MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

# Global Data Sharing and Transparency Initiatives

**Barbara E. Bierer, MD**

bbierer@partners.org

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F494: The New World of Transparency for Clinical Trial Results

# Disclaimer:

- The opinions contained herein are those of the authors and are not intended to represent the position of Brigham and Women's Hospital or Harvard University.
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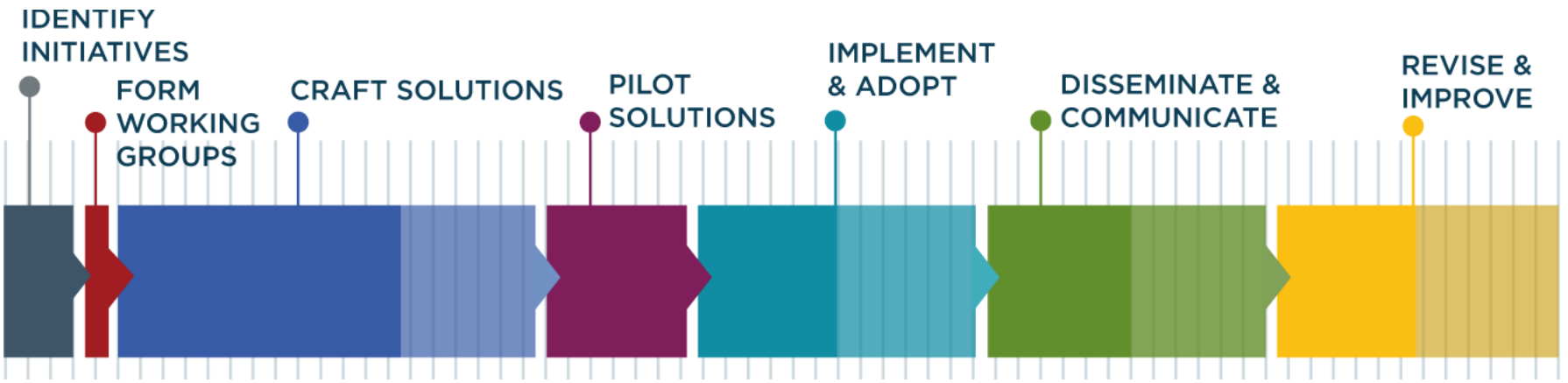
- We are committed to autonomy in our research and to transparency in our relationships. The MRCT Center—and its directors—retain responsibility and final control of the content of any products, results and deliverables.

# Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.

# MRCT Current Project Status




- Protocol Ethics
- Return of Aggregate Results
- Training and Competencies
- Global Regulatory Engagement
- Data Sharing and Transparency
- Post-Trial Responsibilities
- Individual Return of Results

# Purpose-driven data sharing will enhance scientific discovery and public trust

- Benefits are substantial (e.g.):
  - Eliminate duplicative trials
  - Evaluate common AEs by compound class or subpopulation
  - Identify surrogate endpoints
  - Enhance correlative and explanatory science
- But benefits only realized if:
  - Risks are minimized, with attention to participant privacy
    - Attention to informed consent and respect for consent
    - Data anonymization
  - Data are interoperable, data sets can be pooled
    - Data standards are available, or alternative methodology
    - Metadata is shared
    - Real-time analytics are available
  - State-of-the-art security is in place

# 2012-2015 Major Milestones in Clinical Trial Data Sharing: Platforms

- **GSK** and the Clinical Study Data Request (**CSDR**) platform, a multi-sponsor request site where data are used in a secure environment
- **J&J** - **YODA** project through which Yale partners with J&J and Medtronic
- **Pfizer's** Integrated System for Pfizer PI Initiated Research (INSPIIRE) Portal
- **Duke** Clinical Research Institute – Bristol Myers Squibb Strategic Initiative (SOAR), which supports open access to clinical trials data
- **NIH** BioLINCC data repository and others
- **FDA** -Project Data Sphere (cancer comparative data) and High-Performance Integrated Virtual Environment (**HIVE**), a private, cloud-based environment that comprises data storage library, algorithms for analysis, and computational capacity

**However these are not interoperable nor are these systems integrated**
**Few voluntary academic or biotech data generator participants**

# Access to documents
# Requests for information

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

- Policy published November 2010
- 'Outputs' table to guide implementation
- Change in access policy had big impact on Agency operations
- Average 450-500 requests for information each month
- But information only goes to the requester and although they may share, it is less visible

# Clinical trial transparency

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

**EU Clinical Trials Register**

**Proactive publication of clinical study reports – Policy 70**

**Clinical Trial Regulation and EU Portal and Database – public information clinical trials authorized in EU**

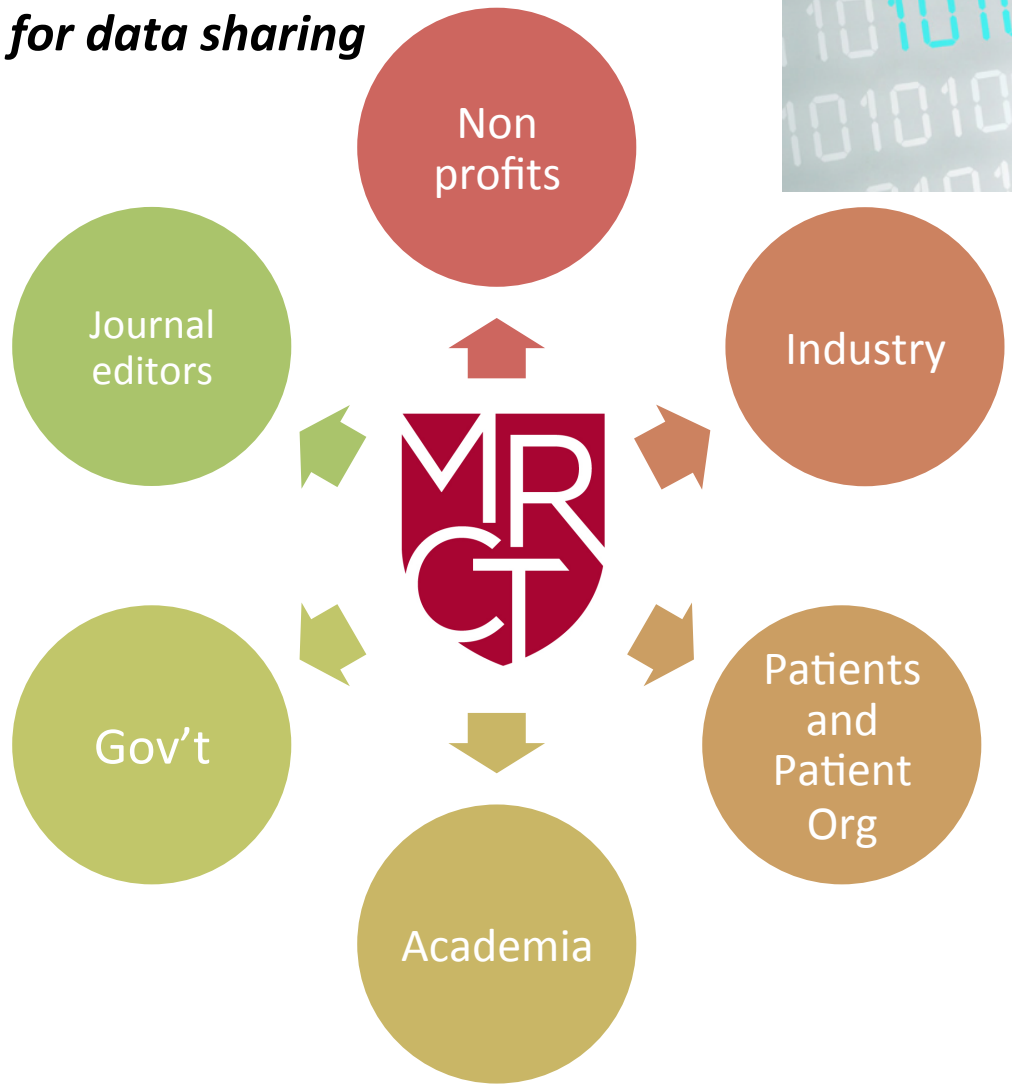
# ICJME data sharing proposal, 26 Jan 2016

- The ICMJE defines a *clinical trial* as any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention and a health outcome.
- "As a condition of consideration for publication of a clinical trial report in our member journals*, the ICMJE proposes to require authors to share with others the deidentified individual-patient data (IPD) underlying the results presented in the article (including tables, figures, and appendices or supplementary material) no later than 6 months after publication.* The data under-lying the results are defined as the IPD required to re- produce the article's findings, including necessary metadata. This requirement will go into effect for clinical trials that begin to enroll participants beginning 1 year after the ICMJE adopts its data-sharing requirements."*
- Anyone can provide feed-back at www.icmje.org by 18 April 2016.

http://www.icmje.org/news-and-editorials/M15-2928-PAP.pdf

# MRCT Center's Role as a Neutral Convener

***To create implementable solutions for data sharing***

# The Phases of Our Work in Data Sharing

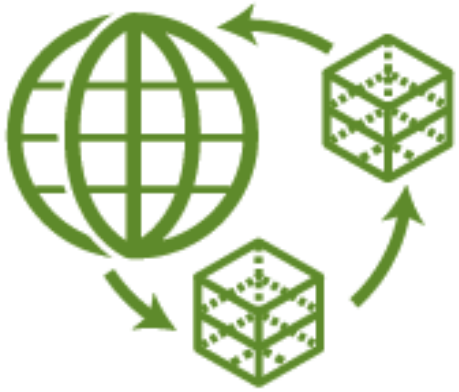
**PHASE 1**

Four Methods of Data Sharing & Framework

**CONFERENCE AT HARVARD**

Consensus Building of the Issues & Case Studies in Clinical Trial Data Sharing Conference March 30-31, 2015

**PHASE 2**



Implementation of Solutions for Data Sharing

# 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 u

sed 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 _____, 20 (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 secretes, 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.

*Panel at 2:30 today will discuss issues in informed consent

# Data Sharing Conference: Consensus of Future Vision March 30-31, 2015

- 70 representatives of pharma, biotech, patient/patient advocates, foundations, academics, journal editors and others:
- **Consensus on future strategic vision:**

1. Expectations and practices of registration and results reporting of all clinical trials would be regularized among industry and academia;
2. Greater access to participant-level clinical trial data could be facilitated;
3. Researchers would be able to access and combine data across various platforms and sponsors, to multiply opportunities for data analysis; and
4. Research participant privacy must be safeguarded, through IT design as well as conditions imposed on data users.

*Sponsored by the MRCT Center, Laura and John Arnold Foundation and Wellcome Trust*

# March 2015 Data Sharing Conference: Future Vision

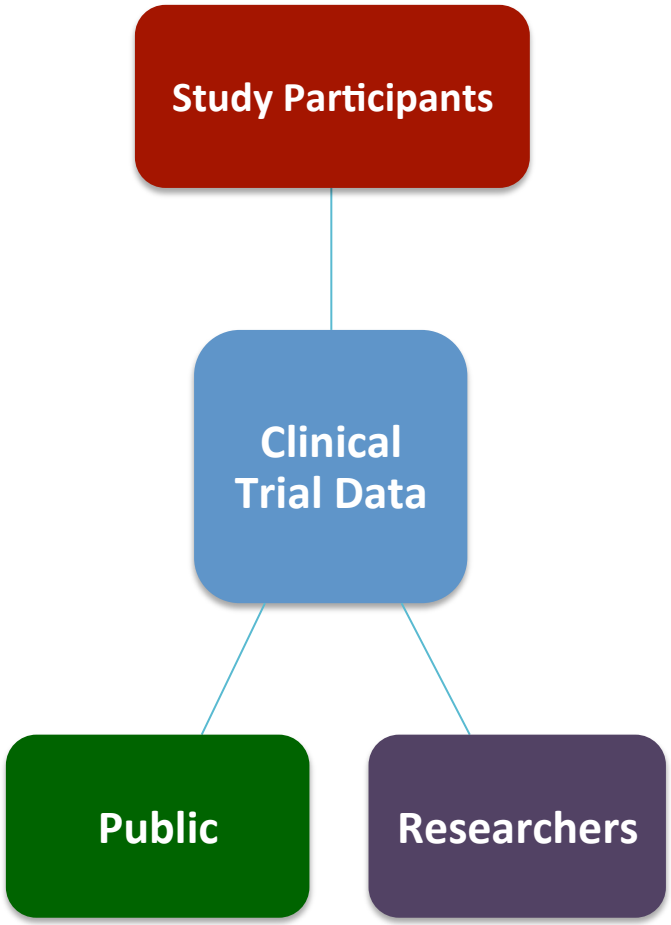
- **Organizational structure and Governance** - A coordinating, centralized, international, not-for-profit organization with accountability;
- **A centralized and single portal** - A central user interface with a robust search engine functionality, including information on trials around the world;
- **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 needs: ability to host data, access data from third party hosts, or download data if freely available. Ability to utilize middleware to communicate with analysis applications. Analytic flexibility necessary.

# Clinical Trial Data Sharing and Transparency Project

The MRCT Center, the Wellcome Trust, and Arnold Foundation and collaborators have spearheaded a major initiative related to sharing of clinical trials data, to enable stakeholders to comply with ICMJE proposed requirements, pending EU regulations, and IOM guidelines *inter alia* on clinical trial data sharing.

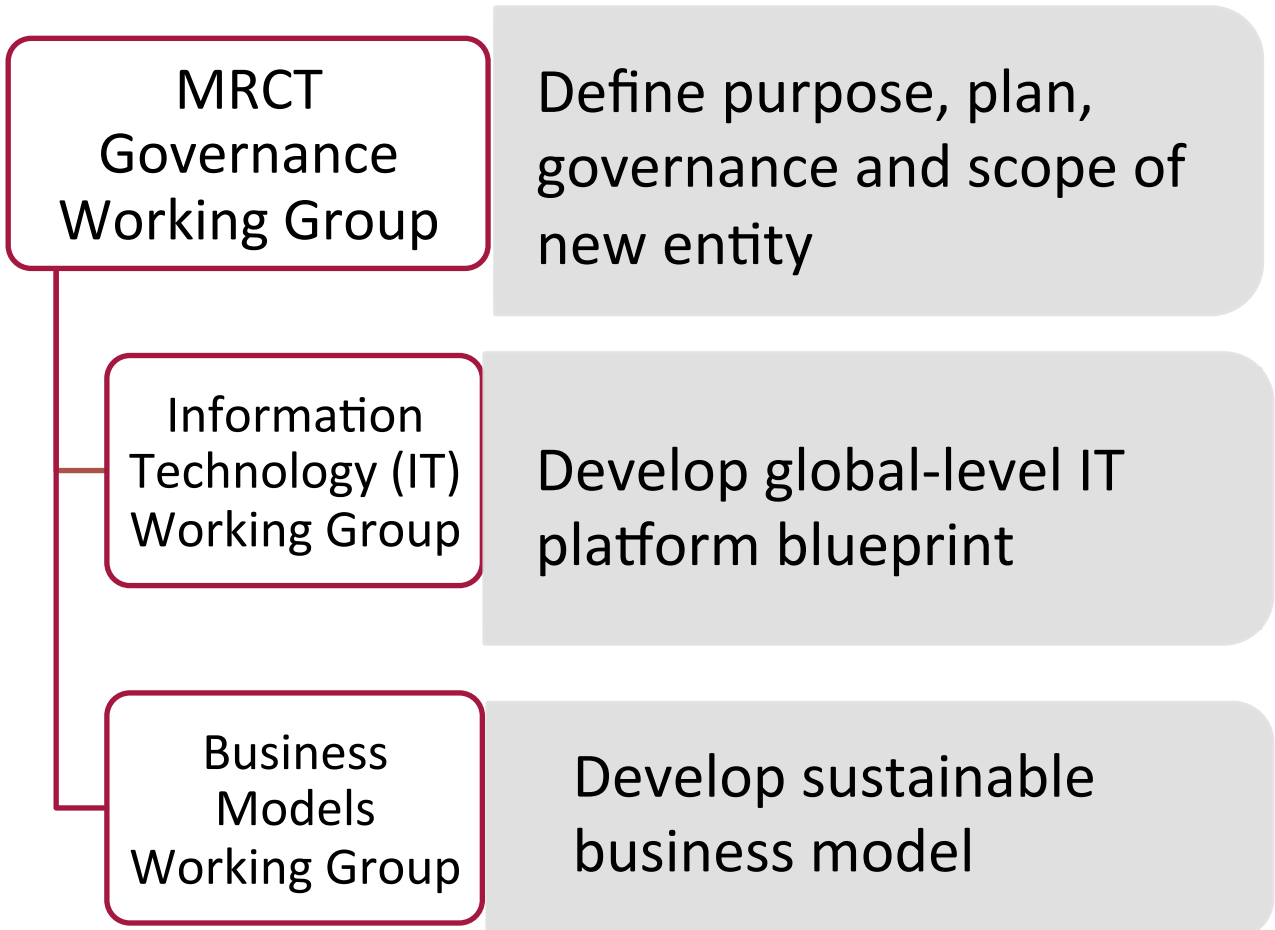
Our goal is to ensure a collaborative, unified approach to a common platform and portal.

We convened stakeholders from the US and Europe and beyond on March 21-22, 2016 at the Wellcome Trust to vet the vision of a global, federated portal of all data sharing sites from industry, academia and others with the capacity to host data and render such data interoperable.



# Data Sharing: Strategy Phase

- In Strategy: We have launched 3 integrated working groups to develop organizational blueprint for the suggested not-for-profit entity:



# The MRCT Center's Data Sharing Workgroup Members

| Governance Work Stream | IT Work Stream | Business Models Work Stream |
|---|---|---|
| **Co-Chairs:**<br>**MRCT Center**<br>**Wellcome Trust**<br>**Arnold Foundation** | **Co-Chairs:**<br>**Ida Sim (UCSF)**<br>**Barbara Bierer (MRCT)** | **Co-Chairs:**<br>**Wellcome Trust**<br>**MRCT Center** |
| Team Members:<br>Mark Barnes **(MRCT Center)**<br>Barbara Bierer **(MRCT Center)**<br>Stuart Buck **(Arnold Foundation)**<br>Marla Jo Brickman **(Pfizer)**<br>Nina Hill **(Pfizer)**<br>Rebecca Li **(MRCT Center)**<br>Nick Lingler **(Deloitte Consulting)**<br>Justin McCarthy **(Pfizer)**<br>Heather Marino **(MRCT Center)**<br>Sandra Morris **(Johnson & Johnson)**<br>Jennifer O'Callaghan **(Wellcome Trust)**<br>Nicola Perrin **(Wellcome Trust)**<br>Paul Seligman **(Amgen)**<br>Ida Sim **(UCSF)**<br>Jessica Scott **(GlaxoSmithKlein)**<br>Catrin Tudur Smith **(University of Liverpool)** | Team Members:<br>George Alter **(U of Michigan)**<br>Munther Baara **(Pfizer)**<br>Barbara Bierer **(MRCT Center)**<br>Kris Bolt **(MRCT Center)**<br>Brian Bot **(Sage Bionetworks)**<br>Anne Claiborne **(IOM)**<br>Khaled El Emam **(U of Ottawa)**<br>Ghassan Karam **(WHO)**<br>Michael Khan **(U of Colorado)**<br>Sean Khozin **(FDA)**<br>Rebecca Kush **(CDISC)**<br>Rebecca Li **(MRCTCenter)**<br>Gene Lichtman **(HCRI)**<br>Michelle Mancher **(IOM)**<br>Heather Marino **(MRCT Center)**<br>Chris Mavergames **(Cochrane)** | Team Members:<br>Barbara Bierer **(MRCT Center)**<br>Patrick Cullinan **(Takeda)**<br>Rebecca Li **(MRCT Center)**<br>Peter Lyons **(Deloitte)**<br>Heather Marino **(MRCT Center)**<br>Nicola Perrin **(Wellcome Trust)**<br>Rohin Rajan **(Deloitte)** |

# Vision

To advance human health through clinical trials data sharing, thereby respecting and honoring the contributions of sponsors, funders, investigators and, most essentially, clinical trial participants

# Mission

**Promote, coordinate, and facilitate clinical research data sharing through the creation and implementation of a sustainable global data-sharing enterprise that will:**

- Protect study participants' privacy and respect the legitimate interests of data generators, funders and sponsors
- Encompass the full breadth of clinical trials funded and conducted by academia, government, industry and others
- Respect and bridge to or incorporate existing data sharing platforms
- Provide the capability to host and analyze data, as well as to enable discovery of data on external or generator platforms.
- Interact with and complement current registries, results reporting platforms, and regulatory initiatives
- Provide an independent review process for data requests, where required
- Develop global, fair data sharing policies and practices

# Scope

This data sharing initiative will function as a platform for the sharing of clinical trials data by hosting data for stakeholders that may lack the necessary resources to do so and by coordinating and integrating existing initiatives, as appropriate.

Phased approach:

- Phase I launch, with definition of minimum viable product (MVP)
- Phase II and beyond: acquisition and development of additional functionalities

Focus on IPD

# The data sharing organization: identity and brand

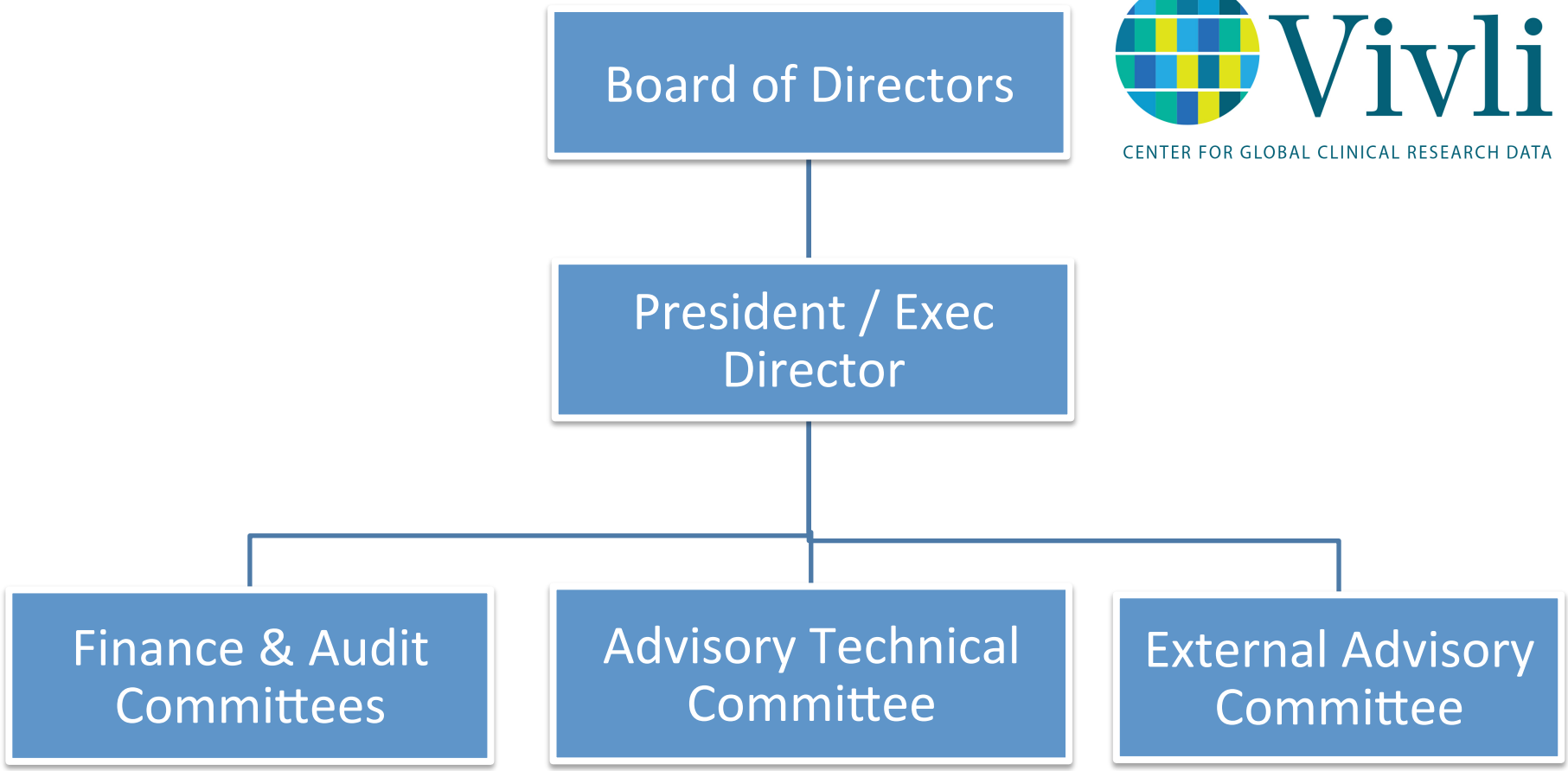

- *Vivli*, adapted from the Greek word for library, ‘vivliothiki,” and the Latin root “viv,” or life.
- We hope Vivli “the library of life,” will evoke cooperation, collaboration and a determination to respect the altruism of clinical trial participants worldwide for the benefit of medicine and public health.

# Vivli to establish resources and expertise to promote transparency, standards and equity

Vivli
CENTER FOR GLOBAL CLINICAL RESEARCH DATA

- Ability to host data and aggregate data
- Dynamic analytic tools
- Common templates and resources:
  - Public education and tools
  - Informed consent templates, optimized for country and purpose
  - Data contributor agreements
  - Enforceable data requester and data use agreements, specific for purpose, that prohibit re-identification inter alia
- Independent review panels (or reliance agreements) for data that are subject to intermediary review
- Data standards and data curation
- Risk-based data anonymization
- Development of standards and frameworks to integrate data platforms
- State-of-the-art security provisions to minimize risk

# Proposed Organizational Structure for Non Profit Vivli

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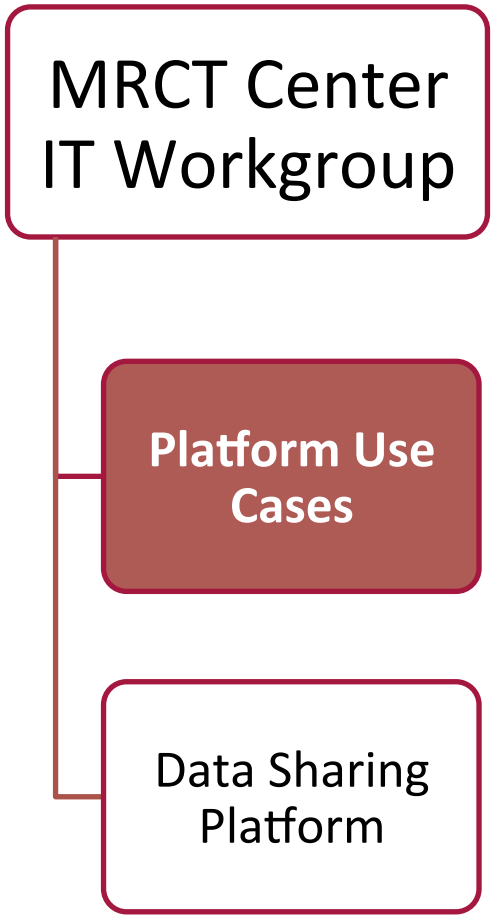
# Approach to the Work



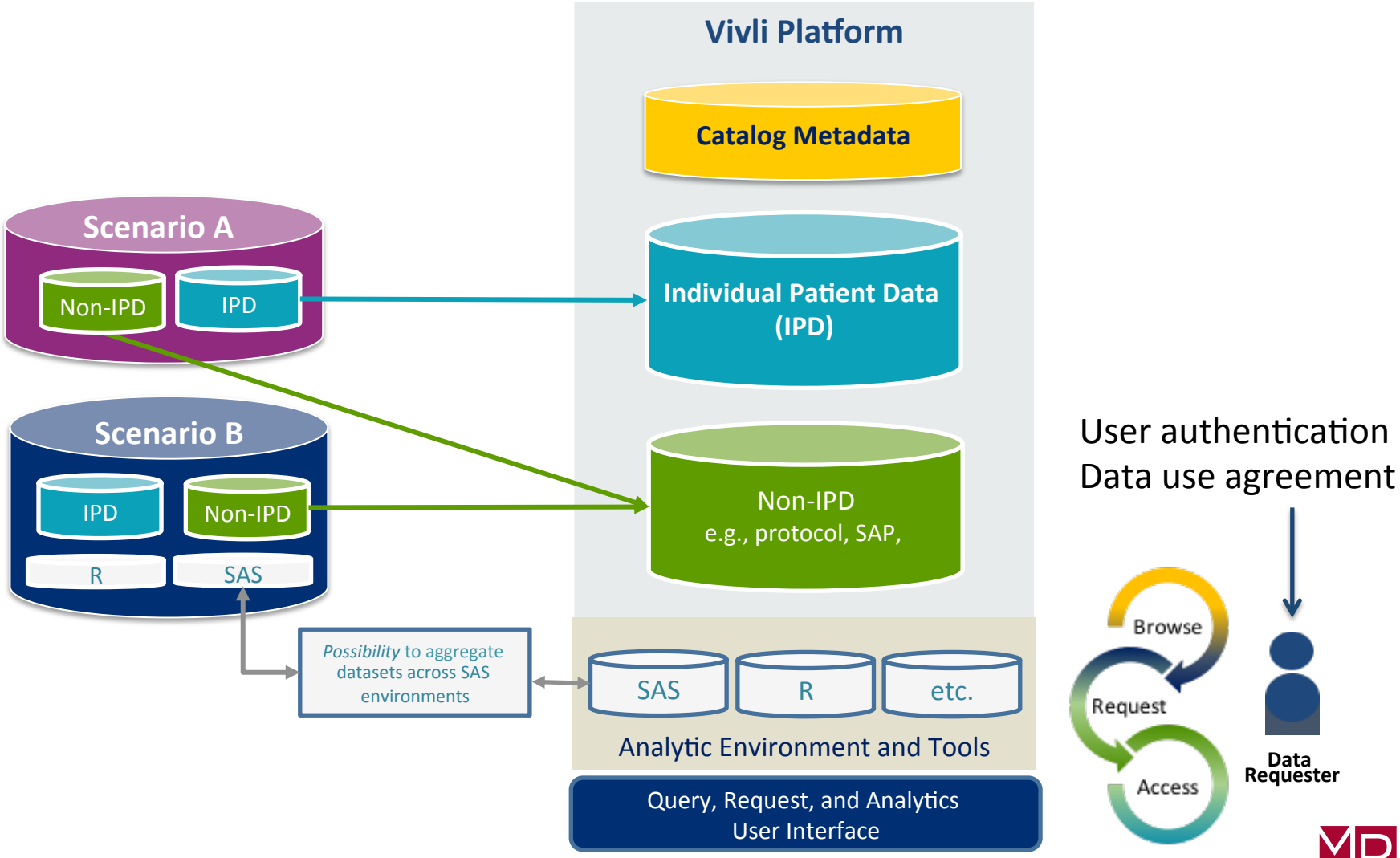

**Use Case Documents** –Define scope, utility and feature set of IT platform including:

- **Data Analysis Use Cases**
  - Outline how data users will interact with the platform to find, request, and analyze data
  - Analyzing published and unpublished data from studies
- **Data Submission Use Cases**
  - Outlines how data generators will deposit data in the platform
  - Addresses anonymization and data standardization issues

# 5 Essential Domains for Platform

| Platform Topics | |
|---|---|
| **IPD Intake and Curation** | Must be able to intake and curate data with flexibility to scale to new types of data |
| **Catalog Metadata and Dataset Identifiers** | Must have accurate structured metadata and unique identifiers for each dataset, to enable precise granular searching |
| **Review Process for Requests** | Must be able to accommodate different review requirements and processes |
| **Anonymization and DUAs** | Critical to maintain participant privacy |
| **Analysis Tools and Workspace** | Must have a secure analysis space, enabling as much cross-dataset aggregration as possible, with the flexibility to develop accommodation of many types of tools |

# Overview of platform data sharing scenarios



# Platform Participating Trials (e.g Sponsors)

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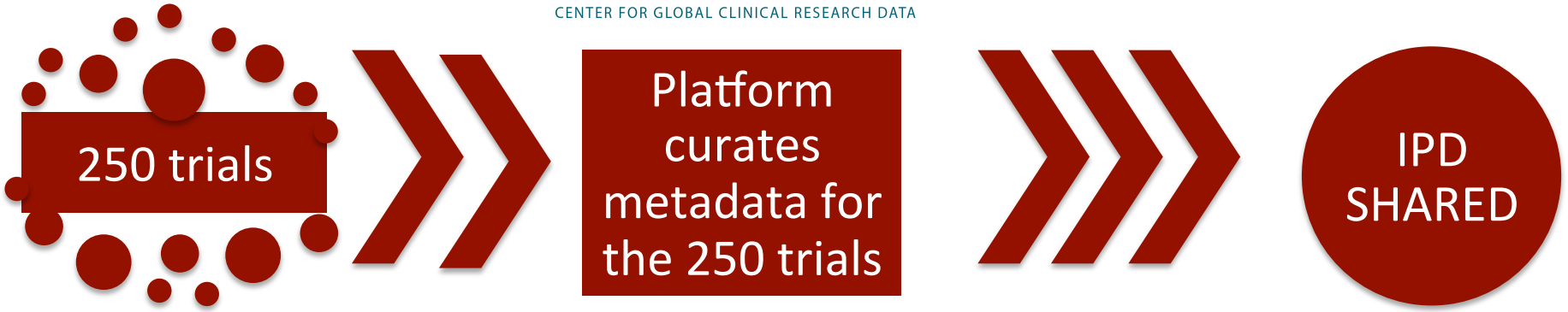


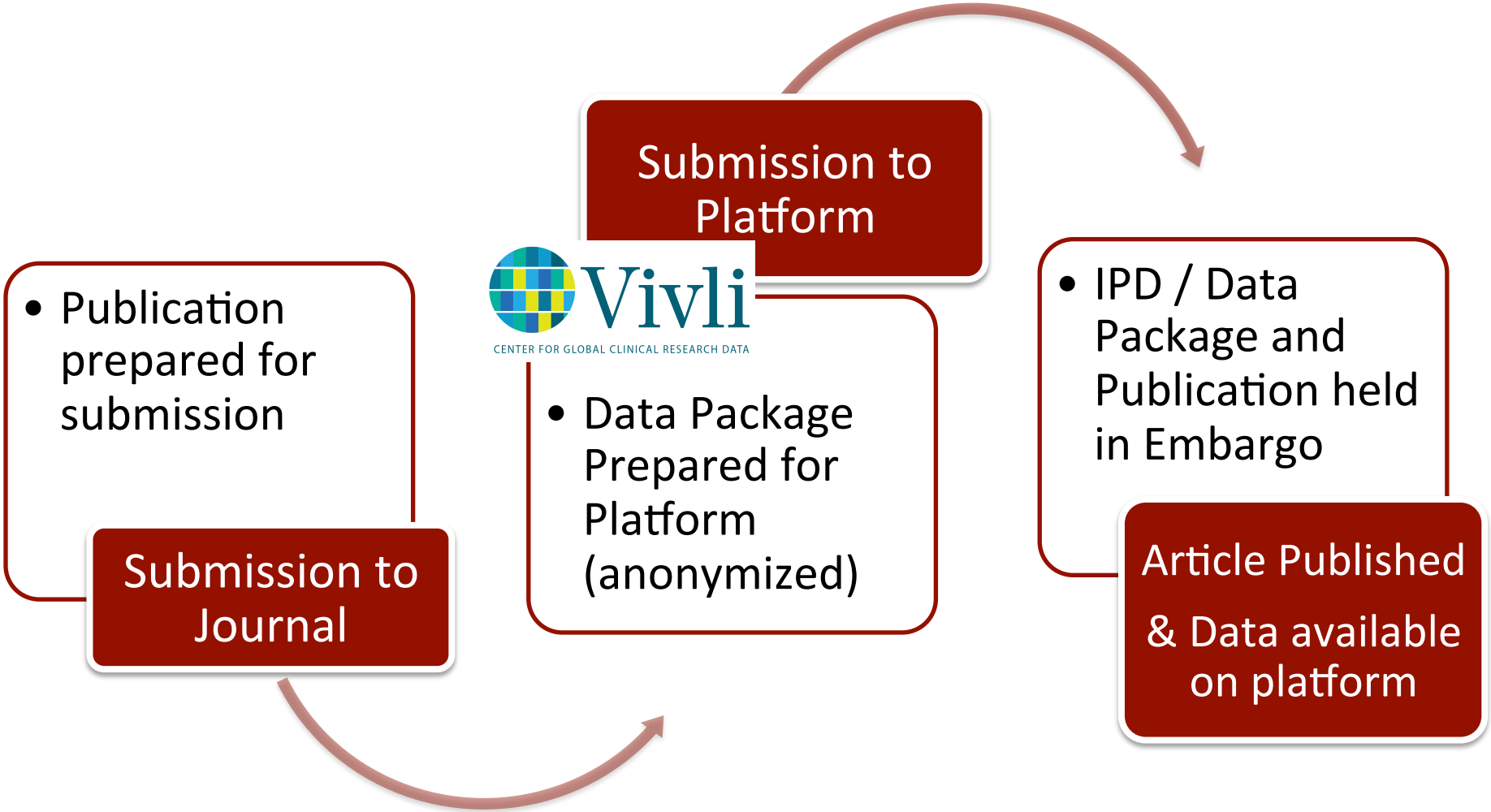

*Sponsor notifies platform of # of participating trials*

*Searchable terms match available IPD*

*Review process*

- No IRP review
- Platform review
- Data generator review

# Platform Participating Trials (e.g. Publication-based)



# Why Vivli is Needed

- Data hosting capacity
- Analytic functionality / value
- Economies of scale
  - Technical
  - Policy
  - Operational
- Lower costs secondary to economies of scale

➢ Building upon, leveraging, and partnering with existing platforms and creating anew only that which is essential

# A new global platform for data sharing

*Connecting current clinical trial platforms*

*Hosting trials that do not currently have a home*

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*Offering additional services*

- *Advanced search capabilities*
- *Anonymization*
- *Statistical analysis tools*

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# Comments, questions and discussion