Responsible Sharing of Clinical Trial Data: An FDA Perspective

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Data Sharing – Critical Path 2004

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**.
FDA Experience – A Few Examples

**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 External Data Sharing at FDA

• Legal
  – Data ownership
  – HIPAA/privacy
  – Proprietary information

• Technical/Practical
  – Format
  – Data standards
  – 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.
- 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.
- 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 sought 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: Additional Considerations

• Emphasis: targeted opportunities to advance regulatory science

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

• 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

• We are encouraged by independent organized efforts to create, curate and share clinical trial datasets from all sources
Current status of FDA’s proposal

- Received over 60 comments
- Several made specific legal points, these are under review by the Office of Chief Counsel
- FDA is considering next steps, including a possible pilot project
  - ECG data warehouse availability for specific projects
  - Data de-identified and may only use placebo and standard comparator data, possibly class data but not from specific test agents
  - Prior to moving forward with the pilot, FDA intends to:
    - Hold public meeting or workshop
    - Issue FR notice with greater detail
IOM Report and the FDA

- FDA was a strong supporter of IOM’s study and wanted to consider the results before proceeding
- Overall respect for the results
- Specific recommendations for regulators
  - Work with stakeholders to develop a new clinical study report template that is free of CCI and personally identifying information
  - Regulatory harmonization of requirements to support data sharing
Return of Clinical Trial Results to Participants

- FDA supports providing accurate information to patients that is not misleading, particularly so for participants of clinical trials.
- FDA regulatory and policy considerations:
  - No regulation or guidance directly on this issue.
  - FDA has regulations and guidance on manufacturer dissemination of information.
  - Maine issued an advisory to industry after consulting with FDA’s OPDP (formerly DDMAC) about posting study results on a public database; the advisory provided advice on how to avoid the posted content being regulated as promotion by OPDP (formerly DDMAC).
- In light of emerging case law, FDA is currently engaged in a comprehensive review of its regulations and guidance documents relating to the manufacturer dissemination of truthful, accurate, and non-misleading information.
Points to Consider

• Note that PHRMA and MRCT have put forward principles, guide, and a toolkit
• The devil is in the details
• FDA’s points to consider
  – Truthful, accurate, and non-misleading information about trial results may benefit participants
  – More specifically
    • The language should be simple and factual, neutral in its description
    • The information should not be selective
    • The information cannot make pre-approval claims of safety or effectiveness in a promotional context
Guidance can help provide clarity

- The FDA has already issued draft guidance in the area of unsolicited requests and the distribution of scientific and medical reference texts, that includes recommendations for the distribution of third-party clinical practice guidelines
  - (Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices Practices – December 2011)

- FDA plans to issue guidance that addresses unsolicited requests, distributing scientific and medical publications on unapproved new uses, and manufacturer discussions regarding scientific information more generally.

- The time may be ripe for FDA to consider the development of specific guidance to enable study results to be returned to participants without being considered promotional.