IRB Considerations for Biorepository Research

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Investigator’s Reaction
Research Coordinator’s Reaction

IRB’s Reaction
Agenda

• Agreeing on the definitions
• Components of a Repository
  – Specimen Source; the collectors
  – Repository Bank and its management
  – Specimen Recipients; the investigator users
• Regulatory issues and compliance
• Writing a long-term, useful biorepository consent and conducting a truly informed consent

Agreeing on the Definitions

Tissue, specimen and sample are terms often used interchangeably.

• Any biological specimen obtained from patients or research subjects.
• This includes: fixed, frozen or fresh pathology or autopsy specimens, blood, urine, saliva, CSF, semen, breast milk or other biological material and any purified DNA, RNA, proteins, or cell lines.
Agreeing on the Definitions

Research Repository, Biorepository and Bank are terms often used interchangeably

- An entity involved in procuring, processing, storing and/or distributing tissue (specimens or samples) expressly for research use.
- Data may also be procured, processed, stored and distributed.

Agreeing on the Definitions

Registry, Repository and Database, Biorepository, Databank and Tissue bank are often used interchangeably (and imprecisely) to mean the same thing . . .

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<th>Workable definitions for:</th>
<th>Receive a collection of data from multiple sources</th>
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Agreeing on the Definitions

*When research data and samples are collected, stored and distributed, you have a Repository AND Registry study, and the name should reflect that. Whatever you call it, they are all considered a repository for regulatory purposes (45 CFR 46 and 45 CRF 160,164).*
3 Components of a Biorepository

1. Specimen Sources

2. Biorepository Itself

3. Recipient/Investigator User
The Specimen Sources

**How will the specimen be obtained?**
- As part of clinical care (left-overs)
- Simultaneously with clinical care (piggyback)
- Specifically for research

**Will the specimen be identifiable?**
- Direct identifiers
- Coded information with no access to the link to the code
- Coded information with access to a link to the code
  - Is access to medical records allowed
  - Is recontact of participants allowed

The answers to these questions will determine the IRB regulatory requirements
Specimen Sources

It’s not always easy to tell . . .

Distinction between a clinically derived sample and a research sample.

• Research sample will require IRB review, informed consent--or not
• Clinical sample that is identifiable will require IRB review, informed consent--or not
• Clinical sample can be stripped of identifiers and be determined not human subjects--or not

Request IRB approval for what you want and need as specimen sources, not for what you think is “allowable”!
Components of a Biorepository

Specimen Sources

Repository Bank

Who owns this bank? Who runs the bank?
- For-profit or not-for-profit
- Academic Medical Center
- Single vs. multiple institutions
- HIPAA covered or not

Why was this bank created?
- To share sample and/or data for future research
- For a specific phenotype, disease or disease category or anything “interesting”
- For a specific organ or type or every available specimen
- Exclusively research and/or clinical specimens
Repository Bank

What services does the Bank offer?

• Process specimens in any way; separate cells, DNA, tumors, etc
• Validate for clinical diagnosis (CLIA compliant)
• Access updated clinical information related to the specimen
• Return of results to participants of any research that utilized the Bank’s specimens (sticky wicket for genetic studies)

Repository Bank

How does the Bank deal with deposits?

• Is an MTA, DTA required?
• A single Repository consent or separate consent form for each study?

How does the Bank deal with withdrawals?

• Who is the gatekeeper?
• What are the eligibility rules?
• Who, what, how, where do requests get processed/tracked?

The answers to these questions will determine the IRB regulatory requirements
Request IRB approval for what you want and need in the Bank, not for what you think is “allowable”!

Components of a Biorepository

Specimen Sources

Bank

Recipient/Investigator User
The Recipient/Investigator User

- Can the recipient obtain identifiable specimens?
- Can the recipient obtain updated clinical information?
- Is the recipient expected to share any research results with the bank?
- What are expectations for publications?
- Are there expectations for return of results for genetic “incidental findings”?
- Who is responsible for posting genetic data to dbGaP?
- The answers to these questions will determine the IRB regulatory requirements

Request IRB approval for what you want and need from the Users, not for what you think is “allowable”!
Regulatory Issues and Compliance

Repository Consent Form must address all 3 components

1. Purpose
2. Procedures
3. Population
   • Intake of specimens (source)
   • Physical location, processing (if any) and maintenance of specimens (bank)
   • Output of specimens to requesting researchers (users)

Writing the BioRepository Consent Form

1. Determine the Investigator’s desired plan to all 3 elements of the Repository for the long-term and state the plan very clearly.

2. Write that samples and data will be widely shared with other qualified investigators for future research.

3. Always opt for broad statements of use. Don’t limit the consent to a specific disease or disorder. Use larger categories of disorders such as “cardiac”, “gastrointestinal” “reproductive” “metabolic” “neurological”, etc.
Writing the BioRepository Consent Form

4. Strongly suggest ICF opt in/out language for re-contact of participants for original and other research projects.

5. Include the possibility that genetic tests may be done on the collected sample.

6. Strongly suggest putting GWAS language and permissions in the ICF.

7. Strongly suggest obtaining a federal Certificate of Confidentiality to as an assurance of compliance.

8. Write there is no expected benefit to participants. Do mention that some people will feel pride in their participation to help advance medical science.

9. If necessary, write that participants will not be notified when, where, how or even if their samples/data are used in future research. Participation is voluntary.

10. State plainly that if a participant has discomfort in sharing samples and/or data for unspecified research investigations—They should not join the Repository.
Consenting the Participant into a BioRepository

1. The Consentor needs to know the regulatory inconsistencies in “Informed consent”:
   a. “identifiable”:
      • 18 HIPAA elements per Privacy Rule
      • “Readily identifiable” per Common Rule
      • Not defined per FDA regulations
   b. “unspecified future research”
      • Requires specificity of authorization per Privacy Rule
      • Unspecified allowed per Common Rule
      • Unspecified allowed per FDA regulations
   c. “IRB ability to grant a waiver of permission”
      • Allowed (under certain conditions) per Privacy Rule
      • Allowed (under certain conditions) per Common Rule
      • Waiver of consent rarely allowed per FDA regulations

Consenting the participant into a BioRepository

2. Be clear about a description and purpose of the Repository.
   • Collection of samples/data for future research
   • Long term storage
   • Wide Sharing among other investigators
   • Goal to learn more about human disease

3. Be clear about the lack of benefit to participants. Don’t fail to acknowledge the participant’s ‘gift to science’.
Consenting the participant into a BioRepository

4. **Be clear about the primary risk of loss of confidentiality.** You cannot promise no privacy breach will occur or what other privacy risks will occur in the future.

5. **The volunteer nature of this request to join a Repository.**

6. **Be clear about the limited reversibility of their decision.** Samples/data can be destroyed later, but not if already shared in a de-identified manner.

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A consent form is not always needed because...

1. Waiver of consent can be granted by the IRB per 45 CFR 46.116(d) if:
   - Minimal risk
   - Not adversely affect rights and welfare
   - Not practical without a waiver
   - Participants will be given pertinent info (rarely applies)

2. Waiver of Authorization (HIPAA) can be granted by the IRB per 45 CFR 164.512 if use of PHI is minimal risk based on:
   - Adequate plan to protect identity and,
   - Adequate plan to destroy identifiers ASAP and
   - Adequate written assurances that PHI will not be reused or disclosed
   - Not practical without a waiver or access to and use of PHI
A consent form is not always needed because ...

3. Alternatives to Waivers to use and disclose research PHI
   • Deceased participant info
   • Anonymized information
   • Limited data sets
   • Reviews preparatory research without prior authorization

Have you learned that Biorepositories are:
   Complicated?
   Multi-dimensional?
   A Moving Target?
Get HELP!!!

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Help and understanding the issues means a new reaction:
Copacetic!