The Final Common Rule: What Does It Mean for Health and Life Sciences Stakeholders?

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Federal Policy for the Protection of Human Subjects ("Common Rule")

- Research oversight framework adopted by 15+ federal Departments and Agencies
- Not materially updated since original 1991 publication
- Revisions had been in progress for 5+ years
- Most of the more aggressive proposals ultimately were not finalized
- Compliance Date:
  - January 19, 2018 for nearly all changes
  - January 19, 2020 for new cooperative research IRB requirement requiring centralized IRB

1991 – Common Rule Published

July 2011 – ANPRM

September 2015 – NPRM

January 2017 – Final Rule
Presentation Overview

- Evolution of Final Rule
- Substance and Impact
  - Common Rule Jurisdiction and Scope
  - Definitional Changes
  - Key “Streamlining” Changes: Improved Alignment of Risk with Scope of IRB Review
  - Changes to Basic Informed Consent Requirements and New “Broad Consent” for Secondary Research
  - New Key Exempt Categories Relating to HIPAA and Secondary Use
  - Takeaways and Remaining Friction with HIPAA
- Common Thread: New Explicit Focus on Privacy Risk and Secondary Research
Overall Theme of the Changes

- Modernize the Common Rule so as to recognize and respond to:
  - Changes in technology
  - Proliferation of and demand for data sharing for research
  - Corresponding proliferation and demand for storage and use of data and biospecimens for secondary research
  - Increasing role of genomics in research and precision medicine

- Streamline and simplify the Common Rule’s process for IRB oversight of the design and implementation of research studies so as to facilitate and accelerate biomedical research and discovery
Common Rule Jurisdiction & Scope

Did not extend of Common Rule to all clinical trials regardless of funding source

Extends direct oversight and enforcement authority to “independent” IRBs (i.e., those unaffiliated with FWA-holding institutions)

Eliminates 4b Federalwide Assurance (FWA) elections – OHRP no longer permitted to exercise oversight/enforcement authority over non-federally funded human subjects research, even if conducted by institution receiving federal funding for other human subjects research

Did not finalize proposed “exclusion” categories

Practice Note for FWA Institutions
- May continue to rely on internal policies and oversight mechanisms that reflect Common Rule requirements (so as to apply the same standards to all human subjects research, irrespective of funding source)
- However, self-oversight of compliance will be necessary
- Need to honor or amend current contractual commitments to comply with Common Rule and develop contracting position going forward
Changes to “Human Subject” Definition

- Clarified definition to expressly include biospecimens as well as data
- Did not finalize proposal to treat all biospecimens as “human subjects”
- Definition: A living individual about whom a researcher:

**ORIGINAL**

- (1) Obtains data through *intervention* or *interaction* with the individual; OR
- (2) Obtains identifiable *private information*

**FINAL RULE**

- (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*.
Changes to “Human Subject” Definition: More to come regarding Identifiability of Data and Biospecimens?

- **Identifiable private information and identifiable biospecimens:**
  - Key phrase in definition: Where identity “is or may readily be ascertained”

- Final Rule requires HHS to periodically confer with experts to reassess:
  1) The meaning of identifiability in the Common Rule context
     - Permits HHS to “alter the interpretation” of definitions relating to “identifiability” based on reassessments, as appropriate and permitted by law, including through issuance of guidance rather than formal rulemaking
  2) New technologies and techniques that can generate identifiable private information or identifiable biospecimens
     - HHS must publish a list of technologies/techniques that meet this requirement with opportunity for public notice and comment
     - Use of technologies and techniques on this list may de facto require consent or waiver
     - HHS “expects” whole genome sequencing to be one of the first evaluated for inclusion
Changes for Common Rule-Regulated Studies

▪ Cooperative research
  – Single IRB must be used for multi-site studies conducted in the U.S.
    ▪ Only limited exceptions
  – Compliance date: January 19, 2020

▪ Common Rule departments and agencies must harmonize future guidance before issuance
Research “Streamlining” Changes:
Improved Alignment of Risk with Scope of IRB Review: Continuing Review

- Unless IRB determines otherwise, continuing IRB review is not required for any of the following:
  - Research that qualifies for expedited review
  - Research initially subject to only limited IRB review (e.g., exempt categories)
  - Research for which only data analysis remains
  - Research for which only assessment of follow-up clinical care data remains
Research “Streamlining” Changes:
Improved Alignment of Risk with Scope of IRB Review: Recruitment

- **Certain preparatory to research activities** (scope is narrower than HIPAA)
  - IRBs may now approve proposals in which researcher obtains information or biospecimens for screening, recruiting, or study eligibility purposes **without** informed consent (or waiver thereof)
  - Researcher would obtain data from individual through oral or written communication, or access stored / archived identifiable materials
  - Reflects effort to align with FDA and HIPAA requirements and ease administrative burden **BUT NOTE THAT DIFFERENCES REMAIN:**
    - Common Rule still requires IRB review even though consent/waiver is not required
    - Scope of HIPAA’s preparatory to research pathway is limited
      - A HIPAA authorization waiver may be required even if Common Rule consent waiver is not (but note new HIPAA-related exemption (discussed later) that will reduce instances in which both HIPAA and Common Rule apply)
Scenario 1: Research Site Opportunity

A Hospital is approached by a for-profit industry sponsor to serve as a research site. The Hospital wishes to administer a short questionnaire to patients who come in for certain procedures to determine their eligibility for the study.

**Question:** If the Hospital complies with the HIPAA preparatory to research rule, does the Hospital have any additional compliance obligations under the Common Rule?
Scenario 1: Research Site Opportunity

- **Question:** If the Hospital complies with the HIPAA preparatory to research rule, does the Hospital have any additional compliance obligations under the Common Rule?

- **Analysis:**
  - Consider funding source
  - Review new screening pathway under the Common Rule (if applicable)
    - Note IRB review is still contemplated under this pathway
Informed Consent: Significant Changes
New Requirements for Obtaining Consent

- Final Rule includes new requirements for obtaining informed consent
- Content, Organization, and Presentation
  - Must “begin with a concise and focused presentation of the key information” pertinent to the individual’s decision
  - Mere recitation of facts is not sufficient. Information must be organized and presented in a way that supports the individual’s understanding of the pros and cons of participating in the research study
  - Must include information that a reasonable person would want to have to make an informed decision
- Concise and focused presentation requirement may not be omitted or altered by IRB
Informed Consent: Significant Changes
New Requirements for Obtaining Consent

▪ IRB should focus on the **content** rather than the length of the form

⚠️ However, the “concise and focused” beginning section should be **no more than a few pages for a complicated clinical trial**

• Beginning of consent form would typically include/describe:
  ✓ Statement that participation is voluntary
  ✓ Purpose of research, duration of participation, and research procedures
  ✓ Reasonably foreseeable risks and discomforts
  ✓ Benefits
  ✓ Any alternatives

▪ **Does not finalize** NPRM’s proposed “dual document” system that requires certain information to be included only in appendices
## Informed Consent: Significant Changes

New Key Consent Elements For Secondary Use, Genomic Research, and Discoveries

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Requirement</th>
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<tbody>
<tr>
<td>If study collects identifiable private information/specimens:</td>
<td>• Statement that identifiers might be removed and then the data/specimens could be used or distributed without additional consent, <strong>or</strong> a statement that this will not occur (BASIC ELEMENT)</td>
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<td>If study contemplates commercial profit from biospecimens:</td>
<td>• Statement regarding the profit and whether subject will share (ADDITIONAL ELEMENT)</td>
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<td>If study plans to disclose clinically relevant research results:</td>
<td>• Statement describing disclosure and conditions for disclosure (ADDITIONAL ELEMENT)</td>
</tr>
<tr>
<td>If study will or may include whole genome sequencing of specimens:</td>
<td>• Statement indicating such (ADDITIONAL ELEMENT)</td>
</tr>
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Informed Consent: Significant Changes
IRB Waiver or Alteration of Consent Changes

- Adds new criterion modeled after a HIPAA waiver criterion:
  - Investigator must demonstrate that the research could not practicably be carried out without using the information or biospecimens in an identifiable format
  - Designed to protect privacy and promote use of non-identifiable information as possible
- HHS declined to define “practically”
Informed Consent: Significant Changes
New Broad Consent Pathway for Repositories and Secondary Use

- New **one-time upfront broad consent** pathway for researchers who wish to store and maintain identifiable private information/specimens and for subsequent secondary use of the stored information

⚠️ Available for **secondary research only** (i.e., this broad consent pathway is not available for the primary collection of information/specimens through an intervention with a subject)

- Described as an optional **alternative** to study-specific consent, waiver of consent, or research with de-identified information/specimens – not a mandate
- Not entirely new – the pre-2018 Common Rule already allowed researchers to obtain consent for future use
Informed Consent: Significant Changes
New Broad Consent Pathway for Repositories and Secondary Use: Elements

- Examples of information that must be included in a broad consent (IRB cannot omit or alter):
  - Unless subject will receive details about specific research studies, a statement that s/he will not be informed of details of any specific research studies that may be conducted using his/her identifiable private information/specimens, and that s/he might not have chosen to provide consent for some of these specific research studies.
  - Statement regarding any use of specimens for commercial profit and whether subject will share (if applicable).
  - If the research will or may include whole genome sequencing (if applicable).
  - Statement that clinically relevant research results will not be disclosed back (if applicable).

But IRBs still may omit or alter elements of study-specific consent.

- Query: Is study-specific consent still an option for obtaining consent for storage/maintenance/secondary use for which broad consent could have been obtained?
• Obtaining broad consent is one of the criteria under the two new exempt research categories that allow investigators to obtain only limited IRB review and be exempt from continuing review for the:
  (1) Storage and maintenance, or
  (2) Secondary research use of identifiable private information/specimens (see later slides).

• More prescriptive – requires the disclosure of more information than under pre-2018 Common Rule, some of which may cause individuals to be more reluctant to provide the broad consent.

• More rigid – IRBs cannot omit or alter any elements

• IRB may not waive if individual was asked to and declines to provide broad consent. Thus, need broad consent tracking mechanism.
Informed Consent: Significant Changes
New Broad Consent Pathway: Implications

- Do the incentives outweigh the potential drawbacks?
  - Rate of adoption by researchers remains to be seen
  - NPRM sought public comment on how likely investigators are to seek broad consent
  - A majority of the 30 commenters who responded said they would not use broad consent “if other options were available”

- Did OHRP include this pathway in anticipation of changes it may make in the future to the identifiability standards (through guidance or after notice and comment)?
Scenario 2: Biospecimen Research Repository Start-Up

Using federal funding, a Hospital wishes to create a biospecimen research repository using leftover biospecimens originally obtained in connection with diagnosis or treatment.

▪ **Question:** What are the pros and cons of its various options (e.g., de-identified data, waiver, or identifiable)?

![Diagram showing Hospital, Leftover biospecimens from medical Dx / Tx, and Proposed biospecimen research repository.]
## Scenario 2: Biospecimen Research Repository Start-Up

<table>
<thead>
<tr>
<th></th>
<th>Pros</th>
<th>Cons</th>
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<tr>
<td><strong>Broad Consent</strong></td>
<td>• Access to identifiers useful for research</td>
<td>• Costly and burdensome</td>
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<td></td>
<td>• Component of two exempt categories that involve limited review and no continuing IRB review</td>
<td>• Prescriptive (no elements can be waived/ altered)</td>
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<td></td>
<td>• Opportunity for individual to decline</td>
<td>• IRB cannot later waive if broad consent was declined</td>
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<td></td>
<td>• Sign of the future as identifiability standards change?</td>
<td>• HIPAA and state law considerations</td>
</tr>
<tr>
<td><strong>Study-Specific Consent</strong></td>
<td>• Access to identifiers useful for research</td>
<td>• Costly and burdensome</td>
</tr>
<tr>
<td></td>
<td>• May be viewed as more supportive of subject autonomy and agency</td>
<td>• Prescriptive</td>
</tr>
<tr>
<td></td>
<td>• Opportunity to ask IRB to omit/ alter certain elements</td>
<td>• Must seek new consent for future studies if not included in scope of consent provided</td>
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<tr>
<td><strong>Waiver</strong></td>
<td>• Access to identifiers useful for research</td>
<td>• May not meet waiver criteria</td>
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<tr>
<td></td>
<td>• Less administrative burden and cost</td>
<td>• Patient/subject relations (less autonomy)</td>
</tr>
<tr>
<td><strong>De-identified or Coded</strong></td>
<td>• Less administrative burden</td>
<td>• HIPAA and state law considerations</td>
</tr>
<tr>
<td></td>
<td>• Once de-identified or coded, ongoing/additional compliance obligations are minimized</td>
<td>• May not meet research needs</td>
</tr>
<tr>
<td></td>
<td>• Outside scope of HIPAA and many state laws</td>
<td>• Patient/subject relations (less autonomy)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Identifiability debate not over. Sustainable?</td>
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<td>• More difficult with unstructured data</td>
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Overhaul and Expansion of Exemption Pathways

- Did not adopt proposed “exclusion” categories
  - Excluded research would not have been subject to Common Rule
  - Some proposed “excluded” categories were incorporated as new exemptions
- Establishes new and expanded “exempt” categories
  - Includes, among others, new or expanded exempt categories that are of significance for entities that either:
    - are also regulated under HIPAA or
    - seek to engage in the banking and secondary use of identifiable private information or biospecimens
Overhaul and Expansion of Exemption Pathways: Secondary Research Without Consent, Including Certain HIPAA-Regulated Activities

New expanded exempt category permits secondary research with identifiable private information or identifiable biospecimens *without subject consent* in 4 instances:

- Study only collects and analyzes identifiable private information and is regulated as “research,” “health care operations,” or for “public health activities and purposes” under HIPAA, OR
- Where identifiable private information or identifiable biospecimens are publicly available, OR
- Data is recorded in a manner by which subject’s identity can’t readily be ascertained, AND researcher will not re-identify subjects, OR
- Research conducted by or for Federal agency using government-generated or –collected info first obtained for non-research purposes, if certain storage, maintenance, and compliance requirements are met
Overhaul of Exemption Pathways: Secondary Research Without Consent: HIPAA Considerations

- New HIPAA exempt category is notable for covered entities, business associates, and entities that receive data from them
  - Provides welcome easing of administrative burdens (but be mindful of HIPAA obligations)
  - May reflect HHS’s view that the primary risk of these activities is the risk to privacy, such that need for additional protections under the Common Rule do not outweigh the administrative burden

But note:
- Despite exemption, researcher must still work with IRB or privacy board if the research activity requires a waiver of HIPAA authorization
- Example: Researcher seeks to create large repository of identifiable data using old clinical records, where it would be impracticable to obtain a HIPAA authorization from each patient
Overhaul of Exemption Pathways: Secondary Research with Identifiable Information and Specimens Using Broad Consent

Storage / Maintenance for Potential Secondary Research

• Broad consent is properly obtained, **AND**
  • IRB conducts limited review and confirms that:
    • broad consent was properly obtained and is properly documented (unless documentation is waived), and
    • provisions protecting privacy and confidentiality are in place if a change to the manner of storage or maintenance is made

Secondary Research Use

• Broad consent was properly obtained when first storing the information,
• Documentation that consent was properly obtained (or waiver of documentation),
• IRB conducts limited review and confirms study falls within scope of broad consent, **AND**
• Official protocol does not include return of individual research results
Overhaul of Exemption Pathways: Secondary Research with Identifiable Information and Specimens Using Broad Consent

- These two exemptions effectively function as a “safe harbor” from Common Rule requirements. If new broad consent requirements and other exempt criteria are satisfied, the research is subject to more limited IRB review.

⚠️ Practical utility is unclear:
- **Broad consent for initial storage / maintenance of identifiable information in a repository is required in order to obtain the broad consent exemption for future research use of the repository information**
- IRB review ultimately still required (even if limited)
- Use of secondary research exemption would require working with repositories that had obtained upfront broad consent in compliance with the Common Rule, even if the repository itself was not federally funded or otherwise subject to Common Rule requirements.
  - **Key if the creator of the repository and the subsequent user of the information/specimens are not the same**
Revisiting Scenario 2: Biospecimen Research Repository Start-Up

Using federal funding, a Hospital wishes to create a biospecimen research repository using leftover biospecimens originally obtained in connection with diagnosis or treatment.

- **Question:** *Is the new HIPAA-related exemption available if the repository contains identifiable specimens?*
Revisiting Scenario 2: Biospecimen Research Repository Start-Up

- **Question:** Is the new HIPAA-related exemption available if the repository contains identifiable specimens?
- **Analysis:**
  - Note scope of HIPAA-related exemption (information collection and analysis)
Scenario 3: Leveraging Registry Data for New Federally-Funded Study

A Hospital wishes to conduct a research study using identifiable private information from its research registry. The registry was not federally funded at its creation, and no upfront consent was obtained. The Hospital is also weighing whether to accept an offer of funding from a for-profit, private research institution, or to pursue federal funding for the study.

Question: What are Hospital’s options to conduct the research study if it accepts the private grant? What if it obtains federal funding for the study?
Scenario 3: Leveraging Registry Data for New Federally-Funded Study

Analysis:

- If the Hospital accepts the **private funding**:  
  - Consider new, more limited scope of the Common Rule  
  - Option to voluntarily comply and self-regulate compliance  
  - Note HIPAA requirements still apply

- If the Hospital accepts the **federal funding**:  
  - Note new HIPAA-regulated secondary research exemption  
  - Some HIPAA pathways to consider: IRB waiver of authorization or using a limited data set (if feasible based on research needs)  
  - Decision to accept federal funding may depend on current research programs and administrative burden (e.g., if already conducting other federally-funded human subjects research)
Major Stakeholder Takeaways

- Despite decision to forego the controversial changes, the changes made impose new notable requirements
  - Changes to consent models may discourage some from obtaining consent for biobanking and future use
  - Identifiability standard remains in flux
- Does not fully resolve friction between Common Rule and HIPAA regarding:
  - Status of Limited Data Sets under the Common Rule
  - Common Rule’s treatment of Quality and other Health Care Operations activities
    - HHS did not adopt the proposal to “exclude” certain quality assurance / quality improvement activities from the Common Rule
- But new exemption for certain HIPAA-regulated activities may reduce need to grapple with interplay between HIPAA and the Common Rule
- Note certain areas that are expected to be updated by future guidance
  - Reshaping of identifiability standard
  - Development of “exemption determination” tool or other materials to help assist with exemption determinations (as contemplated in the NPRM)
  - Additional color about key information to be included in consent forms
  - Guidance for IRBs in making new waiver determinations
Major Stakeholder Takeaways

▪ For more information, please see Publication available at: https://www.mwe.com/en/thought-leadership/publications/2017/02/hhs-finalizes-common-rule-overhaul
Thank you