

25.3 Research Involving Data and/or Biological Specimens

25.3.1 Overview

Storing data and/ or biological specimens for research and the use of data and/or biological specimens in research may require IRB approval (or exemption) and informed consent for any of the following:

- Data and/or biological specimens collected for research purposes
- Data and/or specimens collected, stored, and/or distributed for *future research uses*
- Previously collected data/specimens used for *secondary research*.

25.3.2 Definitions

Anonymous: Unidentified (i.e., personally identifiable information was not collected, or if collected, identifiers were not retained and cannot be retrieved); information or materials (e.g., data or specimens) that cannot be linked directly or indirectly *by anyone* to their source(s).

Coded: Direct personal identifiers have been removed (e.g., from data or specimens) and replaced with words, letters, figures, symbols, or a combination of these (not derived from or related to the personal information) for purposes of protecting the identity of the source(s); but the original identifiers are retained in such a way that they can be traced back to the source(s) by someone with the code. *Note: A code is sometimes also referred to as a “key,” “link,” or “map.”*

De-identified: All direct personal identifiers are *permanently* removed (e.g., from data or specimens), no code or key exists to link the information or materials to their original source(s), and the remaining information cannot reasonably be used *by anyone* to identify the source(s). *Note: For purposes of HRPP SOP, protected health information (PHI) is de-identified when it does not contain any of the 18 identifiers specified by the Health Insurance Portability and Accountability Act (HIPAA) at 45 CFR Part 164 or has been determined to be de-identified by a statistician in accordance with the standards established by the Privacy Rule. For more information, including the list of identifiers that must be removed to de-identify health information, see [HIPAA and Human Subjects Research](#).*

Repository: Also: **bank, database.** Collection of data and/or specimens obtained and stored for future research uses and/or distribution, including a collection not originally or primarily obtained for research purposes.

Specimen: Also: **sample.** Human biological material includes sub-cellular components such as DNA or RNA, Gametes (e.g., ova and sperm), embryos and fetal tissue, breast milk, exhaled air, including solid material (e.g., tissue, organs), body products (e.g., teeth, hair, nail clippings, sweat, urine, feces, saliva, semen, cerebrospinal fluid), blood and blood fractions (e.g. plasma, serum, buffy coat, red blood cells) and cells. Exceptions include organisms, such as bacteria and viruses isolated from human specimens are not human biological specimens

Leftover/Remnant Specimen: Remaining portion of a specimen obtained for clinical purposes that is no longer needed for its original purpose and that would otherwise be discarded.

Secondary Research: Study of existing information or materials (e.g., data or specimens) that have been previously collected for a purpose (including non-research purposes) other than the currently proposed activity.

25.3.3 General Information

Prospective collection of data and/or specimens for research purposes (e.g., additional questions added to routine surveys being performed for non-research purposes, an extra tube of blood taken at the time of clinical blood drawing, etc.) is “research involving human subjects,” and IRB review and approval is required. Informed consent (and HIPAA authorization for data that include PHI) must also be obtained.

Collection and storage of data and/or specimens for *future research uses* and/or distribution (i.e., rather than using data/specimens only for pre-defined analyses as described in a specific IRB-approved protocol) are activities that meet the definition of “research involving human subjects;” and IRB review and approval is required (see “Repositories – Collection, Storage, and/or Distribution of Data/Specimens” below). Informed consent (and HIPAA authorization for data that include PHI) is also required.

When the data and/or specimens to be stored for future research uses are generated as part of another research study (e.g., clinical trial), a separate protocol describing repository activities must generally be submitted for IRB review and approval before the protocol that collected the data and/or specimens is closed, unless the bank is externally controlled (see “Repositories – Collection, Storage, and/or Distribution of Data/Specimens” below). *Note: Sponsor-mandated data sharing may not require a stand-alone repository submission.*

In some cases, secondary uses of previously collected data and/or specimens meet the definition of “research involving human subjects,” and IRB approval or exemption is required (see “Secondary Uses of Previously Collected Data/Specimens” below).

Certain activities involving data and/or specimens do not meet the definition of “research involving human subjects” and do not require IRB approval or exemption, as described below.

25.3.4 Activities That Are Not Human Subjects Research

Laboratory research with *commercially available* tissue specimens, cell lines, or other human cells does not meet the definition of “research involving human subjects” and may

be performed without IRB approval or exemption as long as the work is not FDA-regulated (see “Research Subject to FDA Regulations” below).

Research with *autopsy* specimens does not meet the definition of “research involving human subjects” and may be performed without IRB approval or exemption. Research involving decedents’ PHI is subject to HIPAA regulations. HIPAA authorization (or waiver) is generally not required for use or disclosure of PHI for research involving decedents only, with appropriate representations from the researcher. For more information, contact the UVA Health System Privacy Officer at 434-924-5024.

Research with previously collected *anonymous* (see “Definitions” above) data and/or specimens does not meet the definition of “research involving human subjects” and may be performed without IRB approval or exemption *only* when the data/specimens to be studied were not collected specifically for the current research. Note: An investigator may not de-identify data and/or specimens under his or her control (e.g., data collected by the investigator for another study) for future research uses without IRB review.

Research with previously collected *coded* data and/or specimens does not meet the definition of “research involving human subjects” and may be performed without IRB approval or exemption *only* when **all** of the following conditions are met:

- The data and/or specimens to be studied were not collected specifically for the current research
 - Investigator(s) cannot “readily ascertain” the identity of the source(s) of the coded data or specimens because one or more of the conditions below is met:
 - 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 source individuals are deceased)
 - IRB-approved written policies and procedures for the repository or data coordinating center prohibit the release of the key to the investigators under any circumstances (until the source individuals are deceased).

Research with *leftover* specimens does not meet the definition of “research involving human subjects” and may be performed without IRB approval or exemption *only* when their use meets the conditions for *anonymous* or *coded* specimens above. Note: An investigator may not de-identify data and/or specimens under his or her control (e.g., specimens generated by the investigator from a clinical procedure) for future research uses without IRB review.

The research uses of previously collected data and/or specimens described above *may* be defined as “research involving human subjects” under FDA regulations and may require IRB approval and participant informed consent, depending on the nature of the research (see “Research Subject to FDA Regulations” below).

25.3.5 Exempt Research

Research involving *existing* data and/or specimens is exempt when **all** of the following conditions are met:

- All data and/or specimens are available, or “on the shelf,” at the time the research is submitted for an exempt determination
- The sources of the data and/or specimens are publicly available or the information is recorded by the investigator in a way that participants cannot be identified, directly or through identifiers linked to the participants
- The research is not subject to FDA regulations.

Note: An investigator may not de-identify data and/or specimens under his or her control (e.g., data collected by the investigator for another purpose or study) for future research uses without IRB review.

Prospective collection of biological specimens is not exempt from IRB review. Prospective data collection may be exempt in certain cases (e.g., some research qualifying under exempt category #1), depending on the nature of the data and population from whom the information is collected. For more information see HRPP SOP [[Exempt Research](#)].

25.3.6 Secondary Uses of Previously Collected Data/Specimens

IRB approval or exemption is required for secondary research uses of previously collected data and/or biological specimens, unless only *anonymous* or *coded* data/specimens are used as described above (see “Activities That Are Not Human Subjects Research”).

Secondary research uses of *non-research* collections of data/specimens (e.g., data or specimens that are retained for purposes other than research, such as clinical or educational records, archived pathology specimens, etc.) require IRB approval or exemption, as such collections have not been established as repositories with IRB-approved procedures for releasing materials that consider human subjects protection requirements.

Secondary (i.e., “new”) uses of data/specimens obtained for *primary research purposes* by an investigator with IRB approval (or exemption) require IRB review of an amendment or a new protocol describing the proposed secondary use, depending on the previous approval (or exemption) and the new research objective(s). Informed consent may also be required for this new use (as described below), depending on the scope of the original consent and the newly proposed research.

Research using previously collected data and/or specimens must be consistent with the scope and terms described in the original informed consent process/document, as applicable. If consent was not obtained (e.g., data/specimens obtained for non-research

purposes) or the original consent does not adequately include the proposed secondary use, specific informed consent for the new research may be required. De-identification or coding of data/specimens should not be used as a means for circumventing the original terms of consent. Except in unusual circumstances, informed consent is required when identifiable data and/or specimens are used.

Informed consent (and HIPAA authorization, when applicable) can be waived by the IRB for minimal risk non-exempt research with previously collected data and/or specimens when the research meets the regulatory criteria for waiver (see “Informed Consent Requirements” below).

Protocols for using previously collected data and/or biological specimens for research purposes should include the following information, as applicable:

- Purpose of using data/specimens
- Type(s) of data/specimens to be studied
- Source(s) and circumstances under which the data/specimens were collected
- State of the data/specimens to be obtained (i.e., identifiable or coded)
- If the data include individually identifiable protected health information
- Whether informed consent (and HIPAA authorization, when applicable) was obtained for collection and future use of data/specimens
- Physical location/equipment and security provisions for data/specimen storage
- Plan for destruction or de-identification of identifiable or coded data/specimens at the end of the retention period.

Investigators may not share data and/or specimens with collaborators (internal or external to UVA) for secondary research purposes without IRB approval. Distribution of data and/or specimens for secondary research uses beyond a single transfer described in a specific IRB-approved protocol generally requires approval for a repository (see “Repositories – Collection, Storage, and/or Distribution of Data/Specimens” below).

Confidential disclosure agreements (CDAs), data use agreements (DUAs), or material transfer agreements (MTAs) may be required for sharing research data or specimens with non-UVA collaborators. For more information and signatory authority, see or contact the UVA OSP office or the School of Medicine Grants and Contracts Office if within the School of Medicine

Access to and/or use of identifiable patient information from medical records or clinical databases for research purposes must comply with the requirements of the HIPAA Privacy and Security Rules and university policy [e.g., [University Hospital Policy 09-11: Use of Patient Information by Hospitals and Medical Staff](#)]. For more information, contact the UVA Health System Privacy Officer at 434-924-5024.

The proposed use of student education records in research must comply with the requirements of the [Family Educational Rights and Privacy Act \(FERPA\)](#). For information about the release of student records at UVA, see [Privacy and Release of Student Education Records](#) or contact the Office of the IRB for Social & Behavioral Research at 434-243-2915 or the Office of the University Registrar at 434-924-4122.

25.3.7. Repositories – Collection, Storage, and/or Distribution of Data/Specimens

Data and specimen repositories/banks may range from materials held by a single investigator in his/her office or laboratory to large networks with central coordinating centers. Although the size, purpose, types of information and materials stored, and populations from whom the data/specimens are collected may also vary widely, creating a data and/or specimen bank for *future research purposes* (i.e., rather than using data/specimens only for pre-defined analyses as described in a specific IRB-approved protocol) is defined as “research involving human subjects;” and IRB review and approval is required.

Informed consent is required for collection of data and/or biological specimens to be stored for future research (see “Informed Consent Requirements” below). HIPAA authorization is also required when the data include protected health information.

Banking should be understood as the collection and storage of biological samples for future undefined research.

Caution should be taken when requiring participants to agree to the banking of their tissue for future undefined research or for research unrelated to the study at hand as a condition for entry into a trial that offers the potential participant the prospect of some direct benefit. Mandatory banking may be more acceptable if the future research will be related to disease process under study.

The final determination as to whether the proposed mandatory banking for future unrelated research is acceptable will be made by the IRB on a case by case basis.

Protocols for creating data and/or biological specimen repositories for research purposes should include the following information, as applicable:

- Purpose of collecting and storing data/specimens
- Type(s) of data/specimens to be collected and stored
- Source(s) and circumstances of data/specimen collection (i.e., obtained directly from participants or from a secondary source)
- How the data/specimens will be stored (i.e., identifiable, coded, or de-identified)
- If the data include individually identifiable protected health information
- Physical location/equipment and security provisions for data/specimen storage

- Length of time data/specimens will be stored
- Any limits on data/specimens' intended future use (e.g., for cancer research only)
- With whom data/specimens may be shared (including non- UVA researchers)
- Process for requesting and releasing data/specimens
- How data/specimens will be released (i.e., identifiable, coded, or de-identified)
- Procedures to withdraw participants' data/specimens from future research
- Plan for continuing repository operations in the absence (or departure) of the principal investigator
- Process for destruction or de-identification of identifiable or coded data/specimens at the end of the retention period.

Consideration should be given to obtaining a National Institutes of Health (NIH) Certificate of Confidentiality to protect the confidentiality of banked identifiable or coded data/specimens. Certificates of Confidentiality are intended to protect information that, if disclosed, could have adverse consequences for research participants or damage their financial standing, employability, insurability, or reputation. Examples include information about the following:

- Sexual or gender preferences or practices,
- Misuse of alcohol, drugs, or other addictive products,
- Illegal conduct
- Sensitive information pertaining to mental illness,
- Sensitive genetic information.

For more information about Certificates of Confidentiality, see “NIH Certificates of Confidentiality” in HRPP SOP [[Privacy and Confidentiality](#)] or NIH “[Certificates of Confidentiality Kiosk](#).”

Methods for handling and storing data (including the use of personal computers and portable storage devices) must comply with university policies. Restricted data, including protected health information, must be encrypted if stored or used on portable devices, if removed from a secure university location, or if electronically transmitted. For more information, see the [UVA Electronic Data Removal Policy](#) and [UVA Electronic Storage of Highly Sensitive Data](#) Policy.

Investigators and IRBs should consider when research involving the collection and storage of personally identifiable information (i.e., information that can be used to distinguish an individual's identity, such as name, social security number, date of birth, etc., or information linked to an individual, such as medical, financial, or employment information) might expose research participants to the risk of fraud or identity theft. This is especially important in research linked to “fee-for-service” activities, where federal financial regulations for protecting consumers against identity theft may apply. In such cases, plans for handling and storing

personally identifiable information must comply with university policy and Federal Trade Commission rules. For more information, see the [UVa Data Protection Standards](#).

Medical Center Policy # 0119] stipulates that unless specifically exempted from evaluation by the Operating Room Committee, all human tissue and objects/ devices obtained by surgical procedure, traumatic excision, or disease associated sequelae (e.g., vascular auto-amputation) from a patient in any area of the Medical Center, including the Main Operating room, the Outpatient Surgery Center, ambulatory clinics, the Emergency Department, and any procedural area shall be sent to the University of Virginia Department of Pathology for evaluation prior to any substantive treatment, including but not limited to, surgical procedures or radiation therapy. The Operating Room Committee does exempt the requirement for pathology examination of diagnostic surgical tissue/specimens prior to collection of these materials for research purposes if the subject has signed consent.

25.3.8. Informed Consent Requirements

Informed consent must be obtained for collection and storage of data and/or biological specimens for future research and should generally be obtained separately from consent to other research participation. HIPAA authorization is also required when the data include protected health information. For more information on the requirements for obtaining and documenting informed consent, see HRPP policies [] and [].

Investigators and IRBs should balance the ethical obligation to provide sufficient information regarding possible *future research uses* of stored data and/or specimens during the consent process for banking with the practical issues of trying to anticipate and describe all possible research uses of these materials. However, the consent process for collecting and banking data and/or specimens should be as specific as possible regarding the circumstances and any risks associated with data/specimen collection, as well as the procedures for maintaining the security and confidentiality of the stored materials. In addition to the required elements of informed consent, the consent process should include the following information, as applicable:

- Description of the data/specimens to be collected and how they will be obtained
- Any risks associated with obtaining the data/specimens
- How the data/specimens will be used (to the extent known) • Any limits on data/specimens' intended future use (e.g., for cancer research only)
- Whether any identifying information will be retained, and if so, how it will be stored
- Certificate of Confidentiality information (when a Certificate is obtained)
- Description of the repository, including physical location, security procedures, etc.
- Who will have access to the data/specimens
- How long the data/specimens will be stored

- With whom data/specimens may be shared (including non-UVA researchers)
- How to withdraw data/specimens from future research
- Whether or not participants may be re-contacted in the future (e.g., for consent to future research, to return research results, etc.).

HIPAA allows UVA to provide identifiable patient data or specimens (PHI) to a sponsor/grantor (with appropriate consent/authorization or waiver) in return for payments in the form of grants or contracts for UVA to perform research activities, because any provision of PHI to the sponsor/grantor is a byproduct of the service being provided to the sponsor/grantor. However, a disclosure of PHI to an outside entity where no research is being performed by UVA in exchange for the payment would be considered a “sale of PHI,” for which UVA must have a signed authorization from the patient that discloses the payment, unless the payment is only a reasonable cost-based fee to cover the cost to prepare and transmit the data and the PHI consists only of a “Limited Data Set” covered by a Data Use Agreement or is provided under a waiver of authorization granted by an IRB. For questions, contact the UVA Office of University Counsel at 434-924-3586.

When identifiable specimens and/or genetic information are stored and may be released for future research, the consent process/document should also include language describing the protections provided by the Genetic Information Nondiscrimination Act. For specific language, see the consent form templates from Protocol Builder.

The informed consent process/document must not include any exculpatory language through which subjects are made to waive or appear to waive any legal rights regarding the collection or use of their data and/or specimens. For more information see HRPP SOP [[Informed Consent Process and the Elements of Informed Consent](#)].

Research using previously banked data and/or specimens should be consistent with the scope and terms described in the original informed consent process/document, as applicable. If consent was not obtained (e.g., data/specimens obtained for non-research purposes) or the original consent does not adequately include the proposed secondary use, specific informed consent for the new research may be required. Except in unusual circumstances, informed consent is required when identifiable data and/or specimens are used.

Informed consent (and HIPAA authorization, when applicable) can be waived by the IRB for minimal risk non-exempt research with previously collected data and/or specimens when the research meets the regulatory criteria for waiver. Waiver of HIPAA authorization can also be granted (when applicable) by the Privacy Board for secondary uses of existing data and/or specimens in exempt research. For more information on waiver of informed consent, see HRPP SOP sections 11.9: Waiver of Informed Consent and 23: Health Insurance Portability and Accountability Act (HIPAA).

25.3.9. Research Subject to FDA Regulations

Activities involving data and/or specimens that do not require IRB approval under DHHS regulations (see “Activities That Are Not Human Subjects Research” above) must still receive IRB approval if the activities are subject to FDA regulations (e.g., involving FDA-regulated products or submission of data/results to FDA). Activities with data and/or specimens defined by FDA as “research involving human subjects” include testing of *in vitro* diagnostic devices using biological specimens and the use of clinical data for historical “controls” in investigational drug studies.

FDA regulations do not permit waivers of the informed consent requirements in research, except for emergencies (i.e., emergency use of a test article or emergency research) or in certain types of military research. However, under specific circumstances *in vitro* diagnostic device studies may be performed with biological specimens without informed consent, as described below.

FDA intends to exercise “enforcement discretion” regarding the requirements for informed consent in an *in vitro* diagnostic device study involving biological specimens when **all** of the following criteria are met:

- The study meets the IDE exemption criteria
- The study uses leftover/remnant specimens, specimens obtained from repositories, or unused specimens that were previously collected for other research purposes
- The specimens are not individually identifiable
- Clinical information accompanying the specimens does not make the specimen source identifiable
- Individuals caring for the patients from whom the specimens were obtained do not share information with the investigator(s)
- Specimens are provided to the investigator(s) without identifiers, and the supplier has established policies to prevent the release of personal information
- The study has been reviewed and approved by an IRB.

For more information see FDA [“Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable.”](#)

25.3.10. Applicable Regulations/Guidance

- FDA “Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable”(04/25/06);
- National Bioethics Advisory Commission “Research Involving Human Biological Materials: Ethical Issues and Policy Guidance” (08/99);

- NIH “Research Repositories, Databases, and the HIPAA Privacy Rule” (07/02/04); OHRP
- “Guidance on Research Using Coded Private Information or Specimens” (10/16/08);
- OHRP “Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards” (03/24/09);
- OHRP “Issues to Consider in the Research Use of Stored Data or Tissues”(11/07/97);
- “Report of the Public Responsibility in Medicine and Research (PRIM&R) Human Tissue/Specimen Banking Working Group”(03/07);
- The Secretary’s Advisory Committee on Human Research Protections (SACHRP)“FAQs ,Terms, and Recommendations on Informed Consent and Research Use of Biospecimens” (07/20/11)