The Common Rule NPRM:
Most Critical Issues
Agenda

• Background
• NPRM Significant Provisions
  – Biospecimen Research
  – Informed Consent
  – Exclusions and Exemptions
  – IRB Review
  – Data Security Safeguards
  – Harmonization and Extension of Common Rule
• Implications for Research and Clinical Practice
• Conclusion
In 1979, following reports of numerous unethical research studies, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research developed the Belmont Report. The Belmont Report identified three fundamental ethical principles for all human subjects research:

- Respect for Persons
- Beneficence
- Justice
Background: Common Rule

• In 1991, the Department of Health and Human Services (HHS) developed a set of regulations, adopted by 14 other federal departments and agencies, known as the Common Rule

• Intended to create a uniform body of regulations to protect human subjects involved in clinical research

• Applied Belmont Report’s three principles
Background: Changes in Research Landscape

- Since 1991, the nature, volume, and settings of clinical research have changed considerably
- More research is being conducted in outpatient clinics and in physician group practices, as well as in clinical care settings that combine an individual’s research and medical data
- The number of biospecimen repositories and large clinical databases has risen dramatically
- Research is also expanding in geographic scope, with studies often conducted at multiple domestic and international sites and across research networks
- Changes in nature of risks
  - Researchers may not interact directly with research subjects, instead analyzing information obtained from medical records, administrative claims data, and existing biospecimens stored in repositories
  - Risks are largely related to privacy and confidentiality, not physical harm
Background: ANPRM

On July 26, 2011, HHS, in coordination with the Executive Office of the President’s Office of Science and Technology Policy, published an advanced notice of public rulemaking (ANPRM) to request comment on how to modernize and improve the effectiveness of the Common Rule.

ANPRM posed 74 questions to the public.
ANPRM identified five significant possible changes to the Common Rule:

1. Establishing mandatory data security and information protection standards for identifiable information
   - Establish rules protecting against the inappropriate re-identification of de-identified information that is collected or generated as part of a research study
   - Intended to minimize informational risks and thereby eliminate the need for IRBs to review informational risks of the research
2. Continuing Review

- Would be eliminated for all minimal risk studies that undergo expedited review, unless the reviewer explicitly justifies why continuing review would enhance protection of research subjects.

- For studies initially reviewed by a convened IRB, continuing review would not be required, unless specifically mandated by the IRB, after the study reaches the stage at which procedures are limited to either:
  
  A. Analyzing data (even if it is identifiable); or
  
  B. Accessing follow-up clinical data from procedures that subjects would undergo as part of standard care for their medical condition or disease.
3. Expedited Review

- Mandatory regular updating of the list of categories of research that may be reviewed under this mechanism
- Creating a presumption that studies utilizing only research activities that appear on that list are minimal risk
- Providing for streamlined document submission requirements for review
4. Exempt Research

- Require that researchers file with the IRB a brief form to register their exempt studies, but generally allow the research to commence after the filing

- Clarify that routine review by an IRB staff member or some other person of such minimal risk exempt studies is neither required nor even recommended

- Expand the current exemption (regarding the collection or study of existing data, documents, records and biospecimens) to include all secondary research use of identifiable data and biospecimens that have been collected for purposes other than the currently proposed research, provided that specified new consent requirements are satisfied
5. Consent for Future Biospecimen and Data Research

- Generally require written consent for research use of any biospecimens and data collected for clinical purposes
- Such consent could be obtained by use of a brief standard consent form agreeing to permit unspecified future research
- This brief consent could be broad enough to cover all biospecimens and data to be collected related to a particular set of encounters with an institution (e.g. hospitalization) or even to any biospecimens and data to be collected at any time by that institution
- These studies using biospecimens and data collected for clinical purposes also would not require IRB review but would be subject to the data security and information protection standards
• HHS received 1126 comments to the ANPRM
• On September 8, 2015, HHS issued the NPRM, joined by 15 other federal departments and agencies
• Marks the first systematic attempt to overhaul the Common Rule since its promulgation in 1991
• NPRM aims to “protect human subjects involved in research, while facilitating valuable research and reducing burden, delay, and ambiguity for investigators”
• The 90-day comment period closes on December 7, 2015, though could be extended; many requests to extend are already filed
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Biospecimen Research: Current Common Rule

At present, OHRP does not consider research involving only coded private information or specimens to involve “human subjects” if:

- The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and

- The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
  - The investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators;
  - There are IRB-approved written policies for a repository that prohibit the release of the key to the investigators; or
  - There are other legal requirements prohibiting the release of the key to the investigators
Biospecimen Research: Public Comments to ANPRM

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Biospecimen Research: “Human Subject” (§.102(e)(1))

• NPRM would expand the Common Rule’s definition of “human subject” so that it covers all research uses of biospecimens, irrespective of whether the biospecimens are identifiable.

• Consent for the secondary research use of biospecimens could be waived in extremely limited circumstances, but otherwise would have to be study-specific or broadly applicable to future, unspecified research (“broad consent”)
  – Waiver limited to “compelling” research needs
  – Waiver would be granted rarely
Biospecimen Research: Alternative Definitions of “Human Subject”

• For public comment, the NPRM preamble identifies two alternative approaches, which would expand the definition of “human subject” to include the following:
  
  1. Whole genome sequencing data, or any part of the data generated as a consequence of whole genome sequencing, regardless of the individual identifiability of the biospecimens used to generate such data; or

  2. Research use of information produced using a technology applied to a biospecimen that generates information unique to an individual such that it is foreseeable that, when used in combination with publicly available information, the individual could be identified (“bio-unique information”)
Biospecimen and Identifiable Private Information Research: Broad Consent (§_.116(c))

• Consent would be required for identifiable private information and for both non-identified and identifiable biospecimens

• Consent may be broad or study-specific (§_.116(a), (b))

• The proposed requirements for broad consent are separately listed in the NPRM regulatory text (§_.116(c))

• Broad consent would include:
  – 4 basic elements (§_.116(a))
  – 3 additional elements (§_.116(b))
  – 8 new elements (§_.116(c))
NPRM would require that broad consent include:

- Basic elements under §_.116(a)(2),(3),(5), and (7)
  - Description of reasonably foreseeable risks or discomforts
  - Description of any benefits to the subject or to others that may reasonably be expected
  - A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
  - An explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject
• Additional elements under §116(b)(7)-(9)
  – A statement that the subject’s biospecimens may be used for commercial profit and whether the subject will or will not share in this commercial profit
  – A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions
  – An option for the subject or the representative to consent, or refuse to consent, to investigators re-contacting the subject to seek additional information or biospecimens or to discuss participation in another research study
New elements for broad consent

- General description of the types of research that may be conducted with information and biospecimens
- Information that is expected to be generated from the research
- Types of information or biospecimens that might be used in research
- Types of institutions that might conduct research with the biospecimens or information
• The scope of the informed consent
  – A clear description of the types of biospecimens or information that were or
    will be collected and the period of time during which biospecimen or
    information collection will occur
    • May include all biospecimens and information from the subject’s medical
      record existing at the institution at the time informed consent is sought
    • The period of time during which biospecimen or information collection will
      occur cannot exceed 10 years from the date of consent
    • For research involving children, the time period cannot exceed 10
      years after parental permission is obtained or until the child reaches
      the legal age for consent.
  – Time limitations do not apply to biospecimens or information collected for
    research purposes because such materials generally would be described in
    the initial consent document
  – In contrast, in the clinical context, the biospecimens and information are
    usually less predictable and defined, and thus would not be as readily
    understood to subjects.
• Ability to withdraw consent
  – NPRM would require that subjects be informed that at any time and without penalty or loss of benefits, they may withdraw consent, if feasible, for research use or distribution of the subject’s information or biospecimens
  – However, information that has been stripped of identifiers might not be traceable
  – Thus, it might not be feasible to withdraw consent for future use or distribution
  – Statement must make clear that data or biospecimens already distributed for research use may not be retrieved
• Public posting of non-identifiable data
  – This proposed element of broad consent would include an option, “if relevant,” for an adult subject to consent or refuse to consent, to the inclusion of the subject’s data, with removal of the identifiers listed in the HIPAA Privacy Rule, in a database that is publicly available and openly accessible to anyone
  – Under this provision, the consent document would be required to note the option prominently, and to include a description of the risks associated with public access to the data
  – This provision may be misaligned with recent regulatory requirements, including those imposed by EMA and some journals, that all such subject-level de-identified data be posted publicly or otherwise be made available to third-party researchers
• To facilitate the use of broad consent, the NPRM proposes that HHS Secretary will publish in Federal Register broad consent templates containing all required elements of consent.

• NPRM notes that at least two broad consent templates would be developed for:
  1. Information and biospecimens originally collected in the research context; and
  2. Information and biospecimens originally collected in the non-research context.
• Health care providers and all settings where biospecimens are regularly collected (e.g. physician offices, school clinics, public health clinics, mental health agencies, developmental disability settings, nursing homes) – if they wish to be able for biospecimens to be used for future downstream research – will be required to secure broad consents from patients

• Consent or refusal to consent to broad future uses of biospecimens must be recorded and tracked

• Research biospecimens are less difficult, as broad consent can be built into the research consent
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Informed Consent Requirements (§_.116)

• NPRM proposes to modify the informed consent regulations to facilitate shorter and more understandable consent forms.

• NPRM aims to address unduly long documents in which important information may be difficult for a subject to find.
Facilitate Consent Comprehension

- NPRM emphasizes the need that consent forms provide information that a reasonable person would want to know in order to make an informed decision about whether to participate, and to provide an opportunity to discuss that information.

- Would require that information in consent forms be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject’s understanding of the reasons why one might or might not want to participate.
Presentation of Consent Information

• NPRM also proposes that in obtaining informed consent, the investigator be required to present first the Common Rule-required information, before providing other information, if any, to the subject

• Consent document would only include the elements of consent that were required by the Common Rule, with any other information included in an appendix

• NPRM intends for this scheme to shorten consent forms substantially and avoid burying key information in a long and overly complex document
HIPAA Authorization in Consent Form (§ 1.116)

- Under NPRM, if a HIPAA authorization is combined with a consent form, the required HIPAA authorization elements must be included in the consent document and not the appendices.
“Legally Authorized Representative”

- Current Common Rule defines “legally authorized representative” (LAR) as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research.
- NPRM preamble notes that this definition has been problematic for states in which there is no applicable law permitting an LAR to consent in either a clinical or a research context.
- In the absence of such a law, generally community or other standards (such as institutional policies) define hierarchies or identify individuals who may provide legally effective consent, for clinical purposes, on behalf of others who cannot consent for themselves.
- NPRM seeks comment on revising the current definition to also permit an LAR for research purposes to be determined by an accepted common practice standard that is used in a state for determining who can legally consent to clinical care.
New Basic Element of Consent (§.116(a)(9))

- Under the NPRM, research with non-identified data would continue to be regarded as not involving “human subjects”
- NPRM proposes a requirement to ensure that subjects are informed of the possibility that identifiers could be removed from collected data, and then the non-identified data could be used for secondary research studies without the Common Rule protections
- New basic element of consent would apply to all research collecting identifiable private information
- Based on the investigator’s plans, consent form would need to inform subjects either that:
  A. Identifiers might be removed from the data and that the non-identified data could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject; or
  B. Subject’s data collected as part of the research would not be used or distributed for future research studies, even in a non-identified form
NPRM also proposes additional elements of consent:

1. Statement that subject’s biospecimens may be used for commercial profit and whether the subject will or will not share in this commercial profit

2. Statement whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions

3. An option for subject to consent, or refuse to consent, to investigators re-contacting the subject to seek additional information or biospecimens or to discuss participation in another research study
Posting of Consent Forms (§_.116(h))

• NPRM: an additional means of increasing transparency and facilitating the development of more informative informed consent forms is to require that a copy of the final version of the consent form for clinical trials conducted or supported by a Common Rule department or agency be posted on a publicly available Federal website.

• Within 60 days after the trial closes to recruitment, the awardee or the federal department or agency conducting the clinical trial would be required to post the consent document, the name of the clinical trial and information about whom to contact for additional details about the trial.

• NPRM: “The primary purpose of this provision is to improve the quality of consent forms in federally funded research by assuring that—contrary to current practices, under which it is often very difficult to ever obtain a copy of these documents—they eventually would become subject to public scrutiny.”
Waiver of Consent: New Criterion (§_116(f)(1))

• NPRM proposes to add a new waiver criterion: for research involving access to or use of identifiable biospecimens or identifiable information, the research could not practicably be carried out without accessing or using identifiers.

• NPRM modeled this on the similar criterion in the HIPAA Privacy Rule, which requires that the research could not practicably be conducted without access to and use of the protected health information.
Waiver of Consent:
Additional Criteria for Biospecimen Research (§_.116(f)(2,3))

• Additional, more stringent waiver conditions would apply to research involving biospecimens:
  1. “Compelling scientific reasons” for the research use of the biospecimens; and
  2. Research could not be conducted with other biospecimens for which informed consent was or could be obtained

• NPRM would prohibit IRBs from waiving informed consent if individuals were asked and refused to provide broad consent to the storage and maintenance for secondary research use of biospecimens and identifiable private information
  – Implication is that broad consent or refusal to consent must be recorded and tracked
Waiver of Consent: Recruiting and Determining Eligibility (§_.116(g))

• NPRM would allow an IRB to approve a research proposal in which investigators, for eligibility screening and recruitment, obtain identifiable private information from prospective human subjects of research without informed consent, provided that the research proposal includes an assurance that the investigator will implement standards for protecting the obtained information.

• Under the current Common Rule, IRBs generally waive the requirement for informed consent.

• FDA’s regulations do not require informed consent or a waiver of informed consent for such activities.
Waiver of Informed Consent: “Practicability”

- NPRM preamble offers new insight into how OHRP interprets the standard
- OHRP states its agreement with position of HHS Secretary’s Advisory Committee on Human Research Protections (SACHRP), which has identified the following concepts to help an IRB determine whether the research could not be practicably carried out without the waiver of consent:
  1. Scientific validity would be compromised if consent were required;
  2. Ethical concerns would be raised if consent were required;
  3. There is a scientifically and ethically justifiable rationale why the research could not be conducted with a population from whom consent can be obtained; and
  4. Practicability should not be determined solely by considerations of convenience, cost, or speed.
Waiver of Documentation: Distinct Cultural Groups (§117(c)(1))

• NPRM would allow waiver of documentation if subjects are members of a distinct cultural group or community for whom signing documents is not the norm, if:
  – Research presents no more than minimal risk of harm to subjects; and
  – Appropriate alternative mechanism for documenting that informed consent was obtained

• Study documents must include a description as to why signing forms is not the norm for the distinct cultural group or community
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Exclusions (§ 101(b))

- NPRM proposes new section of the regulation for research that would be excluded from the Common Rule
- 11 specific types of excluded activities, some of which are “exempt” under the current Common Rule
- Unlike exempt research, “excluded” activities would not be expected to undergo any institutional, administrative or IRB review to determine whether the activity is excluded
- Investigators would be responsible for self-determining whether their research is excluded
- Excluded research should still be conducted consistently with the principles outlined in the Belmont Report
Exclusions: Categories of Exclusion Types

• Six exclusions are activities that are not “research”
  – The NPRM proposes to list these exclusions explicitly to eliminate confusion that exists under the current Common Rule regarding whether the activities are research

• Four exclusions are activities that are “low risk” or subject to sufficient protections independent of the Common Rule
  – “Low risk” means activities that do not entail physical risk and the probability of other risks is hypothesized to be low

• One exclusion is for a specific type of biospecimen research
Exclusions:
Activities Deemed Not “Research” (§.101(b)(1))

• Program Improvement Activities
  – Includes data collection and analysis, including the use of biospecimens, for an institution’s own internal operational monitoring and program improvement purposes, if (i) originally collected for any purpose other than the currently proposed activity; or (ii) obtained through oral or written communication with individuals (e.g., a survey)

  • Example: a survey of hospital patients to evaluate and improve the quality of delivered meals

  • An example not meeting this exclusion is a prospective observational study of patient treatments to analyze the comparative effectiveness of two different standard of care treatments
Exclusions:
Activities Deemed Not “Research”

• Quality Assurance and Quality Improvement Programs
  – This exclusion covers the implementation of an **accepted practice** to improve the delivery or quality of care or services, **if the purposes are limited to altering the utilization of the accepted practice and collecting data or biospecimens to evaluate the effects on the utilization of the practice**
  – Exclusion would encompass quality improvement activities aimed at implementing practices that are already accepted, with the goal of improving the delivery or quality of treatments or services
    • Example: Randomized study of the implementation of an accepted practice in which half the staff carrying out the practice participate in an educational program regarding the practice whereas the other half do not
  – Would **not** include evaluations of different accepted practices, however, such as activities designed to determine whether a particular accepted medical treatment is or is not more effective than another accepted treatment
Exclusions: Activities Deemed Not “Research”

• Public health surveillance
  – Exclusion category would encompass public health surveillance activities, including the collection and testing of biospecimens, necessary to allow public health authorities to assess potential public health signals or the onset of a disease outbreak
    • Example: FDA’s adverse event reporting systems
  – Subsequent research using information collected during the public health surveillance activity does not meet the exception
Exclusions: Low-Risk and Subject to Other Controls (§ 101(b)(2))

- Collection or Study of Publicly Available or Non-identifiable Information
  - Exclusion would cover research involving the collection or study of information that has been or will be acquired solely for non-research activities or was acquired for research studies other than the proposed research study, if:
    1. Sources are publicly available; or
    2. Information is recorded such that human subjects cannot be identified, directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects or otherwise conduct an analysis that could lead to creating individually identifiable private information
  - This category would not include the secondary research use of biospecimens
Exclusions: Low-Risk and Subject to Other Controls

- HIPAA-Covered Activities
  - NPRM proposes this category to cover activities that are regulated under the HIPAA Privacy Rule
  - These activities involve risks related only to privacy and confidentiality, and are already subject to independent controls provided by HIPAA
  - **NPRM proposes that research involving the use of protected health information by a HIPAA-covered entity for “health care operations,” “public health activities,” or “research,” as those terms are defined under the HIPAA Rules, would be excluded from the Common Rule**
  - Proposed exclusion would not apply if the investigator who receives and uses individually identifiable health information for a research study is not part of an entity that is subject to the HIPAA Rules, even if the entity disclosing the individually identifiable health information to the investigator is itself covered by the HIPAA Rules
**Exclusions**: Low-Risk and Does Not “Meaningfully Diminish Subject Autonomy” (§_.101(b)(3))

- New regulatory standard, based on Belmont Report’s principle of respect for persons
- NPRM proposes to exclude secondary research use of a non-identified biospecimen that is designed only to generate information about the person that is already known
- **Very narrow exclusion**
- This exclusion would include:
  - Development and validation of certain tests and assays, e.g., research to develop a diagnostic test for a condition using specimens from individuals known to have the condition and those known not to have the condition; and
  - Quality assurance and control activities
Exemptions (§_104)

- Current Common Rule’s exemption categories continue in the NPRM, either as exemptions or exclusions (and thus not subject to administrative or IRB review)
- Exempt studies remain subject to certain, specified requirements
- NPRM proposes an important modification to the exemption regulations to assist investigators and institutions in making timely and accurate exemption determinations:
  - Development by federal departments and agencies of a voluntary “exemption determination tool” or algorithm
  - Institutions would be able to rely on the use of the federally developed tool as a “safe harbor” for this determination, so long as the information that has been provided to the tool is accurate
  - Use of the tool would be voluntary
Exemptions:
Low-risk interventions (§.104(d))

- New category involving “benign intervention” and collection of data from adult subject
  - “Benign interventions” would be brief in duration, harmless, painless, not physically invasive, and not likely to have a significant adverse lasting impact on the subjects
  - Investigator would have to have no reason to think the subjects would find the interventions offensive or embarrassing
  - Examples: subject is asked to read materials, review pictures or videos, play online games, solve puzzles, or perform cognitive tasks
  - Subject would need prospectively to agree to the intervention and data collection, and:
    - Information obtained would have to be recorded in such a manner that human subjects could not be identified directly or through identifiers linked to the subjects; or
    - Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation
- Subject only to requirement that a record be kept to demonstrate that the exempt determination was made
Exemptions:
Collection of Sensitive Information (Except Biospecimens) (§.104(e))

- New exemption for secondary research use of identifiable private information originally collected for non-research purposes, if prior notice has been given to the individuals that such information may be used in research
  - Differs from exclusion for non-identifiable information because it permits the investigator to record non-public information in an identifiable fashion
- Under the current Common Rule, IRBs frequently waive consent for research involving the secondary use of identifiable private information, particularly when the data sets are large or drawn from multiple institutions
- Subject to documentation requirements and standards for data security
Exemptions: Biospecimens and Identifiable Information (§_.104(f))

Two exemptions exist to enable the storage of biospecimens for secondary research and the performance of research on such biospecimens

1. Exemption for **storage or maintenance** for secondary research use of biospecimens or identifiable private information that has been or will be acquired for research studies *other than for the proposed research study*, or for non-research purposes, if:
   - Written consent for storage, maintenance, and secondary research use of the information or biospecimens is obtained using the broad consent template; and
   - IRB conducts a limited review of the broad consent process

2. Exemption for **secondary research** use of biospecimens or identifiable private information stored pursuant to the storage and maintenance exemption described above
   - If individual research results will be returned to subjects, then the research is **not** exempted and must be reviewed by the IRB, and standard informed consent for the research must be obtained
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Single IRB Review for Cooperative Research (§ 114)

- NPRM would mandate that all institutions located in the United States engaged in cooperative research rely on a single IRB as their reviewing IRB for that study.

- Reviewing IRB would be selected by the federal department or agency supporting or conducting the research, or by the lead institution if there is no such funding agency or department.

- Requirement would not apply to:
  1. Cooperative research for which more than single IRB review is required by law (e.g., FDA-regulated devices); or
  2. Research for which 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 study.
• NPRM clarifies that this proposal would not relieve any site of its other obligations under the regulations to protect human subjects

• Although a local IRB may conduct its own additional internal review, such a review would not be binding on the local site if not adopted by the single IRB, and its terms would not be enforced by OHRP
IRB Review:
Return of Results (§111(a)(8))

• As a new criterion for IRB approval, NPRM proposes that if an investigator develops a research plan for returning clinically relevant results to subjects, the IRB must determine that the plan is appropriate.

• IRBs do not need to determine whether there should be a plan for returning individual research results.

• NPRM recognizes that challenges can arise regarding return of individual research results when it is not clear if the findings have clinical validity or utility, or when the knowledge imparted may cause psychological distress or social harm.
IRB Review: Continuing Review (§_.109(f))

- NPRM would eliminate continuing review for minimal risk studies that qualify for expedited review unless the reviewer documents why continuing review should occur.

- For studies initially reviewed by a convened IRB, continuing review would not be required, unless specifically mandated by the IRB, after the study reaches the stage when the study involves either:
  - Analyzing data (including identifiable private information);
  - Accessing follow-up clinical data from procedures that subjects would undergo as part of standard care for their medical condition or disease.
IRB Review: Expedited Review (§__110)

- NPRM would allow expedited review to occur for studies on the HHS Secretary’s list unless the IRB reviewer(s) determine(s) that the study involves more than minimal risk
  - Reversal of current Common Rule default position
    - Current: IRB use the expedited review procedure only if IRB reviewer determines that the research involves no more than minimal risk
    - Proposed: IRB use the expedited review unless IRB reviewer determines that research involves greater than minimal risk
  - Minimal risk would be clarified through new HHS Secretary list of minimal risk activities, to be evaluated every 8 years and amended, if appropriate, after consultation with Common Rule agencies and departments and after publication in Federal Register for public comment
  - IRB would document any determination that activity on minimal risk list involved more than minimal risk
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Data Security Safeguards (§_.105)

• NPRM proposes to set uniform standards that would help to assure reasonable and appropriate privacy and confidentiality protections
  – Concern that IRBs often lack expertise in evaluating privacy and confidentiality risks

• NPRM proposes to require that investigators and institutions implement reasonable and appropriate safeguards for:
  – Protecting against risks to the security or integrity of biospecimens or identifiable private information; and
  – Protecting from any intentional or unintentional use, release, or disclosure

• Uniform standards would eliminate need for IRBs to review individual plans for safeguarding biospecimens and research so long as there is compliance with standards
Data Security Safeguards (cont’d)

• The NPRM would allow investigators and institutions to implement either:
  – A list published by the Secretary of HHS of specific measures that an institution or investigator can use to meet the requirements; or
    • Security safeguards to limit access to physical biospecimens or information
    • Access to electronic information is only authorized for appropriate use
    • Information/biospecimens posing informational risks to subjects would be protected
  – Safeguards that meet the standards in the HIPAA rules
    • Institutions not subject to HIPAA could voluntarily adopt
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Harmonization (§_101(j))

- NPRM includes a provision that would require that federal guidance on the requirements of the Common Rule be issued only after consultation, to the extent appropriate, with other Common Rule departments and agencies, if feasible
  - No requirement for consistency, only consultation

- While FDA is not a Common Rule agency, the preamble specifies that FDA intends to modify its regulations in light of this NPRM, to the extent appropriate, considering FDA’s unique statutory framework and regulatory mission

- NPRM preamble further states that FDA and OHRP will continue to work together in developing guidance on their respective regulatory requirements that are found both in FDA regulations and in Common Rule, to the extent feasible
Regulate Unaffiliated IRBs (§_.101(a))

- NPRM proposes to authorize Common Rule departments and agencies to enforce compliance directly against unaffiliated IRBs that are not operated by an assured institution
  - Proposal addresses concerns about OHRP’s current practice of enforcing compliance with the Common Rule only through the institutions that are engaged in human subjects research, even in circumstances when the regulatory violation is directly related to the actions of an external IRB
    - Concerns were one source of lack of support for single IRB review mandate
- NPRM also proposes that the institution and the IRB should establish and follow written procedures identifying the respective compliance responsibilities of each entity
NPRM would extend the scope of the policy to cover all “clinical trials” regardless of funding source:

- Conducted at a U.S. institution;
- Institution receives federal funding for non-exempt human subjects research; and
- Not subject to FDA jurisdiction

The NPRM would define “clinical trial” as:

Research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes

This expanded scope would ensure that all “clinical trials” are covered by a set of federal research ethics regulations
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Implications

• As described, the NRPM includes extensive and substantive revisions to the Common Rule
• NPRM seeks active public engagement on the proposed codified text, on the numerous questions identified for public comment, and on the alternative schemes discussed in the preamble
• NPRM will be open for public comment until December 7, 2015
Implications: Compliance Dates

• **Effective date of final rule**: one year after publication in the Federal Register

• **Compliance dates of final rule**:
  - Generally, 1 year from the publication of the Final Rule
  - 3 years for new rules covering all biospecimen research and the mandate of a single reviewing IRB

• **Transition period**: research involving the use of prior collections of biospecimens would be permitted if the biospecimens were collected before the effective date of the final rule, and the individually identifiable information associated with the biospecimens has been removed
Implications: Compliance Costs

• $12 billion estimated 10 year costs of requiring consent for secondary use of biospecimens and identifiable private information

• NPRM estimates that investigators could seek consent (or waiver) for secondary research use of biospecimens from 15 million individuals annually

• Institutions creating research repositories would need to develop and implement tracking systems to monitor which biospecimens or what information may be used in secondary research by investigators, and what refusals to consent have occurred
Implications: Benefits

• $1.1 billion estimated 10 year cost-savings for mandated single IRB review for cooperative research

• Putative non-quantitative benefits:
  – Improved human subjects protections in clinical trials and biospecimen research not currently subject to oversight;
  – Enhanced oversight in research reviewed by unaffiliated IRBs;
  – Increased uniformity in regulatory requirements among Common Rule agencies;
  – Ethical benefit of respecting an individual’s wishes in how his or her biospecimens are used in future research;
  – Standardization of human subjects protections when variation among review IRBs is not warranted;
  – Improved informed consent forms and processes;
  – Improved protection of biospecimens and identifiable private information; and
  – Better ensuring availability of biospecimens for future research activities
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Conclusion

- Industry and research institutions must carefully review the NPRM and assess how the proposals could affect:
  - Institutional policies and practices
  - Institutional capabilities (personnel, resources, technologies)
  - Legal, regulatory, compliance, and risk management strategies
  - Business and financial operations

- Determine whether to submit public comment

- Anticipate that unless there is a shift in Administration policies or significant public comments, the rule may be finalized largely as is, potentially by end of 2016
For CLE credit, complete and return Attorney Affirmation form within 48 hours.

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**Note:** A recording of today’s presentation will be made available.
Questions?

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The Common Rule NPRM: Most Critical Issues

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