



# Stratton VA Medical Center IRB Standard Operating Procedure: Collection, Banking and Use of Human Biological Specimens for Research Purposes

## PURPOSE

This SOP establishes policies and procedures for the collection of human biological specimens for research purposes, the reuse of previously collected research specimens, and the storage of human biological specimens for future research use. It also addresses the collection and storage of clinical data that may be linked to those human biological specimens. This SOP applies to all such activities that are carried out at Stratton VAMC or by persons acting under the authority of the Stratton VAMC.

## SCOPE

- The availability of human biological specimens for research is crucial for the advancement of medical knowledge and for understanding, diagnosing, and treating diseases that affect the veteran population. This SOP is intended to provide Stratton VAMC investigators with policy and guidelines regarding the collection, banking, and use of banked human biological specimens.
- The provisions of this SOP apply to all research that is conducted completely or partially at Stratton VAMC facilities, conducted in approved off-site locations and facilities, and/or conducted by Stratton VAMC researchers while on VA official duty time. The research may be VA-funded, funded from extra-VA sources, or conducted without direct funding. The same policies are applicable to veteran and non-veteran subjects.

## DEFINITIONS

- For the purposes of this SOP, the following definitions are used and listed alphabetically.
  - **Approved Research Protocol.** The detailed specification of a particular research activity that has been reviewed and approved by the Stratton VAMC oversight committee(s), including the Institutional Review Board (IRB) and Research and Development (R&D) Committee.

- **Banked Specimen.** A specimen and its related biomaterial (e.g., DNA) collected and stored for future research purposes that are not specified in the original research protocol or collected under a protocol designed only to collect specimens is considered a “banked specimen”. Also included in this category is a specimen and its related biomaterial that is collected under a particular protocol but reused for a new research protocol, or a specimen that remains after the research protocol under which it has been collected terminates.
- **Biorepository.** A place or unit that stores human biological specimens and exercises control over access to those specimens. It may also store linked clinical and demographic data including individually identifiable health information.
- **Biorepository Director.** The person with overall responsibility for managing the biorepository.
- **Case Report Form.** A printed or electronic document designed to record all of the protocol-required information to be reported on each study subject.
- **Clinical Trial.** Biomedical or health-related research study in human beings that follows a pre-defined protocol.
- **Coded.** Coded means that (i) 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 (ii) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens. For Stratton VAMC, the code must not include any of the 18 HIPAA identifiers and must not be derived from one of the HIPAA identifiers.
- **Common Rule.** The Federal Policy for the Protection of Human Subjects adopted by Federal departments and agencies conducting or supporting human subjects research. The Common Rule is codified for VA at 38 CFR Part 16.
- **Confidentiality.** The prevention of unauthorized disclosure of personal information pertaining to a research subject.
- **Data Use/Data Transfer Agreement.** A written agreement between the provider and the recipient of data that are transferred from one to the other. It defines what data may be used, who may

access and use the data, how the data must be stored and secured, and how the recipient will dispose of the data after completion of the research.

- **De-identified Data.** Data that meet the HIPAA Privacy Rule (45 CFR 164.514(b)), VHA Handbook 1605.1, and the Common Rule (38 CFR Part 16) definitions of de-identified.
- **Genetic Testing.** The analysis of deoxyribonucleic acid (DNA), ribonucleic acid (RNA), chromosomes, proteins, or certain metabolites that convey information about a person's genotype.
- **HIPAA.** The acronym HIPAA means The Health Insurance Portability and Accountability Act of 1996 (HIPAA).
- **HIPAA Authorization.** Written permission for use and disclosure of protected health information (PHI) from the information's source person/research subject or legally authorized personal representative, as required under law, including the HIPAA Privacy Rule. The written permission is documented on an authorization form.
- **Human Biological Specimens.** Human biological specimens are defined as materials derived from living human subjects, such as blood, urine, tissue, organs, hair, nail clippings, buccal swaps or any other materials that are either collected specifically for research purposes or as residual specimens from diagnostic, therapeutic or surgical procedures.
- **Informed Consent.** Free and knowledgeable agreement to participate in research as required under the human subject protection regulations at 38 CFR 16.116. The written document approved by the Institutional Review Board (IRB) is sometimes referred to as the informed consent form and, when signed by a research subject, the written informed consent. Also see guidance at: [http://www.research.va.gov/programs/tissue\\_banking/Non-profit-Informed-Consent.pdf](http://www.research.va.gov/programs/tissue_banking/Non-profit-Informed-Consent.pdf)
- **Institutional Review Board (IRB).** Committee responsible for the review, approval, and continuing oversight of research involving human subjects in accordance with 38 CFR Part 16 and VHA Handbook 1200.05.
- **Interventional Clinical Trial.** Studies in which the research subjects are assigned by the investigator to a treatment or other intervention and their outcomes are measured.

- **Limited Data Set.** Data that meet the HIPAA Privacy Rule (45 CFR 164.514(e) definition of a limited data set. See Appendix B.
- **Materials Transfer Agreement.** An agreement describing the material (such as human biological specimens) to be transferred. It states that the owner grants the recipient access to the material and the rights to use it for a specified purpose, within the recipient's facilities, and by a specified researcher or group. It also specifies what happens to the material once the research is completed.
- **Minimum Necessary.** Minimum amount of protected health information necessary for the intended purpose.
- **New Use.** The use of human biological specimen for purposes not specifically defined in the research protocol under which the specimen was collected, the use of a specimen collected under a protocol designed to bank specimens, or the use of human biological specimen collected for general medical care for research purpose. This is sometimes termed “reuse.”
- **Non-banked Human Biological Specimens.** Specimens collected under a Stratton VAMC approved research protocol and used for the specific objectives outlined in the approved research protocol and are destroyed when the specific test/analysis is complete or at the termination of the research project.
- **Principal Investigator (PI).** Qualified person or persons designated by an applicant institution to direct a research project or program and who usually writes the grant application. The PI oversees scientific and technical aspects of a grant and the day-to-day management of the research. In the event of an investigation conducted by a team of individuals, the PI is the responsible leader of that team. (FDA considers Investigator and Principal Investigator to be synonymous.) A Stratton VAMC Principal Investigator must hold at minimum a paid 5/8ths VA appointment. *Note: To meet special needs of Stratton VAMC, exceptions to this requirement are considered on a case-by-case basis. Such requests must be submitted by the medical center Director with the endorsement of the ACOS/R&D and the Chief of Staff in a letter to the CRADO.*
- **PI-dedicated Biorepository.** A biorepository where the PI is collecting and banking specimens only for his/her studies and specimens will not be shared with researchers other than his co-investigators.

- **Privacy Board.** A Privacy Board is a review body that may be established to act upon requests for a waiver or an alteration of the Authorization requirement under the Privacy Rule for uses and disclosures of protected health information (PHI) for a particular research study. A Privacy Board may waive or alter all or part of the Authorization requirements for a specified research project or protocol. A covered entity may use and disclose PHI, without an Authorization, or with an altered Authorization, if it receives the proper documentation of approval of such alteration or waiver from a Privacy Board.
- **Protected Health Information (PHI).** PHI is individually identifiable health information maintained in any form or medium.  
*Note: PHI excludes health information in employment records held by a covered entity in its role as an employee.*
- **Research and Development (R&D) Committee.** The committee responsible for oversight of the Stratton VAMC facility's research program under VHA Handbook 1200.01.
- **Research Protocol.** The formal written plan for conducting a research investigation, including but not limited to biomedical, behavioral, social, health service, or educational research investigations, as well as clinical trials.
- **Shared Biorepository.** A biorepository where specimens are collected and banked for one or more researchers and shared with other researchers inside or outside of the VA
- **Specimen.** Biological material stored in a biorepository (tissue bank).
- **VA Investigator.** Any individual who conducts research approved by the Stratton VAMC Research and Development Committee while acting under a VA appointment, including full and part-time employees, without compensation (WOC) employees, and individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA) of 1970. A VA investigator must comply with all applicable VA and VHA regulations and policies.

## NON-BANKED HUMAN BIOLOGICAL SPECIMENS

- Human biological specimens collected under a Stratton VAMC-approved research protocol are **not** considered “banked specimens” if the specimens are
  - Used only for the specific tests/analyses outlined in the approved research protocol and informed consent and
  - Destroyed when the specific tests/analyses are complete or at the termination of the research project.
- Any new use of non-banked specimens or samples may not occur unless the institutional review board (IRB) and Research and Development (R&D) Committee have approved that use through a new protocol or an amendment to the original protocol. The informed consent under which the specimens were collected must be consistent with the new use.
  - New consent must be obtained if the original consent does not allow for new use.
  - A written HIPAA authorization must be obtained also unless all criteria are met for waiver of the HIPAA authorization by the IRB or a Privacy Board.
- **NOTE:** *If the new use is under a new protocol, the specimen then becomes a banked specimen. See section 5.*
  - Non-banked specimens must be labeled with a code that does not contain any of the 18 HIPAA identifiers or is not derived from one of the HIPAA identifiers (see Appendix A). The coding method, as well as other means to protect confidentiality, should be defined in the protocol reviewed by the responsible IRB and R&D Committee. The key to the code must not leave the Stratton VAMC.
  - All applicable VA policies and procedures must be followed.
  - If non-banked specimens are sent to an institution outside of the Stratton VAMC for tests/analyses, then the following additional rules apply:
    - The PI of the protocol collecting specimens must hold at minimum a paid 5/8ths VA or obtain a waiver from the Chief Research and Development Officer.

- The remainder of the specimen must be destroyed or returned to VA for destruction after the specific tests/analyses have been performed.
- If the specimen is destroyed at the non-VA site, a certification of destruction for each individual sample must be obtained for the VA study files. This notification must be sent to the principal investigator (PI) on at least a quarterly basis.
- If the non-VA entity is a non-profit institution (e.g., university, private research organization) or other government agency (e.g., National Institutes of Health, Department of Defense) and if the specimens are outside of the VA for 5 or more years while awaiting or undergoing analyses, then the study must be registered with the VA Office of Research and Development (ORD). See the guidance document found at [http://www.research.va.gov/programs/tissue\\_banking/non-profit.cfm](http://www.research.va.gov/programs/tissue_banking/non-profit.cfm) for the registration form.
- If non-banked specimens are sent outside of the VA to a **for-profit institution for greater than 90 days for research** tests/analyses, then the following additional rules apply:
  - The PI must obtain a waiver before any specimens leave the VA facility. The procedures for applying for a waiver can be found at <http://www.va.gov/vaforms/medical/pdf/10-0474-fill.pdf> .
  - At the time of continuing review, the PI must provide yearly updates to the Stratton VAMC facility's research office, which will forward them to ORD. See the guidance document found at [http://www.research.va.gov/programs/tissue\\_banking/for-profit.cfm](http://www.research.va.gov/programs/tissue_banking/for-profit.cfm) for details.
  - Any data sent to the for-profit institution must be de-identified according to the HIPAA Privacy Rule (45 CFR 164.514(b)), VHA Handbook 1605.1, and the Common Rule (38 CFR Part 16) definitions of de-identified.
  - Case report forms may not contain any code derived from a HIPAA identifier, including initials and scrambled social security numbers, if they leave the Stratton VAMC.

- In addition to conforming to the requirements in Appendix C of VHA Handbook 1200.05, the informed consent under which the specimens are collected must
  - Be written in lay language in a way that the purpose and procedures are clear and transparent.
  - Include the elements listed in the guidance document found at [http://www.research.va.gov/programs/tissue\\_banking\\_for-profit.cfm](http://www.research.va.gov/programs/tissue_banking_for-profit.cfm) .
- The HIPAA authorization must have an expiration date. That date should be the shortest interval possible needed to collect follow-up data but cannot be more than 10 years after the date of the subject's enrollment.
- Specimens must be destroyed within 1 year of the study completion date.
- During the study (prior to mandatory destruction), a subject may request that his/her specimens(s) be destroyed. The Stratton VAMC PI will send the subject's code to the for-profit institution, and the company will confirm the destruction in writing.
- Whenever possible, aggregate results should be made available to the subjects during and/or after the study.
- If a research monitor or a pharmaceutical company needs access to electronic health records in VISTA, current Stratton VAMC policies and procedures must be followed.
- Individual raw genetic data (e.g., sequence, single nucleotide polymorphisms) from veteran subjects must be destroyed within 1 year of the study completion date.
- If the institution is in a foreign company, the study may be considered international research and require a waiver. See VHA Directive 2005-050 for details.
- If non-banked specimens are sent outside of the Stratton VAMC to a **for-profit reference laboratory** to confirm diagnosis/eligibility or to perform safety tests (i.e., for non-research analyses) for a research study, then the rules in section 4.f. do not apply. The use

and destruction of these specimens should be explicitly stated in the protocol, contract, or in a materials transfer agreement.

## **BANKED HUMAN BIOLOGICAL SPECIMENS**

- Human biological specimens collected and stored for future research purposes that are beyond the scope of work described in the original protocol or those collected under a protocol designed for banking of specimens are considered banked human biological specimens. Those specimens must be collected under a Stratton VAMC-approved protocol, including an informed consent process and written HIPAA authorization when required, that allows for such future use. Specimens collected under a protocol designed to collect human biological specimens for future research are considered banked specimens as soon as the specimens are obtained.
- **On-Site Biorepositories**
- On-site biorepositories include biorepositories (places that store human biological specimens and exercise control over access to those specimens) at the investigator's Stratton VAMC, another VA Medical Center with an established tissue bank, or at the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC) core laboratory at the VA Boston Healthcare System, which serves as the Cooperative Studies Program (CSP) Genetic Tissue Core Laboratory.
- There are two types of on-site biorepositories. One is where the PI is collecting and banking specimens only for his/her studies and specimens will not be shared with researchers other than his co-investigators (PI-dedicated biorepository). The second is where specimens are collected and banked for one or more researchers and shared with other researchers inside or outside of the VA (shared biorepository).
  - **The following apply to a VA PI-dedicated on-site biorepository:**
    - The VA PI serves as the biorepository director.
    - A PI-dedicated biorepository established at a Stratton VAMC site by a Stratton VAMC PI must be approved by the ACOS/R&D or designated person in the Stratton VAMC facility's research office.
    - In addition to the protocol(s) under which the specimens are collected, the PI must establish a banking protocol, which must undergo continuing review at least annually by the IRB and R&D Committee.

- At the time of continuing review, the PI must provide annual updates to the Stratton VAMC facility's research office, which will forward them to ORD. See the guidance document found at [http://www.research.va.gov/programs/tissue\\_banking/non-profit.cfm](http://www.research.va.gov/programs/tissue_banking/non-profit.cfm) and [http://www.research.va.gov/programs/tissue\\_banking/Tissue-Banking-FAQ81409.pdf](http://www.research.va.gov/programs/tissue_banking/Tissue-Banking-FAQ81409.pdf) for details.
- The biorepository must undergo an annual compliance audit by the Stratton VAMC facility's Research Compliance Officer. The results of the audit must be sent to the Office of Research and Development and the Office of Research Oversight. See the guidance document referred to in this SOP.
- In addition to conforming to the requirements in Appendix C of VHA Handbook 1200.05, the informed consent under which the specimens are collected must
  - Be written in lay language in a way that the purpose and procedures are clear and transparent.
  - Include the elements listed in the guidance document found at [http://www.research.va.gov/programs/tissue\\_banking/Tissue-Bank-Operations-Sheet.pdf](http://www.research.va.gov/programs/tissue_banking/Tissue-Bank-Operations-Sheet.pdf) .
- Banked specimens must be labeled with a code that does not contain any of the 18 HIPAA identifiers or is not derived from one of the HIPAA identifiers (see Appendix A). The coding method, as well as other means to protect confidentiality, should be defined in the protocol reviewed by the responsible IRB and R&D Committee. The key that links the code to the subject's identity must be maintained at the Stratton VAMC in a locked file cabinet or in a password-protected electronic file.
- Specimens must be destroyed upon the subject's request.
- Upon IRB approval, the PI may destroy specimens when they are no longer of scientific value.
- Identifiable data linked to the specimens must be stored at the Stratton VAMC in a locked file cabinet or in a password-

protected electronic file. Genetic sequence data should be treated as identifiable data.

- If data linked to the specimens contain any of the 18 HIPAA identifiers or a code derived from them and are transferred outside of the Stratton VAMC to a co-investigator, as necessitated by the protocol, then the external database must be encrypted according to FIPS 140-2 standards.
- The following biorepository best practices must be followed:
  - Specimens must be stored in a secure location that has limited access. The room or freezers should be locked when not in use.
  - The PI should maintain records of all specimens deposited in the bank, including type of specimens; the dates specimens were banked; and copies of the protocols, including the consent form under which specimens were collected.
  - In the event of power failure, a backup generator or dry ice should be available. In the event of a freezer failure liquid nitrogen storage or dry ice should be available.
- All applicable Stratton VAMC policies and procedures must be followed.
- If the biorepository closes (for example, PI does not receive funding for additional studies), then the specimens must be destroyed.

#### **ROLE AND RESPONSIBILITIES OF THE RESEARCH COMPLIANCE OFFICER**

The research compliance officer is responsible for performing annual compliance audits of both PI-dedicated and shared on-site biorepositories and forwarding the results of the audit to ORD and the Office of Research Oversight.

#### **ROLE AND RESPONSIBILITIES OF THE IRB**

- The IRB of record for the Stratton VAMC facility that houses the on-site biorepository is the IRB responsible for the biorepository.

- This IRB is responsible for the following:
  - Complying with all requirements in VHA Handbook 1200.05
  - Conducting review of the biorepository's banking protocol and activities at least once a year.
- This IRB is not responsible for approving individual research protocols that propose to use data from the biorepository unless one or more of the investigators is from the same VA facility that houses the biorepository.
- The IRB is responsible for ensuring that all elements listed in the guidance document found at [http://www.research.va.gov/programs/tissue\\_banking/Tissue-Bank-Operations-Sheet.pdf](http://www.research.va.gov/programs/tissue_banking/Tissue-Bank-Operations-Sheet.pdf) and [http://www.research.va.gov/programs/tissue\\_banking/Non-profit-Informed-Consent.pdf](http://www.research.va.gov/programs/tissue_banking/Non-profit-Informed-Consent.pdf) are included in the for all protocols that it reviews that involve
  - Banking human biological specimens at on-site or off-site biorepositories
  - Non-banked human biological specimens that are sent outside of the VA to a for-profit institution for greater than 90 days for research test/analyses.

#### **ROLE AND RESPONSIBILITIES OF THE R&D COMMITTEE**

- The R&D Committee of record for the Stratton VAMC facility that houses the biorepository is responsible for oversight of the biorepository.
  - The R&D Committee is responsible for conducting a review of the biorepository's banking protocol and activities at least once a year.
  - The R&D Committee is not responsible for approving individual research protocols that propose to use specimens from the biorepository unless one or more of the investigators is from the same Stratton VAMC facility that houses the biorepository.

#### **ROLE AND RESPONSIBILITIES OF THE INVESTIGATOR**

- The Stratton VAMC investigator is responsible for obtaining a waiver
  - Prior to banking human biological specimens outside of the Stratton VAMC.
  - Prior to sending non-banked specimens outside of the Stratton VAMC to a for-profit institution for greater than 90 days for research test/analyses
- The Stratton VAMC investigator is responsible for obtaining approval from the ACOS/R&D prior to establishing a PI-dedicated or shared on-site biorepository.

## **Appendix A: The Eighteen HIPAA Identifiers**

1. Names and initials
2. All geographic subdivisions smaller than a state
3. All elements of dates (except year) and all ages over 89
4. Telephone numbers
5. Fax numbers
6. E-mail addresses
7. Social security numbers or parts of them, scrambled or unscrambled
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web URLs
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including fingerprints and voiceprints
17. Full-face photographic image
18. Any other unique identifying number

## **Appendix B: Direct Identifiers That Must Be Excluded From a Limited Data Set**

1. Names and initials
2. Postal address information, other than town or city, state, and zip code
3. Telephone numbers
4. Fax numbers
5. E-mail addresses
6. Social security numbers or parts of them, scrambled or unscrambled
7. Medical record numbers
8. Health plan beneficiary numbers
9. Account numbers
10. Certificate/license numbers
11. Vehicle identifiers and serial numbers, including license plate numbers
12. Device identifiers and serial numbers
13. Web URLs
14. Internet Protocol (IP) address numbers
15. Biometric identifiers, including fingerprints and voiceprints
16. Full-face photographic image