

Revising the Common Rule: The HHS Notice of Proposed Rulemaking

Heather H. Pierce, JD, MPH
Senior Director, Science Policy
Regulatory Counsel
September 18, 2015

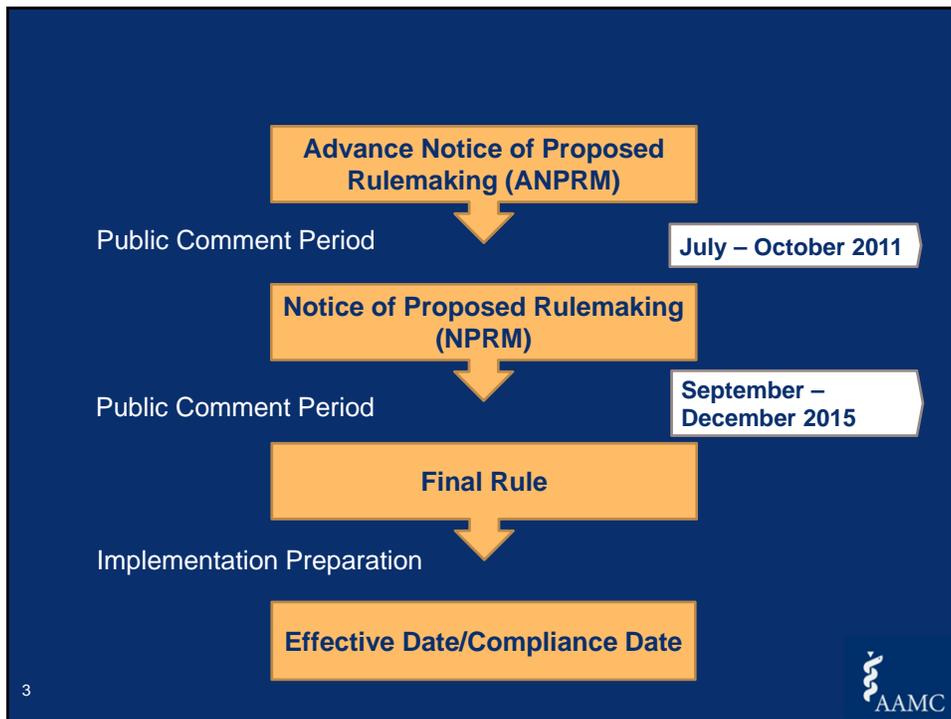
Learn
Serve
Lead



Association of
American Medical Colleges

Agenda

- Goals and Overview of the NPRM
- Most significant changes
 - Biospecimens
 - Jurisdiction
 - Exclusions and Exemptions
 - IRB Review
 - Cooperative Research
 - Informed Consent
 - Privacy Standards
- Other Provisions and Opportunities for Comment
- How to Provide Your Input



Goals of the Proposed Rule

1. Increase human subjects' ability and opportunity to make informed decisions
 2. Reduce potential for harm and increase justice
 3. Facilitate current and evolving types of research
 - Reduce ambiguity in interpretation
 - Increase efficiencies
 - Reduce burden on investigators
- Firmly rooted in the principles of the 1979 Belmont Report
 - Beneficence
 - Respect for Persons (autonomy)
 - Justice
- 4
- AAMC

Overview of the NPRM

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

Executive Summary (p. 53933)

Discussion of Major Proposals (p. 53942)

- NPRM Goal
- Current Rule
- NPRM Proposal
- What would change?
- Specific questions for public comment

Regulatory Impact Analysis (p. 53993)

Summary of ANPRM Comments (54033)

Regulatory Text (p. 54044)



Most significant changes

- Most research with biospecimens would require written informed consent
- Federal jurisdiction would extend to all clinical trials at federally funded institutions and to IRBs that review research
- Some activities would be specifically excluded from the rule
- Changes to IRB review process would include exempt research, limited review, continuing review
- Cooperative research would require a single IRB of record
- Format and elements of informed consent documents would change
- Standard privacy and security safeguards would be established for biospecimens and data

6



Research with Biospecimens

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

Obtains, uses, studies, or analyzes biospecimens

- This does not change the definition of identifiable, but instead sweeps all research with biospecimens, *identified or non-identified* under the Common Rule
- Primary 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

7



Research with Biospecimens – Broad Consent Requirements

- Four elements from the basic elements of informed consent
 1. Reasonably foreseeable risks/discomforts
 2. Benefits
 3. Confidentiality
 4. Contact for questions and concerns
- Three additional elements if applicable:
 1. Potential for commercial profit
 2. Return of results
 3. Discussion of recontacting for more data/biospecimens or other research

8



Research with Biospecimens – Broad Consent Requirements

- Eight elements specific to the broad consent document

Element 1: “A general description of the types of research that may be conducted with the information and the biospecimens and the information that is expected to be generated from the research, the types of information or biospecimens that might be used in research, and the types of institutions that might conduct research with the biospecimens or information”

9



Research with Biospecimens – Broad Consent Requirements

- Eight elements specific to the broad consent document
 1. Element 1
 2. Description of types of biospecimens or information to be collected over what time period
 3. How long an investigator can conduct the research
 4. Voluntary participation statement
 5. If no notification will be provided about future research conducted
 6. If applicable, a statement on potential for sharing
 7. Institution or institutions where collection will take place
 8. If relevant, consent or refusal to include de-identified data in a publicly available database

10



Research with Biospecimens – Broad Consent

Of note:

- Biospecimen or data *collection* (outside of the research context) cannot exceed 10 years from the date of the consent
- HHS will develop templates for the broad consent document
- Refusal to consent must be documented

11



Extension of Federal Jurisdiction

1. Institutional Review Boards (IRBs) reviewing research that is subject to the policy must comply with the regulations
2. Applies to all clinical trials, irrespective of funding source, if:
 - At an institution that receives *any* federal funding for non-excluded, non-exempt human subject research
 - Not regulated by the FDA
 - Conducted at an institution in the U.S.

12



Excluded Activities

Three categories of “excluded” activities deemed to be outside the regulations and require no review:

1. Activities “deemed not to be research”
2. Activities “considered to be *low-risk* human subjects research, when already subject to independent controls”
3. A low-risk activity that does not “meaningfully diminish subject autonomy”

13



Certain excluded activities (not complete list)

Category 1

- An institution’s operational monitoring and program improvement
- Oral history, journalism, biography, historical scholarship
- Quality assurance or improvement activities involving the implementation of an accepted practice to improve health care delivery

Category 2

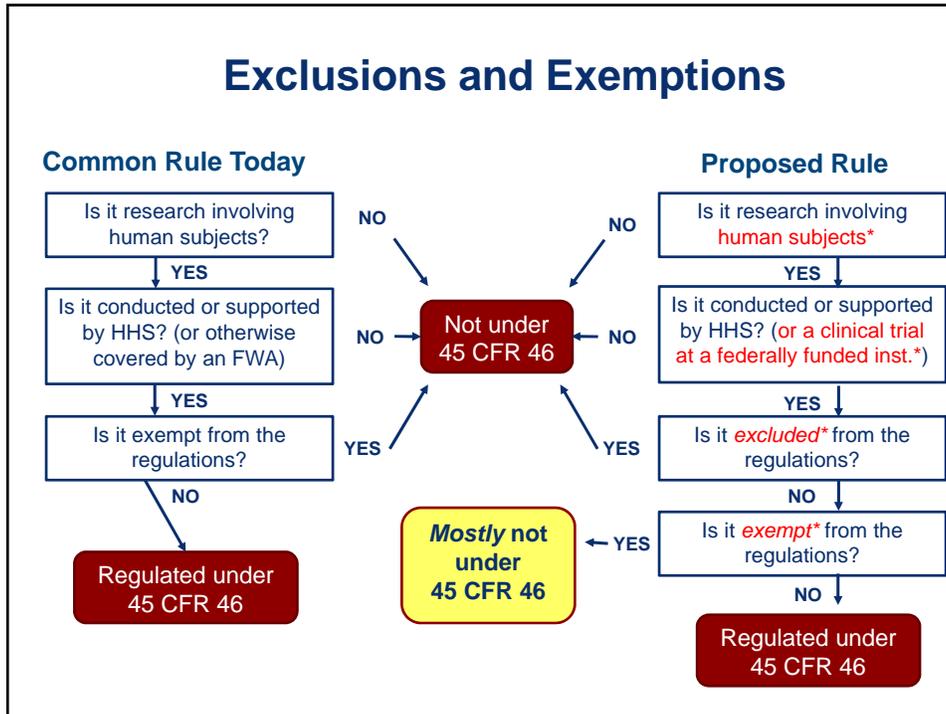
- Tests, surveys, interviews or observation, if subjects cannot be identified OR disclosure would not put subjects at risk OR subject to the Paperwork Reduction Act of 1995/Privacy Act of 1974 (*previous exempt category 2*)
- Collection or study of information gathered for non-research purposes if the sources are publically available OR not identifiable (*previous exempt category 4, modified*)

Category 3

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



Exclusions and Exemptions



Changes to the IRB Review Process – Exempt Research

- Exempt research – 3 new categories, all must be recorded
 1. Low-risk Interventions
 - Privacy/security standards do not apply
 2. Collection of Sensitive Information
 - Not including biospecimens
 - Privacy/security standards do apply
 3. Storage of biospecimens or data obtained in other research or non-research context OR research on such stored biospecimens
 - Broad informed consent
 - Limited IRB Review
 - Privacy/security standards do apply

Changes to the IRB Review Process – Exempt Research

- Determination of whether research is exempt accomplished through HHS-developed “decision tool”
- “Safe harbor”: If information entered into tool is accurate, determination made by tool assumed by federal agencies to be appropriate
- Retention of completed decision tool will meet recording requirements

17



Changes to the IRB Review Process – Continuing Review of Research

- Proposes circumstances under which continuing review will not be required:
 1. Research eligible for expedited review
 2. Research that only involves data analysis and/or accessing follow-up clinical data from standard of care procedures
 3. Research that has undergone “limited review”
 - Limited review implements exemption for “storage or maintenance for secondary research use of biospecimens or identifiable private information”
 - 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

18



Mandated Single IRB of Record for Multisite Studies

- Questions raised by ANPRM
 - (and answers from the NPRM)
 - What types of research and how many sites?
 - All types, more than one site conducting research in U.S.
 - How would the IRB be selected?
 - Funding agency would select
 - If no federal funder, the lead institution will select
 - How would the roles and responsibilities be defined to address liability and logistic concerns?
 - New authority to enforce compliance against unaffiliated IRBs
 - Institution and IRB should establish and follow procedures
 - How would local context issues need to be addressed?
 - If required by law or deemed that a single IRB is not appropriate, multiple IRBs may be used
 - Most issues can be addressed through mechanisms other than IRB review

19



Mandated Single IRB of Record: Questions Asked in the NPRM

74. Is mandated single IRB review for all cooperative research a realistic option at this time? *Please provide information about the likely costs and benefits to institutions.* Will additional resources be necessary to meet this requirement in the short term? Should savings be anticipated in the long run?
75. What areas of guidance would be needed for institutions to comply with this requirement? Is there something that OHRP could do to address concerns about institutional liability, such as the development of model written agreements?
76. Would it be useful for this requirement to include criteria that Federal departments or agencies would need to apply in determining whether to make exceptions to the use of a single IRB requirement? If so, what should these criteria be?
77. Are the exceptions proposed appropriate and sufficient, or should there be additional exceptions to this mandate for single IRB review than those proposed in the NPRM?
78. Is three years appropriate timing to establish compliance with this provision?

20



Changes to General Informed Consent

Goal: “to facilitate prospective subjects’ decision about whether or not to participate in a research study, thereby enhancing autonomy”

Primary changes:

- Emphasize the need to get essential information to prospective subjects
- Organize document to provide sufficient detail but also facilitate understanding
- Present core information first, including only required elements and including all other information in appendices

21



Changes to General Informed Consent

Basic elements of informed consent are largely unchanged, with one new element:

- A statement about whether or not the subject’s data will be used for future research studies if the identifiers are removed

Additional elements are generally unchanged and three elements have been added:

1. Potential for commercial profit
2. Return of results
3. Discussion of recontacting for more data/biospecimens or other research



Other Changes to Informed Consent and Waivers

- IRB may approve screening, recruiting, or eligibility determinations without consent with assurance of protections
- Final consent forms would be posted on a federal website
- Waivers
 - Written informed consent related to biospecimens should be waived very rarely
 - Waiver of written informed consent possible if subjects are members of a “community in which signing forms is not the norm”



Uniform Privacy and Security Standards

Certain exempt research and all non-exempt research must implement “reasonable and appropriate safeguards” to protect biospecimens and identifiable private information

- IRB review is generally not required
- HHS will establish specific measures that will satisfy the requirements
- Institutions and investigators can choose to implement HHS standards or to comply with HIPAA rules (voluntarily or as already required)

This would apply to IRB records if they contained identifiable private information



Additional Important Proposals

- Existing biospecimens would not be subject to new requirements and could still be used for research if not identified
- Ongoing human subjects research:
 - Most new provisions would not apply if initiated before effective date
- Effective date and compliance date one year from final rule with two exceptions
 - Regulatory flexibility provisions may be implemented 90 days after effective date
 - Single IRB and consent for biospecimens would be not be required 3 years
- Harmonization of agency guidance

25



Terms that are not defined in the proposed rule

- Benign intervention (criteria but not definition)
- Biospecimen
- Low-risk
- Behavioral health-related outcomes (in context of clinical trial definition)

Definitions that have not changed substantially in the proposed rule

- Research
- Minimal risk (but HHS will publish a list of activities)
- Legally authorized representative (LAR)

26



Key Reminders

- The NPRM is not a final rule
- Your input matters to AAMC
 - What do you need to better understand and respond to this proposal?
 - What is the most concerning proposal? The most beneficial proposal?
 - Draft AAMC letter will be made available prior to comment deadline
- Your comments matter to HHS
 - Alternatives are essential
 - Numbers count
 - Data helps

27



Providing Input on the Proposed Rule

HHS Comment Deadline: 5 p.m. **December 7, 2015**

Comment letters may be submitted to HHS at
www.regulations.gov

Reference docket ID HHS-OPHS-2015-0008

Provide your feedback to AAMC by **November 2, 2015**

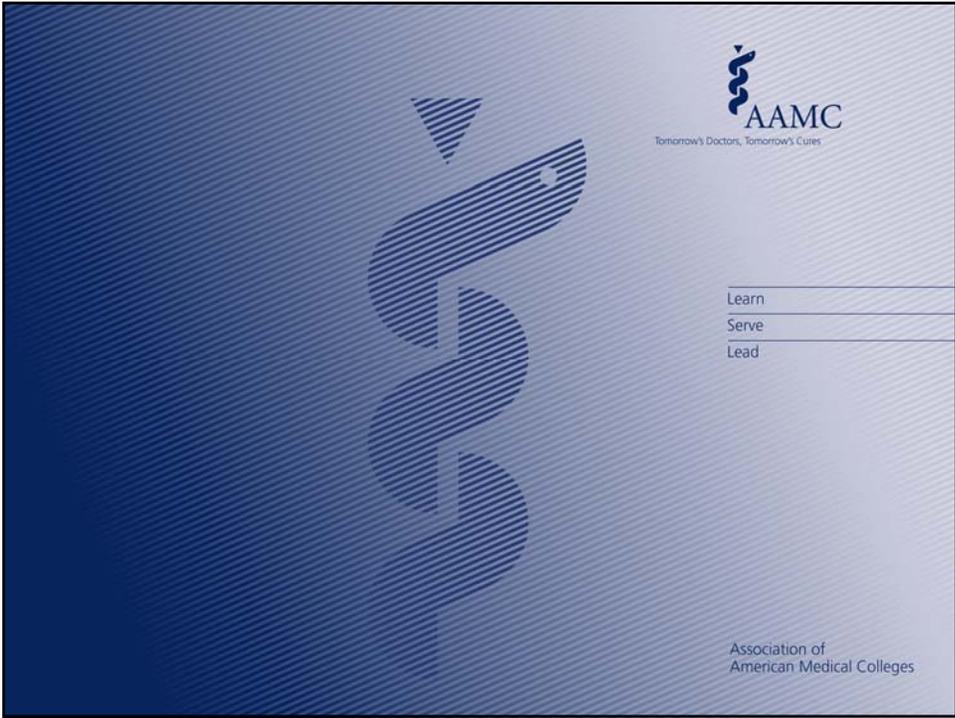
Heather Pierce

hpierce@aamc.org

(202) 478-9926

28






AAMC
Tomorrow's Doctors, Tomorrow's Cures

Learn
Serve
Lead

Association of
American Medical Colleges