Updating Regulations for Human Subjects Research: The new Common Rule has arrived! What changes are coming?

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Disclaimers

- The opinions expressed are my own and do not necessarily reflect the policy of U.S. EPA (or any other federal agency).
- I participated in the federal Interagency Working Group to revise the Common Rule, but am not representing that group.
- I am not speaking for the IRBs at UNC-Chapel Hill.
Outline

- What is the Common Rule?
- Why was it revised?
- Why did it take so long?
- What proposed changes were NOT adopted?
- What are the key changes?
- What does this mean for you?
Current Regulations Provide a “Patchwork Quilt” of Protections

Federally Funded
18 Departments & Agencies

DHHS

45 CFR 46
Subpart A
Subpart B
Subpart C
Subpart D

Common Rule

FDA

HIPAA

Research Involving Human Subjects
Why revise the Common Rule?

- Oversight system no longer accommodates research (esp. clinical research) as conducted today
- Evolving notions of identifiability
- Multiple areas of inefficiency or ineffectiveness
- Recalibration of protections to burden

Changes proposed to “better protect human subjects while facilitating valuable research and reducing burden, delay and ambiguity for investigators”
The Federal Rulemaking Process

Advance Notice of Proposed Rule Making (ANPRM)
- July 26, 2011
- Open Comment period through Oct 26, 2011

Notice of Proposed Rule Making (NPRM)
- Sept 8, 2015
- Open Comment period through Jan 6, 2016

Final Rule
- Jan 19, 2017
Federal Rulemaking Process

• The Rulemaking involved Health and Human Services (HHS) and 15 other federal agencies, coordinated by White House (EOP and OMB)
• First substantial revision to the human subject protection regulations since 1981
  • First issued in 1974 → substantially revised in 1981 → adopted by other agencies as the Common Rule in 1991
• Advance Notice of Proposed Rulemaking (ANPRM) released in 2011
  • 1,100 public comments
• NPRM released in 2015
  • 2,100 public comments
• Final Rule published in Federal Register on Jan 19, 2016
Proposed Changes

- Informed Consent
- Biospecimens
- Single IRB
- Continuing review
- Extension to clinical trials
- Privacy safeguards
- Exclusions
- Exemptions

... and the KITCHEN SINK
Proposal to Define All Biospecimens as Human Subjects, Regardless of Identifiability (with Mandated Consent)

Public Comments on 2011 ANPRM
Cadigan, Nelson, Henderson, Nelson and Davis (2015)

Public Comments on 2015 NPRM
OHRP (2016)
What proposals were NOT adopted?

- Extension of Common Rule to cover research using non-identified biospecimens, which would almost always require consent
  - More stringent criteria to make waiver of consent “very rare”
  - Differential handling of biospecimens vs. data
- Extension of Common Rule to clinical trials that are not federally funded
- Creation of an exemption decision tool
- Creation of a broad consent template
- Development of standardized privacy safeguards
Level of Risk Determines Level of Review

- Minimal Risk?
  - Is it on the list?

- Is it on the list?

- 2. Are there Human Subjects?
  - 1. Is it Research?

- Convened Meeting
- Expedited
- “Exempt”
- Not Human Subjects Research

RISK
OK... so what DID change??

“The announcement of the changes really went well.”
Definition of “Human Subject” – Clarifying Changes

Human subject - a living individual about whom an investigator conducting research

(1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens

§.102(e)(1)(i)
Addressing the Evolving Concept of “Identifiability”

Federal agencies’ commitment to collaborate at least every 4 years to:

- Reexamine the meaning of identifiability
- Identify analytic techniques capable of generating identifiable private information or biospecimens

§.102(e)(7)
Definition of “Research: Activities Deemed Not To Be Research”

- Scholarly and journalistic activities
  - Focus on the specific individual about whom information is collected
  - Excludes certain activities, not entire academic fields

- Government functions with separately mandated protections
  - Public health surveillance activities
  - Collection of information for criminal justice purposes
  - Operational activities for national security purposes
Public Health Surveillance Activities
Deemed Not to be Research

- Limited to:
  - Those conducted, supported, requested, ordered, required or authorized by a “public health authority.”
  - Those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance, including trends, signals, risk factors, patterns of diseases, or increases in injuries from using consumer products.

§.102(I)
Changes to Informed Consent

1. General Improvements to Informed Consent
2. Broad Consent
3. Posting of Consent Form for Clinical Trials
4. Waiver and Alteration of Informed Consent
Promoting Autonomy

Changes are intended to make informed consent more meaningful so that research subjects will have the necessary information to make informed decisions.
General Improvements

The revised Common Rule explicitly establishes a new standard: to provide the information that a reasonable person would want to have in order to *make an informed decision about whether to participate*.

§__.116(a)(4)
General Improvements

Information presented in **sufficient detail**, and **organized and presented** in a way that facilitates subject’s understanding of reasons why one might or might not want to participate

- **i.e., do not merely provide lists of isolated facts**

§_.116(a)(5)(ii)
General Improvements

The revised Common Rule has a new requirement that certain key information must be provided first.

§.116(a)(5)(i)
Concise and Focused: Key Information

That first section must provide a **concise and focused** presentation of **key information** regarding **why one might or might not want to participate**

§._.116(a)(5)(i)
Elements of Informed Consent

One new BASIC element:

- Notice about possible future research use of information or biospecimens stripped of identifiers:
  - Notifying prospective subject that subjects’ information or biospecimens could be used for future research without additional consent; or
  - Notifying prospective subject that subjects’ information or biospecimens will not be used for future research.

§_.116(b)(9)
Elements of Informed Consent

Three new ADDITIONAL elements:

• Notice about whether clinically relevant research results, including individual research results will be given to subjects, and if so, under what conditions

• Notice about possible commercial profit, and whether subject will share in this profit (for research involving biospecimens)

• Notice about whether research might include whole genome sequencing (for research involving biospecimens)
Allowing the Use of Broad Consent for Secondary Research

• **OPTIONAL:** An alternative to traditional informed consent or waiver of informed consent

• **Applicable to:**
  - The storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens
  - Collected for either a different research study, or for non-research purposes

• **Creates future regulatory flexibilities**
What is Secondary Research?

Research use of information or biospecimens collected for either research studies other than the proposed research, or for nonresearch purposes (e.g., clinical care, public health, education)
Posting of Consent Forms for Clinical Trials

- For clinical trials supported by federal funding, one IRB-approved consent form used to enroll participants must be posted on publicly available Federal website to be designated.
- Post after recruitment closes, no later than 60 days after last study visit.
- Federal department or agency may permit or require redactions.

\$116(h)
Waiver of Consent

- New waiver criterion for research with identifiable private information or identifiable biospecimens
- The IRB must determine that the research could not \textit{practically} be carried out without accessing or using identifiers
- \textit{Non-identified} information should be used whenever possible in order to respect subject’s autonomy

§116(f)(3)(iii)
No Waiver if Broad Consent Refused

IRB cannot waive consent if individuals were asked, and refused, to provide broad consent to the storage, maintenance and use of identifiable private information or identifiable biospecimens.

§.116(f)(1)
### Summary of Changes to Exemptions

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<th>Pre-2018 Rule (Current)</th>
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*New Exemption 7
*New Exemption 8
*New - Limited IRB Review
Exemption Applicability - Subparts C&D

- **Pre-2018 Rule (Current)**
  - Subpart C prisoners research – none apply
  - Subpart D children research - exemption 2 for research involving survey or interview procedures or observations of children by investigators who participate in the activity being observed does not apply; other exemptions apply

- **Revised Common Rule**
  - Subpart C prisoners research expanded – exemptions do not apply except for research aimed at involving a broader subject population that only incidentally includes prisoners
  - Subpart D children research:
    - Same restrictions as above for exemption 2 plus new provision §_.104(d)(2)(iii) also not applicable
    - New exemption 3 does not apply
Exemption 1: Restrictions Added

- Normal educational practices in established or commonly accepted educational settings
- New: normal educational practices that are not likely to adversely impact students’ opportunity to learn required educational content, or
- The assessment of educators who provide instruction

§.104(d)(1)
Expanding Exempt Research: Exemption 2

Educational tests, surveys, interviews, and observations of public behavior exemption when

- Information recorded cannot be readily linked back to subjects, or
- Any information disclosure would not place subjects at risk of harm, or
- Identifiable information recorded with limited IRB review for privacy and confidentiality protection under §.111(a)(7)

§.104(d)(2)
What Happened to Exemption 3?

- Removed from revised rule: Research involving the use of educational tests, survey procedures, or observation of public behavior if:
  - The human subjects are elected or appointed public officials or candidates for public office, or
  - Federal statute requires protects confidentiality without exception.
- Almost all such research would be exempt under the new exemption 2. If researchers record sensitive identifiable information about public officials, it must be kept confidential.
Expanding Exempt Research: New Exemption 3

New exemption for research involving benign behavioral interventions with adults who prospectively agree when information collection is limited to verbal or written responses (including data entry) or audiovisual recording, and:

- Information recorded cannot be readily linked back to subjects, or
- Any information disclosure would not place subjects at risk of harm, or
- Identifiable information recorded with limited IRB review for privacy and confidentiality protection under §111(a)(7)

§104(d)(1)
Exemption 3, Cont’d

• What are “benign behavioral interventions?”
  • Brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing

• Includes authorized deception research

§_.104(d)(3)
Secondary research use of identifiable private information or identifiable biospecimens (materials no longer need to be “existing”) if:

1. Identifiable private information or identifiable biospecimens are publically available, OR

2. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot be readily ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects or re-identify subjects, OR
Secondary research use of identifiable private information or identifiable biospecimens for which consent is not required, if:

3. Investigator’s use is regulated under HIPAA as “health care operations,” “research,” or “public health” OR

4. Research is conducted by, or on behalf of, a Federal agency using data collected or generated by the government for non-research purposes, and the information is protected by federal privacy standards

§.104(d)(4)
Exemption 5: Expanded

Public benefit and service programs research and demonstration projects

- Expanded to apply to federally-supported research; no longer limited to federally-conducted research
- Added requirement that Federal agency publish a list of projects covered by this exemption prior to commencing the research

§_.104(d)(5)
Exemption 6: No Change

- Taste and food quality evaluation and consumer acceptance studies

§.104(d)(6)
Expanding Exempt Research
New Exemptions 7 and 8: Require Broad Consent

- Exemption 7: Storage or maintenance of identifiable private information or identifiable biospecimens for secondary research
- Exemption 8: Secondary research using identifiable private information or identifiable biospecimens

§.104(d)(7)and (8)
“Limited” IRB Reviews

- Required for exemptions 2(iii), 3(i)(C), 7, and 8 in the revised Common Rule
- Exemptions 2(iii) and 3(i)(C) review:
  - For privacy and confidentiality protection under §._.111(a)(7)
- Exemptions 7 & 8 reviews:
  - For other safeguards related to privacy and confidentiality protection, and broad consent
Updating and Simplifying Expedited Review

- List will be reviewed every 8 years and updated if necessary.

- Presumption that activities listed are minimal risk.
  - Unless expedited reviewer determines otherwise, which would make the study not expeditable and would need to be documented.

- Limited IRB review has been added to list of permissible use of expedited review mechanism.

§_.110, §_.109(f), and §_.115(a)(8)
Eliminating Certain Continuing IRB Reviews

- In general, no continuing review required for:
  - Research approved by expedited review
  - Exempt research requiring limited IRB review
  - Research has completed interventions and only involves:
    - Analyzing data, including analyzing identifiable private information or identifiable biospecimens
    - Accessing follow-up clinical data from clinical care procedures
  - IRB can override this default and require continuing review, but this must be documented

§.109(f) and §.115(a)(3)
Single IRB Review for Multisite Studies

● Applies to:
  ● U.S. institutions engaged in cooperative research for the portion of the research conducted in the U.S.

● Does not apply:
  ● When more than single IRB review is required by law (including tribal law)
  ● Whenever any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context – flexibilities allowed

§_.114(b)
Other Changes to Reduce Burden and Increase Flexibility

- Eliminating IRB roster reporting to OHRP
- Eliminating grant application review
- Eliminating the option on Federalwide Assurance (FWA) to “check the box”
Transition and Implementation
Implementation Dates

- Before January 19, 2018, all activities must comply with the pre-2018 rule
  - Note that you can implement revised Common Rule provisions that do not conflict with the pre-2018 rule
- Any study started on or after January 19, 2018 must comply with the revised Common Rule
- The requirement for single IRB review in multi-institutional studies goes into effect January 20, 2020
General Implementation of the Transition Provision

Transition date for revised Common Rule

Pre-2018 Rule applies to all studies

Studies initially “approved” before January 19, 2018
• Presumption: Pre-2018 rule applies
• Institution may elect to apply the revised Common Rule. IRB must document this in writing.

Studies initially “approved” on or after January 19, 2018: Revised Common Rule applies

January 19, 2018
Where are the potential landmines?

- FDA is not a Common Rule agency and has not revised their regulations, which apply to some of the same studies.
- When you’ve seen one IRB… you’ve still seen one IRB.
- How will IRBs implement “limited” review?
Questions About the Revisions?

- OHRP will be developing resources to explain the revised Common Rule. Check out [www.hhs.gov/ohrp](http://www.hhs.gov/ohrp)

- Submit your questions to [OHRP@hhs.gov](mailto:OHRP@hhs.gov)
Acknowledgments

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