



# Banking/Storing Biospecimens: VA Institutional and IRB Issues and Considerations

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# Objectives

- Identify issues related to the storage and banking of de-novo collected specimens
  - Discuss the difference between “banking” and “storing” biospecimens
  - Identify when a biorepository is a VA biorepository vs. a non-VA biorepository
  - Define a “shared” biorepository” and identify common configurations
  - Discuss IRB and Institutional considerations when reviewing research involving biospecimens

# “Banking” vs. Storing” Biospecimens

## BANK



Associated with reuse of biospecimens  
in future research (reuse)

## STORAGE UNIT



Usually associated with current  
study only (no reuse)

1. A VA Investigator states in his or her research protocol that after biospecimens are drawn and analyzed, the biospecimens will be placed in his or her lab for 10 years.

**Answer: Storage**

2. A VA Investigator is conducting an industry-sponsored clinical trial involving 102 VA and non-VA sites involving the collection of biospecimens. The biospecimens are sent to a central lab for analysis within 24 hours of obtaining the biospecimen from the subject. The remaining biospecimen aliquots are sent to the industry sponsor for the remainder of the 5 year study and then will be used for future biospecimen studies.

**Answer: Storage and Banking**

3. A VA Investigator is conducting a single site research study involving collection of a single biospecimen for DNA analysis. Neither the informed consent document nor the research protocol states what will happen to the biospecimens after the analysis.

**Answer: Insufficient Information**

## Banking or Storing Biospecimens

- Understanding the disposition of biospecimens is a critical IRB and institutional consideration when evaluating the activity.
  - Banked for future use
  - Stored for specified period
  - Destroyed
- Sometimes the protocol or informed consent document is not clear or in conflict with each other and/or a clinical trial agreement (if an agreement is required) and the conflict must be resolved.
  - Example: Protocol states that biospecimens sent to the industry-collaborator will be placed in a biorepository for future use;
  - Informed consent document states that all biospecimens obtained and analyzed for the study will not be reused; and the
  - Clinical trial agreement states that biospecimens will be reused by the industry collaborator as agreed to in the subject's informed consent document.

## Identify when a Biorepository is a VA Biorepository vs. a non-VA Biorepository

- Applicable VA Policy Statement
  - VA research is research that is conducted by VA investigators (serving on compensated, WOC, or IPA appointments) while on VA time. The research must be approved by the R & D Committee before it is considered VA research and before it can be initiated.  
*VHA Handbook 1200.02, Paragraph 3(g)*
- VA only has authority over that which is approved as VA research
  - Example: A VA Investigator is conducting a clinical trial on his/her VA time. It must be approved as VA research.
- VA does not have authority over non-VA research
  - Example: A Dual-Appointment Physician is conducting a clinical trial at his/her University on his University time. No VA time is involved. Some research subjects are recruited by the Dual-Appointed Physician who are also Veterans, but there is no active recruitment at the VA. This activity is not VA research.

## Identify when a Biorepository is a VA Biorepository vs. a non-VA Biorepository

- Key Considerations to differentiate a VA Biorepository vs. a Non-VA Biorepository:
  - Where are the biospecimens located?
  - Who has control over accessing the biospecimens in the biorepository?
  - Who will be held accountable for any biospecimens lost or misused which are placed in the biorepository?
  - Who is responsible for the operating procedures for the biorepository?

## VA Biorepository or non-VA Biorepository?

1. A VA Investigator has consented VA subjects in an industry-sponsored clinical trial to send their biospecimens to the industry-collaborator for future use. This is part of the IRB-approved protocol.

**Answer: Non-VA Biorepository**

2. A VA Investigator has consented VA subjects in an industry-sponsored clinical trial to obtain an additional biospecimen for future use by his/her VA Facility. The biospecimens will be placed in his/her biorepository. This is part of the IRB-approved protocol.

**Answer: VA Biorepository**

3. A VA Investigator has consented VA subjects to place biospecimens in a repository at the academic affiliate. This is an IRB protocol approved solely for the collection and sending of the biospecimens to the VA academic affiliate. The academic affiliate's biorepository contains biospecimens for 112 different institutions. The biorepository samples will be shared with VA and Non-VA researchers.

**Answer: Non-VA Biorepository**

## “Shared” Biorepositories

- What is a “shared” repository?
  - Non-regulatory term
  - Usually associated with biorepositories which “share” biospecimens with multiple institutions
  - Not associated with storage of biospecimens; it is associated with placement of biospecimens into a common biorepository managed by an institution in which different users can request biospecimens
  - Rules of shared repository mandate who can request biospecimens for projects
    - Only institutions who have placed biospecimens into the repository
    - Any user requesting biospecimens

## Are these Examples of “Shared” Biorepositories?

1. An industry collaborator obtains biospecimens for future use which are stored in their biorepository. The biospecimens will only be used by the industry collaborator.

**Answer: No**

2. A VA investigator establishes a biorepository for use within his or her VA Facility?

**Answer: Yes**

3. An academic institution establishes a biorepository populated with biospecimens from 9 different institutions. Only institutions which contributed biospecimens may request access to the biospecimens.

**Answer: Yes**

4. A VA Investigator establishes a biorepository for future use of research studies conducted by himself or herself.

**Answer: No**

## IRB and Institutional Considerations When Reviewing Research Involving Biospecimens

1. Are the biospecimens identifiable, coded, or not-identifiable?
2. Does the activity require IRB review and approval?
3. Is the activity subject to FDA regulations?
4. If the proposed project involves a secondary use of the specimens, is the secondary use consistent with the consent under which the research biospecimens were obtained?
5. If the biospecimens are to be stored or banked, does the protocol indicate where the biospecimens will be located?
6. If the biospecimens are to be stored or banked, does the protocol indicate the time period?
7. If the biospecimens are to be stored or banked, does the protocol indicate what is the final disposition of the biospecimens if the biospecimens will not be kept until all biospecimen material is used.
8. What are some of the applicable privacy issues from a HIPPA perspective?

# Are the Biospecimens Identifiable, Coded, or not-Identifiable?

- **Identifiable:**

(1) If either condition in following subparagraphs 6a(1) or 6a(2), is met, the data are identifiable.

(a) The identity of the subject is or may be readily ascertained by the investigator or research team member or others from the information contained with in the data. The information is considered private information as defined in 38 CFR 16.102(f)(2) if it includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record or information about specific beliefs) or

(b) The subject is identifiable by HIPAA Privacy regulations because:

1. The data contain one or more of the eighteen types of identifiers listed in the HIPAA Privacy Rule in 45 CFR. 164.514(b) (2) (see App. B),
2. The covered entity has actual knowledge that the information could be used alone or in combination with other information to identify an individual who is the subject of the information; (i.e., there are other data that when combined with the dataset will allow the identification of any individual) (45 CFR 164(b)(2)(ii)), or
3. The data have not met the criteria for de-identification by statistical means as outlined in 45 CFR 164.514(b)(1).

Source: VHA Handbook 1200.12: Paragraph 6(a)(1)

# Are the Biospecimens Identifiable, Coded, or not-Identifiable?

- **Coded:**

(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.

- **Not-Identifiable: Also known as de-identified**

De-identified data is health information or other information on human subjects that:

(1) Does not meet the common rule definition of human subjects, and

(2) Meets the HIPAA de-identification requirements:

(a) No longer contains any of the eighteen types of identifiers listed in Appendix B, or

(b) Meets the criteria for de-identification by statistical means as outline in 45 CFR 164(b)(1).

Source of Not-Identifiable: VHA Handbook 1200.12, Paragraph 6(b)

## Identifiable or Not-Identifiable (De-identified)?

1. Investigator requests and receives biospecimens from a biorepository. The biospecimens are labeled with a code, but no identifying information is associated with the code. No associated information accompanies the biospecimens.

**Answer: De-Identified**

## Identifiable or Not-Identifiable (De-identified)?

2. An Investigator has obtained identifiable biospecimens from 900 University patients with lung cancer and placed those biospecimens in a biorepository accessible to both VA and non-VA users. The Investigator submits a proposal to the VA using 150 of the coded biospecimens from University subjects to be combined with another 150 coded biospecimens from Veteran subjects he obtained from another VA biorepository. The biospecimens are labeled with a code, but no identifying information is associated with the code. No associated information accompanies the biospecimens.

The Investigator sends a request to the IRB for a determination of non-human subjects research indicating that all the biospecimens he will use for the VA project will be de-identified.

**Answer: Follow-up needed. The VA biospecimens would be de-identified for purposes of the use in the VA research. However, it is unknown whether the biospecimens from the University to be used in the VA research activity are de-identified? Does the Investigator have access to the key to the code for the University subjects?**

## Does the Activity Require IRB Review and Approval?

The research does not require review and approval under the Common Rule if both 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, there are agreements, IRB-approved policies and procedures, or legal requirements in place that prohibit the release of the key to the code to the investigators under any circumstances until the individuals are deceased.

## Is the Activity subject to FDA regulations?

- Certain research studies involving medical devices and tissue specimens will qualify as clinical investigations under the FDA regulations.
- Most commonly, devices that are tested using tissue samples are In Vitro Diagnostic (IVD) devices.
- Under the definition of a human subject in FDA device regulation 21 CFR 812.3(p), “Subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.”
- Thus, if tissues are used to establish the safety and effectiveness of a device, then the FDA regulations apply.
- Under the FDA regulations, IRB review (21 CFR Part 56) is always required, and consent of the subject (21 CFR Part 50) is usually required. HOWEVER . . .

# FDA Guidance – Change in Informed Consent

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## IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects

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### Guidance for Sponsors, Investigators, and Institutional Review Boards

**This guidance is for immediate implementation.**

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(3) without initially seeking prior comment. The Agency has determined that prior public participation is not feasible or appropriate because this guidance presents a less burdensome policy that is consistent with the public health. Although this guidance document is immediately in effect, it remains subject to public comment in accordance with the Agency's good guidance practices regulation (21 CFR 10.115).

You may submit comments or suggestions at any time. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD

<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM566948.pdf>

## Is the Activity subject to FDA regulations?

- FDA does not “intend to object to an IRB approving a consent procedure that does not include, or that alters some or all the element of informed consent set forth in 21 CFR 50.25,” as long as the IRB **finds and documents** that:
- The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subject;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The clinical investigation could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

[IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects:](https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM566948.pdf)

<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM566948.pdf>

**If the proposed project involves a secondary use of the specimens, is the secondary use consistent with the consent under which the research biospecimens were obtained?**

- **Evaluate the nature of the proposed secondary research**
  - Sound research design
- **If the secondary research involves consented biospecimens, could it reasonably be understood to fall within the scope of research that was described in the original consent form?**
  - If the original consent form specifically prohibited the proposed research activity, it is presumed the research is not allowable
  - De-identification should be used as a mechanism to get around a subject's prohibition against reuse
- **Does the new research use impose new or significantly greater risks (including privacy risks) not described in the initial consent form?**
  - Example: Secondary research proposes GWAS (Genome Wide Association Testing). The original consent did not reference any genetic testing for future use.
- **Are there known concerns of the study population(s) about the proposed new use?**
  - Example: Secondary research proposes to send biospecimens to multiple countries.

## If the Biospecimens are to be stored or banked, does the protocol indicate where the Biospecimens will be located?

- Does the protocol indicate where the biospecimens will be banked and/or stored?
- Does the protocol indicate who will have access to the biospecimens?
  - VA
  - Academic partners
  - Non-profit organizations
  - Industry
  - Industry agents

## If the Biospecimens are to be stored or banked, does the protocol indicate where the Biospecimens will be located?

- Does the informed consent describe where the biospecimens will be banked and/or stored?
  - Specificity should be carefully evaluated for purposes of the informed consent.
    - Biospecimens will be stored in Room 612 and used only by the VA research Investigator for the next 10 years
- vs.
- Biospecimens will be stored at the VA Facility and may be moved to another secure VA location if approved by the IRB.

## If the Biospecimens are to be stored or banked, does the protocol indicate the time period?

- If the biospecimens are to be stored, is there a rationale for the length of time the biospecimens will be stored?
- If the biospecimens are to be banked, is there a rationale for the length of time the biospecimens will be banked?
- Does the informed consent document inform the prospective subject how long his or her biospecimens may be stored or banked?

If the biospecimens are to be stored or banked, does the protocol indicate what is the final disposition of the biospecimens if the biospecimens will not be kept until all biospecimen material is used?

- Many protocols and informed consent documents are silent on the final disposition of biospecimens.
- Disposition is not equivalent to destruction. Disposition can include:
  - Destruction
  - Return to the institution supplying the biospecimen
  - Use of the biospecimen until the biospecimen no longer exists
- Does the protocol indicate the final disposition of the biospecimens?
- Does the subject's informed consent (if applicable) indicate the final disposition of the biospecimens?

## What are some of the applicable privacy issues from a HIPAA perspective?

- Biospecimens are not data, but the data produced from biospecimens will be protected health information if the data is identifiable and the data is either produced by a covered entity or is being used by a covered entity.
- If the information associated with the biospecimen is de-identified in accordance with the HIPAA Privacy Rule, HIPAA does not apply.
- VA does not use broad HIPAA authorizations. An authorization for use and disclosure and protected health information must be study specific.



# Questions?

