BRIGHAM AND WOMEN'S HOSPITAL

Guiding Principles for Clinical Trial Data Sharing

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- **Conflict of Interest :** The speaker has no personal relevant financial relationships with industry.
- **No Commercial Support** was provided for this talk.
- **MRCT at Harvard** is a multi-stakeholder initiative that receives support from pharmaceutical companies (e.g. Amgen, Merck, Pfizer, Sanofi, etc.), clinical research organizations, independent IRBs, not-for-profit organizations (foundations, patient support groups, academic institutions, professional organizations, etc.).

IOM Proposed Principles

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- Respect the individual participants whose data are shared
- Maximize benefits to participants in clinical trials and to society, while minimizing harms
- Increase public trust in clinical trials
- Carry out sharing of clinical trial data in a manner that addresses fairness.

Or

- Respect for persons
- Beneficence
- Justice (fairness)
- Public trust

Core Principles

- Protect research participants
- Advance innovation and public health
- Balance risks with benefits of data sharing
- Treat all data generators equally
- Make data disclosure practicable by avoiding undue burdens on data generators and requesters
- Provide timely access to data
- Ensure adequate transparency
- Ensure accountability

Details are important: applicability, practicability, transparency and accountability

Global application

- All countries
- All data generators
- All data requestors
- All data holders

1. Data sharing rules should apply to equally to all study sponsors and data generators, and to all data holders
2. Something beyond a purely voluntary regime is desirable to create a level playing field
3. There should be standard formats for clinical-trial data and documents, common definitions and metadata, and ability to combine datasets
4. The rationales and benefits presuppose that initial and re-analyses of shared data will reflect sound science
   - Data sharing system should have mechanisms for promoting responsible use of data
   - Accountability standards should be similar for the initial sponsor and data generator, and a researcher conducting a re-analysis
5. Data sharing system must be practical and transparent

6. Many of the rationales/benefits require participant-level datasets
   - Facilitate secondary analysis to verify results, regulatory decisions, public policy
   - Improve safety surveillance
   - Speed new discoveries
7. Important mechanisms for a data sharing system:
   - Ensure adequate scientific expertise among the analytical team
   - Provide technical support sufficient to permit users to understand the data
8. Some benefits are difficult to achieve in a sponsor-controlled model
9. Timing of availability for both summary and participant-level data should be pre-determined (e.g. 1 year after primary study completion).
   - Assuming an adjudicated process to obtain participant-level datasets, evaluation of the purpose for the participant-level datasets could be different ('tighter') prior to product approval.

Operating guidelines

- Requests and decisions posted on the web
- Requesters pre-commit to an analytical plan
- Requester's identity and scientific plan are publicly disclosed
- Requester signs a data use agreement

  (See EMA suggestions for elements of DUA)
- Decisions about data releases include both the data generator and other parties

Does de-identification of data solve the problem of risks to participant privacy and confidentiality?

- De-identification is not consistently defined; EMA definition is more vague, less detailed and thus possibly quite different than the HIPAA definition
- The use of data items in combination presents greater risk than each alone
- Removing HIPAA identifiers does not (necessarily) anonymise data
- De-identification is a moving target due to improving technology, *e.g.*, genetic information is becoming increasingly identifiable, which may make the HIPAA de-identification standards obsolete
- Degree of de-identification is inversely related to data usefulness: *the more identifiers removed, the less useful the data become to subsequent researchers*
- Acknowledges that risks are informed both by (a) the probability of re-identification and (b) the consequences of re-identification
- Needs to be layered with system design e.g. controlled access, DUA etc.

Provide guidance for retrospective and prospective study consent

Principles

1. Informed consent document, and contract with the subject, should be honored
2. If unclear whether, how or what data sharing is allowed, ethics committee of the data generators should be decide
3. If regulations require data sharing and inconsistent with ICF, data generators should not be liable for breach of contract or failure to comply
4. Prospective consent should explain process, benefits and risks of sharing
5. Compound consent should be avoided and "choice" will impact representation and/or statistical validity of study
6. Public education essential

1. Provide access sufficiently broad to achieve the sought-after benefits
   - At a minimum, prospectively apply to approved drugs, devices, and biologics
2. Ensure responsible use of data
   - Data generators should be held harmless for compliance
   - Company confidential information should be withheld from public view
3. Protect participants' privacy and conformance with informed consent
4. Treat all qualified data requesters and trial sponsors evenhandedly
5. Hold data requesters and generators accountable
   - Data requestors are accountable for quality, scientific integrity, and expertise; commit to an analytic plan; honoring specific requests, confidentiality of participants, and held to same standards as data generators.
   - Data transparent, principled decisions about data releases
6. Responsibilities of regulators for results and analysis of secondary data should be determined prior to implementation
7. Ensure practicability
   - Common platforms for data, definitions, and metadata
   - Ability handle large volume and variety of trials
   - Globally harmonized standards