MULTI-REGIONAL CLINICAL TRIALS

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

THE FUTURE OF CLINICAL TRIALS DATA SHARING

MEETING PROCEEDINGS

MARCH 21-22, 2016

HOSTED BY THE WELLCOME TRUST

MULTI-REGIONAL CLINICAL TRIALS CENTER OF BRIGHAM AND WOMEN'S HOSPITAL AND HARVARD UNIVERSITY

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EXECUTIVE SUMMARY

The agenda is included in Appendix I.

The major themes of the 2016 Future of Clinical Trials Data Sharing Conference included:

- Presentation of plans for Vivli, a new entity for global data sharing
- Presentation from experts in data sharing responding to plans for new entity
- Feedback from participants

Plans for the new entity, Vivli, were presented based on the work performed by the Governance, Business Models and Data Sharing Platform Workgroups. In addition, invited speakers and panelists presented their perspectives in relation to clinical trials data sharing and the Vivli proposal:

- Fergus Sweeney, Ph.D. of the European Medicines Agency opened the meeting by discussing the importance of clinical trials data sharing and Policy 70 on publication of clinical trial data
- Frances Nuttall, MSc. of the European Medicines Agency explicated Policy 70 further and detailed its potential benefits
- Jeff Drazen, M.D. of the New England Journal of Medicine spoke on the value of data sharing and the mandates being put forward by ICMJE to encourage data sharing
- Shasha Jumbe, Ph.D. of the Bill and Melina Gates Foundation highlighted the work being done by the Gates Foundation to promote clinical trials data sharing for studies performed in low and middle income countries
- Karla Childers, M.S. of Johnson & Johnson gave an overview of the YODA system and its impact on clinical trial data sharing
- Bernard Lo, M.D. of the Greenwall Foundation focused on the hurtles that need to be addressed when attempting to set up a data sharing initiative
- A panel of IT and Data Sharing Platform experts reflected on the Vivli platform and recommended flexible and limber decision-making, aiming to disrupt the current data sharing environment and to move quickly
- A panel of five discussed transparency, reflecting governance of the Vivli platform and recommended that the platform assess current initiatives before moving forward. They further recommended rapid development of a prototype pilot program.

Principles consensus recommendations of the outlined plan for Vivli included:

- Strengthen the Vivli value proposition to ensure that the Vivli initiative will address a clear gap
- Accelerate the timeline to create Vivli and to launch a pilot program
- Respect existing platforms and take the existing efforts into account when developing the Vivli platform

WELCOME AND INTRODUCTIONS

Nicola Perrin, Wellcome Trust
Nicola Perrin welcomed the group to the meeting with noted the strengths and diversity of the assembled group. She commented that, although there are efforts being made to further sharing of clinical trial data, there is insufficient data sharing happening today and current initiatives have been disjointed. The 2016 Meeting on the Future of Clinical Trial Data Sharing's builds on the prior March 2015 meeting held at Harvard and advances the work that has been done by the workgroups over the past year.

Barbara Bierer, Multi-Regional Clinical Trials Center
Dr. Barbara Bierer presented an introduction and background of the Multi-Regional Clinical Trials (MRCT) Center and the Data Sharing and Transparency Initiative. The MRCT Center acknowledges the researcher's responsibility to the public and the study participants during clinical trials as well as the responsibility to other researchers through the sharing of clinical trial data. In everything that follows, Dr. Bierer noted that the expectation of clinical trial registration and results reporting were a threshold expectation. The benefits of data sharing are substantial since they will be able to advance new science (e.g. evaluate common AEs by compound class or subpopulation, identify surrogate endpoints and enhance correlative and explanatory science) and potentially to eliminate duplicative trials that put participants at risk unnecessarily. However, these benefits can only be realized if risks are minimized, state-of-the-art security is in place, there is wide participation of all data generators, data are interoperable and data sets can be pooled.

Dr. Bierer noted that data sharing is supported by several recent policies and specifically noted the ICMJE proposal which was released 26 January 2016. The proposal states:

> *"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 de-identified 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 underlying the results are defined as the IPD required to reproduce 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."*[1]

The March 2016 meeting was the culmination of the second phase of the data sharing and transparency project. The first phase was the development of the four methods of data sharing, the elucidation of a "learned intermediary" model for data sharing, and a framework for its approach.[2] Phase one ended with the 2015 Conference at Harvard University in which 70 representatives of pharma, biotech, patient/patient advocates, foundations, academics, journal editors and others. During the meeting a consensus on the future strategic vision was reached:

[1] Policy can be found at: http://www.icmje.org/news-and-editorials/M15-2928-PAP.pdf
[2] Mello paper.

- Expectations and practices of registration and results of all clinical trials would be regularized among industry and academia;
- Greater access to participant-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 must and can be safeguarded with established, trusted anonymization techniques.

The participants endorsed further exploration of a centralized single portal with organizational structure and governance that contains data requirements, shared or common services and flexibility in order to facilitate the sharing of clinical trial data.

The next steps were to develop a timeline:

- Strategy (August 2015 – March 2016)
- Construction (March 2016-September 2017)
- Implementation (September 2017-Forward)

Three work streams (Governance, Business Models and IT Platform) were developed in order to drive this work forward.

The progress which has been made by these workgroups culminated in the proposal for a new not-for-profit entity, that we have termed Vivli:

Identity and Branding:

Vivli
CENTER FOR GLOBAL CLINICAL RESEARCH DATA

Vivli, adapted from the Greek word for library, 'vivliothiki' and the Latin root 'viv' for life.
We hope that 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.

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.
A phased approach is planned:

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

Dr. Bierer introduced the work groups that would present the various pieces of the platform and new entity. She urged the audience to pay close attention to how each piece would function but to remember how all of this will fit together to form the new not-for-profit entity. Feedback and discussion were welcomed.

The Importance of Data Sharing and Transparency

Fergus Sweeney, European Medicines Agency (EMA)
Dr. Fergus Sweeney presented background on the work done by the European Medicines Agency (EMA) that highlight how data sharing and transparency fit closely into the mission of the EMA, most particularly in providing quality and independent information regarding the medicines it evaluates to patients and healthcare providers.

Dr. Sweeney discussed the three pillars of clinical trial data transparency within the EMA including:

- EU Clinical Trials Register: Launched in March 2011, where information and structured results summaries on all clinical trials authorized in the EU dating from 2004 o are made public, including information on pediatric clinical trials and in Pediatric Investigation Plans. www.clinicaltrialsregister.eu

- Policy 70 on publication of clinical data: Policy 70 covers the proactive publication of clinical trial data, and in particular clinical study reports, submitted in Marketing Authorisation Applications to the EMA as of 1 Jan 2015. http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000555.jsp&mid=WC0b01ac05809f363e

    - Policy 70 Phase 1: Publication of clinical study reports and aggregate data tables, and other clinical data summaries, expected to be operational as of September 2016

  - Policy 70 Phase 2: The Agency will review various aspects in relation to IPD, including finding the most appropriate way to make IPD available, in compliance with privacy and data protection laws.

- New EU Clinical Trial Regulation - EU Portal and Database: where information, including structured summaries of results and layperson summaries on all Phase I-IV clinical trials conducted in the EU will be made public at the time of their authorization and 12 months after the end of each trial. Notably for "category 1" trials (essentially non-therapeutic trials in particular phase I) there may be a deferral of publication of results up to 18 months maximum.
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000629.jsp&mid=WC0b01ac05808768df

Discussion
There was some discussion about how Vivli would define a clinical trial. It was noted that 300-600 clinical trials are registered each week. Given that volume, Vivli would be advised to define which subset we intend to capture lest the volume be too large. The EMA trial registers include interventional clinical trials of medicinal products, and the Marketing Authorizations focus on trials with medicinal products. MRCT may also want to capture device trials and observational studies.

GOVERNANCE WORKGROUP

Rebecca Li, MRCT Center
Dr. Li gave an overview of the main outputs and deliverables from the Governance Workgroup including:

- Presentation of the Proposed Vivli Governance Structure
- Presentation of the Platform Review Process
- Discussion of the Platform Participating Trials
- Recommendations on Data Packages
- Presentation of the Resource Kit
- Presentation of the Data Sharing Case Studies

Proposed Governance Structure of Vivli
The governance of Vivli will consist of a Board of Directors that oversees a President or Executive Director. The Board will have several committees including finance & audit committees, advisory technical committee and external advisory committee.

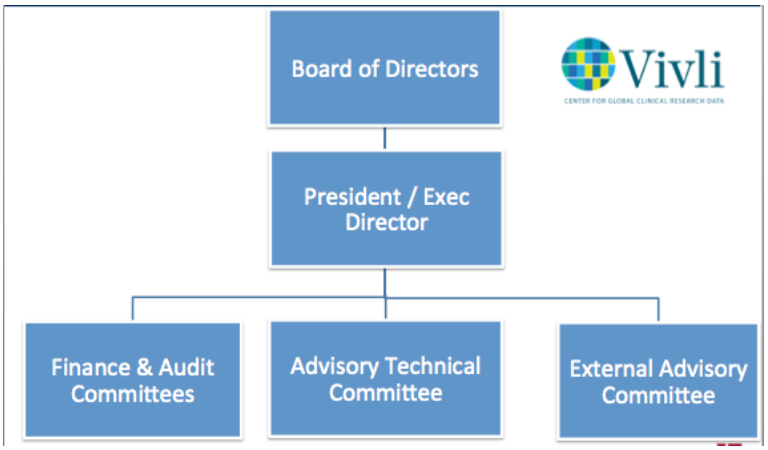

Figure 1

The governance of Vivli is suggested to be a Board of Directors composed of contributors to the organization (often financial) and "at-large" positions. Contributor representatives to the board will be nominated by the contributing entities and be approved by the board. The board nominating committee will appoint at-large members, the process for which will be defined.

Platform Review Process

Vivli will act as a "data library" that will respect both the needs of the requesters and the concerns of the donors. Any data requestor would sign a data use agreement (DUA) as a condition of access, including commitments to publish results of the secondary analyses, not to re-identify participants and not to share data beyond those specified in the DUA. In addition, those that donate data to Vivli would be able to choose a tier for further review of data access:

Tier 1: Data generator would donate data that would not require a further review process.
Tier 2: Data generator would cede review to the platform's selected Independent Review Panel (IRP).
Tier 3: Data generator would maintain own review process. Platform will forward requests for review.

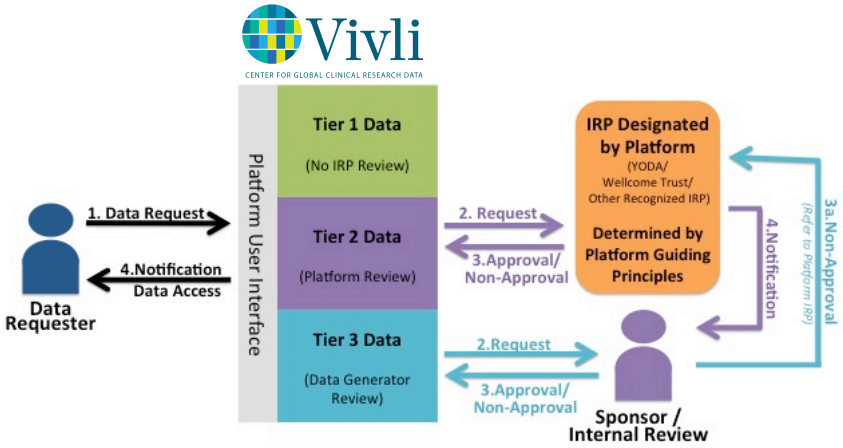

Figure 2

Vivli would begin with the three tiered review system in which data generators would have the choice of maintaining autonomy in the review process. However, we hope that the organization would eventually be able to move towards harmonization of the process and, as an aspirational goal, eventually move towards a two-tiered system

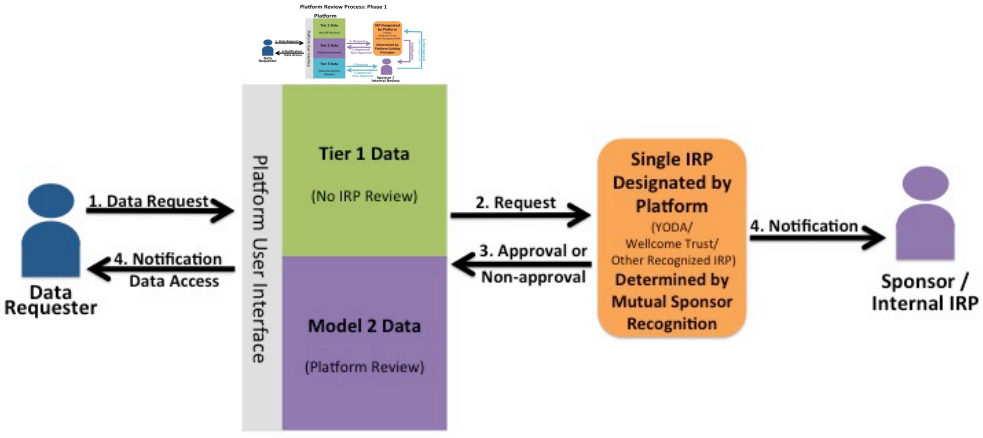

Figure3

Platform Participating Trials
Trials participating in the platform will be defined as trials which are registered in an internationally recognized clinical trial register. These trials will have associated metadata as well as IPD that is or will be made available. The platform will not prescribe the trials that are present but will accept all trials moving forward as offered.

Recommendation on Data Packages
The basic package recommended for submission to the platform would include:

- Analyzable individual participant-level dataset (IPD)
- Final study protocol + amendments
- Statistical analysis plan
- Other items that may be included but would not be required:
    - Annotated case report forms
    - Analytic code supporting the published results
    - Redacted CSR

Data Sharing Case Studies
The MRCT Center summarized below five case studies to demonstrate the effective use of data sharing:

Table 1

Data Generator	Data Recipient	Impact
(1) ITN Network – RAVE Trial – NIAID (funder)	Investigators at the Institute for Computational Health Sciences, University of California, San Francisco	Reanalysis of the RAVE trial demonstrated a correlation between patient's granulocyte subsets at baseline with the likelihood of remission at 6 months following either cyclophosphamide or rituximab in patients with ANCA-Associated Vasculitis.
(2) Pfizer, GSK, Lundbeck	Investigators at the University of Gothenberg, Sweden, Swedish Research Council (funder)	In a post-hoc analyses of 18 trials of SSRIs utilizing a single rating scale versus the Hamilton depression rating scale, SSRIs were shown to be more consistently effective than placebo in the treatment of patients with major depression.
(3) Medtronic – YALE YODA (intermediary)	Investigators at the University of Colorado Department of Orthopedics	Meta-analysis of 4 trials demonstrated that, for patients with degenerative disc disease following lumbar arthrodesis, the presence of radiographic fusion was correlated with improved clinical outcomes compared to radiographic non-union (Oswestry Disability Index - ODI; Numeric Rating Scales (NRS) for back and leg pain).
(4) J&J, Amgen, Hoffman-LaRoche and 5 independent investigators	Investigators at University of Bern; German Federal Ministry of Education and Research, Medical Faculty of University of Cologne and Oncosuisse (funder)	Meta-analysis of 18 trials (13,933 patients) demonstrated that administration of erythropoiesis-stimulating agents in oncology patients increased mortality compared with transfusion therapy alone. The increase in mortality must be balanced against the potential benefits of erythropoiesis -stimulating agents in this patient population.
(5) Pfizer, Sanofi	Investigators at University of North Carolina	Mitoxantrone added to prednisone in the treatment of patients with post-docetaxel, metastatic, castrate-resistant prostate cancer showed no survival benefit over the use of prednisone alone and may be associated with increased toxicity.

Discussion
Moderated by Barbara Bierer, Multi-Regional Clinical Trials Center

Timeline

Several questions were posed on timeline for the process. Some were wondering when academics would be brought into the planning process. It was highlighted that all work streams contained diverse membership that included academic representation.

Data Packages
There were several questions surrounding the data packages and upload of data to the platform. Some wondered whether it was necessary for the platform to host data or whether it should be a directory for where data can be found.

Others commented that since the platform will have a governing body and membership it would have the power to place requirements on those that joined. Although this is the case, Vivli will want to be inclusive rather than too prescriptive. Finding solutions that encompass and include the current initiatives is the best way to ensure initial buy in.

Review
Some concerns were expressed around the proposed review process and the tiered data system. Attendees at the meeting expressed the hope that the platform review process would be as transparent as possible, including making the data requests transparent (perhaps after an embargoed period). It was noted that the 3-tier process was developed in order to accommodate data generators who may not be comfortable with ceding the review process to the platform, particularly at the beginning of operations.

Attendees also noted that internal review does not equate with rejection of requests: many sponsors have not rejected any requests for data sharing.

General Governance
There was a question on whether there would be an adjudication process for a finding derived through data sharing that does not agree with the original findings of the data generator. The platform will need to determine whether and how to deal with this type of situation. It was also mentioned that Journals are currently trying to come up with best practices for secondary analysis. It has been proposed that those trying to conduct secondary analyses demonstrate that they can come to the same conclusion as the primary analysis in order to prove their understanding of and familiarity with the dataset. There was no consensus as to whether that requirement should be a condition of access.

It was also noted that Vivli should not try to "take on too much." The platform will not be able to fulfill all needs for every audience. Instead, Vivli should set certain principles and goals to pursue in the development of the organization and platform.

Business Models Workgroup

Rohin Rajan, Deloitte Consulting
Dr. Rohin Rajan presented the work conducted by the Business Models Workgroup. The priorities of this group were to develop a plan reflected the Governance and IT vision and by which Vivli would be able to launch and to achieve sustainability.

Approach

The business models workgroup developed their proposal using the following approach:

- **Landscape**: Performed an external scan of existing clinical trial data sharing technologies and platforms
    - Found that several approaches currently exist but none can be described as a "silver bullet"
    - Several groups are involved in at least two data sharing initiatives
    - Smaller groups do not have models for data sharing
- **Capabilities:** Defining high-level functionality and capabilities of the desired platform / system / entity
- **Operating Model:** Define potential operating models that would enable the capabilities required for Vivli
- **Timeline:** Determine near-term and long-term opportunities for Vivli to evolve flexibly

Potential Operating Models

Based on the external scan and capabilities needed by the platform, several operating models were proposed. Dr. Rajan noted that, although these models are presented as individual approaches, in all likelihood the final model will,be a combination of several of these models:

- **Advocate and Lobby:** Engage in advocacy for policy and practical changes to increase transparency and cooperation in clinical trial data sharing with existing efforts (platforms / systems / regulators, other stakeholders)
- **Assemble:** Find, support, and render specific solutions to address existing and emerging gaps in clinical trial data sharing, to facilitate exchange between platforms
- **Partner:** Identify and partner with existing initiatives (e.g. Project Data Sphere, CSDR) to enable immediate access to current capabilities / functionality as a foundation for growth
- **Build and Develop:** Build and develop capabilities as needed to facilitate the exchange of clinical trial data

These four potential models were evaluated for their capability, dynamism, investment, stakeholder risk, control and time to build. The summary of this analysis is in the following diagram and others.

Comparison across dimensions

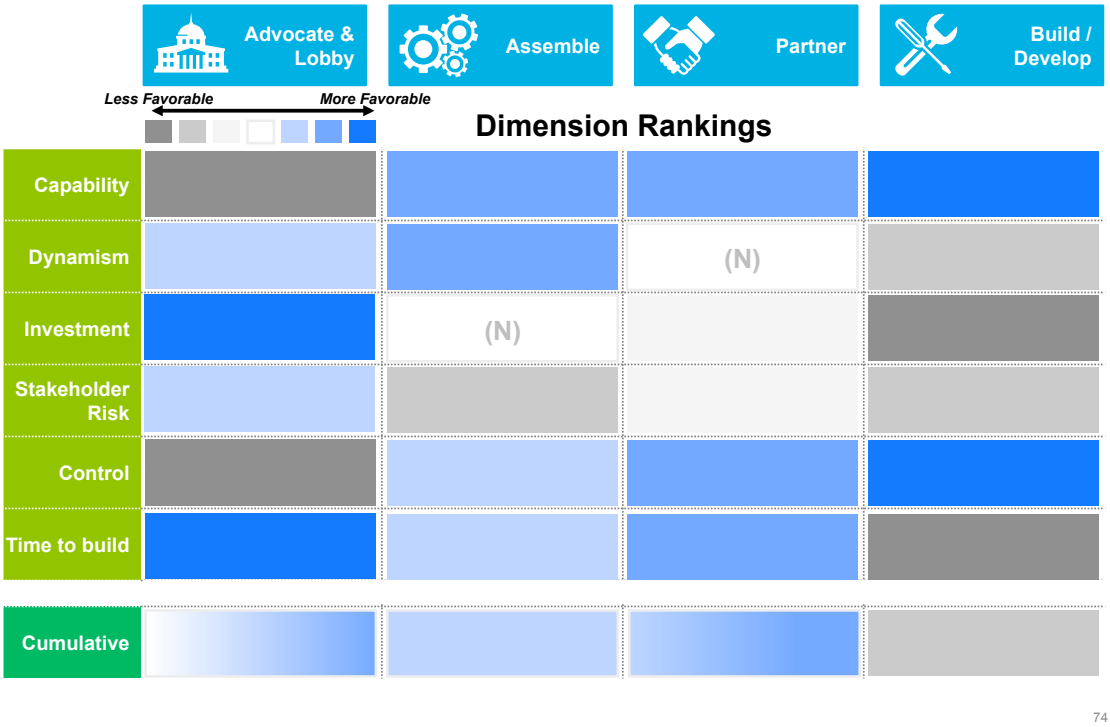

Figure 4

Finally, Dr. Rajan presented a timeline for the development of the platform and the entity and capital needed for each stage of development:

- **0-6 Months:** Clarify vision, mission and timeline for Vivli, increase awareness, identify service offerings partners and targets
    - **Investment:** $400-$500K for Operational Costs
- **6-18 Months:** Develop agreements and partnerships, clarify scope and roles of Vivli and complementary organizations, participation and sign-on of biotech companies and academic organizations
    - **Investment:**
        - Capital: $5M – 10M
        - Operational: $2-4 M
- **18-36+ Months:** Grow user base, develop technological capabilities, develop sufficient revenue flow
    - **Investment:** Unknown

Discussion
Moderated by Frank Rockhold, Duke University

Relationship with Other Data Sharing Initiatives
During discussion, there were some questions expressed surrounding other existing data sharing initiatives and the relationship between those initiatives and the Vivli platform. The audience was reminded that groups such as CSDR, WHO, University of Oxford and others--that were not explicitly discussed during this meeting but had been presented in the March 2015 meeting--have developed data sharing platforms. While most of these are for specific data sets or addressing specific diseases, many of these platforms may have similar functionality to that which is being proposed. Presenters explained that these platforms will be options that are explored when assessing the partner/assemble options for the business model.

Regulation of Data Sharing
It was noted that regulatory agencies might not finalize and post requirements for data sharing as believed which might make adoption and utilization of Vivli more challenging. However, it is difficult currently to pass these regulations since there is no location for small biotechnology companies and academics to share their data securely and responsibly. It was pointed out that if such a place were to exist, it would be more feasible for data sharing to be mandated. Vivli is positioned to be one such place.

Genomics
It was noted that genomic data were not mentioned during the presentations. Participants believed that genomics data needed to be considered in the initial planning phase, as these data become more common and more research studies move toward inclusion of genomic and genetic data.

Non-profit vs. For-Profit
There was significant discussion surrounding the choice for Vivli to exist as a not-for-profit rather than as a for profit company. The intent behind the not-for-profit decision was to build trust in the field and to encourage collaboration rather than competition among those who already exist in the marketplace. Any margin generated from the platform would be reinvested into data sharing, further decreasing the costs and lowering barriers to participation.

Charging for Service
Since Vivli will be striving toward a sustainable business model, many wondered who specifically would be charged for the services that Vivli is providing. Presenters noted that the cost will need to be balanced between those who are sharing data and those who are requesting it. The threshold will be low initially and cost will be re-assessed before the platform goes live. The intent is to be self-sufficient but conservative.

Incentives for Use
Several noted that to be successful, incentives are required for data generators to use this platform. For academic investigators, the "academic coin" is in publishable material and working towards tenure. The platform will need to find a way to encourage academics to take on the cost of sharing their data.

EMA Policy on Publication of Clinical Trial Data for Medicinal Products for Human Use

Frances Nuttall, EMA
Frances Nuttall presented the purpose and objectives behind the EMA Policy 70 and commented on its impact on clinical trial data sharing.

The new policy was published on October 2, 2014 and came into effect January 1, 2015. The policy covers clinical reports moving forward from January 1, 2015, and does not cover legacy data. The policy has two phases. The first is to ensure the publication of clinical reports once the regulatory decision has been taken. These clinical reports will be text searchable PDF documents which will have commercially confidential and personal information anonymized/redacted. Once this has been achieved, the EMA will investigate publication of IPD. The form in which IPD will be required to be shared has not been decided yet.

There is a new section of the EMA website that is being set up to access the published clinical reports. There are two access options: (1) view only and (2) downloadable clinical reports from the site for registered users. The site is anticipated to go live in September 2016. There is a back log of cases that need to be prepared for publication. EMA has already contacted the first companies that are affected; others are being asked to wait for the time being.

This policy will be beneficial since it will increase transparency and public information and will prevent clinical trial duplication while promoting enhanced scientific knowledge.

Data Sharing Platform Workgroup

Ida Sim, University of California, San Francisco
Dr. Ida Sim presented the work conducted by the Data Sharing Platform Workgroup. The Data Sharing Platform Workgroup was tasked with developing the Data Sharing Platform Blueprint as well as making recommendations that will enable broader sharing of clinical trial data.

Data Browse, Request and Access
Existing systems currently do not support accurate or precise queries on study design features. A more precise query requires study design features to be more computable, structured and accurately completed. Vivli will create added value through searchable, curated catalog metadata with specific elements. Through curation, the platform will be able to attest to a certain level of accuracy for the metadata that exists.

Submission of Catalog Metadata
During phase 1, the platform will use human curation in order to develop the catalog metadata. Vivli will learn from lessons in ClinicalTrials.gov, the WHO ICTRP, and others to develop best practices. The human curation will provide quality assurance to assumptions and contributors or sponsors

will be able to review fields for accuracy. In phase 2, Vivli will move toward a semi-automated curation with natural language processing and text mining. More computable information will be extracted from the protocols while human curation will provide monitor for accuracy and for support.

Submission of IPD
The Vivli Platform will allow for two separate scenarios for data sharing (Fig 6):

- ***Scenario A:*** This scenario will allow for IPD and Non-IPD to be stored on the platform for analysis and combination with all other data shared on the platform. The data generator will have no further ongoing maintenance of the data set after submission to the platform.

- ***Scenario B:*** This scenario will allow for Non-IPD to be copied to the platform for analysis and combination with all other non-IPD on the platform. This does not allow for IPD to be stored on the platform and data generator will maintain an analysis environment separate from the Vivli platform.

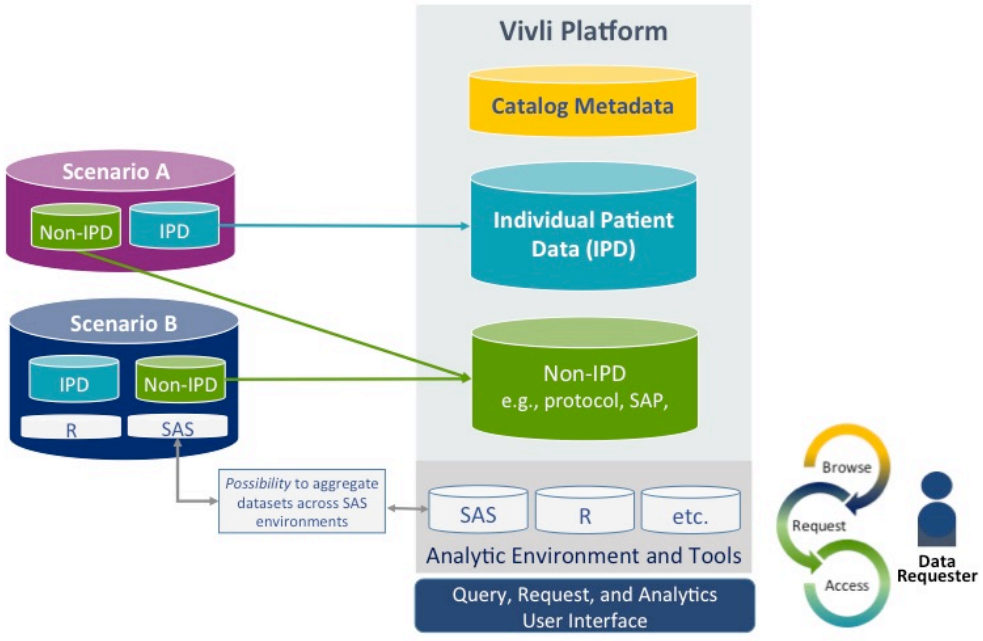

Figure 5

IPD that is submitted through the platform will enter into a curation queue. During curation, Vivli will ensure that all IPD is properly anonymized/de-identified and standardized and a digital object identifier (DOI) will be minted. The curated IDP will be indexed to the other contents of the platform and will become accessible to platform functionality.

Phased Approach
The platform will be developed in a phased approach with phase one consisting of the minimum viable product (MVP) for launch of Vivli. Phase one plus items are stretch goals for functionalities that will be "nice to have" for the launch of the platform but are not required for the initial launch. Finally, phase two consists of goals for the platform but will not be present in the initial build.

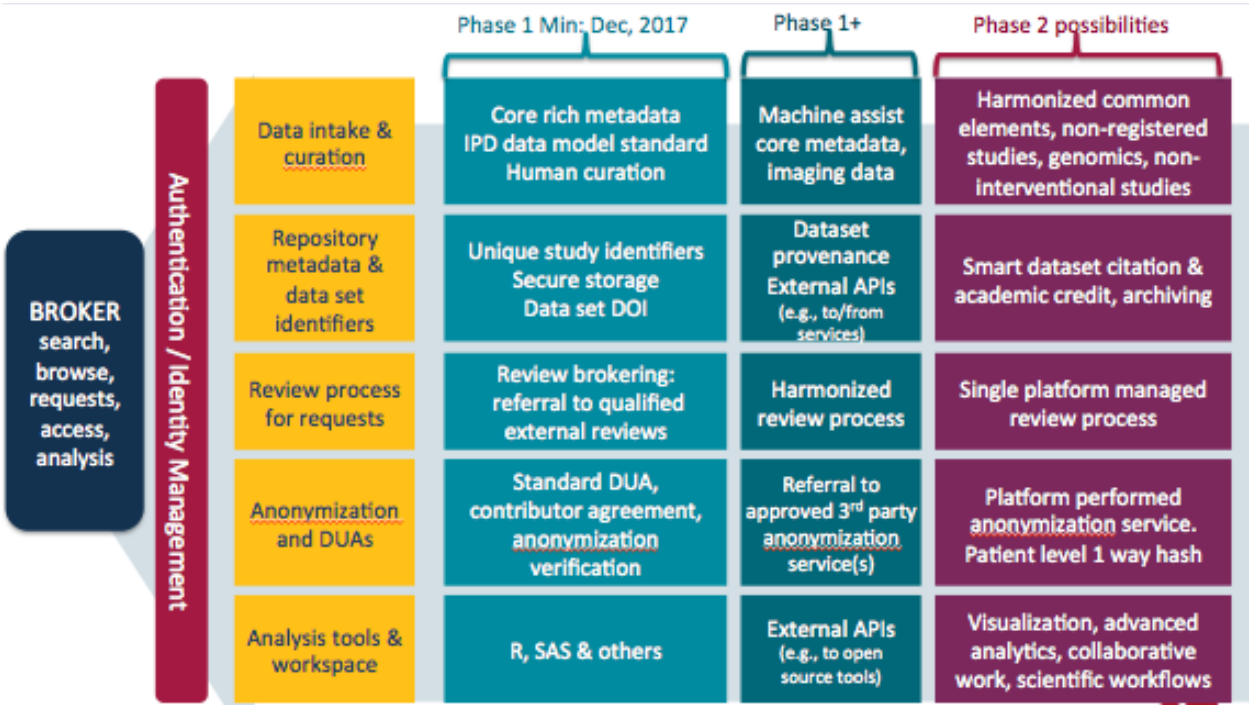

Figure 6

Discussion
Moderated by Brian Bot, Sage Bionetworks

Existing Initiatives
As with the discussion during the business models section, there was concern about the disruption of other current data sharing and clinical trials registration initiatives. Some were worried that Vivli may interfere with trial registration initiatives since this would only give a small snapshot of clinical trials which exist or it could lead to selective reporting. A proposed solution was to ask current trial registries to expand their searches and include directories to where IPD is stored.

Others were concerned that the Vivli platform would create competition to the current platforms that share IPD. Some similar platforms mentioned include CSDR, YODA, BIOLINCC, and the WWARN Neglected Tropical Disease Network. SAS is one commonality among many of these platforms so it may be a good vendor or partner to consider in the build/assemble process; however, it was noted that SAS is not universally used due to expense and complexity. It was recommended that Vivli

consider the various platforms that exist and assemble the best aspects of these platforms to inform final construction.

Attribution of Credit
Some were concerned about the quality of data that is uploaded to the platform. The proposed DOI system in which the platform would mint DOIs in order to attribute each data set to the data generator would allow the sets to be linked to the person who collected the data and created the data set. This, combined with the curation of data, will allow for some quality assurance of data.

Journal Requirements
It was suggested that although the ICMJE has put forward a proposal for the requirement for the sharing of IPD data, many journals may not be willing to make such a requirement until there is a place for the data to be securely stored and shared. Presenters noted that until there is market for such a repository, potential builders of any platform would be hesitant to undertake such effort fearing that no one will use the platform. Therefore, these two groups will likely have to work together to release a product and requirements in a similar timeframe.

Security
Data shared on this platform will be de-identified individual participant data (IPD). Some concern was raised regarding re-identification of patients using the data that is shared on the platform. There will always be some risk of re-identification, although sufficiency of anonymization and execution of a data use agreement will mitigate the risk. Further, Vivli will publish standards for the level of de-identification for data that is shared on the platform to further minimize risk.

Informed Consent
Some attendees questioned whether the executed informed consent documents would allow for data to be shared on the platform. Informed consent is a recognized concern of sponsors. It is recommended that Vivli carefully check the wording in informed consent forms for legacy trials; for prospective trials Vivli should provide recommended informed consent language to address the sharing of trial data.

Requiring the Use of Vivli
Some wondered whether sponsors of the Vivli platform would require those who they are sponsoring to use Vivli as a means for data sharing. While the working groups never envisioned mandatory use of Vivli, several funders confirmed that it will be difficult to require the use of a specific platform until data sharing and data publication are more commonplace.

FACILITATED DISCUSSION FEEDBACK

For the facilitated discussion section, there were seven breakout groups of 12-15 participants, each of which either discussed the Governance and Business Models proposal or the Data Sharing

Platform Proposal. After an hour and a half, the groups reported the results of their discussion. Group summary reports are collated and listed below based on discussion topic.

Governance and Business Models Discussions

- Vivli should be a non-profit organization.
- Gap analysis for Vivli should be clarified. The development of the gap analysis, and how Vivli will fill that gap, will increase the quality of the proposal
- The Governance and Business Models groups should make sure efforts are not being duplicated
- Data generators will need to be held accountable for the data that they put onto the platform.
- There should be a clear incentive for sharing data that is captured through the Vivli Platform
- Vivli will need to think about how it will address the market. Academics are different from sponsors and Vivli will need a marketing plan
    - Biotechs and academics have been largely missing from the discussion so far
- There will need to be a clear plan for how revenue will be generated
    - Begin with grants
    - Later on, revenue could be gained through membership fees of funders and user institutions
    - Advertising on the site is also a source of revenue
    - User fees could be constructed based on quantity of data or datasets requested (e.g. browse is free, use of X datasets free, >X datasets pay for service)
- A step-wise approach will be needed in the development of Vivli in order to build trust in the company and brand
- Vision needs to expand to include the unique selling point, gap analysis and data on what else already exists
- Mission needs to be expanded to include incentives for using the platform

Data Sharing Platform Discussion Points

It is important for all stakeholders to be on or be able to access the platform but the value is not the same for all groups

- Portal may want to provide credit or incentives for negative trials to be uploaded on the platform
- Some additional use cases might be beneficial:
    - How do funders fit into the proposal?
    - What different analytical tools will be on the platform? – SAS, R, Others?
- May want to provide a "Blue Button" option for return of individual results
- Technical questions and considerations:
    - Many large datasets may not be feasible to curate manually
    - What is the capacity for datasets on the platform
    - Can machine learning be obtained early?
    - There are different expectations of data standards and a need to set standards
    - Need to have a compute functionality / capacity

- If external codes are allowed on the platform, code review and additional security provisions should be considered
- The capacity to perform meta analysis of data across studies is important and needs to be prioritized
- User interface must be easy to use

A Vision Comes Together

Mark Barnes, MRCT Center

Mr. Mark Barnes gave a short closing statement for the day with conclusions and considerations for day two. He confirmed the need for a crisper rational for platform differentiation from other existing data sharing initiatives. The Vivli platform will provide the ability to do meta-analyses and combine individual patient data across different trials and sponsors. It will be neutral, and disease agnostic. Vivli will work with ClinicalTrials.gov and other registries to build on what already exists with trial registration.

Mr. Barnes also noted the need for standardization of the data curation and security standards. Vivli will work toward the harmonization of DUA terms and conditions as well as work toward a common language for Informed Consent Forms. Vivli will also, ideally, have methods and the ability to enforce the provisions of the DUA commitments. Tiers within the platform will move toward a common IRP, principles and other practices.

The governance of Vivli would ensure that the organizations that commit to the success of Vivli at the start will have representation in governance, and that the control may evolve as the organization becomes more self-sustainable. There will be an increasing demand for this type of product once regulations come into place. The goal is not to disrupt the current market but to coordinate and collaborate with existing groups.

Day 2

Unique Selling Point

Ida Sim, University of California, San Francisco
Dr. Sim opened day 2 with a short clarification on the vision of Vivli and its potential fit into the field of data platforms.
Vivli will provide both data hosting capacities as well as analytic functionalities. Current federated architectures give limited analytical options; the proposed platform would allow for both meta-analyses and analysis with IPD data. Vivli will therefore act as a global neutral convener offering general access to IPD hosting and secure analyses, eventually to host and/or utilize the majority of the world's IPD.

Data Sharing Mandates Presentations

Jeff Drazen, New England Journal of Medicine
Dr. Drazen demonstrated the value of data sharing using a case of sharing data on adjuvant chemotherapy for colon cancer. Through this demonstration, he commented on the value to the community to make new advancements through existing data.

Dr. Drazen commented that data sharing and open data began with trial registration. This was advanced when journal editors began requiring trial registration, however, journals will not be able to require data sharing until there is a place for this to happen. Journals hope for at least one user-friendly and strong plaform for IPD generated in clinical trials.

Dr. Drazen concluded with four points. The data sharing plan proposed at trial outset can specify the means of access but that access will need to be a third party. Data underlying results reported will need to be placed on a public repository within six months. Data users will have an obligation to show that they can reproduce original results. And there should be a means of rewarding data gatherers.

Shasha Jumbe, Bill and Melinda Gates Foundation
Dr. Jumbe opened his talk reminding attendees that clinical trial patients need to be remembered and that their contribution is significant. With de-identification, we often "forget the people or children who are behind the numbers." He stated that in the field of medicine and health research, there is much less collaborative work being done then in other industries.

Dr. Jumbe highlighted the work that is being done by the Gates Foundation to facilitate data sharing. Groups who are members of the data sharing initiative all agree to share data with the platform and are then able to receive data from the platform. Code on the platform is available to all data generators and recipients.

In conclusion, Dr. Jumbe stated that the technical field is moving very quickly and that global data should be translated into further knowledge through data sharing.

Karla Childers, Johnson & Johnson
Ms. Karla Childers presented the collaborative work being done between Johnson & Johnson and the Yale Open Data Access Project (YODA) to share clinical trials data. YODA is used by Johnson & Johnson for data sharing because it is a neutral platform with an understanding of research and development. Together, YODA and J&J have a shared vision for the future of data sharing.

The YODA project commits to review all requests for data that come through; Johnson & Johnson are blinded to the identity of the requester until access has been approved. Though this process, Ms. Childers stated that they have learned several valuable lessons. They have negotiated revisions to the DUA. A mechanism was established to provide feedback to requesters for more robust proposals. And researchers have expressed the desire to have access to different analytical tools.

Bernard Lo, The Greenwall Foundation
Dr. Lo began his presentation with comments on the presentations from day one of the conference. He focused on the risk of re-identification with the sharing of clinical trials data and noted that there will need to be specific informed consent language developed in order to address data sharing. In addition, he mentioned the need for a tracking system for data sets in order to both gain academic credit and citations for the sharing of data.

Dr. Lo also noted that it is not easy to work with another person's data set. Often documentation does not resolve problems or questions and the data user may need to return to the original data generator for clarification. He also noted that additional challenges (e.g. responding to unscientific analyses) may arise.

DATA SHARING PLATFORM PANEL DISCUSSION

Panel Participants:
Adam Asare, *Immune Tolerance Network, Massachusetts General Hospital*
Daniel Bergqvist, *Google*
Christoph Gerlinger, *Bayer Pharma Aktiengesellschaft*
Vahan Simonyan, *US Food and Drug Administration*
Kenji Takeda, *Microsoft Research*
Moderator: Juergen Klenk, *Deloitte Consulting*

Based on the presentations on the proposed platform, how would you achieve this platform and put it to use?
Panelists expressed excitement for many of the proposed features of the platform including the ability to combine datasets from different sponsors and the inclusion of other items in the data packages such as code or protocols. Panelists also noted that, in order to be successful, the platform

should be disruptive of the current market and move beyond a registry-like system. It was recommended that Vivli "aim for a moonshot," work to build trust and stay abreast of technical advances to ensure that users continue to utilize Vivli.

Is this proposal thinking too traditionally? What other components should be considered?
Panelists recommended that the designers of the platform take on a "start-up mentality." In order to be successful, Vivli should ensure that there is a clear value proposition and that the end user be the main focus with platform capacities focusing on their needs. It was also recommended that the timeline be short and a product be released for pilot quickly. Future users should be recruited to test the initial pilot and provide feedback along the way. Code for the site should be kept open source and the project should be completely transparent.

Given that biomedicine has not been exposed to the start-up process and mentality, what are some reactions to that mindset?
There was a very positive reaction to the recommendation that the project be completely open and code be provided as open source. The main concern expressed by biotechnology panelists was the security of the data. They wanted to ensure that personal data would remain secure even if the timeline for development were expedited. They recommended working under a proof of concept option in which the pilot works with a specific disease category before branching into the sharing of all clinical trials data.

Can components be removed from the MVP to have a simpler initial product?
Panelists highlighted that this is a very complex problem that will need a complex solution. Although there were no recommendations for removal of items from the minimum viable product, several noted that Vivli should ensure that high quality data is offered on the site to ensure continued success.

Additional Items to be considered in the build
Panelists echoed previous speakers in the need to find a way to include academic credit to incentivize academia to join the platform. In addition, they commented that "IPD as a service" should be explored. Pricing structures for various services should be explored with potential users.

Enabling, Harmonizing and Integrating Global Transparency Initiatives Panel

Panel Participants:
Robert Frost, *GlaxoSmithKline*
Trish Groves, *BMJ*
Rebecca Kush, *CDISC*
Trudie Lang, *University of Oxford*
Deborah Zarin, *National Institutes of Health (NIH)*
Moderator: Jeff Drazen, *New England Journal of Medicine*

What is needed for global data sharing initiatives to be more effective?

Many of the panelists suggested that all data sharing initiatives should not only build on what has previously been learned from past initiatives but also use tools and processes currently available. Specific examples included using a common process, ensuring flexibility and adhering to an independent review process. Panelists also mentioned that any initiatives should uphold and support the entire trial reporting process, not just the sharing of IPD. Data should also be shared in a standard format to ensure maximum usability after sharing. In addition, several panelists commented that, if a group would like to start a global initiative, it should ensure that it has global reach. Data sharing projects should enable low- and middle-income countries (LMIC) to also become data generators.

Panelists noted that, by increasing incentives and ensuring maximum discoverability within these initiatives, it would promote greater sharing of data and decrease the occurrence of small, poorly conducted trials.

Why is the uptake of data sharing initiatives so low?
Panelists believe that the bar is too low for clinical trials to be approved and conducted. It is easy to conduct your own clinical trial so there is little motivation to use another's data. To help solve this problem, panelists recommended that regulators increase the difficulty of beginning a clinical trial and funders put out calls for secondary analyses. Additionally, by increasing training and skills in secondary analysis and meta-analysis, more individuals will be interested in and capable of conducting these kinds of studies.

Some panelists noted that increasing trainings could help in areas such as increasing the occurrence of data standards and helping to enable LMIC researchers to become data generators.

Is it possible that increasing data sharing could lead to a greater gap between high income and low- and middle-income countries?
The increase of data sharing will have to come along with incentives so that "data parasites" do not develop. Research is done to better the health of everyone so data sharing should come along with some incentives in order to change the culture and behavior around research. This can be improved by ensuring that there are fewer overall clinical trials and increasing the demand and reward for sharing data.

The Challenges of Privacy Laws Globally

Moderator: Beth Thompson, Wellcome Trust

Nick Tyler, Takeda Pharmaceuticals
Mr. Tyler discussed the challenges of data privacy laws globally but focusing on European requirements and the forthcoming European General Data Protection Regulation as they set the highest standard.

He first commented that because there was no consistent approach to addressing compliance with data privacy laws across the industry or across multiple jurisdictions, the data protection laws themselves may be perceived to be a problem when in fact there is a significant lack of awareness and understanding, amongst regulators, policy makers and the general public of how clinical trial data is used beyond the provision of healthcare. The most significant challenge to the industry and our representative bodies is in terms of communications and stakeholder engagement around this topic.

Mr. Tyler discussed the difference – from a legal standpoint - between anonymization, a process in which the data is stripped entirely of identifiers and can no longer be attributed to an individual person, and pseudo-anonymization, where a code can be used to re-identify the patient if needed. He summarized the proper application of data privacy principles required to ensure fair and lawful processing of personal data and to provide safeguards to protect patients through the application of technical and organizational measures to ensure data minimization. It was noted that alternative legal bases to consent (including scientific research) were important in this context but must be based on EU or Member State law with suitable and specific safeguards for the fundamental rights and interests of individuals. In relation to the publication and re-use of clinical trial data he concluded that while anonymization is preferred if the scientific purposes can be achieved there is now legal recognition for the proper application of pseudo-anonymization techniques in this context.

Khaled El Emam, Children's Hospital of East Ontario

Dr. El Emam opened by stating that there are not many regulations dictating which data can and can not be shared. Therefore, if data has been anonymized, it is considered to be a permitted use of data in most countries. There are many types of data that can be anonymized but, notably, genomics data cannot be. There are general requirements for the anonymization of data and a systematic review found that no data that was correctly anonymized has been successfully attacked.

In addition to anonymization, Dr. El Emam noted that additional layers of security can be added such as contracts, security controls and perturbed data to ensure that it is more difficult to re-identify. There is a finite but specific risk with any anonymization; this risk can be mitigated through these additional measures.

Discussion

One audience member asked about whether there is a clause for someone to withdraw their data from a dataset and if this would still be possible once the dataset is anonymized. Dr. El Emam responded that this is an important factor of informed consent, however, there is still progress to be made in the effective processing of these requests.

Others expressed concern about other personal identifying data that may be shared by individuals on the internet and whether this impact how well IPD can be de-identified. De-identification techniques are still being developed. And, although it may be possible for close friends and relatives to identify a person's data, it is much more difficult for anyone else to identify.

Finally, it was noted by the audience that it is important to develop a specific risk-based approach. All researchers are responsible for complying with data security and working to reduce risk to an acceptable level.

Closing Remarks

Barbara Bierer, MRCT Center

Dr. Bierer gave a short closing statement for the conference confirming for all stakeholders that the feedback had been absorbed and the proposal would be modified. The aim is to clarify that the intention of Vivli is to partner with existing platforms and respect existing communities. A crisper value statement will be communicated to the stakeholders and collaborators. Presenters and participants were thanked for their valuable comments and continued support of MRCT initiatives.

TABLES AND FIGURES:

APPENDIX 1: AGENDA

Day 1

Monday, 21 March 2016	
9:00 AM - 9:30 AM	**Breakfast, Registration**
9:30 AM – 10:30 AM	**Welcome and Introductions:** Nicola Perrin, Wellcome Trust • **Overview of MRCT Center progress** in data sharing and rationale for current project • **Scope of the clinical trial data sharing program** – Vision and mission • **The Importance of Data Sharing and Transparency (EMA)** ***Speakers***: Barbara Bierer, *MRCT Center* Fergus Sweeney, *European Medicines Agency*
10:30 AM - 11:10 AM	**Governance Workgroup** *The governance workgroup is tasked with developing the organizational structure and leadership for the new entity* Key Workgroup Deliverables: ○ Review Process ○ Platform participating trials ○ New Entity reveal ○ Charter & Governance structure ○ Data Sharing Guidance and Resource Kit ***Presenter:*** Rebecca Li, *MRCT Center* **Moderated Participant Q&A** ***Moderator:*** Barbara Bierer, *MRCT Center*
11:10 AM - 11:25 AM	**Break**
11:25 AM - 12:15 PM	**Business Models Workgroup** *This workgroup's objectives are develop sustainable business models for the new entity* Key Workgroup Deliverables ○ Assumptions ○ Case Studies ○ Recommended funding and cost models ○ Launch and long term sustainability needs ***Presenter:*** Rohin Rajan, *Deloitte Consulting LLC* **Moderated Participant Q&A** ***Moderator:*** Frank Rockhold, *Duke University*
12:15 PM - 1:00 PM	**Lunch**

1:00 PM – 1:30 PM	**EMA Policy 70 Implementation – Clinical Data Publication** ***Presenter:*** Frances Nuttall, *European Medicines Agency*
1:30 PM – 3:00 PM	**Data Sharing Platform Workgroup** *This workgroup's objectives are develop the IT blueprint including recommendations for the platform that would enable broader data sharing of clinical trials data* ○ IT Platform – Overview ○ IT approach and summary of use cases ○ Key requirements for data packages ***Presenter:*** Ida Sim, *University of California, San Francisco* **Moderated Participant Q&A** ***Moderator:*** Brian Bot, *Sage Bionetworks*
3:00 PM - 4:30 PM	**Facilitated Discussion** *Facilitated discussion on vision, governance, sustainability, data sharing platform and clinical data publication (EMA). Invitation for collaboration, specific feedback, and constructive critique.* *Break at 3 PM*
4:30 PM – 5:15 PM	**A Vision Comes Together** *Integrating the Governance, Business Models and IT Platform* ***Moderator*:** Mark Barnes, *MRCT Center*
5:15 PM – 5:30 PM	**Wrap Up Remarks**: Day 1 ***Speaker:*** Jeremy Farrar, *Wellcome Trust*
6:00 PM	**Dinner at the Royal College of GPs** *30 Euston Square, London NW1 2FB, United Kingdom*

Day 2

Tuesday, 22 March 2016	
8:00 AM - 8:30 AM	**Breakfast**
8:30 AM - 8:45 AM	**Day One Summary** ***Speaker:*** MRCT Center

8:45 AM - 10:00 AM	**Data Sharing Mandates** ***Speakers:*** Jeffrey Drazen, *New England Journal of Medicine* Shasha Jumbe, *Bill and Melinda Gates Foundation* Joanne Waldstreicher, *Johnson & Johnson* Bernard Lo, *The Greenwall Foundation* ***Moderator:*** Barbara Bierer, *MRCT Center*
10:00 AM - 11:15 AM	**Moderated Panel Discussion** *Data Sharing Platform* • Feedback on the proposed platform specifications • Challenges in implementation • Opportunity ***Panelists:*** Adam Asare, *Immune Tolerance Network, Massachusetts General Hospital* Vasa Curcin, *Kings College London* Christoph Gerlinger, *Bayer Pharma Aktiengesellschaft* Vahan Simonyan, *US Food and Drug Administration* Kenji Takeda, *Microsoft Research* **Moderated Participant Discussion** ***Moderator:*** Juergen Klenk, *Deloitte Consulting LLC*
11:15 AM - 12:15 PM	**Enabling, Harmonizing and Integrating Global Transparency Initiatives** Policy, Standards, etc. ***Panelists:*** Robert Frost, *GlaxoSmithKline* Trish Groves, *BMJ* Rebecca Kush, *CDISC* Trudie Lang, *University of Oxford* Deborah Zarin, *National Institutes of Health (NIH)* **Moderated Participant Discussion** ***Moderator:*** Jeffrey Drazen, *New England Journal of Medicine*
12:15 PM - 1:00 PM	**Lunch**

1:00 PM - 1:45 PM	**The Challenges of Data Privacy Laws Globally** ***Speaker:*** Nick Tyler, *Takeda Pharmaceuticals* Khaled El Emam, *Children's Hospital of East Ontario* ***Moderator:*** Beth Thompson, *Wellcome Trust*
1:45 PM - 2:45 PM	**One singular vision for the new entity - Uniting the platform, governance and business model** • What are the challenges of this approach? • What are the benefits? • What assumptions must hold true for this approach to be successful? **Next steps: Plan for next 18 months** **Moderated Participant Discussion** ***Moderators:*** Barbara Bierer, *MRCT Center* Mark Barnes, *MRCT Center*
2:45 PM - 3:00 PM	**Closing remarks** ***Speaker:*** Rebecca Li, *MRCT Center* Nicola Perrin, *Wellcome Trust*
3:00 PM- 4:00 PM	*Project leadership and Workgroup Members Debrief in* ***Mendel 1***

APPENDIX 2: VIVLI STRATEGY DOCUMENT

Vivli Strategy

Since 2013, the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard University (MRCT Center) has been deeply involved in the public debate regarding the sharing of, and access to, clinical trials data around the world.

On March 21-22, 2016 the MRCT Center and the Wellcome Trust hosted a private meeting of the MRCT stakeholders and collaborators, entitled *The Future of Data Sharing*. The goal of this meeting and of related efforts of the MRCT Center has been to establish an independent general access electronic data repository, interactive server, and search engine through which data from clinical trials conducted by researchers in academic, industry, foundation and non-profit entities can be hosted, shared and accessed. This solution would fill identified gaps in the availability of clinical trials data worldwide. To that end, a new not-for-profit entity, Vivli, should be formed as the organized, permanent vehicle for governance and management of this effort.

Attended by over 100 participants from academia, government, not-for-profit organizations, journal editors and industry, *The Future of Data Sharing* was intended to allow open discussion and consideration of strategy, goals, and tactics of Vivli. Discussion at the meeting clarified and refined the original proposal. The plans for Vivli now include:

- Directing, implementing, and governing a global clinical trials data-sharing platform, search engine and outward-facing, publicly-accessible software capacity to connect data requestors to data generators and their archived data.
- Functioning as a global, neutral platform for the hosting of clinical trials data.
- Providing for hosting of anonymized individual patient level data (IPD) as well as facilitating the integration of data from multiple sources. A key goal will be to bring a high degree of integrated search functionality through enhanced computability of clinical trials metadata. This will allow trials to be more discoverable and facilitate secondary uses of data, especially meta-analyses of aggregated data.

A wide array of analytical tools and services will be made available through the platform, including anonymization, de-identification, and if needed, the analysis tools themselves. Vivli will also provide harmonized and centralized data request services, a uniform approach to data use agreements and research participant protections, and capacity to enforce the terms and conditions of data use agreements.

Keys to Success:

- **UNIQUE NICHE -** The Vivli platform will host academic clinical trials data the vast majority of which do not currently have hosting options. Vivli will also aim to facilitate a data requester's ability to combine anonymized IPD from different hosts and all types of data generators, including industry, bringing economies of scale to technical, operational, and policy concerns. The curated metadata and analytic functionality will be augmented by services such as anonymization or standardization.
- **TIMING -** We had initially proposed a 12-18 month process to launch Vivli (anticipated December 2017); at the meeting on March 21-22, 2016, however, we heard a clear mandate to accelerate the timeline to launch. There is a clear and acute need for such a platform to serve multiple stakeholders, and timing is

critical. In response we have shortened the timeline to launch the platform within 12 months through partnership and collaboration, and to postpone or eliminate the RFP selection step by selecting partners based on specific requests (see Table 1 below).

- **MESSAGING**:
    - Moving forward we will define and convey the value proposition more crisply, specifically differentiating this platform, operating system and search capacity from other existing clinical trials data platforms and systems.
    - Provide clarity on intent to respect existing platforms, operating systems, and disease and research communities, including incorporating, partnering and assembling current technologies and functionalities
- **PRIORITIZE THE REMIT OF VIVLI -** Two major priorities emerged **-** meeting mandates (ICMJE, PhRMA/EFPIA, NIH, Gates) and conducting research by allowing the interdigitation of datasets across various stakeholders (industry, academia etc.). Both of these are important, but the Vivli proof of concept should prioritize one of these remits first to ensure focus.
    - The participants agreed that ensuring academia had a place for data hosting was a critical need and should be prioritized.
    - Creating bridges to existing platforms was also a critical imperative, but was considered somewhat secondary to creating a user-friendly environment for trial/research data that currently do not have a platform, including data from academia-sponsored or -funded trials.
- **PATH TOWARD IMPLEMENTATION** – Vivli should partner with existing, proven electronic data sharing systems as the most efficient and effective strategy of enabling data sharing. For those capabilities that do not currently exist, Vivli should assemble or build them in order to fill in gaps in the availability, accessibility and usability of clinical trials data.
- **CHALLENGES**
    - Journal editors challenged us to move as quickly as possible to create these electronic capacities, as journals await an organized, reliable mechanism to allow researcher-authors to meet the ICMJE requirements on data sharing.
    - Proof of concept – Zika virus or a similar urgent public health or scientific need could serve as a proof of concept for the platform and its technological capacities
- **CREATION OF AN INCENTIVE STRUCTURE - A**ssuring academic or professional credit to data generators can be a major incentive to spur data sharing among those not currently sharing as well as to recognize those who have invested effort and funds to collect specific trials data. This platform can link to elements within existing trial registries that currently capture data sharing as a component of trial registration.
- **FINANCIAL STRUCTURE –** Maintaining a low barrier to entry, over a defined start-up period, for independent researchers and for researchers within academia, government and start-up entities.

In summary, the MRCT team and collaborators continue to consult with key stakeholders to raise funds and engage an appropriate interim leadership team to establish VIVLI under a formal governance structure. Once Vivli is launched as an independent entity, the MRCT center will participate as one stakeholder among many potentially as one member of the Board.

APPENDIX 3: WORK GROUP MEMBERS

Governance Work Group Co-Chairs: **MRCT, Wellcome Trust, Arnold Foundation**
Mark Barnes **(MRCT Center)** Barbara Bierer **(MRCT Center)** Stuart Buck **(Arnold Foundation)** Marla Jo Brickman **(Pfizer)** Nina Hill **(Pfizer)** Rebecca Li **(MRCT Center)** Nick Lingler **(Deloitte Consulting)** Justin McCarthy **(Pfizer)** Sandra Morris **(Johnson & Johnson)** Jennifer O'Callaghan **(Wellcome Trust)** Nicola Perrin **(Wellcome Trust)** Paul Seligman **(Amgen)** Ida Sim **(UCSF)** Jessica Scott **(GlaxoSmithKlein)** Catrin Tudur Smith **(University of Liverpool)** Natalie Zaidman **(Pfizer)**

Data Sharing IT Work Group Co-Chairs: Ida Sim **(UCSF)**, Barbara Bierer **(MRCT)**
George Alter **(U of Michigan)** Munther Baara **(Pfizer)** Barbara Bierer **(MRCT Center)** Kris Bolt **(MRCT Center)** Brian Bot **(Sage Bionetworks)** Anne Claiborne **(IOM)** Khaled El Emam **(U of Ottawa)** Nick Ide **(NIH)** Ghassan Karam **(WHO)** Michael Khan **(U of Colorado)** Sean Khozin **(FDA)** Rebecca Kush **(CDISC)** Rebecca Li **(MRCT Center)** Gene Lichtman **(HCRI)** Michelle Mancher **(IOM)** Chris Mavergames **(Cochrane)** Eric Perakslis **(Takeda)** Frank Rockhold **(GSK)**

Business Models Work Group Co-Chairs: **Wellcome Trust, MRCT Center**
Barbara Bierer **(MRCT Center)** Patrick Cullinan **(Takeda)** Rebecca Li **(MRCT Center)** Peter Lyons **(Deloitte)** Nicola Perrin **(Wellcome Trust)** Rohin Rajan **(Deloitte)**