Human Research Protection Program
Policies & Procedures

Banking of Data and Biological Specimens for Future Uses (Registries, Repositories and Data Banks)

Version 1.0
Date Effective: 5.4.2010

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BACKGROUND

Data and specimen repositories (sometimes called registries, banks, or libraries) are used to store data and/or specimens for future research use. Federal regulations and OHSU policies that protect the privacy of patients and research subjects apply to both the creation and the use of research repositories. Repositories involve the collection, storage and later distribution of information and/or biological specimens for some future purpose. Repository activities involve three components: 1) the collection of materials, 2) the repository storage and data management and 3) the use by recipient investigators. Each component of the repository is governed by Federal regulations. Some repositories are created and maintained explicitly for research purposes. Others are created and maintained for non-research purposes, but may be accessed for research uses. The purpose of establishing a formal research repository is to give the investigator the authority and responsibility for distributing data and/or specimens from the repository, to minimize the regulatory paperwork burden and to define future uses in a fashion that protects participants' rights yet supports scientific inquiry.

1. SCOPE

This policy applies to human subject research repositories established by OHSU investigators for the purpose of storing data and/or specimens for future research purposes.

This policy does not apply to data/specimens that are collected and stored as part of routine clinical care or hospital procedures, for example, blood banks, pathology, surveillance, or quality assurance. However it does apply to data/specimens from these sources that are then stored for future research.

2. POLICY

A. Any repository holding identifiable or coded data/specimens for research purposes must comply with this policy.

B. The collection and storage of specimens/data becomes a research repository when there is a specific intention for the data/specimens to be used repeatedly for research purposes, or stored for future research or shared with other investigators.

i. The prospective collection and storage of data/specimens for defined research purposes (including holding samples to "batch" them for assays), as part of a single IRB-approved protocol is not considered a repository.

ii. If there is no explicit plan to destroy the data/specimens when the specific original research project ends, the investigator may maintain the data/specimens under continued IRB approval for uses as approved in the original protocol.

iii. Once a use is desired beyond the primary research goals of the original protocol, the PI must establish an IRB-approved research repository protocol for any future research uses or submit data/specimens into an existing IRB-approved repository.

C. All research repositories, except those qualifying as non-human subjects research, requires review and approval by the IRB.

i. Non-Human Subjects Research – this is an activity that doesn't meet the definition of human subject or research.

a. Research projects that are originally deemed non-human subjects (NHS) research and converted to a repository are considered NHS repositories.

b. Data/specimens that are de-identified as part of the original research protocol will likely be deemed NHS repositories.

c. A request for determination should be sought to have the IRB confirm the NHS status.

ii. Exempt Repositories – these meet the regulatory definition of being exempt from the full requirement of IRB oversight.

a. For repositories that are exempt, continuing oversight by the IRB is limited to annual renewals.

b. Repositories will NOT be found to be exempt if the data/specimens retain any identifier or link that would permit anyone to identify, directly or indirectly, the person whose data/specimens are stored.

iii. Non-Exempt Repositories

a. The operation of any non-exempt research repository requires standard continued oversight by the IRB.

b. Creating a repository specific protocol will be required for the review.

c. The IRB will review and approve the repository protocol specifying the conditions under which data and specimens may be accepted into the repositories, how they will be securely stored, and the procedures under which they will be shared in order to ensure that adequate measures are employed to protect the privacy of subjects, maintain the confidentiality of the data and the integrity of specimens.

D. Revisions to a repository protocol must be approved by the IRB prior to implementation.

E. Research repositories require either consent and authorization (C/A) by participants for the storage and future research use of their data/specimens <u>OR</u> a waiver of consent and/or authorization by the IRB.

F. Requests by a recipient investigator to access identifiable data and/or specimens from any existing non-exempt research repository requires IRB approval. The OHSU PI must comply with all requirements of the repository and terms of any usage and/or submittal agreements

G. Research repositories will be required to provide a summary report to the IRB of all collections, releases or destruction of data/specimens from the repository at each continuing review.

H. Genetic opt out requirements, per the Oregon Genetic Privacy Act, may be required for coded and anonymous genetic research.

3. PROCEDURES

A. Submitting an application for IRB approval of a research repository.

i. The electronic IRB (eIRB) contains a specific application for the creation of new research repositories.

ii. Any existing study that is completed but has collected data and/or specimens for future research purposes may choose to convert the study to a repository via a modification of continuing review application.

iii. It is recommended that a request for determination be sought from the OHSU IRB whenever there is a question of IRB oversight requirements. This can be accomplished through a repository Initial Review Questionnaire (IRQ).

iv. **Database/Repository is Maintained at OHSU -** When the database/repository is maintained partly or completely at OHSU, a separate repository protocol must be submitted for the database/repository itself.

v. **Database/Repository is Maintained Outside of OHSU -** When an investigator is contributing data/specimens to a repository not held by OHSU, the OHSU IRB must approve at a minimum the collection protocol, the consent process and the submittal agreement. This can be done as a new application or an amendment to an existing study. However, not all submittals meet the requirements for engagement in human subjects research and a request for determination may be sought.

vi. **Requesting Data/Specimens from a Repository**

a. When an investigator is requesting coded or identifiable data from an established repository, a study submission is required either as a new study or as a modification to an existing study. The OHSU IRB must approve at a minimum the protocol, data collection tools, the usage agreement, consent process (most likely a waiver), and IRB approval of repository from which the request is being made.

b. For anonymous and some coded data, a request for determination should be submitted.

B. General Repository Protocol Requirements – All repository protocols must include information regarding the following:

i. **Purpose of the Repository.**

ii. **<u>Collection</u> - Data/specimens to be included.** Describe the data/specimens to be included, their sources, and the process of acquisition. If some of the data/specimens have been or are to be collected at sites outside of OHSU for storage at OHSU, include a collection plan and C/A document for distribution to data/specimen collectors and use by their local IRBs. Indicate conditions under which data/specimens may be accepted. Confirm that documentation of local IRB approval will be provided to the OHSU IRB for each site contributing data/specimens to the OHSU database/repository.

a. **Consent and authorization (C/A).** Describe how C/A has been or will be obtained from subjects, or why waiver of C/A is justified.

- **Consent** - The C/A form should contain all the basic elements for C/A required by federal regulations. It must have a clear statement in the C/A form that the subjects are giving permission for their data and/or specimens to be stored in the database/repository in order to be used in future research studies... This statement may be specific or broad; however it will dictate the limits on future uses.

- **Waiver of C/A –** A waiver for C/A may be granted by the IRB if all of the requirements for waiver are met. Keep in mind that data collected and stored under a waiver may have more limitations on future use.

iii. **Maintenance –**

a. **Security and confidentiality.** Describe how and where data/specimens will be stored, and how the privacy of subjects and the confidentiality of data will be protected, including if a Certificate of Confidentiality will be obtained.

b. **Access to the data/specimens.** Describe who will have access to the data/specimens, what the requirements for access are, and who is designated as the Guardian. A complete description of the process for requesting and releasing data must be included. Submit a template usage agreement.

iv. **Release - Mechanisms release of data/specimens**. A statement should be made in the repository protocol that separate IRB approval/determination will be required for each specific human subject research activity that uses identifiable data/specimens from the repository. Each study is considered to be a research activity that is separate from the repository itself.

C. **Repository Protocol Operating Procedures** - The repository protocol must describe the operating procedures for how the repository will perform the following required activities:

i. Identifying when and what material (data or/or identifiable specimens) is originally received.

ii. Documenting whether the person from whom the material was obtained signed a legally effective consent and authorization (C/A) or there was an IRB approved waiver of C/A.

a. Any IRB approved consent forms for the collection of the material being submitted to the repository should be included with data/specimen submissions.

b. Consent for storage into an OHSU repository will preferably use the stand-alone banking C/A.

iii. Certifying that the material collection protocol had IRB approval from the home institution. A copy of the approval letter should be submitted.

iv. Identifying data/samples for which consent has been withdrawn and will ensure no future use.

v. Identifying data/samples which have limitations on future uses and ensuring that future uses are not contrary to those limits.

vi. Certifying genetic opt out status with OHSU officials, if applicable.

vii. Securing submittal agreements from investigators placing data/specimens in the repository. For those obtained under waiver of C/A, it should also contain an acknowledgment that collector-investigators are prohibited from providing recipient-investigators with access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained without prior IRB approval.

viii. Securing Usage Agreements from recipient investigators.

ix. Ensuring that material transfer agreements are used when necessary for the transfer of biological materials. LINK to MTA

D. Security and Confidentiality – The security and confidentiality of the materials must be protected. The following minimum measures must be described in the repository protocol:

i. Coding. A method to code the data/specimens, including a process to protect/maintain the key to the code and limit access to the key. The coding system must be adequate to reduce the possibility of re-identification.

ii. Control of access to the data/specimens - access to the un-coded data/specimens must be restricted to a limited number of repository staff. Accountability for controlling and monitoring access must be provided.

iii. Security procedures - a method to limit access to the coded data/specimens (including computer security and specimen storage security measures) must be provided.

iv. Data transfer security – methods to ensure confidentiality during the collection and release of data and specimens.

v. Location and housing of data/specimens.

vi. **Certificate of Confidentiality (CoC)** - Recommended for all repositories, but not required, as an additional protective measure. The IRB may require a CoC for repositories housing potentially sensitive information. LINK to CoC Policy

E. Guardian - A Guardian must be appointed for each repository. Guardians are responsible for:

i. Ensuring that data/specimens are received and released according to OHSU policy and the IRB approved repository protocol.

ii. Executing a usage agreement each time data or specimens are released for research purposes.

iii. Ensuring the security and confidentiality of stored data and specimens,

iv. Secure data and specimen distribution.

v. Tracking acquisitions and release of data and specimens.

F. Study Specific Repositories - When collecting data/specimens in the course of a study and depositing them into a database/repository that will be used only for the research goals of that specific study:

i. A separate repository protocol/consent form is recommended.

ii. If a separate repository protocol is not created, the study protocol/consent form must contain the following information about the database/repository:

a. Method of data/specimen storage and use;

b. Data points and specimens to be stored. Include all identifiers.

c. Designated repository guardian and list of who will have access to the repository; and

d. Methods to protect confidentiality

e. A statement that the samples/information may be used for future research. This statement may be specific or broad; however it will dictate the limits on future uses.

iii. Any proposed use beyond the original study will require creation of a repository protocol.

G. Conversion of a Clinical Database/Repository to a Research Database/Repository. Data/specimens that have been stored in a database/repository solely for clinical, QI purposes or other standard non-research purposes in the past can be moved into a research database/repository under an IRB waiver of C/A.

H. Conversion of a Research Study Protocol to a Research Database/Repository Protocol. Some currently approved IRB protocols include not only a specific research study, but also a research database/repository to store data/specimens for future studies. When the research database/repository is maintained at OHSU for use in future studies, a single IRB submission can be maintained while the research study is still in process. Within that single IRB submission, there should be a separate protocol for the specific study and a separate protocol for the database/repository, with separate C/A forms. In order to be compliant with this policy, it may be necessary to create or revise existing study documents and C/A forms to meet the requirements outlined above. Subjects who are currently enrolled under the study protocol usually will not have to be re-consented because they have already given C/A for both the specific study and the database/repository. Future subjects in the research study must sign separate C/A forms for the specific study and the database/repository. Once the research study and subsequent data analysis are complete, the repository protocol can be separated into a repository specific IRB submission and the original research study submission can then be terminated. This can be done at continuing review or via a modification.

I. Terminating a Repository

i. When there is no intent to continue to operate a repository for future research or if the data/specimens are being transferred to another repository, the repository should be terminated via a modification in the eIRB. Termination Policy

ii. The termination request must include the disposition of the data and samples, including details on transfer, donation or destruction of specimens or data in a secure way.

iii. When applicable, a description of any communications with research participants regarding disposition of data and samples should be submitted for approval.

4. DEFINITIONS

A. Guardian: A person who has primary control of data and specimens and maintenance of the repository. This person may be delegated by the Principal Investigator; however the PI retains ultimate responsibility for the oversight of the repository.

B. Non-Human Subjects Research (NHS): activities that do not meet the 45 CFR 46 definition of human subject research.

C. Repository: Registries, data banks, and tissue banks are all considered “repositories” for regulatory purposes. Any reference in this policy to repositories applies equally to data banks, tissue banks, and registries. Generally, a repository collects, stores and distributes human tissue, specimens and/or data for use in future research projects. Any collection of human biological materials (including data) is considered to be a repository when there is no

explicit plan to destroy the materials when the specific research project that generates the materials ends.

D. **Submittal Agreement:** An agreement that attests that specimens collected were obtained with written informed consent of the donor-subjects utilizing an informed consent document approved by the local IRB or under an IRB Approved waiver of informed consent.

E. **Usage Agreement:** An agreement that details the conditions for receipt and future receipt use of data and/or specimens from a repository.

Guidance on Defining Repositories

The terms ***database, registry, data bank, repository,*** **and** ***tissue bank*** are often used imprecisely, and sometimes interchangeably. The following definitions are not universally accepted, but are provided solely to clarify

Database. A database is collection of information elements (i.e., data) arranged for ease and speed of search and retrieval. Most databases are now maintained electronically, but the term can also be applied to paper record systems.
Examples of databases include the following:

- A set of observations (i.e., data) resulting from a research study
- An electronic file of a medical provider's patients
- A collection of diagnosis, treatment, and follow-up information for a hospital's oncology patients
- A file of outcomes information complied for quality assurance activities
- A list of potential research subjects

Registry. A registry or "data bank" is a collection of information elements or databases whose organizers:

- Receive information from multiple sources
- Maintain the information over time
- Control access to and use of the information by multiple individuals and/or for multiple purposes, which may evolve over time

Registries often contain codes that link information and specimens to their donor's identify. Examples of a few well-known registries and data banks include:

- Centers for Disease Control & Prevention (CDC) State Cancer Registries
- Familial Gastrointestinal Cancer Registry
- National Registry of Myocardial Infarction (NRMI)
- National Registry of Veterans with Amyotrophic Lateral Sclerosis
- The National Library of Medicine Hazardous Substances Data Bank (HSDB)
- The National Practitioner Data Bank
- The US Census 2000 Data Bank

Repository. A repository or "tissue bank" is a collection of biological specimens whose organizers:

- Receive specimens from multiple sources
- Maintain the specimens over time
- Control access to and use of specimens by multiple individuals and/or for multiple purposes, which may evolve over time

Repositories usually include demographic and/or medical information about the individuals from whom the specimens were obtained. Repositories often maintain codes that link the information and specimens to their donor's identify. Examples of a few well-known repositories include:

- The National Human Radiobiology Tissue Repository
- The National Institute of General Medical Sciences (NIGMS) Human Genetic Cell Repository
- The National Institute on Aging Cell Repository
- The National Marrow Donor Program (NMDP) Research and Outcomes Repositories
- The National Surgical Adjuvant Breast & Bowel Project (NSABP) Data and Tissue Banks