



Title:	Data or Biological Sample Repositories		
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1 Data or Biological Sample Repositories

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

These policies and procedures apply to both data and biological sample repositories. For simplicity, both will be referred to as samples in this document.

There are two type of repositories:

- 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 that are altered to facilitate research (e.g., through the addition of data fields not necessary for the core purpose of the repository) are considered research repositories.

1.1 Non-research Repositories

Even though repositories were not created for research purposes, they may contain information that is of great interest to researchers. 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).

- 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.
- The IRB may require researchers to obtain the informed consent of subjects for research involving information or specimens contained in non-research databases or repositories. The IRB can waive the requirement for informed consent if the research meets the criteria in the regulation

1.2 Research Repositories

Research repositories involve three components:

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

1.2.1 Sample collection

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 information should include:

- 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 information, such as the length of time that data will be stored, subjects' access to information learned from the research, and secondary uses of the samples should be considered as appropriate.

Repositories should have data submission policies to ensure that the data was collected in an ethical manner, such as informed consent and IRB approval.

- Sample Storage and Management
- 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 identifier
 - Certificates of Confidentiality

1.2.2 Recipient Investigators

Recipient-investigators should have a written agreement with the repository. The 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.

1.2.3 IRB Oversight

Operation of a research repository and its data management center under the auspices of the UNC-Chapel Hill is subject to oversight by the UNC-Chapel Hill IRB. Proposals to establish a repository must be submitted to the IRB specifying the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. The IRB also reviews and approves a sample collection protocol and informed consent document for distribution to sample collectors and their local IRBs.

2. Biological Specimens

All activities involving the collection of human biological specimens for research purposes, as well as the research use of specimens collected for clinical care, must be conducted under the terms of an IRB approved research protocol. The collection and use of human biological specimens (either identifiable or de-identified) must comply with all applicable laws and regulations for research involving human biological specimens or superseding requirements. .2

2.1 Regulatory Oversight

Under HHS regulations, a human subject is a living individual about whom an investigator conducting research obtains

- data through intervention or interaction with the individual, or
- identifiable private information

Whether research involving biological specimens meets the definition of human subjects research is based on a) how the specimens were obtained and b) whether the specimens

include identifiable private information. If the specimens are obtained specifically for research purposes, then they have been collected through intervention or interaction with the individual and, thus, the research meets the definition of human subjects research. If the specimens were not collected for research purposes but as part of routine clinical care or other non-research purpose, then the research only meets the definition of human subjects research if the specimens include identifiable private information.

An exception to this is federally-funded research involving Newborn Blood Spots. Per the Newborn Screening Saves Lives Reauthorization Act of 2014 (Public Law No: 113-240), federally-funded research funded using newborn dried spots is considered human subjects research regardless of whether the specimens are identifiable. Further, the law eliminates the ability of the IRB to approve alterations or waivers of informed consent under 45 CFR 46.116(c) and 116(d) for research involving newborn dried blood spots.

3. Research use of cord blood from births at UNC Hospitals

According to UNC Hospitals policy (February 15, 2000), any collection for research use of placental tissue, umbilical cord tissue or cord blood from births at UNC Hospitals will require written consent of the mother. Investigators seeking to acquire such specimens for research use should prepare an IRB application including a consent form. They must also notify the Department of OB/GYN, since protocols involving obstetrical patients also require review by the OB/GYN Department Research Committee and requests for cord blood may need to be prioritized. Investigators will be responsible for making arrangements for obtaining consent and collecting the specimens.

This policy is based on the following considerations:

1. Cord blood and placental tissue are a unique source of stem cells and other biologic materials, with great therapeutic potential. Consequently there is increasing demand.
2. Certain research uses of these tissues already require informed consent. In particular, the recent designation of UNC Hospitals as a collection site for an NHLBI-sponsored Cord Blood Bank for stem cell research will result in approaching most if not all mothers for permission to collect cord blood for this purpose.
3. Certain ethnic groups do not view the placenta and placental blood as waste, but as sacred objects. Using tissues from such persons without their consent would constitute a serious violation of their rights.

FDA regulations do not apply to biological specimens unless they are gathered as part of a clinical investigation involving human subjects or being used to test a medical device. HIPAA does not cover biological specimens but does cover protected health information (PHI) linked to the specimens.

Registries are sometimes created by a public authority (e.g., the North Carolina Central Cancer Registry was created by the North Carolina Legislature, see [North Carolina General Statute Chapter 130A - Article 7](#)) If the research meets the definition of human subjects research, then all of the requirements of this document apply.

3.1 IRB Review

Research involving only biological specimens may be exempt under Exemption Category #4: “Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.” However, in order to qualify under this category, all of the specimens must exist prior to the research being submitted to the IRB. Additionally, this exemption cannot be applied to federally-funded research involving Newborn Blood Spots.

Non-exempt research only involving biological specimens may be eligible for expedited review if it is minimal risk and falls within one of the following categories:

- Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture [with restrictions]
- Prospective collection of biological specimens for research purposes by noninvasive means.
- Research involving materials... that have been collected, or will be collected solely for nonresearch purposes

All non-exempt research involving biological specimens that are not eligible for expedited review must be reviewed at a convened IRB meeting.

For all non-exempt research involving biological specimens, informed consent and documentation of consent is required unless waived by the IRB. Informed consent is required for all federally-funded research using Newborn Blood Spots.

3.2 Coded Human Data or Biological Specimens

The UNC-Chapel Hill IRB policy is based on the OHRP guidance document entitled, “Guidance on Research Involving Coded Private Information or Biological Specimens” (October 16, 2008 <http://www.hhs.gov/ohrp/policy/cdebiol.html>). This document:

1. Provides guidance as to when research involving coded private information or specimens is or is not research involving human subjects, as defined under HHS regulations for the protection of human research subjects (45 CFR part 46).
2. Reaffirms OHRP policy that, under certain limited conditions, research involving only coded private information or specimens is not human subjects research.
3. Clarifies the distinction between (a) research involving coded private information or specimens that does not involve human subjects and (b) human subjects research that is exempt from the requirements of the HHS regulations.
4. References pertinent requirements of the HIPAA Privacy Rule that may be applicable to research involving coded private information or specimens.

Note: The FDA definition of human subjects differs from the Common Rule definition. Use of coded specimens for FDA-regulated research such as research on In Vitro Diagnostic Devices

requires assessment according to the FDA regulations and guidelines. Investigators should contact the IRB office for guidance.

For purposes of this policy, coded means that: (1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and (2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Guidance:

Obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research. Obtaining identifiable private information or identifiable specimens includes, but is not limited to:

1. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that have been provided to the investigator from any source; and
2. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that were already in the possession of the investigator.

In general, private information or specimens are considered to be individually identifiable when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Private information or specimens are not considered to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Research involving only coded private information or specimens (other than federally-funded research using Newborn Blood Spots) do not involve human subjects per the Common Rule definition if both of the following conditions are 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 because, for example:

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 (note that the HHS regulations do not require the IRB to review and approve this agreement);

In some cases an investigator who obtains coded private information or specimens about living individuals under one of the conditions cited in 2(a)-(c) above may (1) unexpectedly learn the identity of one or more living individuals, or (2) for previously unforeseen reasons now believe that it is important to identify the individual(s). If, as a result, the investigator knows, or may be able to readily ascertain, the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity now would involve human

subjects. Unless this human subjects research is determined to be exempt. IRB review of the research would be required. Informed consent of the subjects also would be required unless the IRB approved a waiver of informed consent.

3.3 Who Should Determine Whether Coded Private Information or Specimens Constitutes Human Subjects Research

The investigator in consultation with the IRB Chair or Director of the IRB Office will determine if the research involving coded information or specimens requires IRB review following the procedures for Human Subjects Research Determinations.

3.4 Sample Storage and Management

Repositories should have written policies on:

- Data and tissue submission requirements
- Informed consent
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3.5 Recipient Investigators

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3.6 IRB Oversight

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4. Gene manipulation in human subjects research

All research involving gene transfer into human subjects or any form of recombinant DNA research must be reviewed by the University's Institutional Biosafety Committee in addition to IRB review. All recombinant DNA research must be reviewed and approved by the NIH's

Recombinant DNA Advisory Committee (RAC). The results of these additional reviews should be submitted to the IRB.

NIH guidelines on recombinant DNA and gene transfer research are available online at:

<http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>

5. Human embryonic stem cell research

Federal regulation of human embryonic stem cell research is both complex and evolving. Research proposals that involve human embryonic stem cells must be submitted to the Embryonic Stem Cell Research and Oversight (ESCRO) committee. Not all such studies (e.g., in vitro studies or animal experimentation) constitute human subjects research requiring IRB review. Studies that do involve human subjects research as defined in the regulations should be submitted to the IRB for review, in addition to the ESCRO committee.

6. Human fetal tissue transplantation research

It is unlawful for any person to knowingly acquire, receive or transfer any human fetal tissue for valuable consideration. It is unlawful for any person to solicit or knowingly acquire, receive or accept a donation of human fetal tissue for transplantation if the tissue is obtained pursuant to an induced abortion and the donation is made pursuant to a promise that it will be transplanted to any specified individual, to a relative of the donating individual, or in valuable consideration for the costs associated with the abortion. Additionally, all other ethical and regulatory requirements for the welfare and protection of human research subjects apply to both the donors and the recipients of human tissue used in transplantation research.

Human fetal tissue may be used only if it has been obtained in accord with the following requirements: (1) the woman providing the tissue must declare in a signed written statement that she is donating the tissue without any restrictions regarding the identity of the transplant recipients and without being informed of the identity of the recipients; (2) the attending physician must declare in a signed written statement that the tissue was donated by the woman and with full disclosure with regard to the physician's interest in the research and any known medical or privacy risks associated with the research. If the tissue is obtained pursuant to an induced abortion, the attending physician must also declare in her or his signed written statement that the consent of the women for the abortion was obtained prior to requesting or obtaining consent for the donation of the tissue, no alteration of the timing, method or procedures used to terminate the pregnancy was made solely for the purpose of obtaining the tissue; and the abortion was performed in accordance with applicable state law; and (3) the PI for the research must declare in a signed written statement that: the tissue is human fetal tissue; the tissue may have been obtained pursuant to a spontaneous or induced abortion or stillbirth; the tissue was donated for research; the investigator had provided this information to other individuals involved in the research and received written acknowledgement of the receipt of this information; and the investigator has had no influences on the decision to terminate the pregnancy.

(For more information see OHRP Guidance on "Fetal Tissue Transplantation" dated February 7, 2003.