
Yale University Human Research Protection Program

HRPP Policy 445: Use of Stored Data and Biological Specimens in Human Research

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Scope

This policy applies to all members of the Yale University research community who intend to use data and/or biological specimens (materials) derived from living human beings that are stored in repositories, databases or other collections and made available for research purposes.

Policy Statement

Institutional Review Board (IRB) review and approval or determination of exemption as appropriate is required prior to:

- the research use of identifiable data/biological specimens, that are accessed from a data/biological specimen bank,, repository or other collection.

Reason for the Policy

The use of data and/or biological specimens (materials) have proven valuable to researchers in making significant gains in the study of science and medicine. Repositories allow materials and data to be shared by investigators and accessed for multiple research projects, including those that weren't conceived at the time of data/specimen collection. The use of data/specimens from a repository may invoke unique ethical and regulatory issues that necessitate a distinct policy to facilitate proper management of these activities. This policy describes when Yale considers the use of such stored materials to constitute human research requiring IRB review, approval exemption or other determination.

Definitions

Anonymous

Stripped of identifying information and of codes that could be used to link data or samples back to a specific individual. Although anonymous materials do not by definition contain linking codes, they need not necessarily be de-identified (as defined below). Note that materials containing certain demographic information may not be considered anonymous depending on the size of the population from which the materials or data are derived.

Bank or Repository

A collection of human data and/or tissue/specimens collected and maintained for future research purposes. The bank should have written plans for distributing the stored data and/or specimens and may or may not intend to distribute the stored data and/or specimens to other research groups. Example a bank of biological specimens that are collected by clinicians within a department or section and used for their own research purposes.

Coded Material:

Data or specimens for which:

(1) private information (such as name or social security number) that would enable the investigator to ascertain the identity of the individual to whom the data, specimens, records, or other materials 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 information or specimens.

Donor –Subject:

A living individual from whom materials are obtained either through clinical or research intervention or interaction with the individuals.

De-identified Material:

Data, biological specimen or tissue that cannot be linked to a specific individual by either:

1) not including any of the 18 identifiers specified by HIPAA or

2) if a person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable: (i) applying such principles and methods, determines that the risk is very small that the Materials could be used, alone or in combination with other reasonably available information, by the researchers to identify an individual who is the origin of the Materials; (ii) documents the methods and results of the analysis that justify such determination; and (iii) provides that documentation to the IRB.

Materials are not considered de-identified if the researchers know that the materials could be used, alone or in combination with other information, to identify an individual who is the origin of the materials.

See also HIPAA Policy 5039, Use and Disclosure of De-Identified Information and of Limited Data Sets.

HIPAA

The Health Insurance Portability and Accountability Act of 1996 and implementing privacy and security regulations.

Human Subject or Human Participant

A living individual (1) about whom an investigator (whether professional or student) conducting research obtains either (a) data through intervention or interaction with the individual; or (b) identifiable private information; or (2) who is or becomes a participant in research involving drugs or devices, either as a recipient of a test article or as a control. Note that both human subject and human participant are used interchangeably in IRB policies and procedures. While the term “participant” conveys the voluntary nature of an individual’s agreement to participate in the research, it also can convey a sense of partnership which is not reflected in all types of research. In some cases, the research volunteer is in fact more acted upon than truly having any sense of partnership in the research. Hence the term subject is considered more appropriate in such cases.

Individually Identifiable

The identity of the research participant is or may readily be, ascertained by the investigator or associated with the information.

Limited Data Set

A subset of Protected Health Information (PHI) which removes all identifiers related to the individual who is the subject of the PHI, or of relatives, employers or household members of the individual except for one

or more of the following: town or city, State, zip code, dates, including dates of birth, death, and services. See also HIPAA Policy 5039, Use and Disclosure of De-Identified Information and of Limited Data Sets.

Materials

Data, films, biological specimens, or other recorded information that may be useful for research. Examples include vials of blood, medical records, tumor specimens, scans, and videotapes of interviews. Note that sources of “information” or “data” (e.g., facts contained in articles or books) are not affected by this policy because they do not identify any human subjects or contain PHI, or otherwise implicate any unique privacy concerns.

Recipient Investigator

A member of a research team who receives data and/or tissue/specimens from a repository for a single and defined research purpose under an approved protocol or as otherwise permitted by this policy.

Research

A clinical investigation or a systematic investigation, including research and development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Policy Sections

445.1 Research Utilizing Materials from Repositories Requiring IRB Review

Research activities require review by a Yale IRB when:

- Identifiable data or biological specimens stored in clinical, historical or other collections are used for research.
- Identifiable information is seen by the investigator in the source record but redacted or not recorded when gathering the data set for research purposes.
- Limited data set materials are withdrawn from repositories
- Previously coded materials become individually identifiable. (e.g., an investigator learns the identities of the sources of coded biological samples or data sets previously considered anonymous)
- Excess individually identifiable materials that were collected as part of the single IRB-approved protocol are used for a subsequent research project or secondary use not known when the materials were collected
- The utilization of de-identified, coded or anonymous materials for research is required by the repository retaining the material, or when the investigator believes journals or other publication entities will require proof of IRB review.

Requests for de-identified materials do not require documentation of IRB review, approval, exemption or not human subject determination because the project is not considered human subject research.

Research involving only coded materials will not be considered human research by the IRB as defined in 45 CFR 46.102(f), and hence will not require IRB review when the following are both met:

- a. The private information was not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; AND
- b. The investigator cannot readily ascertain the identity of the individual to whom the coded private information pertain because either:
 - i. The key to decipher the code is destroyed before research began, or

- ii. The investigators and the holder of the key enter into an agreement, such as the Internal Data Use Agreement, prohibiting the release of the key.

Determinations regarding whether the data/specimens are individually identifiable may be made by IRB members or staff or by an individual with appropriate training and knowledge of the requirements for de-identifying or making data anonymous. Principal Investigators should be aware that in some cases, journals or funding agencies may require documentation that the IRB, or someone other than the research investigator has determined the data/specimens to not be individually identifiable or de-identified and therefore not subject to IRB oversight.

445.2 Responsibilities of Recipient Investigators Utilizing Materials Stored in Repositories

Investigators wishing to obtain materials from a repository must abide by the operating and distribution conditions specified by the repository and must use the materials solely for the purpose indicated in the application to the IRB and/or repository. This need not, but may, include review and approval of the research by an IRB at the recipient's organization.

445.3 Informed Consent/Authorization Required for the Use of Materials

Consent for the use of materials stored in repositories must be consistent with the requirements noted in IRB Policy 200, and if applicable, for authorization in HIPAA Policy 5032. Consent and authorization for the use of the material may be obtained at the time the material is collected. The IRB will approve the use of such a consent method for future research when the research aim of the individual research project is consistent with types of research described to the subject-donor at the time the material was collected.

A. Waiver of Consent and Authorization

Prior consent and authorization for use of the material in future research may be waived by the IRB in accordance with federal regulations and Yale IRB Policy 200.3 and, if applicable, for waiver of authorization in HIPAA Policy 5032.

B. Re-Consent and Authorization

Re-contacting of donor-subjects for new consent may be required by the IRB when any of the following conditions apply:

- a) The use of the material is not consistent with the original purpose noted in the consent form used at the time the material was originally collected, or
- b) The use of the material falls out of society's mainstream thinking as acceptable; or
- c) The individual donating the material reaches the age of majority and the materials were stored by the donor-subject during his/her childhood,

If the IRB requires new informed consent/authorization, and the original informed consent does not include the donor-subject's permission for future contact, the materials cannot be distributed for new research projects.

C. Consent Not Required

Informed consent may not be required for use of the materials when the materials are truly unable to be tied to an individual.

445.4 Accessing Materials for Research From a Repositories

A. Access to Repositories Including Protected Health Information (PHI) for Pre-Research Activities:

Investigators wishing to access materials or databases for activities considered preparatory to research, e.g., determining sufficient statistical base, are required to provide an appropriate attestation of the activity to the Principal Investigator of the repository.

Appropriate attestations at Yale may be made using the Yale University/Yale-New Haven Hospital Request for Access to Protected Health Information for a Research Purpose Form.

B. Attestation and Documentation of IRB Review of Projects

Investigators should be prepared to provide documentation of IRB review, approval or exemption determination to the Principal Investigator or other person operating the repository when requesting to access or obtain materials.

The following Yale supported repositories require an attestation form in addition to documentation of IRB review when accessing materials.

Yale New Haven Hospital Medical Records: Yale University/Yale New Haven Hospital Request for Access to Protected Health Information for a Research Purpose Form.

Yale Medical Group: PBI Report Request Form for data requests out of IDX.

Yale University Cancer Data Repository (CaDR); Data Requests:
www.yalepath.org/CaDR/data.htm

Yale New Haven Hospital Request for Excess Clinical Samples; Request for Human Subjects Research Form; <http://medicine.yale.edu/labmed/research/testing/initiate.aspx#human>

Materials released to recipient investigators for IRB approved research will be assigned a unique code, unless permission is granted by the IRB to include specific identifiers. Recipient investigators who will have access to directly identifiable materials and who have been granted an exemption from the IRB are prohibited from recording the direct identifiers.

C. Use of Coded Materials

Investigators wishing to withdraw coded materials from repositories should be knowledgeable as to whether or not the repository requires review of the project by an IRB.. Documentation of IRB review may be required by some repositories or for publication in certain journals or other places.

The release of coded materials that retain a link(code) to identifiable information about the donor-subject require that the Principal Investigator of the repository assess that the proposed research is consistent with the scope of research described in the consent/authorization signed by the donor-subject at the time of collection. Release of coded materials also requires that the conditions noted in 445.1(a and b) above be met:

- a. the repository/bank determines that the research does not involve “human subjects” as described in section 400.1; and
- b. the recipient investigator will not be given the identifiable information linked to the material and signs an agreement not to access identifiers or attempt to ascertain the donor-subjects' identity; and

Operators of repositories or data management centers are prohibited from releasing the key to recipient investigators under any circumstances, until the individuals are deceased, or IRB approval is obtained for releasing the identifiable information.

D. Limited Data Sets

Requests from Yale researchers to use limited data sets containing PHI from databases and repositories owned by Yale University or its agents must utilize an Internal Data Use Agreement. Requests to use limited data sets containing PHI from researchers who are external to Yale, must use the Data Use Agreement as provided by Yale or the repository institution.

445.5 Ownership and Transfer of Materials

Investigators wishing to transfer materials outside of Yale must comply with Policy 730 Human Research Record and Biological Specimen Retention and Transfer.

Investigators who are permitted to take such materials elsewhere must provide an attestation that they would treat and work with the materials only in accord with the original consent and HIPAA research authorizations, grants and IRB approved protocols.

The transfer of biological specimens may also be subject to Material Transfer Agreements.

Investigators bringing in research materials previously collected at another institution and intended for future research purposes are required to establish a repository/bank subject to Yale IRB review and approval. See HRPP Policy 440.

Related Information

IRB Policy 100: IRB Review of Research

IRB Policy 200: Informed Consent for Human Research

440 PR 1: Development of Repositories for Research

HIPAA Policy 5039: Use and Disclosure of De-Identified Information and Limited Data Sets

Yale Medical Group: <http://ymg.yale.edu/administration/forms/>

Yale New Haven Hospital Request for Excess Clinical Samples; Request for Human Subjects Research Form; <http://medicine.yale.edu/labmed/research/testing/initiate.aspx#human>

Yale Medical Group: <http://ymg.yale.edu/administration/forms/>

Yale University Material Transfer Agreement

Yale University Research Authorization Form

Yale University/Yale-New Haven Hospital Request for Access to Protected Health Information for a Research Purpose Form.

Yale University Cancer Data Repository (CaDR); Data Requests: www.yalepath.org/CaDR/data.htm

Contacts

Questions can be addressed to:

Subject	Contact	Phone
Submitting protocol-specific conflicts of interest (Biomedical Research)	Human Investigation Committee	203.785.4688 www.yale.edu/hrpp
Submitting protocol-specific conflicts of interest (Social and Behavioral Research)	Human Subjects Committee	203.436.3650 www.yale.edu/hrpp

Roles and Responsibilities

Human Investigation Committee

The HIC I, HIC II, HIC III and HIC IV serve as the Institutional Review Boards or IRBs for biomedical human research conducted at Yale University.

Human Subjects Committee

The HSC is responsible for the review and oversight of social and behavioral research involving human subjects.

References:

National Heart, Lung and Blood Institute; Guidelines for Human Tissue Repository
<http://www.nhlbi.nih.gov/funding/policies/repos-gl.htm>

DHHS, Office for Protection from Research Risks (OPRR), Issues to Consider in the Research Use of Stored Data or Tissues, November 7, 1997
<http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm>

DHHS, Office for Human Research Protections (OHRP), Guidance on Research Involving Coded Private Information or Biological Specimens, October 16, 2008
<http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm>

Mark Barnes and Kathleen T. Uscinski, Secondary Uses of Data, PRIM&R Annual Conference, October 2004

Lawrence H. Muhlbaier and Kathleen T. Uscinski, Primer on Data and Specimen Repositories: How to Establish, Manage, and Be HIPAA Compliant. PRIM&R Annual Conference, November 2007

Partners Human Research Committee Policy on Research Tissue Banks/Repositories, November 9, 2005
 PHRC Policy on Research Tissue Banks/Repositories

UCSF Guide for the Research Use of Human Biological Specimens: Collecting, Banking and Sharing Specimens, May 2005

Revision History