

Revising the Common Rule:

AAMC Member Feedback on Proposed Changes to *Research with Biospecimens*

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Today's Goals

- Brief overview and orientation to proposed changes
- Tell AAMC:
 - What aspects of the proposal make sense to you?
 - What proposed changes are concerning? What is the effect on institutions? Investigators? Research subjects?
 - What data might be persuasive?
 - How do the proposals advance or hinder the stated goals of:
 1. Increasing human subjects' ability and opportunity to make informed decisions
 2. Reducing potential for harm and increasing justice
 3. Facilitating current and evolving types of research
 - Reducing ambiguity in interpretation
 - Increasing efficiencies
 - Reducing burden on investigators

Input Opportunities

Direct Input to AAMC – by November 2

- Heather Pierce: hpierce@aamc.org, 202-478-9926

Conversations with AAMC on Specific Proposals

- Informed Consent – October 13, 2015
- Categorization and IRB Review of Research – October 14, 2015
- **Research with Biospecimens – October 21, 2015**
- The Single IRB Mandate – October 22, 2015

Send Your Comments to HHS – by December 7

- www.regulations.gov (HHS-OPHS-2015-0008)

Overview of the NPRM

80 Fed. Reg. 53933-54061 (September 8, 2015)

- Executive Summary (p. 53933)
- Discussion of Major Proposals (p. 53942)
- Regulatory Impact Analysis (p. 53993)
- Summary of ANPRM Comments (p. 54033)
- Regulatory Text (p. 54044)

Significant Changes for Research with Biospecimens

1. Research with biospecimens would be research with “human subjects”
2. “Broad consent” would be required for storage, maintenance, and secondary use of biospecimens
3. Waiver of informed consent would be severely restricted
4. Excluded activities and exempt research have special rules for biospecimens



Biospecimens Show Up Throughout the NPRM

“Human Subject” is a living individual about whom an investigator obtains, uses, studies, or analyzes biospecimens (§__.102(e)(1)(iii))

Biospecimens are included in 6 of 11 “excluded” activities (§__.101(b)(1) and (3))

Biospecimens are included in 3 of 8 “exempt” activities (§__.104(d)(2) and (f))

Biospecimens collected before the rule and used for research after removing identifiers does not fall under rule (§__.102(k)(2))

Standard safeguards to protect biospecimens required for all non-exempt and some exempt research (§__.105(a))



IRBs must ensure that broad consent and privacy and information protection standards are satisfied in “limited review” of storage or maintenance of biospecimens (§__.111(a)(9))

New element of informed consent: whether biospecimens may be used for commercial profit and if subject will share (§__.116(b)(7))

Broad consent required for storage, maintenance, and secondary research use of biospecimens (§__.116(c)(1))

Consent for continued collection of biospecimens in non-research context lasts 10 years (§__.116(c)(1)(ii)(B))

Refusal to provide broad consent must be documented and prevents later waiver (§__.116(d)(4) and (f)(3))

Additional criteria for waiver of consent for biospecimen research includes “compelling scientific reasons” (§__.116(f)(2))

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Defining Biospecimens as Human Subjects (§__.102(e)(1)(iii); pp. 53944-46)

Proposal: change definition of “human subjects” to include a living individual *about whom* an investigator conducting research:

Obtains, uses, studies, or analyzes biospecimens

- Impact: generally, all research on biospecimens requires prior written informed consent
 - If obtained in other research or non-research context, must comply with new “broad consent” requirements

Questions 2-5 in the NPRM (p. 53946)

- ✓ Q5: “any concerns you have ... including concerns about implementation or burden to investigators and institutions”

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Alternative Proposals to all Biospecimens (pp. 53945-46)

1. Instead of “biospecimens,” include only whole genome sequencing data, regardless of individual identifiability
 - Would apply to the research to generate the data, research with the data, and secondary use of any part of the data
2. Information from “technology applied to a biospecimen” that, when used in combination with publicly available information, could identify the individual (bio-unique data)
 - Would require continual analysis of available technologies and uncertainty in application

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Broad Consent for Biospecimen Storage and Maintenance for Secondary Research

Elements (§__.116(c)(1); pp. 53972-75, 54053)

- Four elements from the basic elements of informed consent (2, 3, 5, and 7)
- Three additional elements if applicable (7, 8, and 9)
- Eight elements specific to the broad consent document

Templates (§__.116(d)(1); pp. 53966-67, 54054)

- HHS will develop for public comment at a later date

Considerations

- Training non-research staff
- Tracking refusals, compliance, and versions

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Excluded Activities with Biospecimens (§__.101(b)(3); pp. 53944-45, 54046)

Category 3 – Excluded as a low-risk human subjects research activity that does not meaningfully diminish subject autonomy

- Secondary use of non-identified biospecimens “to generate information about an individual that already is known” (including validation tests, assays)



Exempt Research with Biospecimens (§__.104(f)(1) and (2); pp. 53965-68, 54049)

1. Storage of biospecimens or data obtained in other research or non-research context
 2. Research on such stored biospecimens
- Broad informed consent needed
 - Limited IRB review
 - Privacy/security standards apply
 - **Questions 54-56 in NPRM**



Continuing Review of Research (§ __.109(f)(1)(iii); pp. 53984-85, 54051)

- Continuing review will not be required for research that has undergone “limited review”
 - IRB must determine only that:
 - broad informed consent procedures were followed
 - privacy and information protection standards are satisfied if there is a change in storage or maintenance

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Key Questions to Determine Requirements for Future Research with Biospecimens

In what context will it be collected?

- Research → Broad consent added to study specific informed consent
- Non-research → Broad consent in clinical setting

Were the individuals asked for consent?

- If no, waiver rarely allowed, additional criteria added
- If yes, and they refused, no waiver allowed
- If yes, and broad consent provided, future research is exempt

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Questions for consideration

- Should biospecimens be treated differently than identifiable private data?
- If the requirements for broad consent were adopted as proposed, is three years sufficient time to implement changes?
 - What would have to happen at your institution?
 - At other clinical sites?
- Are there other ways to address concerns raised that individuals want to know how their biospecimens are being used?
- What would the impact be if few people provided consent or if different populations varied in the likelihood of obtaining consent?

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Important reminders

- The NPRM is not a final rule
- Your input matters to AAMC
- Your comments matter to HHS
 - Alternatives are essential
 - Numbers count
 - Data helps
 - It is better to provide some comments on some proposals than not to send comments on any proposals

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