Biorepositories and Biospecimen Studies Under the NPRM

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January 29, 2016

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