Proceedings
Multi-Regional Clinical Trials Center (MRCT) at Harvard
2nd Annual Meeting

4th December, 2013 • 7:30 AM – 5:00 PM

Loeb House • Cambridge, MA

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MEETING PARTICIPANTS

Name:	Job Title:	Affiliation:	Company:
Kald Abdallah	Vice President	MRCT Sponsor	Sanofi US
Salvatore Alesci	Vice President	MRCT Sponsor	PhRMA
Mohanish Anand	Sr. Director	MRCT Sponsor	Pfizer
Tanya Antonille	Director, Data Management	Work Group Member	Immune Tolerance Network
Jim Armbrust	Head, Clinical Trial Transparency & Task Force	Participant	AstraZeneca Group of Companies
Adam Asare	Director, Bioinformatics	Work Group Member	UCSF
Enrique Aviles	Chief Technology Officer	Participant	Critical Path Institute
Behtash Bahador	Outreach Coordinator	Work Group Member	CISCRP
Raj Bandaru	Clinical Operations Technology Partner	Participant	AstraZeneca
Mark Barnes	Partner	Faculty Co-Chair, MRCT; Meeting Speaker, Work Group member	Ropes & Gray, LLP; Harvard Law School; MRCT
Barbara Bierer	Senior Vice President, Research	Faculty Co-Chair, MRCT; Meeting Speaker; Work Group Member	Brigham & Women's Hospital; Harvard Medical School; MRCT
Martha Brumfield	President & CEO	Work Group Member	Critical Path Institute
Matthew Cahill	Vice President	MRCT Sponsor	Merck
Susan Callery D'Amico	Vice President R&D Quality Assurance	Meeting Speaker	ABBVIE
Anne Claiborne	Senior Program Officer	Participant	Institute of Medicine
Theodora Cohen	Executive Director	MRCT Sponsor; Work Group Member	Harvard Clinical Research Institute
Stuart Coleman	EA to Dr. Murray Abramson & Eileen Gradwell	MRCT Sponsor	Biogen - Idec
Jeffrey Cooper	Vice President Global Consulting	MRCT Sponsor Work Group Member	WIRB Copernicus Group
Alla Digilova	Research Assistant	MRCT	MRCT
Hans-Georg Eichler	Senior Medical Officer	Meeting Speaker	European Medicines Agency
Emily Eldh	Assistant Director of Clinical Research	Participant	Dana-Farber Cancer Institute
John Ennever	Director of IRB Policy Development and Compliance	Participant	Harvard University
Howard Fingert	Senior Medical Director	Participant	Takeda Pharmaceuticals
David Forster	Chief Compliance Officer	MRCT Sponsor; Work Group Member	WIRB Copernicus Group
Jeffrey Francer	Vice President & Senior Counsel	MRCT Sponsor; Work Group Member	PHRMA
Geoff Garabedian	Vice President and Managing Director	MRCT Sponsor	Quintiles
Elizabeth Garofalo	Head Clinical Development Sciences	MRCT Sponsor	Novartis Pharma AG
Cindy Geoghegan	Patient Advocate	Participant	Project Data Sphere LLC
Dean Gittleman	Sr. Director of Operations	MRCT Sponsor	Target Health Inc.

Norman Goldfarb	Managing Director	Work Group Member	First Clinical Research
Eileen Gradwell	Senior Director, Quality Operational Capabilities	MRCT Sponsor	Biogen-Idec
Zach Hallinan	Director	Meeting Speaker	CISCRP
Kimberly Haren	Senior Counsel	Participant	Bristol-Myers Squibb
Sara Harnish	Assistant Director of Non-Clinical Research	Participant	Dana-Farber Cancer Institute
Kate Heffernan	Counsel, Chairwoman Academic and Clinical Research	Work Group Member	Verrill Dana LLP
Cindy Henderson	Vice President Operations	MRCT Sponsor	Veristat
Hon Ho	Physician	Participant	NSMC
Paul Hryvniak	Program Manager	MRCT	MRCT
Elisa Hurley	Education Director	MRCT Sponsor	PRIM&R
John Isidor	CEO	Work Group Member	Human Subject Protection Consulting, LLC
Cheryl Jernigan	Patient/Cancer Research Advocate	Meeting Speaker	Susan G. Komen
Carolyn Jones	Director, Regulatory Policies	MRCT Sponsor	Biogen Idec
Kris Joshi	Global Vice President - Healthcare	Work Group Member	Oracle
Greg Koski	President and CEO	Participant	Alliance for Clinical Research Excellence & Safety
Whitney Lesch	Associate Director, Clinical Trial Transparency	Participant	Bristol-Myers Squibb
Rebecca Li	Executive Director	MRCT Executive Director	MRCT
Craig Lipset	Clinical Innovation	MRCT Sponsor; Work Group Member	Pfizer
Justin McCarthy	SVP and Associate GC	MRCT Sponsor; Work Group Member	Pfizer
Jennifer Miller	E.J. Safra Fellow	Work Group Member	Harvard University
Helia Morris	Administrative Director	MRCT	MRCT
Sandra Morris	VP Strategy Realization	MRCT Sponsor	Johnson & Johnson
Richard Moscicki	Deputy Center Director for Science Operations	Meeting Speaker	Rich Moscicki
Jacquelyn Murphy	Project Manager / Program Administrator	MRCT	Harvard University
Perry Nisen	SVP Science and Innovation	Meeting Speaker	GSK
Jason Nyrop	Senior Consultant	MRCT Sponsor	Deloitte Consulting
Ellie Okada	Social Scientist, President & CEO	Participant	Boston Cancer Policy Institute, Inc
Pearl O'Rourke	Director of Human Research Affairs	Work Group Member	Partners HealthCare Systems
Holly Peay	Vice President	Meeting Speaker	Parent Project Muscular Dystrophy
Doug Peddicord	Executive Director	Meeting Speaker	ACRO
Shawn Pelletier	Director of Transparency and Clinical Science Management	Work Group Member	Bristol-Myers Squibb
Christine Pierre	President	Participant	Society for Clinical Research Sites (SCRS)
Jeannette Potts	Vice President - Legal	Participant	Takeda Pharmaceuticals International Co.

Sandra Prucka	Consultant Scientist	MRCT Sponsor; Meeting Speaker; Work Group Member	Eli Lilly and Company
Joan Rachlin	Executive Director	MRCT Sponsor	PRIM&R
Evgeny Rogoff	Head	MRCT Global Advisor	RosZdravNadzor of Russia
Peter Ronco	Vice President - GDMA, Business Operations and Scientific Writing	Participant	Bristol-Myers Squibb
Dave Rosa	Director	Participant	ClinTec International
Natalie Rossignol	Program Officer	MRCT Sponsor	Bill and Melinda Gates Foundation
Benjamin Rotz	Adviser - Office of Medical Transparency	MRCT Sponsor	Eli Lilly
Michele Russel-Einhorn	Senior Director	Participant	Dana-Farber Cancer Institute
Donald Russell	Senior Director	MRCT Sponsor	Eli Lilly and Company
Jim Saunders	President	Work Group Member	New England Institutional Review Board
Taka Senda	Executive Vice President	Participant	Boston Cancer Policy Institute, Inc
Jessica Scott	Director, North America Medical Advocacy and Policy	Work Group Member	GSK
Tim Shi	Partners HealthCare Privacy Program Manager	Work Group Member	Global MD Organization
Im Hee Shin	Professor / Chair & Director	MRCT Sponsor	1) DCUMC 2)CIMI
Ed Silverman	Editor	Meeting Speaker	Pharmalot
Lynn Sleeper	Chief Scientist	Work Group Member	New England Research Institutes, Inc. (NERI)
Ki Cheul Sohn	COO / Professor	MRCT Sponsor	1) DCUMC 2) CIMI
Donald Stanski	Vice President, Distinguished Clinical Investigator	MRCT Sponsor; Work Group Member	Novartis Pharmaceuticals
Catherine Stehman-Breen	Vice President, Global Development	MRCT Sponsor	Amgen, Inc.
Walter Straus	Executive Director & Head, Scientific Affairs, Vaccines	MRCT Sponsor	Merck
Yoko Tanaka	Research Advisor	MRCT Sponsor; Work Group Member	Eli Lilly and Company
Patricia Teden	Principal	Work Group Member	Teden Consulting LLC
Fabio Thiers	CEO	MRCT Sponsor	ViS Research
James Thomasell	Executive Director	MRCT Sponsor	Association of Clinical Research Professionals
Toshi Tominaga	MRCT Global Advisor	Meeting Speaker	MRCT
Thomas Travison	Director, Biostatistics	Work Group Member	Partners
Pol Vandenbroucke	Vice President, Development	MRCT Sponsor	Pfizer

SPEAKER BIOGRAPHIES

MARK BARNES, J.D., LL.M, focuses his practice in the areas of research, advising clients throughout higher education and the health care industry, including pharmaceutical companies, medical device manufacturers, hospitals, and universities. He has extensive experience in legal issues related to research with humans and animals, stem cell and genetic research, research grants and contracts, research misconduct, and international research. Mark was a partner at Ropes & Gray from 2001-2008, before leaving to serve as Executive Vice President and Chief Administrative Officer at St. Jude Children's Research Hospital. Before returning to the firm, Mark also served as Senior Associate Provost for Research and Chief University Research Compliance Officer at Harvard University. In these positions at Harvard, he supervised the University's sponsored research operations and was responsible for the full range of research policy and compliance issues, including human subjects research, research misconduct, export controls, conflicts of interest, and grants and contracts compliance. Mark's diverse legal background also includes senior policy and administrative positions at the New York State Department of Health and the New York City Department of Health, where, among other duties, he directed the Ryan White CARE Act program providing medical, substance abuse and mental health treatment to New Yorkers living with HIV/AIDS. Mark Barnes co-founded and now serves as Co-director of the Multi-Regional Clinical Trials Initiative at Harvard, a University-wide and collaborative effort to improve standards for the planning and conduct of clinical trials in the developing world.

BARBARA E. BIERER, M.D., a hematologist-oncologist by training, is Senior Vice President for Research at the Brigham and Women's Hospital (BWH) and Professor of Medicine at Harvard. She is the institutional official for human subjects and animal research, for biosafety and for research integrity at the BWH. In addition, Dr. Bierer established the Center for Faculty Development and Diversity at the BWH and serves as its first director. Dr. Bierer is the Co-Chair of the Partners HealthCare Committee on Conflict of Interest and the Program Director of the Regulatory Foundations, Law and Ethics Program of the Harvard Catalyst, the Harvard Clinical and Translational Science Award. In addition to her academic responsibilities, Dr. Bierer served on the Board of Directors of both the Association for Accreditation of Human Research Protection Programs (AAHRPP) and the Federation of American Societies for Experimental Biology (FASEB). She served as the Chair of the Secretary's Advisory Committee for Human Research Protections, Department of Health and Human Services until recently. She is currently a member of the AAMC Forum on Conflicts of Interest in Academe and on the National Academies of Sciences Committee on Science, Technology and the Law. Dr. Bierer co-founded and now serves as Co-director of the Multi-Regional Clinical Trials Initiative at Harvard, a University-wide and collaborative effort to improve standards for the planning and conduct of clinical trials in the developing world.

SUSAN CALLERY D'AMICO, B.S., is a seasoned pharmaceutical industry leader and compliance expert with extensive experience in quality assurance and clinical development. Susan is the VP R&D Quality Assurance at AbbVie, Inc., where she implements, maintains, and ensures the effectiveness of the Quality Systems for pharmaceutical products. She has held senior management QA positions at Reata, Novartis, and RWJPRD (J&J) and has the breadth of drug development experience from early-man to regulatory approval and launch.

HANS-GEORG EICHLER, M.D., M.SC., is the Senior Medical Officer at the European Medicines Agency in London, United Kingdom, where he is responsible for coordinating activities between the Agency's scientific committees and giving advice on scientific and public health issues. Prior to joining the European Medicines Agency, Dr. Eichler was at the Medical University of Vienna in Austria for 15 years.

He was vice-rector for Research and International Relations since 2003, and professor and chair of the Department of Clinical Pharmacology since 1992. His other previous positions include president of the Vienna School of Clinical Research and co-chair of the Committee on Reimbursement of Drugs of the Austrian Social Security Association. His industry experience includes time spent at Ciba-Geigy Research Labs, U.K., and Outcomes Research at Merck & Co., in New Jersey. In 2011, Dr. Eichler was the Robert E. Wilhelm fellow at the Massachusetts Institute of Technology's Center for International Studies, participating in a joint research project under the MIT's NEWDIGS initiative. Dr. Eichler graduated with an M.D. from Vienna University Medical School and a Master of Science degree in Toxicology from the University of Surrey in Guildford, U.K. He trained in internal medicine and clinical pharmacology at the Vienna University Hospital as well as at Stanford University.

DAVID FORSTER, J.D., M.A., C.I.P., joined Western Institutional Review Board (WIRB) in 1996 and is currently the Chief Compliance Officer, Office of Compliance for both Western Institutional Review Board and Copernicus Group Independent Review Board. In this capacity, David oversees the Quality Control, Quality Assurance departments and Board, and is responsible for WCGIRB compliance with FDA and HHS regulations, ICH guidance, and AAHRPP accreditation requirements. David serves as auxiliary faculty at the University of Washington Department of Bioethics and Humanities and co-chairs the SACHRP Sub-Committee on Harmonisation (SOH). He is on the Certified IRB Professional (CIP) Council. He also serves on the Harvard Multiregional Clinical Trials Work Group (MRCT) and the Alliance for Clinical Research Excellence and Safety (ACRES) global steering committee. David completed a four-year term as a member of the Secretary's Advisory Committee on Human Research Protections (SACHRP) in 2012, and was a member of the SACHRP Sub-Committee on Inclusion of Individuals with Impaired Decision-Making in Research (SIIIDR). He also served on the Executive Advisory Committee for the Collaborative Institutional Training Initiative (CITI) Developer's Group. David completed his term as a Member of the Quality Management and Evaluation Advisory Committee (QMAC), World Health Organization.

ZACH HALLINAN, B.S., is the Director of Patient Communication and Engagement Programs at the non-profit Center for Information and Study on Clinical Research Participation (CISCRP). A graduate of the University of Pennsylvania, he oversees CISCRP's programs for better understanding and meeting the needs of clinical research volunteers globally. He has been recognized for his work and scholarship by the American Chemical Society and the National Science Foundation, and was recognized by CenterWatch as one of 20 innovators changing the face of the clinical trials industry.

CHERYL L. JERNIGAN, CPA, FACHE, is a 17-year breast cancer "thriver" and breast health advocate. Ms. Jernigan is the advocate member of the Susan G. Komen® Scientific Advisory Board; and Founding Board member and Chair of the Strategic Missions Committee for the Greater Kansas City Komen Affiliate. She also serves as Komen's representative on the Clinical Trials Transformation Initiative's newly formed Patient Leadership Council. Ms. Jernigan is also Immediate Past Chair of The Advancement Board for The University of Kansas (KU) Medical Center and Hospital and Co-Chair of their Cancer Funding Partners. She is a past Board President and founding board member of Turning Point, which provides psycho-social support services for patients and their families dealing with chronic or life-threatening diseases. Recently, she was selected to serve on National Cancer Institute's (NCI) Central Institutional Review Board (CIRB), and is a past member of the NCI Director's Consumer Liaison Group (DCLG). While on the DCLG, she served as their representative to the National Community Cancer Centers Program. She is a member of DIA's Patient Advocate Fellowship Alumni group; and has served as an advocate reviewer for Komen's Research Program, the U.S. Congressionally-Directed Breast Cancer Research Program, and the

Lance Armstrong Foundation. Ms. Jernigan is also a founding member of Komen's Advocates in Science Steering Committee, and serves on their Clinical Trials Education & Training Working Group.

KRIS JOSHI, PH.D., is global vice president for healthcare product strategy for Oracle Corporation's Health Sciences Global Business Unit. In his prior role at Oracle, he led strategy and operations for healthcare and life sciences, focusing on inorganic growth opportunities. He helped launch the health sciences business unit, and successfully led two acquisitions for Oracle in the life sciences space. Before joining Oracle, Joshi served in senior strategy roles in IBM's Global Sales and Distribution organization. Prior to that, Joshi was with McKinsey and Co, where he served Fortune 500 clients on strategy issues. Joshi has a long-standing interest in bridging the gap between the non-profit and for-profit worlds through entrepreneurship and innovative business models. He holds a bachelor's degree in Mathematics from Caltech, and a Ph.D. in Physics from MIT.

REBECCA LI, PH.D., is the Executive Director, MRCT, and has over 17 years of experience spanning the entire drug development process with experience in Biotech, Pharma and CRO environments. Dr. Li currently serves as the Executive Director of the MRCT Center at Harvard. The Center was chartered to improve the design, conduct and oversight of multi-regional clinical trials in the developing world and simplifying research through best practices. She is also a Fellow in the Division of Medical Ethics at Harvard Medical School. Prior to joining the MRCT Center, Dr. Li served as the Vice President of Clinical Research at the New England Research Institutes (NERI) for 6 years. She also was employed at Wyeth Research (currently Pfizer) and served as the Associate Director in Translational Clinical Research. In this role, she designed protocols and had responsibility for incorporating exploratory clinical biomarkers into trial designs.

CRAIG LIPSET, M.P.H., is Head of Clinical Innovation within Worldwide Research & Development at Pfizer. Craig's team is impacting clinical research through digital tools, innovative research approaches and unprecedented collaborations. Craig previously served as Venture Partner in Pfizer Venture Investments (Pfizer's VC arm), where he focused on diversifying the company's $50M annual budget for private investments in the areas of diagnostics and health technology. Craig was also Senior Director in Molecular Medicine, where he spearheaded initiatives driving innovation in clinical research and personalized medicine by drawing upon tools from health information technology, telemedicine, and eHealth. Craig brings over 15 years of leadership and innovation in the field of drug development. He previously served as Associate Vice President of Program Management at Adnexus Therapeutics (acquired by Bristol-Myers Squibb), and on the founding management team for Perceptive Informatics (now part of PAREXEL International). Listed among the 2010 PharmaVOICE most inspiring people in the life sciences and among Pharmaceutical Executive's 2011 Emerging Leaders, Craig recently served as chair for the 2012 Annual Meeting of the Drug Information Association. His work was recently acknowledged with the 2012 BioIT Best Practices award for Clinical & Health IT. Outside of Pfizer, Craig serves on the Board of Directors for the Foundation for Sarcoidosis Research, the Operations Committee for TransCelerate BioPharma, the Editorial Board for Therapeutic Innovation & Regulatory Science, and as a Mentor at health tech accelerator Blueprint Health.

RICHARD MOSCICKI, M.D., serves as CDER's Deputy Center Director for Science Operations. He shares in the executive direction of Center operations and provides leadership in overseeing the development, implementation, and direction of our programs. Before joining CDER, Dr. Moscicki served as senior vice president (SVP), Head of Clinical Development at Genzyme Corporation. He joined Genzyme in 1992 as medical director and became the chief medical officer and SVP of biomedical and regulatory affairs in 1996 -- holding that post until 2011. Over the past two decades, Dr. Moscicki has been responsible for

worldwide global regulatory and pharmacovigilance matters, as well as all aspects of clinical research and medical affairs for the company. Dr. Moscicki received his medical degree from Northwestern University Medical School. He is board certified in internal medicine, diagnostic and laboratory immunology, and allergy and immunology. He completed his residency with a focus on immunology, followed by a four-year fellowship at Massachusetts General Hospital (MGH) in immunology and immunopathology. He remains on staff at MGH and on the faculty of Harvard Medical School.

PERRY NISEN M.D., PH.D., is the Senior Vice President, Science and Innovation at GlaxoSmithKline. He previously held leadership roles as Chief Medical Officer, Head of Oncology Research and Development, and of Clinical Pharmacology and Discovery Medicine. In those roles he has been engaged in the discovery and development of multiple products. He is a member of key governance, scientific advisory and investment Boards at GlaxoSmithKline. Perry helped establish an end-to-end research and development center in China. He holds a B.S. from Stanford University and M.D. and Ph.D. from the Albert Einstein College of Medicine. Formerly, he was the Lowe Foundation Professor of Neuro-oncology at the University of Texas Southwestern School of Medicine, then Vice President, Cancer Research at Abbott Laboratories.

ANN H. PARTRIDGE, M.D., M.P.H., received her M.D. from Cornell University Medical College in 1995. She completed her residency in internal medicine at the Hospital of the University of Pennsylvania and went on to complete fellowships in medical oncology and hematology at DFCI. Later she received an M.P.H. from Harvard School of Public Health. She is a medical oncologist focusing on the care of women with breast cancer, and she has a particular interest in the psychosocial, behavioral, and communication issues in breast cancer care and treatment.

HOLLY PEAY, M.S., is the Vice President of Outreach and Education for Parent Project Muscular Dystrophy (PPMD), the largest Duchenne-focused advocacy group. She also acts as Director of the DuchennneConnect registry. Her effort is shared between education programs and interventions (to families, healthcare providers and the public) and research conducted through PPMD, and as a Guest Researcher/Contractor at the NHGRI. Her research focuses on decision making and adaptation, with a goal of improving the wellbeing of individuals with and at risk for serious, burdensome disorders. She is the PI of an NINDS-funded study on therapeutic misconception and clinical trial expectations in the Duchenne and Becker muscular dystrophy community. Other ongoing research includes a study of predictors of adaptation in mothers of individuals with Duchenne and Becker muscular dystrophy, and a study of treatment preferences, risk tolerance, and Duchenne-related worries in parents of children with Duchenne muscular dystrophy. Holly has a Masters degree in Genetic Counseling from the University of South Carolina School of Medicine and a Bachelors degree in Biomedical Ethics from the University of Virginia. She has conducted many years of clinical work and social science research. Holly is anticipating completion of a Ph.D. program focused on social/behavioral science at Leiden University Medical Centre in 2014.

DOUGLAS PEDDICORD, PH.D., serves as Executive Director of the Association of Clinical Research Organizations (ACRO). Founded in 2002 by leading clinical research organizations that provide a wide range of research and development support services to pharmaceutical, biotechnology and medical device companies, ACRO works to provide a heightened awareness of the critical role that CROs play in the development of new drugs, new devices, and new treatments. Dr. Peddicord speaks frequently on the subject of the particular role of the CRO (along with the sponsor, investigator, IRB, and regulator) in the 'system' that provides for the protection of human research participants, as well as on broader

issues relating to the conduct of clinical research, including health information privacy, financial conflicts of interest, and the globalization of clinical trials.

CHRISTINE PIERRE, R.N., is the founder of RxTi and the founder and president of The Society for Clinical Research Sites (SCRS). She is internationally known for her passion of clinical research and expertise in clinical research site management and patient recruitment and retention for the clinical trials industry. Prior to founding RxTi, she spent more than 20 years providing site management services to research sites in all types of settings, and additionally provides education, operation and clinical expertise, in addition to training and consultation services with sponsors and CROs. Christine's understanding of the clinical research site's processes allows her to work with sites and sponsors/CROs to help expedite the clinical research recruitment process by bringing study volunteers into a study on a timely and efficient manner and providing high quality research data.

SANDRA PRUCKA, M.S., CGC, LGC, works in the Genetics and Bioinformatics group, within the Tailored Therapeutics group, at Eli Lilly and Company. In addition to providing project management support, she focuses on pharmacogenomics and biomarker sample acquisition from global clinical trials, with expertise in the areas of bioethics, informed consent, and genetic education. Prior to her work in the pharmaceutical industry, she worked as a clinical genetic counselor at the University of Alabama at Birmingham where she also served as the Director of Genetic Counseling Services.

JESSICA SCOTT, M.D., J.D., is the Director, North America Medical Advocacy and Policy at GlaxoSmithKline. Dr. Scott is a graduate of Tufts Medical School, completed residency with the University of Virginia in Family Medicine and practiced medicine for over a decade before attending Campbell University School of Law. Prior to joining GSK, Jessica worked to improve patient safety and health care outcomes and currently, she leads GSK's U.S. medical policy and advocacy.

ED SILVERMAN, M.A., is a prize-winning journalist who has covered the pharmaceutical industry for the past 18 years. Previously, he was a bureau chief for The Pink Sheet, the venerable industry newsletter, and a contributor to its sister publication, In Vivo magazine. Before that, Silverman worked as a business writer for The Star-Ledger of New Jersey, one of the nation's largest daily newspapers, where he conceived and launched Pharmalot Prior to joining The Star-Ledger, Silverman spent six years at New York Newsday and previously worked at Investor's Business Daily, among other newspapers. Silverman has a master's degree in journalism from New York University and a bachelor's degree in accounting from Binghamton University. He is currently an adjunct assistant professor at the Rutgers University School of Health-Related Professions.

WALTER L. STRAUS, M.D., is the Global Director for Scientific Affairs - Vaccines at Merck Research Laboratories, Merck & Co, Inc., where he leads a team that conducts research in vaccine-preventable and other infectious diseases, as well as oncology. The work spans early discovery through post-licensure assessments. As a result, he is involved in issues ranging from molecular epidemiology, to development of patient-reported outcome measures for use in clinical trials, through to assessment of the safety and effectiveness of marketed products. While much of his work is done in support of clinical research, his group is also involved in basic research. Additionally, since so much of the burden of vaccine preventable diseases falls on developing countries, Dr. Straus' team is also involved in epidemiologic assessment of disease in areas of the world normally outside of sphere that has historically characterized pharmaceutical development. This activity has led to his active involvement in internal discussions about proper research ethical considerations for research in developing countries. Dr. Straus is a former Epidemic Intelligence Service Officer at the Centers for Disease Control and

Prevention, and has served as a consultant to the World Health Organization and other non-governmental organizations.

MARC WILENZICK, J.D., is a Life Science attorney with expertise in regulatory law, policy, bioethics and R&D. He serves as a consultant to the ViS Research Institute for Core Risks, Ltd, and as a member of the Board of Directors for the human subject accreditation group, AAHRPP, in addition to advising the Harvard MRCT Center. Previously, Marc served as the Chief Compliance Counsel for R&D, Medical & Safety for a large pharmaceutical company and as their Assistant General for Clinical Trial Policy & Regulatory Law.

MEETING AGENDA

Registration and Breakfast

7:30 – 8:00 am	**Participants' Arrival, Registration, and Breakfast**

Welcome & Introductions

8:00 – 8:40 am	• **Agenda and Expectations** • **MRCT India Update**	**Rebecca Li (MRCT)** **Barbara Bierer (MRCT)** **Mark Barnes (MRCT)**

Keynote Speakers

8:40 -9:30 am	**EMA – Approach to Data Transparency** **GSK – Access to Patient-Level Data** **FDA – Perspective on Data Sharing**	**Hans Eichler (EMA)** **Perry Nisen (GSK)** **Richard Moscicki (FDA)**
9:30 – 10:25 am	**Moderated discussion of EMA, FDA and GSK approaches**	**Moderator:** **Mark Barnes/MRCT**

Break 10:25 – 10:40am

Data Sharing Implementation and Solutions

10:40 – 11:00 am	**MRCT Phase 2 Data Sharing Implementation Solutions :** ***Criteria, informed consent and commercial confidentiality***	**Barbara Bierer (MRCT)** **Jessica Scott (GSK)**
11:00 – 11:30 am	**Moderated discussion of strategies, approach and implementation**	**Participants: ALL**

11:30 – 12:00 pm	**Lunch**

Work Group Updates

12:00 – 12:45 pm	**Data Safety Monitoring Board**	**Barbara Bierer (MRCT)**
	Protocol Ethics Guidance	**Susan Callery D'Amico (Abbvie)**
	Investigator Competence & Training	**Rebecca Li (MRCT)**

Return of Results: Lessons Learned from Current Efforts

12:45 – 1:50 pm	**Moderated by Mary Ann Plummer (J&J)**	
	Pfizer Blue Button Initiative	**Craig Lipset (Pfizer)**
	Patient Perspective	**Cheryl Jernigan (Susan B. Komen)**
	Providing Research Results to Clinical Study Participants	**Sandy Prucka (Lilly)**
	CSCRP Return of Results	**Zach Hallinan (CISCRP)**

Return of Results: Next Steps

1:50-2:15 pm	**Framing the new initiative** - **pushing the envelope on returning results to patients** - **defining best practices** - **planned pilots and focus groups**	**Rebecca Li**

Return of Results: Panel Discussion

2:15 – 3:15pm	**Panel Discussants:** – **Holly Peay (Parent Project MD)** – **Cheryl Jernigan (Susan B. Komen)** – **Sandy Prucka (Lilly)** – **Zach Hallinan (CISCRP)** – **David Forster (Western IRB)** – **Ann Partridge (Dana Farber)**	**Moderators: Craig Lipset (Pfizer) and Sandra Morris (J&J)**

Break 3:15 – 3:30 pm

Emerging Issues in Multi-Regional Clinical Trials

3:30 – 4:30 pm	**Panel Discussants:** – **Kris Joshi (Oracle)** – **Ed Silverman (Pharmalot)** – **Doug Peddicord (ACRO)** – **Christine Pierre (MYSCRS)** – **Walter Straus (Merck)**	**Moderator: Marc Wilenzick (MRCT)**

Conclusion

4:30 – 5:00 pm	**Wrap-up Discussion**	**Barbara Bierer (MRCT)** **Mark Barnes (MRCT)** **Rebecca Li (MRCT)**

Executive and Steering Committee (closed session) in Theatre Room, Harvard Faculty Club

5:00pm-6:30 pm	**2014 Budget** **Goals for 2014** **Review of Regulatory initiatives and planning for 2014**

EXECUTIVE SUMMARY

WELCOME AND INTRODUCTIONS

Barbara Bierer and Rebecca Li.

MRCT CENTER

Purpose: *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.*

MRCT Objectives:

Establish Best Practices	To establish best practices of performance and to enhance the scientific and ethical conduct of multiregional research.
Develop Standards	To establish common, explicit, realistic and ethical standards for conduct of transnational research
Identify Opportunities for Improvement	To align practice with those standards and study barriers to alignment
Improve Transparency	To enhance predictability for the benefit of research participants, regulatory authorities, sponsors and researchers

Meeting Objectives

- Provide an update to all stakeholders regarding current initiatives and progress with a focus on Data Sharing and Return of Results

- Engage regulators in the MRCT initiatives and mission
- Obtain feedback from regulators and stakeholders on MRCT ongoing and planned initiatives
- 2014 Budget and Proposed New Initiatives (EC/SC meeting)

Review of Recent Regulatory Developments on Clinical Trials in India

Mark Barnes, J.D., (MRCT)

Mr. Barnes presented an update on India's recent regulatory reforms, which threaten to limit future conduct of clinical trials there.

In early 2011, following the deaths of seven girls who had received HPV vaccine in an observational study and adverse media criticism of the trial as well as adverse events reported in regard to other clinical trials conducted in India, the Indian Parliament formed a standing committee to report on functioning of the nation's Central Drugs Standard Control Organization (CDSCO). The Committee concluded that the Drug Controller General of India (DCGI) lacked clinical/scientific expertise to evaluate the scientific rationale and appropriateness of conducting clinical trials. In January 2012, a Supreme Court of India ruling suspended the power of CDSCO/DCGI to approve clinical trials, due to what the Court regarded as inadequate oversight and insufficient attention to clinical trial infrastructure to ensure the safety and welfare of clinical trial participants.

In response to the Supreme Court's decision, in January and early February 2013, the Ministry of Health issued new regulations that dramatically changed the present and future conduct of clinical trials in the nation. These included a requirement that sponsors of trials (which could include academic institutions and funders of trials, such as the U.S. NIH) provide medical care and compensation for participants injured in the course of clinical trials. Moreover, in adopting an extremely broad definition of injuries caused by participation in a trial, the regulations significantly expanded sponsors' responsibility for clinical trial participants' illnesses and injuries, even when those illnesses and injuries have no direct relation to clinical trial participation. Under these new regulations, even the failure of an experimental agent to yield the desired health effects would be regarded as an injury that must be compensated by the sponsor. The laws introduced serious penalties for not following the regulations, including barring sponsors from conducting clinical trials in India. Statutory changes now pending before Parliament would add significant criminal penalties for protocol violations.

As a result of these troubling developments, no significant new clinical trials have been initiated in recent months in India, thus depriving a nation of one billion people of new drug development and approvals. Besides their immediate impact, the reforms may also have long-term structural effects, as the clinical trials infrastructure of investigators, CROs and others is currently being underutilized and is thus withering. MRCT, through three trips to India in 2013, has made contact with a number of stakeholders there (ISCR, FERCI, OPPI, MOH, and others) in order to identify any constructive role that MRCT might play in assisting MOH in revising or interpreting the new regulations. In January 2014, MRCT will co-sponsor the annual meeting of the India Society of Clinical Researchers (ISCR) and has scheduled a number of sessions on these regulatory issues. Also in January 2014, MRCT is co-sponsoring, with AIIMS and Apollo Hospitals, a private expert roundtable meeting with clinical research leaders in India to review the regulations, as well as the recently-released expert report from an ad hoc

MOH committee chaired by Dr. Roy Chaudhury, with the goal of making some concrete recommendations to MOH on regulatory interpretations and needed changes.

KEYNOTE SPEAKERS

European Medicines Agency (EMA) Approach to Clinical Trials Data Sharing.

Hans-Georg Eichler, M.D., (EMA)

Dr. Eichler reviewed EMA's views on the risks and benefits of clinical trials data sharing and the need for a regulatory action.

Aiming to promote potential scientific and public health benefits of providing greater access to information from clinical trials, EMA released its Draft Policy for Clinical Trials Data Sharing Policy in June 2013. EMA's draft policy was guided by an understanding that there exists a need to change current state of transparency in clinical trials. The draft policy has triggered a number of responses and initiatives from industry, academia and other stakeholders, which along with EMA have collectively moved data sharing and transparency initiatives forward.

There is a spectrum of benefits associated with providing broader access to clinical trial data, ranging from fostered trust and accountability to improved exploration and discovery. On the other hand, there are commonly identified risks. As a preliminary note, it is important to distinguish between real risks and negligible risk hazards. For example, among commonly cited risks of data sharing is the potential to undermine the integrity of the national regulatory systems by erroneous analyses of data. However, while there may be people who will play with the data and reach unsupported conclusions, such occurrences will not be new. Studies show that only a small fraction of wrong safety signals (6 percent) come from randomized controlled trials. Thus, EMA's data sharing initiative is unlikely to affect false health scares in a major way. Another often-identified problem with data sharing is the potential to encourage or enable "free-riding" in biomedical research. EMA's regulation will, however, protect against the release of companies' commercially confidential information (CCI). While competitors may improve product design and clinical trial processes from an understanding of their rivals' non-CCI information, this is a desired side effect, not a risk, and will render drug development more efficient. Lastly, there is a need to safeguard trial participants' privacy and prevent the risk of re-identification when individual patient data are released. EMA considers this a real risk and will involve all stakeholders to foster common, balanced approaches for individual patient data sharing standards, queries, access and rules of engagement.

GlaxoSmithKline (GSK) Access to Patient Level Data

Perry Nisen, M.D., Ph.D., (GSK)

Dr. Nisen discussed GSK's data sharing initiative's approach to providing access to anonymized patient level data.

Clinical trials data sharing provides many benefits for science and society, including secondary analyses of study conclusions, new hypotheses generation, new methodologies, and improved trust and transparency. GSK's journey to data sharing has been ongoing for many years. In 2004, the company started its first online clinical trials register, which was subsequently expanded in scope and content in

2009. Today, GSK focuses on the next age in its data sharing journey – making individual patient data available to qualified researchers in a responsible way.

GSK's initiative currently includes around 450 studies and will build to include global studies conducted since the formation of GSK in 2000 and all studies initiated in or after Jan 2013. The studies are listed after the drug has been approved by regulators or terminated from development and the study has been accepted for publication. After approval by an Independent Review Panel and signing of a Data Sharing Agreement, external researchers are given access to anonymized patient level data, as well as other clinical trial documents. In designing its data sharing model, GSK carefully considered the issues of protecting trial participants' privacy, ensuring valid scientific investigations, safeguarding against erroneous claims and practicalities of anonymizing data. To address these concerns, GSK's data sharing model is designed to balance the benefits of sharing patient level data with these risks. Among other precautions, investigators applying for access must meet specific requirements as evaluated by an Independent Review Panel, data use must comport with a contractual Data Sharing Agreement, all access is provided in a secure password-protected website, and accessible data cannot be exported or downloaded. GSK reiterates that it is not involved in access evaluation process and all decisions made by the Independent Review Panel are final. The model also includes transparency around the requests, posting of accepted proposals, numbers of requests, denials, enquiries and GSK requires a publication plan as a component of all submissions for data access.

GSK views its data sharing initiative as a step toward the ultimate vision, which is a model using an independent custodian or learned intermediary entity that could administer the initiative and manage review of proposals. Such an approach would provide investigators with access to academic sponsored clinical trial data as well as a broader spectrum of industry sponsored trials. Such a system would enhance a researcher's ability to combine data sets from different sponsors and would foster greater trust in the system. This change will not happen overnight, but GSK has attempted to take the first step in the right direction.

Responsible Sharing of Clinical Trial Data: An FDA Perspective

Richard Moscicki, M.D., (FDA)

Dr. Moscicki discussed FDA's views on clinical trials data sharing.

Sharing data is not a new concept at FDA. The Critical Path Initiative started by FDA in 2004[1] elucidated the need for data sharing to advance science and to address impediments in reaching this goal. Moreover, sharing of clinical data from various trials with analyses of data sets to advance drug development has been going on *within* the agency for quite some time. The agency has also been involved with various consortia efforts to utilize pooled clinical data.

Through its various data sharing efforts, FDA learned that it is possible to combine datasets in a way that provides a rich scientific resource, while preserving commercial interests of sponsors. Most recently, the agency released a Federal Register notice, seeking public comment on whether certain study data could be made available after steps have been taken to remove information that would identify patients, as well as the specific product application or company involved. For various reasons, however, FDA believes that while it has significant expertise to be a source for data sharing, the agency should not focus on such efforts at this time.

[1] For more information, visit http://www.fda.gov/scienceresearch/specialtopics/criticalpathinitiative/default.htm.

The agency's actions in the data sharing sphere are limited by various laws and regulations. FDA believes that it does not own submitters' data and hence cannot release these data without permission. The agency also recognizes issues associated with patients' privacy and informed consent considerations. Some data may not be released due to their status as commercially confidential information or trade secrets. Generally, FDA can proactively disclose non-summary safety and efficacy data from a specific application only in response to a request under the Freedom of Information Act (FOIA). Moreover, from its prior data sharing experiences, FDA has learned that the process of data pooling, curating and release is extremely resource-intensive. Focusing on data sharing would thus detract from FDA's primary mission. Realizing its limitations, the agency encourages independently organized initiatives to create, curate and share clinical trial datasets from all sources. Specifically, the agency urges consideration of third-party models with critical attention paid to issues and implications raised by different models' structures.

Moderated Discussion of EMA, FDA and GSK Approaches

Moderated by Mark Barnes, J.D., (MRCT).

The Questions and Answers session centered on the following themes:

1. Choosing between state-imposed mandatory data sharing program and industry self-regulation
2. Implications for releases of Commercially Confidential Information (CCI)/trade secrets
3. The need to align releases of patient level data with the "spirit" of Informed Consent
4. Privacy concerns over publishing identity of researchers
5. Keeping data sharing systems in check: remedial mechanisms for inappropriate uses

According to Dr. Eichler, EMA has opted for mandatory regulation as a result of the European pharmaceutical industry's being slow to adopt voluntary data sharing measures. The agency shares FDA's view that distributing data is not a regulator's core business and EMA's preference is to see the industry take the initiative. However, believing that there are public health and scientific benefits to be gained from data sharing, and seeing that the industry was not stepping up to the challenge, EMA decided to take the first steps.

The panel participants agree that data sharing models must include appropriate mechanisms to allow companies to protect their CCI/trade secrets. EMA chose an approach under which submitting companies are requested not to include any CCI/trade secrets in their Clinical Study Reports (CSR), which the EMA intends to be released to the public. The industry has a year during which to prepare for this adjustment, a time interval that EMA considers sufficient to redact any existing documents and to adopt appropriate strategies for future CSR submissions. GSK is making the full CSR available publically, redacting only personally identifying information. Lastly, by virtue of applicable regulations, FDA can generally only release redacted CSRs pursuant to a Freedom of Information Act (FOIA) request.

The panel paid particular attention to privacy issues raised by release of participant level data and the way such releases can be aligned with the "spirit" of underlying informed consent forms (ICFs). Not all ICFs expressly permit future use of data for secondary analysis. Moreover, some ICFs may expressly prohibit such use. There was agreement among panel participants that instances of express prohibition must be honored. Going forward, however, there is a need for harmonization of ICF language across study sponsors. Allowing study participants to opt in/opt out of future data use will create significant operational impediments for data sharing and compromise the scientific integrity of any data set.

There are also concerns associated with making public the identity of researchers through a data sharing mechanism. There have been situations where researchers have been targeted for testing specific drugs. The panel participants have considered this issue through their work, and the EMA appears to be reconsidering its position on the release of this identifying information.

Lastly, panel participants agree that a properly designed data sharing system can be safeguarded through data use agreements. Such agreements bind secondary researchers to use data only for specified purposes. Inappropriate uses of data, including re-identification of study participants, would thus be treated as breaches of contract, which can be addressed in court. Details of approved secondary research proposals would be publicly available, so that any deviation from the proposed research is open to public scrutiny. There were concerns raised, however, as to what entities or bodies would be charged with continuing oversight and enforcement of data use agreements, and some acknowledgement that without a robust enforcement mechanism in place, the terms and conditions imposed through such agreements may not be uniformly honored.

DATA SHARING IMPLEMENTATION AND SOLUTIONS

MRCT Phase 2 Data Sharing Implementation Solutions: Criteria, Informed Consent and Commercial Confidentiality

Barbara Bierer, M.D., (MRCT) and Jessica Scott, M.D., J.D., (GSK)

Drs. Bierer and Scott presented a summary of MRCT's Phase 2 work on implementing data sharing models solutions.

In Phase 1 of its work on data sharing, MRCT formulated four potential models/frameworks for the process. The models were presented during *Consensus Building of the Issues and Case Studies in Clinical Trials Data Sharing Conference* held on May 17, 2013 at Harvard Law School. The group's work was also published in The New England Journal of Medicine.[2] Following the conference, MRCT entered into Phase 2 of its work on clinical trials data sharing. During the second phase, the center built on its earlier work to formulate the specifics of implementation of data sharing solutions. MRCT formed four subgroups, each entrusted with a specific focus: developing criteria for data sharing, designing technological methodologies, evaluating informed consent concerns, and clarifying CCI issues. A brief summary of each subgroup's work is presented below.

The Criteria for Data Sharing subgroup focused on developing criteria for selection and rules of engagement for the data requestor and reviewer of data requests in a way that would facilitate access to patient level data to further science while protecting privacy. The subgroup categorized the process of data sharing into six distinct domains: requester, request, reviewers, review, data hosting, and access & export. The subgroup developed a Criteria Framework for learned intermediary data sharing models, characterizing the six domains along three levels of restrictiveness with regard to sharing patient level data. This framework was also applied to existing models of data sharing to understand how current initiatives addressed pertinent issues as represented by the domains. In its next steps, the subgroup plans to draft guidelines for future data sharing projects, based on identified benefits and considerations

[2] *See* Mello, Michelle M., et al. "Preparing for responsible sharing of clinical trial data." *New England Journal of Medicine* (2013), available at http://www.nejm.org/doi/full/10.1056/NEJMhle1309073.

for various permutations of learned intermediary model domains, and develop a model terms of data use agreement.

The Technical Methodologies Task Force was recently launched with the goals of: (1) gathering and summarizing current practices for de-identification and anonymization of patient-level data, (2) determining how to capture risk of re-identification, (3) identifying methodologies that maximize data utility while protecting participant privacy and (4) integrating findings with informed consent issues through collaboration with this subgroup. The subgroup completed its work on clarifying terminology, including distinguishing between "de-identification" and "anonymization" of data. The distinction is important as, currently, the protection given to study participant's data is based on regulatory requirements that differ across countries. Specifically, United States considers "de-identification" of data (e.g. "the removal of 18 identifiers") sufficient while some European Union regulations require "anonymization" (e.g. destruction of any identifying code) in order to meet its standards. It should be recognized, however, that the risk of re-identification does not necessarily track with current regulations or practices. The subgroup recommends new methods that incorporate data security methodology and allow greater protection of privacy while minimally affecting utility. Thus, the subgroup future goals will focus on identifying methods and recommending best practices for enhancing current practices of de-identification.

The Informed Consent subgroup worked on achieving clear definitions of terms used in Informed Consent Forms and interpreting limitations on data sharing imposed by the language in existing ICFs. The subgroup identified four categories of retrospective ICFs: (1) those explicitly permits data sharing, (2) those specifically prohibits data sharing, (3) those silent on data sharing and (4) those with inconsistent/conflicting language with regard to data sharing. The impacts of each type of ICFs on future data sharing were evaluated. Categories 2 and 4 were identified as particularly problematic. The existing variation in ICF language implies that data sharing regulations will create situations where promises made by the data generator to study participants will conflict with the regulatory demands of sharing participant data. Prospectively, ICF language could be proposed that permit secondary data use. In its next steps, the subgroup hopes to develop such model ICF language for patient-level data sharing that would be acceptable to both IRBs and patient groups. To achieve this goal, the subgroup will work with patient groups and IRBs/ECs on appropriate language regarding future data sharing in ICFs.

The Commercially Confidential Information subgroup was entrusted with: (1) delineating what clinical trial information should be considered potentially commercially confidential, (2) providing a clearer understanding of the economic impact of the release of such information, (3) developing a consensus opinion on definition of CCI with relevant examples, and (4) exploring the potential dangers of inappropriate release of CCI. The subgroup defined CCI as information that is not in the public domain and can cause material harm to an entity. Affording protection to CCI requires careful balancing of the need for transparency beneficial for the advancement of science and public health and the need to afford clinical trial sponsors adequate trade secret protection to promote future investment in innovation. Determination of whether a particular piece of data may be CCI is context-specific, requiring consideration of the product, the timing of disclosures, the sponsor, other publicly available information and type of patent application. The subgroup thus envisions a process whereby a determination to protect CCI may be subject to a time-dependent sunset or a process for re-review on request. A learned intermediary would be one model to operationalize such independent review. In next steps, the subgroup will develop a CCI framework and guidance for determining information confidentiality with relevant risks and illustrate the framework's usage with examples.

Moderated discussion of strategies, approach and implementation

Recommendations for MRCT:

1. Conduct empirical research into patients' concerns over secondary use of their data.
2. Consider the implications of proxy ICFs signed by parents on the behalf of their children struggling with degenerative diseases. In such situations, parents make the decision to participate in clinical trials largely based on potential benefits, not altruism. Clinicians working with such parents frequently complain that they do not pay adequate attention to the risks associated with participation in a clinical trial. As a result, there is a concern that a nuanced discussion of risks and benefits of secondary data use may be lost in such circumstances. MRCT is strongly urged to consider addressing this inadequacy.
3. Address unduly broad ICFs, such as typically used in bio-banking, as well as compound ICFs. Unduly broad ICFs risk making patient's consent meaningless by providing vague understanding of how the data can be used in the future. In turn, compound ICFs may limit participation in clinical trials and/or bias the study sample by conditioning participation on agreement to future data sharing. The latter issue is particularly problematic and difficult to address, since the alternative – allowing patients to selectively opt in or opt out of future data use – will result in incomplete data sets for secondary studies.
4. Consider a program to educate IRBs on the new data sharing mandates and how consent language will necessarily be broadened to allow for greater sharing.
5. To inform MRCT's work, involve patient advocates from the start of data sharing model design and interpretation process.
6. Continue to evaluate the unintended consequences of data sharing, and ways in which those consequences might be best avoided.
7. Consider the risks associated with identification of researchers – information can be put out of context and used to damage careers or even compromise personal safety. One organization opted for a one-tiered approach for sharing physician information – with "de-identified" information available publicly *only*. An alternative would be a two-tiered approach, under which additional information can be made available to requestors who meet prerequisite requirements.

WORK GROUP UPDATES

Data Safety Monitoring Board

Barbara Bierer, M.D., (MRCT)

Dr. Bierer presented an update on MRCT's initiative dedicated to training Data Safety Monitoring Board members.

The goal of the MRCT Data Safety Monitoring Board (DSMB) initiative is to identify, train and recruit experts from emerging regions who have expertise in medicine or statistics, experience in clinical trials, and would like to serve on Data Monitoring Committees. The initiative is conducted with a particular focus on building capacity in developing countries. In Phase 1 of the project, MRCT developed a comprehensive curriculum for training DSMB fellows, identified qualified individuals from the developing world, and educated and trained those individuals to qualify as potential members of a DSMB with a focus on trials conducted in the developing world. On May 19, 2013 the MRCT Center at

Harvard trained its inaugural class of Data Safety Monitoring Board Fellows prior to the 34th Annual Meeting of the Society of Clinical Trials in Boston.[3] A number of graduates ("MRCT DSMB Fellows") of the program have been apprenticed as DSMB members to serve on boards. Five of these fellows have initiated MRCT trainings in their home countries (1 complete, 6 planned for 2014). MRCT seeks to continue its work with DSMBs through Phase 2 of the initiative aiming to expand training regionally to build capacity, transform current fellows into DSMB champions in their own countries to implement safety boards locally, and publish a "How To" resource for DSMB roles.

Protocol Ethics Guidance

Susan Callery D'Amico, B.S., (AbbVie)

Ms. D'Amico reviewed MRCT's progress on protocol ethics guidance focus area.

MRCT's initiative on protocol ethics guidance seeks to develop key elements that are recommended for inclusion in multi-regional clinical trial protocols. The group was launched after recognizing limitations of the existing system for reviewing trials, including shortcoming in: (1) efficiency (i.e. the time it takes to get a protocol reviewed), (2) effectiveness (i.e. the quality of the review and its ability to detect ethical problems), (3) expertise (e.g. in some regions, local ECs lack the level of expertise or sufficient resources required to review complex protocols), and (4) consideration of ethical issues (e.g. study teams developing protocols may not have a sufficiently rigorous methodology to ensure that all ethical issues have been properly considered and addressed).

To address these issues the group developed Essential Elements for Ethics Tool Kit, providing a systematic reference for protocol writers who seek assistance in holistically accounting for ethical considerations of their planned clinical trial. The guide includes a "Points-to-Consider" document, which leads the user towards drafting a standardized protocol and an ICF ethics section. The group has also performed a validation survey of 100 protocols from academia, central IRBs and publications for presence/absence of Essential Elements. The results of the study revealed that an average protocol addressed only 49 percent of the Essential Elements. The group hopes that its Tool Kit can remedy this underperformance by providing researchers with an accessible and helpful guidance for covering essential elements in their protocols. To help progress towards this goal, in its next steps, the group will disseminate its guidance documents to ethics committees and protocol writers. Additionally, the group plans to collate use-cases to learn how the Essential Elements may be refined and, once deliverables are complete, meet on ad-hoc basis to address emerging ethics topics in clinical trials.

Investigator Competence & Training

Rebecca Li, Ph.D., (MRCT)

Dr. Li described progress made by the Joint Task Force for Clinical Trial Competency, which was formed with the goals of analyzing and summarizing core competencies required of clinical trials professionals.

Many groups have made attempts to identify the essential competencies necessary for investigators and support professionals to safely and ethically conduct a clinical trial. The Joint Task Force for Clinical Trial Competency was created to review and integrate these efforts, aligning competencies and developing a harmonization strategy. The task force is well-positioned for its role, bringing together a diverse

[3] For more information, visit http://mrct.globalhealth.harvard.edu/people/dsmb-fellows

representation of stake-holders, including MRCT and the Consortium of Academic Programs in Clinical Research. The group's final product identified eight high-level competency domains, grouped according to broad categories of skills necessary for successfully running clinical trials. Harmonized competencies can be used as the basis for various end-uses, including: streamlining education and training requirements; standardizing job descriptions and promotion criteria, defining site qualification, investigator selection, accreditation standards criteria. However, the utility of this approach depends on its wide acceptance. Thus, the task force hopes that its suggestions would be commonly adopted by the various players in the clinical trials process, such as pharmaceutical companies, institutional review boards/ethics committees, regulatory authorities, and the academic community.

RETURN OF RESULTS: LESSONS LEARNED FROM CURRENT EFFORTS

Moderated by Sandra Morris, Ph.D.

Pfizer Blue Button Initiative

Craig Lipset, M.P.H., (Pfizer)

Mr. Lipset described Pfizer's latest initiative in a series of projects aimed at improving patients' experience in clinical trials.

There are number of existing challenges affecting clinical trials, including low participation rates by patients and physicians, as well as limited extent of patients' engagement in the process. Often, trial participants do not even receive the end results of clinical trials in which they participated. Yet studies indicate that most patients want access to aggregate and clinically significant individual study results and would be willing to share medical information if such access were provided. Mindful of these issues, Pfizer has been a leader in improving patients' experience in clinical trials. Pfizer's adoption of the "Blue Button" technology (first launched by the U.S. Departments of Veterans Affairs and Health and Human Services) is the company's most recent initiative in this area.

Pfizer made important steps in addressing patients' wishes to receive trial results. Through the Pfizer-CISCRP Partnership, Pfizer became the first sponsor to return lay language summaries to trial participants. Last year, the company launched the first online network for clinical trial alumni, with the goal of allowing trial participants opt-in into a continuous relationship with Pfizer. The "Blue Button" Initiative, adopted in 2013, builds on these earlier efforts to establish a secured online portal enabling clinical trial participants download their individual study results. The portal not only provides patients with their data, but also includes links to applications and tools to improve data utilization and understanding. Patients are free to use the data as they wish. Among other uses, patients may decide to share the information with their health care providers for better informed treatment decisions or their caregivers to have a more complete picture of their clinical health.

Patients' Perspective

Cheryl Jernigan, CPA, FACHE, (patient advocate, Susan G. Komen Foundation)

Ms. Jernigan provided an insight into patients' perspectives on current practices in clinical trials.

The ultimate goal of clinical trials is to benefit the public. In fact, typical informed consent forms promise prospective trial participants that their contribution will "benefit society." However, present

clinical trials practices make it unclear whether this promise is fulfilled. Society retains the most benefits from well-designed, scientifically valid trials: (1) that accrue and retain patients, (2) whose results are analyzed and published, and (3) that move the body of knowledge forward. However, around 30 percent of phase III trials close due to lack of accrual, thousands of trials go unpublished each year, and study failures are less often disclosed than positive results. These troubling statistics cast doubt on the accuracy of informed consents' promises of social benefit. With numerous studies not moving forward or not sharing findings, and patients typically not being informed of study results, it is unclear whether or how an individual's participation actually benefits the public.

When discussing trials' participants wishes and preferences, it is important to recognize that patients participating in clinical trials are concerned with the "so what?" factor. Specifically, patients are interested in: "So what difference will the study make in how patients feel, function or survive?" How will the study's results and their implications advance research, and ultimately lead to improved treatment, diagnosis, and prevention of complicated or life-threatening diseases? Sharing results is the right choice from an ethical point of view, if society is to gain the most benefit, and patients who dedicated their trust, time and bodies for the trial are to be treated in a respectful, trustworthy and transparent manner. The practice can also benefit overall clinical trials structure by improving physician-patient communication, promoting patient satisfaction, raising the quality of care, generating potential positive impacts for future health, and improving overall trust in the system.

The mechanics of sharing results require detailed consideration of several factors involved in the process. Informed decisions must be made regarding: (a) who in the clinical trials or patient's health care team should do the sharing, (b) when the result should be provided, (c) how they should be shared, and (d) what should be included in the content. Patients should be given the choice of whether they want to receive the results. The content of the study results must be written in a patient-centered way, explaining in language the patient can understand the impact of the study and what it means for the individual. The patient advocacy community should be engaged early in the process of designing research, to ensure that patients' unique perspectives are fully integrated into decisions made at every step of the research process.

Providing Research Results to Clinical Study Participants

Sandra Prucka, M.S., CGC, LGC, (Lilly)

Ms. Prucka discussed potential criteria for determining what individual research results and incidental findings are most appropriate to share with clinical trial participants, explained the current state of Lilly's internal bioethics position paper on this topic, and reviewed a pilot at Lilly that focused on sharing the overall clinical trial results with study participants.

There are ethical justifications for providing patients with individual research results and incidental findings of clinical importance that were identified from samples they have contributed to research. Respect for research participants' contribution also translates to an obligation, at a minimum, to provide a general summary of the findings. In the United States, there are requirements already in place for providing results to trial participants. For example, investigators must notify patients of existence of conditions or illnesses (whether related or unrelated to the study intervention) that require medical care and are readily apparent or identified through study screening procedures. In addition, summary results from some trials must be timely uploaded to clinicaltrials.gov. However, there are no standard criteria

or process that can serve as definitive guidance for determining what research results should be returned and how.

It is important to remember that not all study results are appropriate to provide. Lessons can be learned from the genetics literature that divides individual research results and incidental findings into three categories: (1) those that *should* be offered, (2) those that *may* be offered, and (3) those that *should not* be offered to the patient. On the one hand, there is a consensus that investigators need to provide information relevant to a participant's health status. However, on the other hand, sharing results with uncertain health, reproductive, or personal utility carries more risks than benefits. For individual research results and incidental findings generated *during* the course of the clinical trials, determination of suitability for sharing should rest on the results' quality, validity and well-established association with a substantial risk of a serious disease.

These were the criteria used by Lilly's Bioethics Program for defining results that are most appropriate for providing to interested research participants. Results not meeting these criteria were determined not suitable for return. This established the categorization system utilized by Lilly mirrors that of the literature, but utilizes a two-category system. Results deemed suitable for return but generated *after* the clinical trial were thought to pose unique challenges, many of which stem from the temporary nature of the clinical study relationship and the years that often pass between when samples are collected and meaningful research results. These challenges can be partially addressed through informed consent, by asking patients to update in a timely way their contact information and/or providing for alternative means of communication.

At this stage, Lilly has developed an internal bioethics position, and will next assess how to translate this bioethics guidance into standards and procedures. This process will ultimately allow the company to operationalize a program for consistently providing individual research results and incidental findings to clinical trial participants. Lilly has also initiated a pilot program for providing aggregate results summarizing the overall outcome of the clinical trial to patients after the trials' completion. For this pilot, patients were able to opt in/out of the program through informed consent, were given a timeline for results release during the last visit, and received biannual updates on the results status up until the point when the results were provided. Lilly has plans to extend this pilot program, in order to gain additional experience in this area.

CISCRP Return of Results

Zach Hallinan, B.S., (CISCRP)

Mr. Hallinan described the importance of returning study results to the patients and presented CISCRP Program aimed to help sponsors work through the challenges of the process.

There is a great need for and value in communicating study results to clinical trial participants. Patients from across the globe consistently rank "receiving information about the results after the study has ended" as one of the top factors influencing their decision to participate in research studies. Yet around 91 percent of patients never hear back from study staff or sponsors, and 68 percent indicate that if not informed of results, they would not participate in future trials. Lack of sharing results thus likely contributes to recruitment and retention problems in clinical trials, as well as lack of public and patient trust in the research enterprise. There is awareness of this problem across the research community, with investigative sites, ethics committees, regulatory agencies and policymakers recognizing the need

for returning study results back to the patients and making corresponding recommendations. Substantial progress has been made in returning overall trial results to study participants, but barriers still remain, including concerns that results sharing can be viewed as promotional, and the logistics of stakeholders (sponsors, sites, ethics committees) supporting and integrating new processes.

CISCRP's program for Communicating Trial Results to Study Volunteers helps sponsors overcome these barriers. The program is currently at different stages of implementation by 21 major and mid-size pharmaceutical and biotechnology companies. The CISCRP Program focuses not only on results delivery but also on maintaining ongoing communications between investigators and study participants. Sponsors engaged in the program set expectations for receiving trial results beginning at the point of informed consent review, thank volunteers at the end of the trial and explain timing for receipt of trial results, and send biannual updates on results status up until the point such results are provided. At the end of the trial, CISCRP works with the sponsor to prepare a lay language summary of the study results. Final summaries are produced in various formats to accommodate different patients' learning needs and styles. Sponsors review CISCRP summaries for scientific accuracy and designate an internal team to field investigative site follow-up questions about the results. CISCRP then sends ready-to-go written materials to study site team members who disseminate them to the patients. CISCRP also creates a website and a "hotline" for clinical trial summaries. 2012 qualitative and quantitative evaluations of the program, as well as prior and ongoing evaluations, demonstrate that the program has been well-received by both patients and investigative staff and there are objective and substantial gains in patient understanding following independent review of a lay-language summary.

CISCRP's program engages patients and the public as partners in the clinical research process. By addressing patients' needs and expectations for receiving results and on-going communication, the program helps instill value, meaning and appreciation for study volunteers. In turn, as trial participants' experience with clinical trials improves, CISCRP creates opportunities for participants that have completed a trial to act as ambassadors to the public, helping build support for the clinical research enterprise and enhancing awareness of and openness to participating in future trials. With greater understanding of the process and fostered transparency, the public gains in trust, literacy and support for the research enterprise.

RETURN OF RESULTS: NEXT STEPS

Framing the New Initiative

Rebecca Li, Ph.D., (MRCT)

Dr. Li described MRCT's upcoming initiative focusing on returning clinical trials results back to trial participants.

MRCT's next initiative will focus on returning study results to clinical trial participants. The center believes the time is appropriate for initiating a work group centered on the return of research results: numerous MRCT stakeholders are interested in going beyond current practices; incentives are aligned for patients, providers and clinical researchers; and resulting enhanced trust in the clinical trial enterprise will benefit all stakeholders. MRCT has already formed a "return of results workgroup" that should launch in the near future.

Initial input from the workgroup crystalized a framework for talking about the return of results, focusing on the problems of: (1) *who* receives the results, (2) *what* results are provided, (3) the *process* of returning the results, (4) the *format* of returning results and (5) the proper *timing*. Each of the five questions has several possible solutions associated with particular advantages and disadvantages. Through its work, MRCT hopes to overcome some existing and perceived barriers to results sharing, including overcoming ethical and logistical limitations (especially in trans-national, trans-cultural and resource-poor areas and for multi-regional clinical trials), improving patients' comprehension of results summaries and ensuring that sharing results is not interpreted by regulators as promotional material. MRCT welcomes regulatory input on the last issue as well as general public comments on desired focus areas.

RETURN OF RESULTS: PANEL DISCUSSION

Moderated discussion on current return of results initiatives and areas for improvement.
Moderated by Craig Lipset, M.P.H., (Pfizer) and Sandra Morris, Ph.D., (J&J).

Panel Participants:

- Holly Peay (Parent Project MD)
- Cheryl Jernigan (Susan B. Komen, Patient Advocate)
- Sandy Prucka (Lilly)
- Zach Hallinan (CISCRP)
- David Forster (Western IRB)
- Ann Partridge (Dana Farber)

The Questions and Answers session centered on the following themes:

1. Reasons for existing lack of communicating trial results information back to the patients
2. Determining limitations and needed safeguards for offering different types of results, as well as best modes for sharing information
3. Potential role for IRBs in reviewing lay language study results summaries before they are sent out to the patients
4. Desired scope of study results summaries
5. Recommended future areas of focus/general recommendations for MRCT

Two reasons seem to explain sponsors' current lack of standard practice of assuring communication of trial results: (a) logistical limitations associated with shortage of site staff and/or budgetary constraints and (b) concerns that sharing results can be misinterpreted as promotional material. While there is a range of viewpoints and potential solutions on the first issue, the second concern can be directly addressed by written guidance from FDA and other regulators on how results sharing could be undertaken so as to avoid any suspicion of inappropriate promotional activity.

There are a number of views on what results should be offered to the patients and whether some results should not, or should never, be disclosed. On the one hand, there is a concern that providing too much information, including non-actionable medical data, will worry and confuse patients needlessly. Similarly, some patients who participate in clinical trials may be in advanced stages of disease and have little interest in trial results. On the other hand, there are groups of patients (e.g. parents of children

with degenerative diseases) who strongly advocate for receiving all information in the hope that such information will lead to potential benefits for the child. Moreover, there is a concern that not disclosing certain data will be viewed as paternalistic.

Likewise, there are many potential ways in which clinical trials information could be shared. While some propose that communicating trial results in person by investigative site staff should be the preferred method, this approach faces issues with scalability. An alternative involves posting trial results online, an approach that is more practical, but may discriminate against people with limited computer/internet access. To accommodate different groups of people, a mixed approach could be adopted, under which lay language summaries are generally provided online (either through sponsor-specific websites or a uniform platform, such as clinicaltrials.gov). All participants in this model would be guided to the internet location. In addition, other forms of communication (e.g. in-person, mail) can be used to inform patients with limited computer/internet access.

Panelists and the audience debated the potential role IRBs can play in reviewing lay language summaries before such summaries are disseminated to the participants. On the one hand, ICH guidance states that IRBs should review all materials given to the patients in the course of the trial. Therefore, FDA is likely to require IRBs' input for results shared *while* the study is still open (such as incidental findings). However, there is no consensus on the scope of IRBs' duties in communicating with the patients *after* the study is closed. In such circumstances, IRBs' staff may experience logistical difficulties in locating appropriate study files and dedicating staff resources to reviewing trial results. Some IRBs have already expressed discomfort over adopting this responsibility. It is also unclear whether IRBs have the necessary skillset to review clinical trials summaries. While IRBs may have adequate experience in determining what classes of information may pose hazards if shared, it has been suggested that IRBs may not be best-equipped for reducing technical study results to lay language documents. Furthermore, there is a question of whether a multi-stakeholder approach to designing results summaries would better achieve the purpose of serving patients' interests.

Panelists generally concurred that results summaries should not be limited to the results of the specific study but should be supplemented by important and relevant information learned from other studies, where such information exists. The added perspective can be particularly useful in instances where individual trial results may fail, but overall knowledge gained from many trials can provide the scientific community and the patients with appropriate valuable information. Providing patients with a broader picture will also help improve their understanding of benefits/limits of medications use. This type of broader information can be added to results summaries in the form of "implications" or "next steps" for the patient.

Panelists and the audience recommended the following future areas of focus for MRCT's upcoming work in this sphere:

1. ***Formulating economically efficient models for sharing clinical trials results.*** Considering that one of the greatest barriers to sharing results is resources, a uniformly-accepted model can achieve economies of scale and make the process practically more feasible for many companies and academic institutions/research sites. Another suggestion for controlling costs is to create the capacity for delivering results in the beginning of the trial by allocating appropriate resources to the process.
2. ***Educating clinician/researchers.*** There are misperceptions in the clinical trials community regarding patients' wishes and preferences with respect to receiving study results. An education campaign/program may help to correct existing misunderstandings.

3. ***Establishing best practices for sharing results.*** MRCT can make informed recommendations on what type of results should be shared, the appropriate content of results summaries, and how the results should be disseminated to the patients.
    a. ***Types of results.*** It is important to determine what categories of results should be shared and whether there should be any limitation at all on what kinds of information is provided. One way to approach this issue is to change focus – instead of delineating categories of data appropriate for sharing, sponsors can simply allow patients opt in/opt out of future communications. Another suggestion is to start with classes of information that are universally approved for sharing (e.g. as aggregate data) and formulate best practices for disseminating this type of results.
    b. ***Content.*** Study results summaries must be written in a way that achieves a careful balance. On the one hand, shared information should be easily understood by the patients. At the same time, however, omitting technical information and phrasing results in lay language carries the risk of being misbranded as promotional material. It is recommended that MRCT seeks written guidance from FDA for indication of what should be the appropriate standard for results summaries. Moreover, there is a question of whether results summaries should reach beyond the particular study and provide patients with implication and insights gained from the totality of data on the disease.
    c. ***The process of sharing.*** The practical aspects of sharing results need careful attention. It is unclear who should be responsible for delivering information back to the patients. Burdened IRBs may not have adequate resources for this role, and researchers are not typically funded to undertake this activity. Alternative means of communicating with patients and associated risks/benefits (e.g. letters sent to wrong mailbox, inadequate access to internet) should be considered.
4. ***Involving patient advocates.*** Many benefits can be gained from involving patient advocates in discussions on delivering results and designing appropriate sharing programs/models. If participants' perspective is considered early – beginning with the writing of informed consent language – advocates will be more involved in the overall process. Later in the clinical trials timeline, patient advocates can be particularly helpful in reviewing/drafting lay language summaries.
5. ***Measures of success.*** MRCT should carefully consider and determine what goals should be achieved by sharing study results and how success will be measured. Among suggested alternatives are: increase in proportion of participants who received relevant data, utilization rates for websites dedicated to providing study results, change in health-seeking behaviors and improved attitudes towards participation in research.
6. ***Seek regulatory guidance on IRBs' role in reviewing results summaries.*** There is no established consensus on whether IRBs are best-positioned to review results summaries before they are disseminated to the patients. MRCT can reach out to FDA and other regulatory agencies for written guidance on this matter.
7. ***Broader focus.*** Much of discussion on this issue disproportionately focuses on industry experience. However, clinical trials are not only sponsored by industry but can be sponsored by government agencies (e.g., NIH) as well as by individual academic or clinical institutions. Engaging the academic and broader clinical trials community would give the sharing discourse an appropriately wider perspective.
8. ***Multi-regional perspective.*** Some nations, such as South Africa, require extensive community engagement for successful clinical trials. MRCT is uniquely positioned to review these experiences and find out if there are valuable lessons to be learned for sharing results from

these community engagement efforts. MRCT should include a focus on how best to conceptualize and implement results sharing in trans-national, trans-cultural clinical trials, especially in the emerging economies, where suitable approaches to these issues may differ from approaches adopted in OECD contexts. MRCT is uniquely positioned to analyze the "return of results" issues in the context of global, multi-national clinical trials.

EMERGING ISSUES IN MULTI-REGIONAL CLINICAL TRIALS

Moderated discussion on future opportunities in increasing confidence in multi-regional clinical trials**.** Moderated by Marc Wilenzick, J.D., (MRCT).

Panel Participants:

- Kris Joshi (Oracle)
- Ed Silverman (Pharmalot)
- Doug Peddicord (ACRO)
- Christine Pierre (MYSCRS)
- Walter Straus (Merck)

Building stronger links between clinical research and care delivery. Modern United States health care systems are fragmented, with little connection between research and health care delivery; benefits can be gained from integration. The integration process, however, will need to overcome the barriers involved in pooling and sharing research data. The hurdles are not just technological: presently there is no network that connects investigative sites, drug developing companies and regulators. Thus, a greater democratization of networking capabilities in health care systems should become one of the future goals in improving clinical trials. While the costs of establishing such networks are presently more manageable than in the past, the process may take at least ten to fifteen years to complete.

Improving transparency and public perception of the industry. While the conversation on data sharing has now moved forward, industry has historically lagged in establishing strong transparency practices. As a result, there is a common public view of the industry as a closed entity. This perception is important to keep in mind and must be addressed when companies and other stakeholders design new data sharing models. Even if a model's ultimate goal is to increase transparency, as long as the sponsor is involved in the decision-making process and/or the process is obscure, the public will likely continue to doubt such efforts, and trust in the system may not improve. Therefore, the way in which sharing models/initiatives are handled and presented is crucial. An illustrative example of a missed opportunity to engage public trust can be seen in the industry's handling of recent American Diabetes Association's (ADA) request for data. In June 2013, in response to concerns over safety of several widely used diabetes drugs, the ADA publicly stated that it would request patient-level data from pharmaceutical companies to conduct its own independent review. However, since the statement's release, there has been no public update on the efforts either by the ADA or by the industry. Such silence appears to reinforce the stereotypes of industry's secrecy and unwillingness to be transparent. At the very least, a short statement or progress report could be made available to the public.

Harmonizing privacy with transparency. Resistance to transparency is not limited to the industry. There is also societal resistance to data sharing, best illustrated by regulatory events in Europe. In Europe, there are currently two regulations moving forward – one on clinical trials data sharing and one on data protection. The approaches adopted by the two regulations highlight the central tensions between the use of data based on policy and governance principles versus the use of data based entirely on the consent model, respectively. The data protection regulation's approach does not allow for the

variations of consent language in interpreting the patient's intent, and would thus limit clinical trials data sharing to fully anonymized data. The two regulatory initiatives also highlight a genuine societal conflict, with one side supporting transparency and another side fiercely believing in privacy and personal autonomy. This tension is not an exclusively European experience and future data sharing models everywhere must take into account the competing considerations. While a balanced approach might be found, current transparency initiatives leave unsolved such crucial issues as the appropriate technological platforms for electronic data capture in clinical trials.

Challenges in conducting trials at developing world sites. Many modern clinical trials are conducted in low-income countries with inadequate health care systems, and yet new therapies proven in these trials may not be available in these countries for a long period of time after they are available in the developed economies. There are many challenges associated with conducting clinical trials in resource-limited settings, including beliefs or requirements that sponsors must take on additional health care responsibilities, some of which have been traditionally and may more appropriately be assigned to national governments. For example, trial sponsors have sometimes compensated for the lack of health care infrastructure in developing nations – an expectation that contradicts appropriate limits of clinical research. Similarly, there are expectations concerning post-trial access that sponsors may not be able to fulfill. For example, sponsors may be unable to provide post-trial access to investigative drugs that are not approved by a national government following the completion of the trial, or whose efficacy is so limited or questionable that the company decides not to seek approval for marketing in any jurisdiction and therefore manufactures no supply of the product. A difficult challenge occurs when a drug is licensed in a country, raising the issue of whether former clinical trial participants are entitled to receive the agent. Should sponsor or government offer the therapy provided in the clinical trial or the standard of care in the nation where the study took place? These issues are unresolved and will require a global dialogue between various stakeholders, including such organizations as MRCT, other multi-regional partners, and national governments.

Sustainability of investigative sites. Lack of sustainability of investigative sites is a fundamental problem in the clinical research ecosystem. The issue is highlighted by the number of sites that participate in a single trial, a problem particularly pronounced in developing countries. In such settings, sponsors not only build the physical infrastructure necessary for a trial, but also train investigators in good clinical practices. At the end of the study, the investigators may face limited domestic opportunities to apply their expertise and may choose to leave the country, resulting in an unfortunate loss to the developing and host country.

This practice of failing to re-utilize experienced investigative sites and the difficulties in retaining investigators prevent accumulation of requisite experience and skills necessary for a successful clinical trials enterprise to emerge. The problem is further compounded by misperceptions of its scope – there is an opinion that lack of sustainability has a minor effect on building trials expertise, as investigative sites are commonly located in big academic centers that can absorb the staff at the end of the study. However, in the United States, 60 percent of investigative sites are found outside of academic centers and are typically the ones most able to recruit participants rapidly.

Sites need guidance in setting and meeting expectations that go beyond simple regulatory requirements for clinical trials. Most investigative sites follow the principles of Good Clinical Practices, but have not adopted sufficient standards, guidelines, and continuing education requirements. Today, a number of organizations are involved in developing such standards. It is hoped that establishing best practices will serve as catalysts for sustainability, by better preparing investigators for future research. Moreover,

formulating common technical standards can promote data interoperability, directly assisting in the data sharing efforts. Investigative sites must be collaboratively involved in these standard-setting efforts, as well as broader data sharing and transparency initiatives, as any changes to the operation of clinical trials directly or indirectly affect the sites.

Another suggested approach for fostering investigative sites' sustainability is development of an accreditation model. On the one hand, accreditation can serve as a designation or stamp of "quality," signaling to sponsors requisite ability to engage in clinical trials. If accreditation is paired with improved transparency of accredited site location, such efforts may improve "recycling" and reduce the number of one-time players. However, accreditation will necessarily require establishing best practices and active participation of the sites in the process. Moreover, investigative sites need appropriate tools and financial incentives to undergo accreditation. If overall costs of accreditation will be too high to bear for the majority of the sites, other means of communicating quality should be considered.

CLOSING REMARKS

In his closing remarks, Mark Barnes, on behalf of MRCT, reiterated that the fundamental focus of the Center is to improve the quality and transparency of clinical trials, with a special attention paid to multi-national studies involving the developing world and emerging economies. The various topics raised in the course of the meeting have a direct impact on this international aspect of clinical trials. For example, returning study results to trial participants is part of the overall global efforts to build trust in the research process – a goal requiring attention not only in United States, but also in the emerging economies. Similar international implications are raised by addressing questions of improving data sharing, qualifying investigators, and improving sustainability of investigative sites. In the near future, MRCT plans to continue its work on regulatory developments in India, as changes in this nation affect one sixth of the world population and involve many of the issues commonly affecting clinical trials.

The central goal of MRCT is to create a pre-competitive multi-stakeholder space where issues of quality and safety in clinical trials can be openly discussed, and opportunities identified for improving trials and making them safer and better. Mark Barnes, Barbara Bierer, and Rebecca Li thanked meeting attendants for their time and participation and invited interested stakeholders to join MRCT's Steering and Executive Committees.