Biorepositories and Biospecimen Studies Under the NPRM

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Regulatory status of biospecimens and biorepositories under the current Common Rule

• Exemption at §101(b)(4) is the only mention of specimens in the current regs — and this refers only to pre-existing pathological and diagnostic specimens

• Biospecimens have *no* special status: they come under the regulations only indirectly and via “guidance” of uncertain legal effect

• When intertwined with interaction/intervention to obtain research data

• When associated with identifiable private information
Categories of currently permissible biorepositories and biospecimen studies

• Those that do not directly acquire specimens and obtain only fully de-identified information OR obtain **coded** information, with an agreement to never access the key to the code

• No IRB determinations are strictly necessary

• Those that access identifiable information but record it in a fully de-identified manner

• Require exemption determinations
Categories of currently permissible biorepositories and biospecimen studies

• Those that have been determined to meet all the requirements of §46.111
  • Often under §110 expedited review
  • Including informed consent req’ts (§116)
    • Sometimes with a (four-part) waiver determination
    • Sometimes via interpretation of vague documents
  • Subject to standard continuing review
Ethical questions not confronted by the current regulations

• What level of administrative or peer review is warranted by the risks posed in biospecimen research?

• To what extent is each of the following needed to justify biospecimen research activities: (a) disclosure of storage and research plans to the human sources of the biospecimens; and (b) those individuals’ authorization of those plans?
NPRM and biospecimens

• Themes:

1. Require consent for biospecimen storage and studies

2. Limit administrative review of both biorepositories and biospecimen studies
Biospecimen donors treated as human subjects

- Primary proposal: The regulatory definition of “human subject” would expand to include any living individual about whom a researcher obtains, uses, studies, or analyzes biospecimens. (§102(e)(1)(iii))
  - Would include all biospecimens — in federally funded research or in clinical trials at federally supported institutions — whether de-identified or identifiable; whether originally collected in a non-research or research context.

- Alternative proposals (each less expansive than the primary proposal):
  - A: Definition of “human subject” would expand only to include individuals about whom whole-genome sequencing data is generated.
  - B: Definition of “human subject” would expand only to include individuals about whom potentially identifiable information, generated from biospecimens, is used for research.

- **NOT** about risk to biospecimen donors, but rather about “the majority of the public’s wishes [to be asked for their permission before biospecimens from them are made the objects of research], which reflect legitimate autonomy interests.”
One new “exclusion” category

- Exclusion (§101(b)(3)(i)): applies to use of non-identifiable biospecimens for research designed only to produce already-known information

- No procedural or record-keeping requirements; also applies to vulnerable populations subparts
Two new exemption categories

- Exemptions
  - Exemption determinations must be made by a knowledgable individual or by PI using a decision tool to be developed by HHS
  - Must record: Study name; PI name; Exemption category applied

- Exemption 1 (§104(f)(1)) - Storage and maintenance of biospecimens, conditioned on:
  - Consent of the each individual source, as prescribed
  - Confidentiality protections, according to standards to be developed by HHS (§105)
  - Limited IRB review: determinations only that (1) consent procedures align with §116 preamble, and (2) any changes to storage or maintenance will satisfy the §105 standards (§111(a)(9))

- Exemption 2 (§104(f)(2)) - Secondary research involving biospecimens, conditioned on:
  - Consent of each individual source, as prescribed
  - Confidentiality protections, according to the same standards as Exemption 1
  - No plans to return individual research results
Opt-in, broad consent allowed

- Proposal is to explicitly allow broad consent to future unspecifiable research (§116(c))
  - OHRP had been unable to make broad consent clearly acceptable under the current system
  - Follows OCR’s 2013 re-interpretation of the HIPAA Privacy Rule
  - U-M has already moved toward this model
- Consent requirements for biospecimen activities can still be satisfied by:
  - “Specific” consent (§116(a)) or
  - (Significantly tightened) waiver of consent (§116(e)(2)). Criteria:
    - Compelling scientific reasons to conduct the research and
    - Suitable specimens with broad consent attendant are not available (including by way of new recruitment)
    - Individuals did not decline to give broad consent
Broad consent (§116(c))

• Required elements of broad consent: 4 of the 9 standard elements plus 5-8 additional elements, including:
  
  • Types of biospecimens being collected
  
  • Types of research that might be conducted with the specimens
  
  • Period of time over which biospecimens will be collected, and period of time over which they may be used

  • Broad consent in clinical context expires after 10 years for continuing collection of new specimens (use of those collected can continue indefinitely)

• Declinations of broad consent must be tracked (§116(d)(4))

• U-M repository consent templates would need few adjustments: statement on plans to return research results; opt-outs for recontact and posting to public databases

• Exemptions at §104(f) both additionally require use of a national template, which is to be developed by HHS
Transition provisions

• New set of biospecimen rules would apply prospectively only, beginning 3 years after final rule is issued.

• New rules would not apply to research using non-identifiable (can be coded) biospecimens collected prior to the rules’ effective date.
2,185 comments submitted

- **SACHRP**: Develop a notice-and-opt-out system
- **President’s Commission**: expand the definition of “human subject” according to Alternative B
- **Many others**: codify the current guidance