

Biorepositories and Research on Biospecimens

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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).

IRB Review

- Not human subjects research
 - No identifiable, private information released
- Exemption Category 4
 - Existing data/specimens either publically available or recorded without identifiers
- Expedited Category 5
 - Data/specimens gathered for non-research purposes

Informed Consent

- For exempt research, informed consent not required
- If not exempt, IRB may waive the requirement for informed consent
 - Minimal risk
 - Waiver will not adversely affect subject rights and welfare
 - Not practicable without waiver
- If consent required, subjects should be informed about how data/specimens are to be used

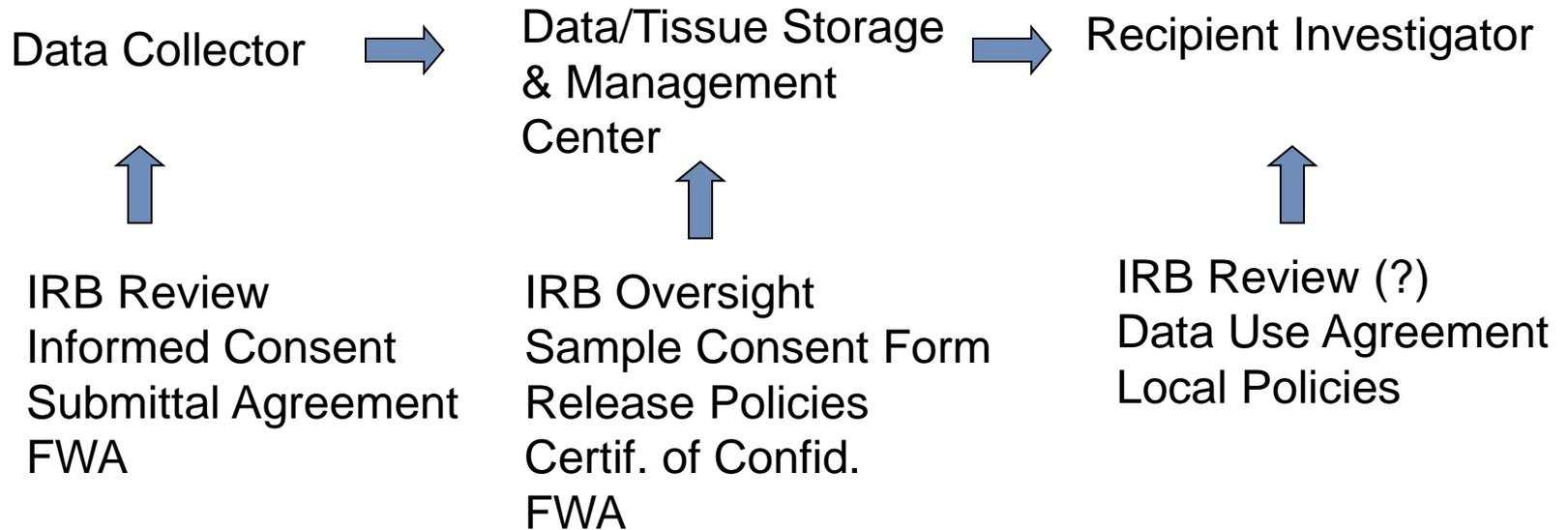
Research Repositories

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
 - Detailed description of facilities, security and oversight procedures, record keeping and access
 - 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

- 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

- 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.

HIPAA Requirements

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 or use of PHI from repositories.

Summary

- Information obtained from non-research repositories may need IRB review and informed consent
- 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