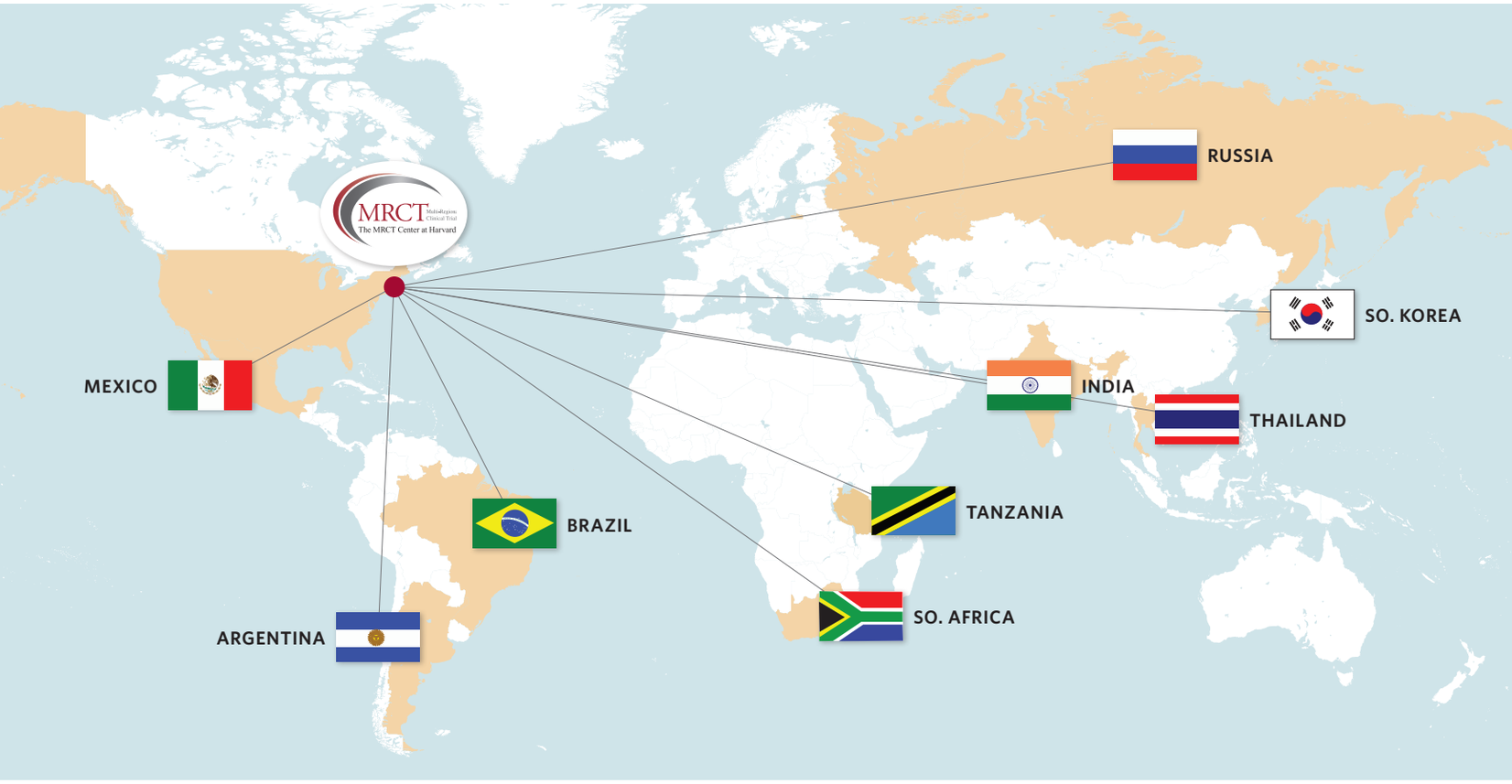
- Key publications authored by the Multi-Regional Clinical Trials Center workgroup appear in *New England Journal of Medicine* and *Bloomberg BNA*
- Multi-Regional Clinical Trials Center presents framework and criteria at key meetings and conferences including DIA and IOM
- Responses to FDA and EMA policies pertaining to data sharing posted

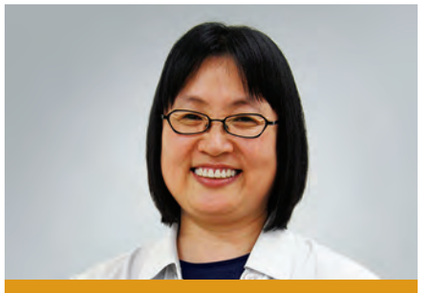
MEMBERS CONTINUED

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 Mitchel, *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 Roin, *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) »





Maria Im Hee Shin, PhD,
DSMB fellow from South Korea

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.

Wasana Prasitsuebsai
Pediatrics, HIV/AIDS,
DSMB fellow from Thailand

MILESTONES

MRCT trained the first class of 11 Fellows from nine countries.

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.

FOCUS AREA 3:

PROTOCOL ETHICS GUIDANCE »

Protocol Ethics Committee convenes to finalize essential elements.

CO-CHAIRS

Susan Callery-D'Amico, *AbbVie*
David Forster, *Western Institutional Review Board*

MEMBERS

Mark Barnes, *MRCT, Ropes & Gray LLP*
Barbara Bierer, *MRCT, Brigham & Women's Hospital*
Amy Davis, *PRIM&R*
Kate Gallin Heffernan, *Verrill Dana LLP*
Elisa Hurley, *PRIM&R*
John Isidor, *Human Subject Protection Consulting, LLC*
Rebecca Li, *MRCT Center at Harvard*
Maeve Luthin, *PRIM&R*
Holly Lynch, *Harvard Law School*
Lindsay McNair, *WIRB Copernicus*
Jennifer Miller, *Harvard University*
Jacquelyn Murphy, *MRCT Center at Harvard*
Rohin Rajan, *Deloitte Consulting*
Marjorie Speers, *AAHRPP*
Toshi Tominaga, *Osaka City University Hospital*
Luann Van Campen, *Eli Lilly*
Mary Wacholtz, *Janssen*
Marc Wilenzick, *MRCT Center at Harvard*
Delia Wolf, *Harvard (HSPH, HDS, HMS)*
Cris Woolston, *Sanofi*

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

Easy to navigate ethics web tool for protocol writers and ethics committees.

1. Addressing Relevant Question
2. Choice of Control and Standard of Care
3. Choice of Study Design
4. Choice of Subject Population
5. Potential Benefits and Harms
6. Informed Consent
7. Community Engagement
8. Return of Research Results and Management of Incidental Findings
9. Post-Trial Access
10. Payment for Participation
11. Study-Related Injury

FOCUS AREA 4:

INVESTIGATOR COMPETENCE & TRAINING INITIATIVE »

DOMAINS AND CORE COMPETENCIES

1. Scientific Concepts and Research Design
2. Ethical Considerations, Patient Care and Safety
3. Medicines Development and Regulation
4. Clinical Trials Operations (Good Clinical Practice)
5. Study and Site Management
6. Data Management and Informatics
7. Leadership and Professionalism
8. Communication & Teamwork

CO-CHAIRS

Sarah Carter, *Amgen*
Sheila Clapp, *FHI*

MEMBERS

Mohanish Anand, *Pfizer*
Mark Barnes, *MRCT, Ropes & Gray LLP*
Barbara Bierer, *MRCT, Brigham & Women's Hospital*
John Constantine, *Merck*
Geoff Garabedian, *Quintiles*
Kim Havens, RN, *PPD*
Agnes V. Klein, *Health Canada*
Rebecca Li, *MRCT Center at Harvard*
Jacquelyn Murphy, *MRCT Center at Harvard*
Jason Nyrop, *Deloitte Consulting*
Christine Pierre, *SCRS*
Rohin Rajan, *Deloitte Consulting*
Anna Ravdel, *Synergy Research Group*
Natalie Rossignol, *Bill & Melinda Gates Foundation*
Tim Shi, *Global MD*
James Thomasell, *Association of Clinical Research Professionals*
Marc Wilenzick, *MRCT Center at Harvard*

For additional information on this focus area:

mrct.globalhealth.harvard.edu/pages/investigator-competence

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 »

GLOBAL REGULATORY MISSION

Understand

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

Engage

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

Act

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.

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.

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.

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.

EXECUTIVE COMMITTEE

Amgen, Inc.
Bill & Melinda Gates Foundation
Brigham and Women's Hospital
Deloitte Consulting
MRCT Center at Harvard
Novartis
Pfizer
PhRMA
Ropes and Gray LLP
Sanofi

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Merck
PRIM&R
Quintiles
School of Medicine, Catholic University of Daegu
Society for Clinical Research Sites
Synergy Research Group
Target Health Inc.
Veristat
ViS Research Institute
Western Institutional Review Board

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

MRCT Multi-Regional Clinical Trials

The MRCT Center at Harvard

Multi-Regional Clinical Trials (MRCT) Center
14 Story Street, 4th Floor
Cambridge, Massachusetts 02138
617-495-4391
mrct@harvard.edu