Responsible Sharing of Clinical Trial Data: An FDA Perspective

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Outline for today

• The Landscape
  – The call for transparency and access
    – Need for reproducibility and credibility
    – The promise vs. fear and loathing
  – What and why
  – The Critical Path Initiative
    – Need for new approaches to drug development

• Data Sharing at FDA
  – History
  – Impediments
  – A possible approach

• Implications of data sharing
Data Sharing

• **Why?**
  – transparency
  – Reproducibility, reanalysis
  – Identify new information: placebo effects, biomarkers, endpoints, trial designs

• **What?**
  – Summary reports
  – Patient or participant level data (how much?)
  – Unselected broad access vs. selected data release or managed analysis

• **For what purpose?**
  – Data dredging?
  – Answer specific questions?
Data Sharing – The Landscape

**Critical Path Report and Opportunities List**

- **Need**: enhance the medical product regulatory science toolkit
- **Barrier**: addressing scientific hurdles to more effective and efficient medical product development and review often requires pooling of effort, data and resources
- **Opportunity**: leverage and analyze pooled clinical and pre-clinical data to (e.g.):
  - Explore new or modified biomarkers or trial endpoints
  - Evaluate the predictability of pre-clinical safety data
  - Understand background rates of AEs in defined patient populations
  - Develop disease models and simulate clinical trials

**Strategic Plan for Regulatory Science**

- **Priority 5 - Harness Diverse Data through Information Sciences to Improve Health Outcomes**
  - “Successful integration and analysis of data from … disparate sources would provide knowledge and insight not possible from any one source alone.”
Data Sharing at FDA

- Analysis of multiple clinical and/or pre-clinical data sets provides an opportunity to advance the science of drug development.
- It may be possible to combine or pool datasets in a way that provides a rich scientific resource, while preserving commercial interests of sponsors.
- Building databases of pooled clinical data around specific disease indications is occurring in numerous consortia (e.g. CAMD).
- Process of gathering, pooling and curating datasets is extremely resource intensive – limited public and private resources should be focused on the most pressing regulatory science questions.
- FDA has historically applied knowledge gained from analysis of pooled data to improving drug development and review - this analysis could benefit from additional external expertise.
Creating Consensus through Consortia

Seven global consortia collaborating with 1,000+ scientists and 41 companies

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<tr>
<th>Consortia</th>
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<td>CAMD</td>
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<td>DRUG SAFETY</td>
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- Biomarkers
- Clinical Outcome Assessment Instruments
- Clinical Trial Simulation Tools
- Data Standards

CDISC
Exploring modified clinical trial endpoints
Earlier sustained virologic response end points for regulatory approval and dose selection of hepatitis C therapies. *Gastroenterology* 2013 Jun;144(7):1450-1455.e2

Quantifying drug efficacy and risks for a specific indication
Exploratory analyses of efficacy data from major depressive disorder trials submitted to the US Food and Drug Administration in support of new drug applications. *J Clin Psychiatry* 2011 Apr;72(4):464-72

Evaluating the predictability of pre-clinical safety data
Predictivity of Non-Clinical Repolarization Assay Data for Clinical TQT Data in FDA Database. *Int J Toxicol* 2013 Jan-Feb;32(1):63

Understanding factors contributing to failure of pediatric trials

Assessing tools for evaluating trial endpoints

Development of disease models
Endpoints and Analyses to Discern Disease-Modifying Drug Effects in Early Parkinson's Disease., *AAPS J* 2009 Sep;11(3):456-64
Impediments to Data Sharing at FDA

- **Legal**
  - Data ownership
  - HIPAA/privacy
  - Proprietary information

- **Technical/Practical**
  - Format
  - Data standards, CDISC
  - Redaction

- **Resources**
  - Need to focus on FDA’s key mission
Disclosure of Product Specific Non-Summary Safety and Efficacy Data

• FDA laws and regulations already specify under which circumstances FDA can disclose product specific (unmasked) non-summary safety and efficacy data, including de-identified patient level data

• The criteria differ depending on the type of regulated product

• The circumstances under which FDA discloses this information and when EMA is contemplating disclosing this information are different.

For example:

– FDA generally discloses non-summary safety and efficacy data from a specific application only in response to a request under the Freedom of Information Act. EMA’s proposal contemplates the proactive posting of certain non-summary clinical trial data from marketing applications.

– EMA is contemplating disclosing the data after it makes a decision on an application, including a decision not to approve an application. FDA’s regulations do not permit us to disclose information when we have issued a complete response letter, if the applicant is working on addressing the application deficiencies.
FR Notice: Masked and De-identified Non-Summary Safety and Efficacy Data

- The FDA is seeking public comments on whether certain study data could be made available after steps have been taken to remove information that would identify patients, as well as a specific product application or company, and whether any limitations should be put in place on its availability.

- Release of confidential commercial and trade secret information is not being considered under this proposal.

- Under this proposal, the FDA does not plan to make available any information related to a company’s business arrangements contained within a product application (e.g. licensing agreements, supplier information).

- FDA does not plan to make available trade secret information under this proposal.

- Such information will continue to be treated in a manner consistent with relevant statutory and regulatory provisions.
FR Notice: Masked and De-identified Non-Summary Safety and Efficacy Data

- FDA invites comments on the issues it should consider with respect to the availability of clinical and pre-clinical study data after steps have been taken to “de-identify” it by removing any personally identifiable information and “mask” it by removing data that could link it to a specific application or sponsor. Specifically, the agency is interested in comments from the public on the following topics:
  - What factors should be considered in masking study data (e.g. should certain data fields be removed or modified; number of different products to pool within a class)?
  - Should there be any limitations on the agency’s ability to make masked data available?
  - In addition to current FDA requirements to remove any names and other information that might identify patients, what other information should FDA consider when de-identifying the data?
  - Would regulatory changes facilitate the implementation of this proposal?
  - In what situations would disclosing masked data be most useful to advance public health?

**FR Notice: Additional Considerations**

- FDA’s approach has been under development for several years – it is not linked to EMA proposal.

- FDA is not contemplating routine preparation and release of de-identified and masked clinical and non-clinical study data
  - resource intensive - would divert scarce resources needed for the evaluation of urgently needed therapies
  - not a central focus of core regulatory mission

- **Emphasis: targeted opportunities to advance regulatory science**

- **Opportunity: focus limited FDA resources to address the most pressing regulatory science questions**

- We encourage independently organized efforts to create, curate and share clinical trial datasets from all sources
Other Efforts at Sharing Data

• **Industry**
  – GSK, Merck

• **Regulatory**
  – EMA

• **Journals**
  – BMJ

• **Institute of Medicine**
  – Forum and Study
Implications of Data Sharing

- Structures and models
  - Third party involvement?
  - Open source vs. requested data
  - Curation
  - Governance to access and analysis
  - Timing
  - Ownership/Donation?
Implications for Drug Development and the Clinical Research Enterprise

• Cost
• Credibility
  – Second guessing of results and regulatory decisions
• Will trial design change?
• Competitive implications
• Impact on academics