Doing Research with Data and Biospecimens Under the Common Rule Part 2 – How Does that Work with Repositories and Future Use?

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Disclaimer

The opinions expressed are those of the presenter and do not necessarily reflect the policy of the U.S. Department of Health and Human Services.

For a complete and accurate description of the regulatory requirements, please refer to the text of the regulations available on OHRP's website.

Scope

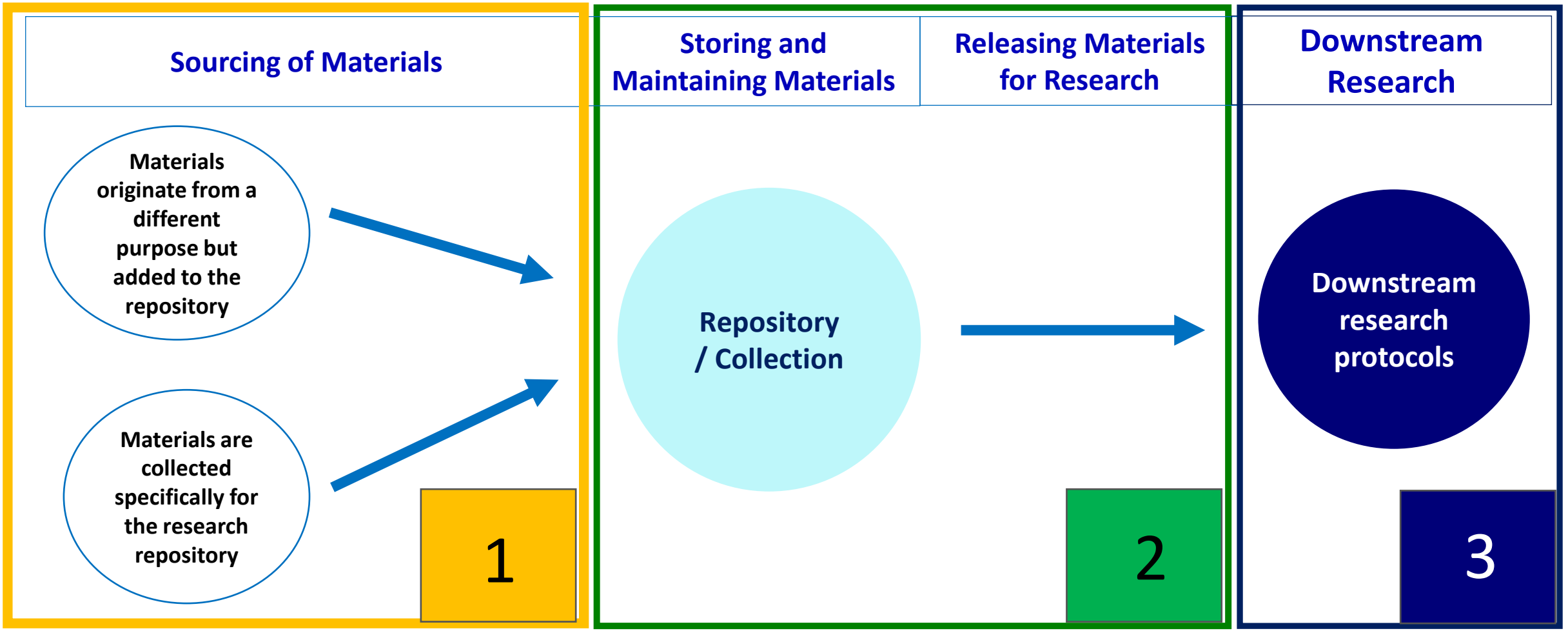
- Repositories supported by HHS funding
  - When there is no funding from HHS (or other Common Rule (CR) agencies), generally, CR has no jurisdiction and does not apply.
- The repositories are created/maintained to support future downstream secondary research.
  - **Reminder**: **secondary research** is the research use of data or biospecimens originally acquired for non-research purposes or for research other than the research being proposed.

Common Rule Considerations for Setting up a Research Repository

OHRP's Guidance on Issues to Consider in the Research Use of Stored Data or Tissues (1997) note:

- Operation of repositories should be subject to oversight by an IRB
- Repository will have policies/procedures for 3 separate components of repository activities to include:
  1. When data/biospecimens are accepted,
  2. The storage and maintenance of the repository, and
  3. The distribution of the repository materials for downstream research

Three Components of A Research Repository



Making Determinations on Whether the Common Rule (CR) Applies to a Repository

Ask these questions <u>in this order</u>:

1. Is the repository supported by ***funding*** from the Department of Health and Human Services (HHS)?
   - Typically, CR considerations are applicable when there is HHS funding for the project.
2. Does the activity involve ***Research***?
   - Is the repository set up/maintained for research purposes?
3. Does the research involve ***Human Subjects***?
   - Does the repository obtain data/biospecimens through intervention or interaction with individual participants? Or,
   - Does the repository receive and/or maintain individually identifiable data or biospecimens?
4. Is the human subjects research ***Exempt***?
   - Does the entire research meet one or more exemption categories (4,5,7,8)?

Repository Accepting Only Secondary Research Data and Biospecimens –

Materials Not Collected Specifically Through Interaction or Intervention with Individual Participants for the Research Repository

Research Repository Accepting Only Data and Biospecimens Not Collected Specifically for the Repository

- There's **no interaction or intervention** with individuals specifically to obtain their private information or biospecimens to put into the research repository.
- Data/biospecimens come from non-research sources or sources other than the proposed research.
- This is **secondary research**.
- Any CR oversight requirements depend on whether the data/biospecimens received are **identifiable or not**.

Data and Biospecimens Without Associated Individually Identifiable Information

If only ***nonidentifiable*** private information or biospecimens are provided to the repository, **no** applicable CR requirements.

- This will be considered ***secondary research that is not human subjects research***.
- Repository should probably know that the sources of materials are proper and legitimate.
- It should have robust policies for protecting confidentiality.
- There should also be policies on the operation of the repository including policies for downstream distribution of materials for research.

Data and Biospecimens With Associated Individually Identifiable Information

If repository will receive *individually identifiable* private information associated with the data and biospecimens but will not keep the identifiers,

- The activity may meet the conditions for exemption 4 at **§46.104(d)(4)(ii)**.
  - Oversight will be similar to that described in the previous slide for materials without associated individually identifiable information.

Data and Biospecimens With Associated Individually Identifiable Information, cont'd

If repository will **receive *individually identifiable*** private information or biospecimens **and keep the identifiers**, check if the activity meets the conditions for exemptions 4 (but not provision ii), 5, or 7.

If not, CR regulatory requirements apply. IRB reviews include (among others):

- The acceptability of the protocol for the sources, the storage, maintenance, and subsequent use of the materials.
- The availability and appropriateness of any informed consent for the materials the repository receives, maintains, distributes for downstream research.
- The appropriateness and adequacy of the measures for protecting privacy and confidentiality of the materials.

Reminder: Possible Exemptions for Secondary Research with *Identifiable* Materials

Main Exemption Categories for *Secondary Research Involving Human Subjects (§46.104(d))*

- Exemption 4: Secondary research use of identifiable biospecimens or private information with four different provisions
- Exemption 5: Evaluation of public benefit and service programs
- *Exemption 7: Storage and maintenance of identifiable materials for unspecified secondary research **with broad consent**
- *Exemption 8: Secondary research use of stored identifiable materials **with broad consent**

* Need limited IRB review to ensure that the conditions described for the exemption have been met.

Informed Consent

Options for Informed Consent

- **Broad consent**
  At § 46.116(d)
- **Standard informed consent**
  At § 46.116 (a)(b)(c)
- **Waiver of informed consent if applicable**
  (*Additional condition*)
  At § 46.116 (f)

Broad Consent Under Revised CR (2018 Requirements)

- An option permissible **only for secondary research**. It cannot be used for specifically collecting identifiable private information or identifiable biospecimens through research interaction or intervention with individuals for the repository.
- Is a means to enable subjects to agree to a broad range of secondary research studies when details of such research may not be available
- Broad consent may be obtained for the secondary research:
  - At the time when standard informed consent is obtained for research involving interaction or intervention with subjects, or
  - In the nonresearch setting when information or biospecimens are collected
- If broad consent is sought and refused, IRB cannot waive the requirement for consent.

Use of Broad Consent

- Main advantage with broad consent is the opportunity to benefit from exemptions 7, 8
- **If used, all of the elements for broad consent must be included** (§46.116(d)), including, amongst others:
  - a general description of the types of research that may be conducted,
  - the types of institutions or researchers who might conduct research with the subject's information or biospecimens

  No flexibility for alteration is allowed!
- Use of broad consent will involve some mechanism for tracking the affected information or biospecimens; the cost and logistical difficulties involved may limit its use

Research Repository Accepting Data and Biospecimens Collected Specifically Through Interaction or Intervention with Individual Participants for the Research Repository

Research Repository Accepting Data and Biospecimens Collected Specifically for the Repository

- There is **interaction or intervention** with individuals **specifically** to obtain their private information or biospecimens for the research repository.
- This is **(*primary) human subjects research*** regardless of whether the data/biospecimens are identifiable or not.
- Unless exemption 5 applies, this primary research is ***non-exempt human subjects research*** that needs to comply with CR regulatory requirements, including IRB reviews, informed consent (broad consent use applicable only to secondary research materials), etc.

Research Repository Involved in Primary Research

- Typically, such a repository is an integral part of a multi-institutional cooperative non-exempt human subjects research project.
- Revised Common Rule has a mandate at §46.114 for institutions engaged in such cooperative research to rely on the review and approval of a single IRB of record (with few exceptions).
  - The institutions document the reliance arrangements and the responsibilities of each according to §46.103(e) .

Subsequent Downstream Research

Third Component - Repository Providing for Downstream Research

- The research repository should follow its own "approved" protocol for the dissemination of data/biospecimens for downstream research.
  - If providing **identifiable** materials for downstream research, repository may need to check the conditions for any applicable consent that may have been provided for the downstream research use.
- If the repository is **solely providing** for downstream secondary research, CR oversight for the downstream research remains **the responsibility of the IRB/IRB office of the requestor-investigators**.
  - For a data repository, solely providing may also include assistance with filtering out appropriate datasets before supplying to downstream investigators for their research.

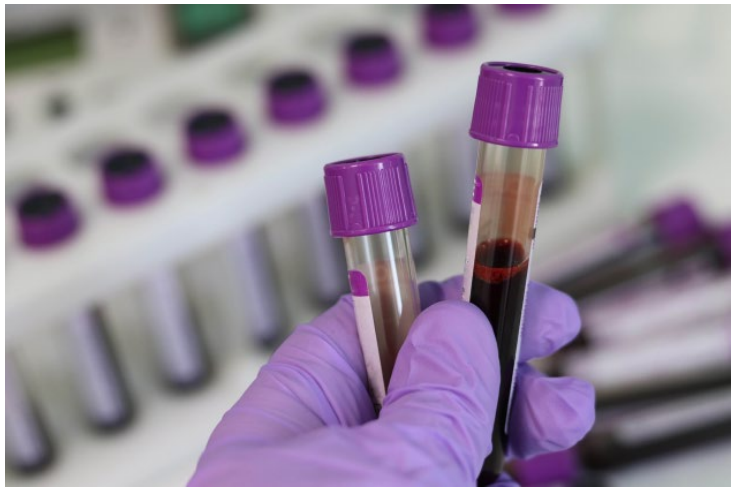
Third Component - Repository Providing for Downstream Research, cont'd

- Beware of any involvement of downstream investigators in the operation of the research repository! For example,
  - When a "repository" takes "orders" from investigators to acquire private information or biospecimens from individuals **specifically** for the purpose of the proposed research, the downstream investigators are conducting **primary human subjects research** and the repository is acting as an agent for the investigators.
    - ✓ The repository will become "engaged" in the research project

Downstream Research – Requesting Investigators' Perspectives

Investigators request data/biospecimens from the repository for their research.

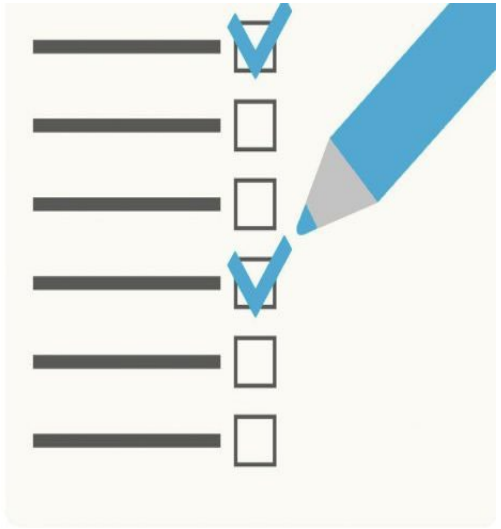
- Typically, this is **secondary research** because the materials the repository provide for the research have not been obtained through interaction/intervention with individuals specifically for the purpose of the proposed research.



Downstream Research – Requesting Investigators' Perspectives, cont'd

The IRB office of the requesting investigators make the following determinations:

- If the investigators receive materials that they cannot readily link back to living individuals from the repository = hence, outside CR, **secondary <u>not</u> human subjects research**
- If the investigators receive materials that have individually identifiable information = **secondary human subjects research** that may or may not meet the conditions for an exemption category (exemptions 4, 5,7,8).
  - If investigators have a role in the operation of the repository, the materials obtained for secondary research will usually be considered identifiable to the investigators.



OHRP Resources

- Issues to Consider in the Research Use of Stored Data or Tissues (1996, 1997) www.hhs.gov/ohrp/regulations-and-policy/guidance/issues-to-consider-in-use-of-stored-data-or-tissues/index.html
- Review video “Doing Research with Data and Biospecimens Under the Common Rule Part 1 – What Researchers Should Know,” – available in due course at https://www.hhs.gov/ohrp/education-and-outreach/human-research-protection-training/ohrp-webinars-on-45-cfr-46/index.html
- Video “Broad Consent in the Revised Common Rule” at https://www.youtube.com/watch?v=jpqH2sHmOF4

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