Clinical Trial Disclosure & Data Transparency – The Expanding Global Environment

September 17–18 | Bethesda, MD
A Future Vision for Data Sharing

Rebecca Li, PhD
Executive Director
The MRCT Center of the Brigham and Women’s Hospital & Harvard

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Topics

- MRCT’s Approach to Clinical Research Transparency
- Returning Results to Participants
- Returning Results to the Public
- Closing Thoughts
The MRCT Center’s vision is to improve the integrity, safety, and rigor of global clinical trials

Our mission:
To engage diverse stakeholders to define emerging issues in global clinical trials and to create ethical, actionable, and practical solutions.
Clinical Trial Data Sharing and Transparency Efforts

MRCT has spearheaded two major initiatives related to sharing of clinical trials data sharing

- Return of summary results to participants
- Data sharing and transparency
- Registration and results reporting
- Participant-level data sharing

Return of Plain Language summary results to participants: Guidance & Toolkit

Return of:
- Incidental findings
- Individual research results
- Study arm results
Returning of Summary Results to Study Participants and the MRCT Mission

► Goals: Returning Clinical Trial Results to study participants

• Develop standards and best practices.
• Create a guidance document, including templates.
• Address perceived barriers to widespread implementation.

► Returning results allows sponsors and investigators to recognize and honor the essential contributions and volunteerism of clinical trial participants.

► Expectations of academic, industry, not-for-profit sponsors similar

► Returning results is a key aspect of Improving Transparency of clinical trials and Increasing Public Trust.

Scope:
Communication and dissemination of summary research results to individual participants
The MRCT Center Deliverables

**MRCT Center Return of Results Guidance** for groups wishing to return results including:

- Content (essential components, source documentation, health literacy considerations)
- Logistics and detailed processes for results sharing
- Timing
- Special considerations

[http://mrct.globalhealth.harvard.edu/file/377001](http://mrct.globalhealth.harvard.edu/file/377001)

**MRCT Center Return of Results Toolkit** including:

- Templates for Phase I, Phase II/III, studies ending early
- Neutral language guide
- Endpoints language guide
- Useful Checklists

[http://mrct.globalhealth.harvard.edu/file/377016](http://mrct.globalhealth.harvard.edu/file/377016)
A Global Approach to Returning Results

• Membership of the return of results group includes academics, industry, regulators, patient advocates and patients, CROs, and IRBs/ECs.

• Our Partners: Dana Farber Cancer Institute, NIH Alliance Working Group, DIA Lay Summary Working Group, the Alliance for Clinical Trials in Oncology, and CISCRP.

• The MRCT working group modified the templates to meet the requirements of Regulation (EU) No 536/2014 (2014).

• Additional feedback is encouraged; the working group will incorporate input from European stakeholders and update the document.
Creation of Summary: Suggestions

• Summary must be unbiased and not promotional
• Summary reviewed by independent editor(s) and patient representative(s)
• Health literacy principles, including clear language
• Translation into other languages (consistent with informed consent)
• An individual from the study site or neutral informed third party should be available to answer questions for participants
• Provisions should be made for vulnerable populations and other instances
• Consideration as to whether to, and whom to, inform in the event of a participant’s death
Emphasis on health literacy

Health Literacy is not the same as one’s ability to read.

refers to the “capacity to make sound health decisions in the context of everyday life – at home, in the community, at the workplace, in the healthcare system, in the market place, and in the political arena.” (Consensus Paper 2013, Making Health Literacy a Priority in EU Policy)

Even those with adequate health literacy can struggle at times to understand health information, and appreciate clear communication.

The complexity of the healthcare system can challenge everyone!
Health Literacy Principles (Implementation)

- Plain language
- Use active voice and short sentences
- Formatting to aid comprehension:
  - Headlines to organize information
  - Presentation of the “big picture” before the details
  - Descriptive headers and subheadings
  - Limited use of tables and charts
  - Adequate “white space”
  - Minimum of 12-point font
  - Sufficient contrast between font and background color
  - Avoidance of text in “all caps”
Numeracy

• The ability to use basic probability and mathematical concepts to explain mathematical and statistical terms.

• Numeracy principles in health literacy focus on simple explanations, instead of using complex fractions, percentages or statistical terms.

• Consider when to include numbers—don’t ignore them!
  - Give people the information they need to make their own choices.
  - Providing necessary numbers can increase comprehension.
Numeracy Example

14%

Or

About 1 in 7
MRCT Center Templates

• Located in ROR Toolkit

• Includes EU required elements

• Examples

• Incorporates principles of Health Literacy and Numeracy

• Templates created for Phase I, Phase II/III, Trials ending early
## Neutral Language

<table>
<thead>
<tr>
<th>Language to avoid</th>
<th>Language to consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study proved...</td>
<td>This study found that... This does not mean everyone in that group had these results.</td>
</tr>
<tr>
<td>This study proved that using (&lt;\text{Drug A}) to prevent (&lt;\text{disease}) is effective.</td>
<td>This study found that people with (&lt;\text{disease}) who got (&lt;\text{Drug A}) had (&lt;\text{primary endpoint}&gt;).</td>
</tr>
<tr>
<td>The combination treatment of (&lt;\text{Drug A and B}) may also help alleviate (&lt;\text{a different disease/condition than what was studied}&gt;)</td>
<td>When (&lt;\text{Drug A and B}) are used together, people in this study had (&lt;\text{study endpoint}&gt;).</td>
</tr>
</tbody>
</table>

*Note: Replace placeholders with appropriate terms.*
Impact and Next Steps

• Creation of a harmonized document that will meet the needs of the US and Europe and others

• TransCelerate Biopharma is using our work to create a harmonized document

• Health Research Authority UK is leveraging our work to develop their lay summary guidelines and those of EU

• Link to MRCT Return of Results overview: http://mrct.globalhealth.harvard.edu/return-results
  Guidance document: http://mrct.globalhealth.harvard.edu/file/377001
  Toolkit (with Templates): http://mrct.globalhealth.harvard.edu/file/377016

• Provide feedback to: mrct@harvard.edu or to any one of us
Collaborations – Next Steps

- Our current Guide and Toolkit are designed for all sponsors (PI-initiated, industry, NIH) to use in all trial types (all phases, FDA- and EU, comparative effectiveness, biobanking, etc).
- Effort made to create harmonized document that will meet the needs of the US and Europe.
- We invite additional collaborators, and welcome your feedback. We will use this feedback to create an updated version.
- Link to MRCT Return of Results overview: http://mrct.globalhealth.harvard.edu/return-results
  Guidance document: http://mrct.globalhealth.harvard.edu/file/377001
  Toolkit (with Templates): http://mrct.globalhealth.harvard.edu/file/377016
- Provide feedback to: Carmen Aldinger (carmen_aldinger@harvard.edu)
MRCT has spearheaded two major initiatives related to sharing of clinical trials data sharing:
- Return of summary results to participants
- Data sharing and transparency
  - Registration and results reporting
  - Participant-level data sharing

Return of:
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- Individual research results
- Study arm results
<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Milestones</th>
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<tbody>
<tr>
<td>February 2013</td>
<td>Working Group launched with 18 stakeholder organizations</td>
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<tr>
<td>March 2013</td>
<td>Convened 4 sub-groups on key issues:</td>
</tr>
<tr>
<td></td>
<td>- Rationales for clinical trial data sharing</td>
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<tr>
<td></td>
<td>- Safeguarding patient privacy, consent principles</td>
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<tr>
<td></td>
<td>- Balancing intellectual property interests</td>
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<tr>
<td></td>
<td>- Implications of patient-level data shared in public domain</td>
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<tr>
<td>May 2013</td>
<td>Co-hosted a conference “Issues and Case Studies in Clinical Trial Data Sharing: Lessons and Solutions”</td>
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**Data Sharing: Common ICF and DUA**

**TEMPLATE ICF LANGUAGE FOR DATA SHARING**

**INFORMED CONSENT LANGUAGE FOR CONFIDENTIALITY AND DATA SHARING**

**What information about me will be used in the study?**

If you join the study, information about you will be used for the study. This information will be called “your data”. Your data includes personal information that can be used to identify you, such as your name or address. It also includes your birth date and information from your medical record. As part of the study we will get new information about you such as heart rate, blood pressure and results of tests on your blood and other samples. By signing this consent form you agree that ‘Your Data’ can be used as described here.

At any time, you may ask the study doctor to see your personal information and ask to correct it if necessary. In some circumstances, you may not be able to see your study information while the study is ongoing. This is to ensure the reliability of the study. However, the study doctor will share any important medical information if it is relevant to your health during the course of the study.

**Who will have access to my information?**

The researchers at the study site (the “Site Study Team”) will give Your Data a unique study code number (such as, 123321). This number will be used in place of your name and other information that directly or easily identifies you (for instance, your address or national identification number.) We will call this new data “Your Coded Data”. The Site Study Team will keep the link between “Your Data” and “Your Coded Data”. They will not send the link to SPONSOR. Your Data that identifies you will remain at the study site. It may be checked by the sponsor, the ethic committee or government agencies that approve medicines to check how the study was run. The Site Study Team will send only Your Coded Data to the sponsor.

**How will my information be used?**

SPONSOR will take steps to ensure that your coded data stays confidential and secure. SPONSOR will protect Your Coded Data in accordance with current law. SPONSOR and those working with SPONSOR will use Your Coded Data for research only. They may:

**DATA USE AGREEMENT TEMPLATE**

**Data Sharing Agreement**

This DATA SHARING AGREEMENT (this “Agreement”) is effective as of _______ (the “Effective Date”) between ____________________ ("Researcher") located at ____________________ and [INSTITUTION NAME] ["[ABBREVIATED NAME"] located at [INSTITUTION ADDRESS].

1) **Definitions**

   a) "[ABBREVIATED NAME] Confidential Information" means all information (including, without limitation, participant-level data, research specifications or protocols, reports, specifications, computer programs, or models and related documentation, know how, trade secrets, or business or research plans) of [ABBREVIATED NAME] or [ABBREVIATED NAME]’s affiliates that are provided to researcher in connection with this Agreement.

   b) “New Intellectual Property” means all discoveries, developments, inventions (whether patentable or not), improvements, methods of use or delivery, know-how or trade secrets that are made by Researcher in connection with the use of [ABBREVIATED NAME] Confidential Information under this Agreement.

   c) “Analytical Tools” includes but is not limited to any methodology, statistical methods, formulae or other methods or tools used by Researcher in conducting the Analysis.

2) **Data Sharing**

   a) [ABBREVIATED NAME] and Researcher intend to establish this Agreement with respect to Researcher’s access to [ABBREVIATED NAME]’s data.

   b) Researcher desires access to certain data collected by [ABBREVIATED NAME] for the sole purpose of analysis according to the Researcher’s approved research plan (the “Analysis”). This plan is detailed in EXHIBIT A, which provides a detailed description of the Analysis and the information required (e.g., diagnosis, gender, age, and other information specified immediately below) to achieve its purpose.

   In addition to restricting its use of any data shared under this Agreement to the Analysis, Researcher agrees to comply with any additional requirements that have been imposed by applicable law or regulation or that were identified by the independent review panel that approved the Analysis. Requirements identified by the independent review panel, if any, are set forth in EXHIBIT B.
70 representatives of pharma, biotech, patient/patient advocates, foundations, academics, journal editors and others:

**Consensus on future strategic vision:**

- Expectations and practices of registration and results reporting of all clinical trials would be regularized among industry and academia;
- Greater access to participants-level clinical trial data could be facilitated;
- Researchers would be able to access and combine data across various platforms and sponsors, to multiply opportunities for data analysis; and
- Research participant privacy can be safeguarded

Sponsored by the MRCT Center, LJAF and Wellcome Trust
Data Sharing: Future Vision

- **Organizational structure and Governance** - A coordinating, centralized, international, not-for-profit organization with accountability;

- **A centralized and single portal** - A central user interface with a robust search engine functionality, including information on trials around the world;

- **Data requirements** – Data standards, definition, data ontology and metadata to allow for and enable the integration of differing datasets for analysis;

- **Shared or common services** – Efficient shared or common services across data generators/sponsors (e.g. policy setting, data de-identification, criteria for independent review panel decisions or reliance, and statistical services); and

- **Flexibility** – Data platform accommodating differing expectations and research needs, including ability to host data for those data generators that do not wish to or cannot do so themselves, access data that is hosted elsewhere, or download data if freely available. Ability to utilize middleware to perform analyses.

Partnering with Wellcome Trust, IOM and Deloitte Consulting to ensure collaborative, sustainable, unified approach to common platform and portal.
Data Sharing: Proposed Model Platform - Draft

PORTAL: Central user interface portal with search engine building upon existing search engines (e.g. ClinicalTrials.gov, ICTRP) to pull information from registries / provide complete and robust “denominator” of existing data

Central multi-stakeholder governance organization

Provides shared services for:
- Administer researcher requests
- Review process
- De-identification
- Setting policies
- Define standards

PLATFORM: federated platform model with optional central component enabling access to data, combining datasets and allowing downloading as appropriate

Researcher

Repository B (other data sets)

Sponsor A Data sets

A

B

Perform feasibility checks

Central repository for academics (or others) who do not wish to “host” data
Vision: To maximize the contribution of clinical trial participants to advance science and patient care through the sharing of participant data for further research.

Mission: To develop and maintain an international non-profit entity to promote, coordinate and oversee clinical research data sharing through the creation and implementation of a sustainable global data-sharing platform that will:

• Protect study participants privacy and confidentiality
• Encourage harmonization, best practices, and regulatory convergence
• Encompass the breadth of clinical trials conducted by academia, government and industry
• Respect and leverage existing platforms, with ability to search and interact
• Provide the ability to access or to host and to analyze data
• Ensure sustainability and efficiency
To create a blueprint for the creation of a new, not-for-profit organization whose goal is to create, direct, implement and oversee a sustainable data-sharing platform.

3 Phases of Realization:

- Strategy
- Construction
- Implementation

Partnering with Wellcome Trust, IOM, Laura and John Arnold Foundation and Deloitte Consulting to ensure collaborative, sustainable, unified approach to common platform and portal.
In Strategy Phase: We have launched 3 integrated working groups to develop organizational blueprint for the suggested not-for-profit entity:

**MRCT Governance Working Group**
- Define purpose, plan and scope of new entity
- Establish new steering committee
- Develop governing principles

**Information Technology (IT) Working Group**
- Report on existing IT infrastructure
- Determine required IT specifications
- Develop global-level IT platform blueprint

**Business Models Working Group**
- Develop sustainable business model, informed by IT Working Group, evaluated by Governance Working Group
- Provide expertise on financial sustainability
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<tr>
<th>Governance Work Group</th>
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<th>Business Models Work Group</th>
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<tbody>
<tr>
<td><strong>Co-Chairs:</strong></td>
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<tr>
<td>MRCT Center</td>
<td>Ida Sim (UCSF)</td>
<td>Wellcome Trust</td>
</tr>
<tr>
<td>Wellcome Trust</td>
<td>Barbara Bierer (MRCT)</td>
<td>MRCT Center</td>
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<tr>
<td>Arnold Foundation</td>
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**Team Members:**
- Mark Barnes (Ropes & Gray/MRCT)
- Barbara Bierer (BWH/MRCT)
- Stuart Buck (Arnold Foundation)
- Nina Hill (Pfizer)
- Rebecca Li (MRCT)
- Nick Lingler (Deloitte Consulting)
- Justin McCarthy (Pfizer)
- Heather Marino (MRCT)
- Sandra Morris (Johnson & Johnson)
- Jennifer O’Callaghan (Wellcome Trust)
- Nicola Perrin (Wellcome Trust)
- Jessica Scott (GlaxoSmithKlein)
- Caroline Stockwell (Pfizer)
- Catrin Tudur Smith (University of Liverpool)

**Team Members:**
- George Alter (U of Michigan)
- Munther Baara (Pfizer)
- Vivien Bonazzi (NIH)
- Brian Bot (Sage Bionetworks)
- Anne Claiborne (IOM)
- Khaled El Emam (U of Ottawa)
- Michael Khan (U of Colorado)
- Ghassan Karam (WHO)
- Rebecca Kush (CDISC)
- Rebecca Li (MRCT)
- Gene Lichtman (HCRI)
- Michelle Mancher (IOM)
- Heather Marino (MRCT)
- Chris Mavergames (Cochrane)
- Eric Perakslis (Takeda)

**Team Members:**
- Barbara Bierer (MRCT)
- Rebecca Li (MRCT)
- Peter Lyons (Deloitte Consulting)
- Heather Marino (MRCT)
- Nicola Perrin (Wellcome Trust)
- Rohin Rajan (Deloitte Consulting)
• Conference in March 2016 in London or Boston to discuss the blueprint for the new governance structure and IT platform for all stakeholders

• New not-for-profit entity will commence operation of directing, implementing and overseeing broad data-sharing platform.

• Sustainable, cost-sharing business model for use of data sharing platform will be implemented to support new entity longitudinally.
Ask