

Tissue and Data Repositories: Issues & IRB concerns

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- Based, in part, on the Stanford University “IRB Guidance on Data and Tissue Repositories”

Overview

- Introduction to Repositories
- IRB Oversight
- HIPAA Requirements



Introduction to Repositories

Definitions

The terms *database*, *registry*, *data bank*, *repository*, and *tissue bank* are often used imprecisely, and sometimes interchangeably.

- Registries, data banks, and tissue banks are all considered “**repositories**” for regulatory purposes.
- A **repository** is a collection of data or biological specimens whose organizers:
 - Receive data or specimens from multiple sources
 - Maintain the data or specimens over time
 - Control access to and use of data or specimens by multiple individuals and/or for multiple purposes, which may evolve over time

Repository Types

- Non-research Repositories
 - Created and maintained for purposes that are totally unrelated to research. Such purposes may include diagnosis, treatment, billing, marketing, quality control, and public health surveillance
- Research Repositories
 - Created and maintained specifically for research purposes. Such purposes may include databases to identify prospective subjects, patient outcome information to evaluate treatment effectiveness, and tissues samples for future research



Non-research Repositories

Non-research Repositories

- Even though repositories were not created for research purposes, they may contain information that is of great interest to researchers, for example:
 - Billing database used for subject recruitment
 - Quality assurance database used to draw general conclusions
 - Tissue repository used for DNA research

Non-research Repositories

- The creation (or operation) of non-research databases or repositories does not involve human subject research and does not require IRB oversight
- However, **IRB oversight is required for use in research** of identifiable private information or identifiable human specimens from non-research databases and repositories (including data/tissue banks and registries).

Non-research Repositories

- When research involves identifiable private information or identifiable human specimens each research use must receive prospective IRB review and approval and continuing IRB oversight
- Researchers should submit an application for IRB review and receive IRB approval before initiating the research.
- Where available, the application should include any available information about the circumstances under which the information or specimens were originally collected.
- Investigators who believe their research may be exempt from the human subject regulations should include a request for exemption #4 with the IRB application.

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Informed Consent

- Because research use was not anticipated at the time of collection, research informed consent has not usually been obtained from the individuals who provided the information or specimens. Standard treatment and surgical consents rarely meet the regulatory requirements for research informed consent.
- IRBs may require researchers to obtain the informed consent of subjects for research involving information or specimens contained in non-research databases or repositories.
- IRBs can waive the requirement for informed consent if the research meets the criteria in the regulation



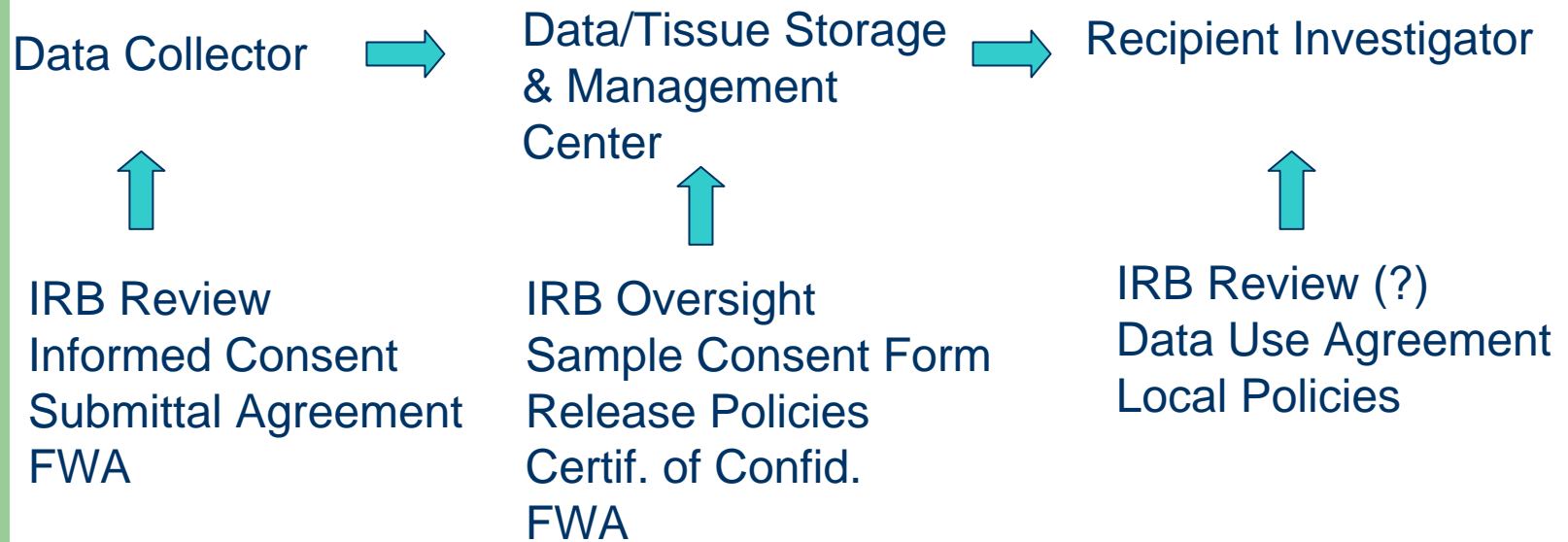
Research Repositories

Research Repositories

Research repositories involve three components:

- the collectors of data;
- the storage and data management center; and
- the recipient investigators.

Research Repositories





Data Collection

Informed Consent

- If the samples were collected for research purposes **or**
- Are associated with information that can identify the donor, **then**
- Informed consent must be obtained from the donor unless appropriately waived by the IRB

Informed Consent Requirements

- A clear description of
 - the operation of the database;
 - the specific types of research to be conducted;
 - the conditions under which data will be released to recipient-investigators; and
 - procedures for protecting the privacy of subjects and maintaining the confidentiality of data
- A statement regarding future withdrawal of the data from the study (i.e., state whether subjects may, in the future, request that their data be destroyed or that all personal identifiers be removed from data).

Other Informed Consent Considerations

- A statement regarding the length of time that data will be stored. If storage time is indefinite, so state.
- A statement regarding subjects' access to information learned from the research, if they so choose
- When human genetic research is anticipated, information should include possible consequences of genetic testing (e.g., insurance risks, misattributed paternity)

Other Informed Consent Considerations

- A statement regarding secondary uses of the samples. For example,
 - state that there will be no secondary use, or
 - subjects have option of allowing secondary use, or
 - subjects will be contacted for additional consent in the future for secondary use, or
 - there will be secondary use only after the banked samples have been stripped of identifiers.

Submittal Agreements

- Collecting investigators must agree in writing to the data collection conditions specified in the repository's policies
- Data collection policies should ensure that the data was collected in an ethical manner
 - Adequate informed consent
 - IRB review when necessary
- Many repositories have sample consent forms



Data Storage & Management

Repository Policies

- Repositories should have written policies on
 - Data and tissue submission requirements
 - Informed consent
 - IRB review
 - Physical and procedural mechanisms for the secure receipt, storage, and transmission of information and specimens
 - Policies on release of information and specimens
 - Coding
 - Release of identifiers
 - Certificates of Confidentiality



Recipient Investigators

Data Use Agreements

- Recipient-investigators should have a written data use agreement with the repository
- The data use agreement should specify under what conditions the data is being released to the recipient-investigator(s)
- The terms under which the data is released determine whether the research requires IRB oversight based on OHRP's Guidance on Coded Data

ORHP Guidance on Coded Data

- Under the definition of human subject at 45 CFR 46.102(f), *obtaining* identifiable private information for research purposes constitutes human subjects research.
 - *Obtaining* means receiving or accessing identifiable private information for research purposes.
 - OHRP interprets *obtaining* to include an investigator's use, study, or analysis for research purposes of identifiable private information already in the possession of the investigator.

ORHP Guidance on Coded Data

- In general, OHRP considers private information to be individually identifiable as defined at 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.
- Conversely, OHRP considers private information not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

ORHP Guidance on Coded Data

- OHRP does not consider research involving **only** coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:
 - (1) the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals;**AND**
 - (2) the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain

ORHP Guidance on Coded Data

Examples of acceptable conditions:

- (a) the key to decipher the code is destroyed before the research begins;
- (b) the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased;
- (c) there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
- (d) there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

ORHP Guidance on Coded Data

- If the investigator(s) later decide to re-identify the subjects then the research activity now would involve human subjects
 - By obtaining the key to the code from the source
 - By deriving the identity through linking the data to other datasets (Deductive Re-Identification)
- Unless this human subjects research is determined to be exempt, IRB review of the research would be required and informed consent would be required unless waived by the IRB



IRB Oversight

Repository Protocols

- Under a repository protocol, the IRB can approve relatively broad parameters for collecting, storing, sharing, and using the repository's information and/or specimens in research.
- A repository protocol may be submitted to the IRB to:
 - Define the operating parameters for establishing and maintaining a research repository, **or**
 - Convert an existing research database, non-research database, or non-research repository into a research repository.

Repository Protocols

- Protocols for establishing and operating a research repository will include at least the following specific information:
 - The specific conditions under which data/specimens may be accepted into the repository, including submission to the repository of a copy of each subject's signed authorization and signed consent document,
 - A detailed description of the physical and procedural mechanisms for the secure receipt, storage, and transmission of information and specimens to ensure the protection of subjects' privacy and the confidentiality of subjects' data/specimens,
 - The specific conditions under which data and/or specimens may be shared with or released to research investigators,

Repository Protocols

- A sample consent form that includes, in addition to the usual elements of consent, a clear description of each of the following:
 - The general concept and purpose of repositories
 - The name and purpose of the specific repository for which consent is being solicited
 - As specifically as possible, the types of research that the repository will support
 - The repository's physical and procedural mechanisms for protecting subjects' privacy and the confidentiality of data/specimens
 - The conditions and requirements under which repository information or materials will be shared with recipient-investigators
 - Specific risks related to a breach of confidentiality related to the information being collected
 - Where human genetic research is anticipated, information about the consequences of DNA typing (e.g., regarding possible paternity determinations) and related confidentiality risks.

Repository Protocols

- Typical IRB protocol forms do not adequately address repository issues and ask for information not relevant to the operation of repositories
- Institutions should develop a separate protocol form to review research repositories



HIPAA Requirements

Non-research Repositories

- PHI in non-research repositories may not be used or disclosed for research purposes unless:
 - Written authorization for use and disclosure of PHI in research has been obtained from the patient-subject, or
 - The IRB approves and documents a formal waiver of the authorization requirement, or
 - The holder of the PHI receives and documents the HIPAA required representations from the investigator and determines that the research involves only one or more of the following: 1) decedents' information, 2) de-identified information, 3) limited data sets, or 4) review preparatory research.

Research Repositories

- HIPAA generally does not apply to research involving tissue samples unless PHI is associated with the samples
- HIPAA does apply to the submission of PHI to research repositories

Research Repositories

- A HIPAA authorization form from patient-subjects for the research use or disclosure of PHI is usually required for submitting PHI to a research repository
- An authorization waiver may be granted if the submission to the repository meets the criteria in the regulations
- Authorization is not required if the research involves only one or more of the following: 1) decedents' information, 2) de-identified information, 3) limited data sets, or 4) review preparatory research.

Research Repositories

- HIPAA does not allow authorization for unspecified future use
- Under HIPAA, PHI can be stored and used for research purposes if:
 - The research is limited to the purpose stipulated in the authorization
 - New authorization is obtained if the PHI is to be released for a new use
 - The IRB grants a waiver of authorization
 - The PHI is only being used for research involving 1) decedents' information, 2) de-identified information, 3) limited data sets, or 4) review preparatory research

Waiver of Authorization

- An IRB (or Privacy Board) can waive the requirement for authorization if the research meets these criteria:
 - (1) The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals based on at least the following:
 - An adequate plan to protect the identifiers from improper use and disclosure; *and*
 - An adequate plan to destroy the identifiers at the earliest possible opportunity unless there is a research or a health justification for retaining them (or retention is required by law); *and*
 - Adequate written assurances that the PHI will not be reused or disclosed to another person or entity (except as required by law, for authorized oversight of the research, etc.).
 - (2) The research could not practicably be conducted without the alteration or waiver.
 - (3) The research could not practicably be conducted without access to and use of the PHI

Waiver of Authorization

- Minimum Necessary Standard
 - When using or disclosing PHI for research without an Authorization, a covered entity must make reasonable efforts to limit the PHI used or disclosed to the minimum necessary amount to accomplish the research purpose
- Right to an Accounting of Disclosures
 - Individuals have the right to receive an accounting of disclosures made for research by a covered entity without the individual's Authorization



Summary

Summary

- Repositories receive data or specimens from multiple sources, maintain the data or specimens over time, and control access to and use of data or specimens by multiple individuals and/or for multiple purposes, which may evolve over time
- There are research repositories and non-research repositories
- Information in non-research repositories may be of interest to researchers and may need informed consent and/or IRB oversight
- Research repositories involve the collectors of data; the storage and data management center; and the recipient investigators, each of which have human research protections concerns
- IRB oversight over research repositories is necessary and there should be a specific repository protocol form
- There are HIPAA issues when PHI is submitted and used for research in a repository

References

- OHRP Guidance, Issues to Consider in the Research Use of Stored Data or Tissues,
<http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm>
- OHRP Guidance on Research Involving Coded Private Information or Biological Specimens,
<http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>
- Stanford University IRB Guidance On Data and Tissue Repositories,
<http://humansubjects.stanford.edu/research/documents/DataTissueRepositories.pdf>
- NIH Guidance, Research Repositories, Databases, and the HIPAA Privacy Rule
http://privacyruleandresearch.nih.gov/research_repositories.asp