



Penn

“This final rule is intended to better protect human subjects involved in research, while facilitating valuable research and reducing burden, delay, and ambiguity for investigators. These revisions are an effort to modernize, simplify, and enhance the current system of oversight.”

The Common Rule

A SUMMARY OF THE PROPOSED RULE MAKING AND HOW THE REVISIONS WILL
IMPACT IRB REVIEW

Outline of Discussion

- ▶ History of Common Rule Revision Process
- ▶ Goals of the Proposed Rule Making
- ▶ Broad Consent Provisions
- ▶ Changes that Impact Convened IRB Review
 - ▶ New Consent Form Regulations
- ▶ Changes that Impact Other IRB Reviews (minimal risk research)
 - ▶ Updated Definitions of Human Subjects and Research
 - ▶ New Exemption Categories
 - ▶ New Ongoing Review Requirements
- ▶ Reliance Agreement Provisions
- ▶ What happens next?



History of Common Rule Revision Process

- ▶ 1974: The National Research Act was signed and the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was established to develop ethical standards for the conduct of research
- ▶ 1979: The Belmont Report was developed as a summary of these ethical considerations
- ▶ 1980s: The Department of Health and Human Services (HHS) and Food and Drug Administration (FDA) revised their human subject regulations
- ▶ 1991: The Federal Policy for the Protection of Human Subjects was published
 - ▶ “The purpose of this effort was to promote uniformity, understanding, and compliance with human subject protections as well as to create a uniform body of regulations across Federal departments and agencies (subpart A of 45 CFR part 46), often referred to as the ‘Common Rule’ for the Protection of Human Subjects”



History of Common Rule Revision Process

- ▶ 2011: HHS announced the Advance Notice of Proposed Rulemaking in an effort to obtain feedback about the human subject protection regulations and how they could be improved
- ▶ 2015: HHS and 15 federal agencies released the Notice of Proposed Rulemaking (NPRM) and outlined suggested revisions to the regulations
 - ▶ “The participating departments and agencies propose these revisions to the human subjects regulations because they believe these changes would strengthen protections for research subjects while facilitating important research”
 - ▶ 2,100+ comments were received in response to the proposal
- ▶ 2017: The Final Rule was published on 1/19/2017
- ▶ 2018: The policy will be effective 1/19/2018
 - ▶ UPDATE: Notification received from the federal government with delay until at least 7/1/9/2018

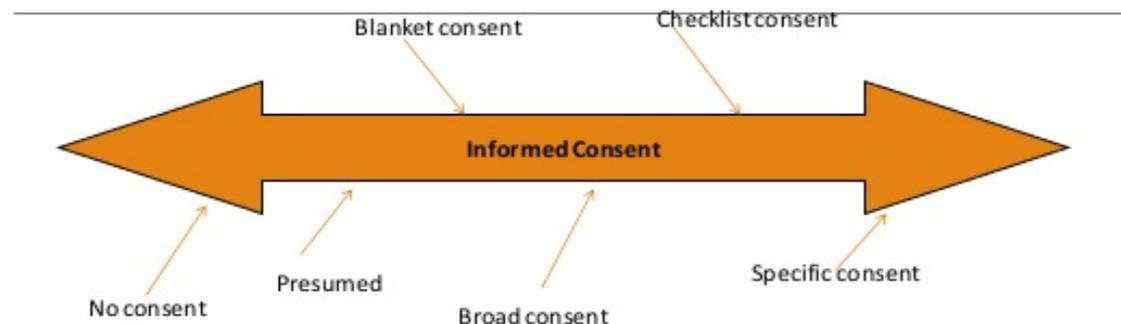


Goals of the Proposed Rule Making

- ▶ Focus resources on the review of greater than minimal risk research
 - ▶ More studies will qualify for exemption from IRB review
 - ▶ Continuing reviews will no longer be required for studies eligible for expedited review, or greater than minimal research that has completed study activities
- ▶ Enhance subject comprehension during the consent process
 - ▶ A summary of key information must be highlighted for subjects
 - ▶ The consent must be organized in a clear, concise way
- ▶ Allow broad consent to be obtained for the use of identifiable private information and identifiable biospecimens
- ▶ Require single IRB review for cooperative research

Broad Consent: Is this actually new?

- ▶ Broad Consent was previously not discussed in the Common Rule.
 - ▶ Previously, an industry standard term for research consent not specific to the primary research project.
 - ▶ Non-specific consent that permits institutions to collect/use/store data/specimens for future research use.
- ▶ Researchers, IRBs, ethicists, and the government have been debating for years Broad vs. Specific Consent.
 - ▶ Both practices are currently in place at Penn.



Broad versus Specific Consent

▶ **Broad consent example**

- ▶ *Your samples, genomic data and health information will be stored and shared with other researchers. The samples and information will be available for any research question, such as research to understand what causes certain diseases (for example heart disease, cancer, or psychiatric disorders), development of new scientific methods, or the study of where different groups of people may have come from.*

▶ **Tiered consent example**

- ▶ *If you wish to participate, please check your answers to the following questions.*
- ▶ *May we collect your tissue samples, health information, and genomic information to study [state specific research project]?*
 - ▶ Yes No
- ▶ *May we share your tissue samples, health information, and genomic information with other researchers to study [state specific disease or disorder]?*
 - ▶ Yes No

Broad Consent Provisions

- ▶ Regulations now define a mechanism for obtaining broad consent from subjects for storage, maintenance, and secondary research use of identifiable private information and identifiable biospecimens
- ▶ This can be accomplished through a separate consent form and process, or as a part of the consent process for another trial
- ▶ Future research involving specimens and data where broad consent was obtained would be eligible for exemption and would not require a waiver of consent

Elements of Broad Consent

- ▶ Description of risks/benefits
- ▶ To what extent confidentiality is maintained
- ▶ Participation is voluntary
- ▶ Specimens may be used for commercial profit, and subjects will not share in this commercial profit
- ▶ Will the research involve genome sequencing?
- ▶ Could a “reasonable person” understand the types of research being conducted?
- ▶ Will sharing of information occur?

Elements of Broad Consent

- ▶ A description of the period of time private information or identifiable biospecimens will be stored
- ▶ Subjects may not be informed of specific research studies conducted
- ▶ Clinically relevant research results may not be disclosed
- ▶ Who do subjects contact with questions?

Implications of Broad Consent

- ▶ Broad Consent allows subjects a mean to exercise their autonomy in deciding whether or not to allow secondary research use.
- ▶ Secondary use of clinical data or biospecimens is still permissible with a waiver of informed consent if it was not practicable to obtain informed or Broad Consent
- ▶ Broad Consent applies to identifiable data or biospecimens
 - ▶ Secondary use of de-identified data would not require Broad Consent

Broad Consent Challenges

- ▶ No Waiver if Broad Consent Refused
 - ▶ IRB cannot waive consent if individuals were asked, and refused, to provide consent to the storage, maintenance, and use of identifiable private information or identifiable biospecimens.
- ▶ The use of Broad Consent will involve a mechanism for tracking the affected information or biospecimens
- ▶ The IRB's role in certifying whether broad consent is properly documented is unclear

Changes that Impact Convened IRB Review: New Consent Form Regulations

- ▶ New requirements were developed for the information that must be given to potential research subjects during the consent process
- ▶ Informed consent must begin with a concise, focused presentation of key information
 - ▶ Summaries will be protocol-specific
 - ▶ Regulations were drafted to allow for flexibility

Changes that Impact Convened IRB Review: New Consent Form Regulations

According to the Common Rule preamble, the following may encompass a “concise explanation”:

- 1 *The fact that consent is being sought for research and that participation is voluntary*
- 2 *The purposes of the research, expected duration of the prospective subject's participation, and procedures to be followed in the research*
- 3 *The reasonably foreseeable risks or discomforts to the prospective subject*
- 4 *The benefits to the prospective subject or others that may reasonably be expected from the research*
- 5 *Appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the prospective subject*

Changes that Impact Convened IRB Review: New Consent Form Regulations

- ▶ The consent document must be organized in a way that facilitates comprehension and presents information in a way that does not merely provide lists of isolated facts, but rather facilitates understanding of the reasons why one might or might not want to participate
 - ▶ How do we accomplish this?
 - ▶ “One pager consent” template document (for purposes of developing a study specific summary document)
 - ▶ Guidance for what information to definitely include, consider including or instructions on how to best assess the specific submission and determine what should be included in the summary
 - ▶ What is most important for the potential participant to remember from the consenting process?

New Elements of Consent

- ▶ Additional Basic Elements of Informed Consent
 - ▶ One of the following statements will be required for any research that involves the collection of identifiable private information or identifiable biospecimens:
 - ▶ A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after removal, could be used for future research studies or distributed to another investigator for future research studies without additional informed consent; or
 - ▶ A statement that subject's information or biospecimens collected as part of the research (even if identifiers are removed) will not be used or distributed for future research studies

New Elements of Consent

- ▶ Additional Elements of Informed Consent
 - ▶ A statement that subject's biospecimens (even if identifiers are removed) 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;
 - ▶ For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e. sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)

Changes in the Common Rule to Reduce Administrative Burden

- ▶ Broader Exemption Categories
- ▶ Eliminating Continuing Reviews for Minimal Risk Research
- ▶ Single IRB Review of Cooperative Research

New studies that can be exempted

- ▶ Surveys/Interviews that collect identifiable data
- ▶ Benign Behavioral Interventions
 - ▶ Deception is permitted if the subject authorizes the deception up front
- ▶ Secondary research using data and specimens subject to HIPAA regulations
- ▶ Storage of specimens and data for secondary research if consent for future research is obtained
- ▶ Secondary research of specimens and data if consent for future research was obtained

New Applications after January 18, 2018 *DELAYED UNTIL JULY OR ACTIVE DATE*

- ▶ You will be able to select these new exemption categories when creating new applications in HS-ERA.
- ▶ IRB staff will review applications and apply new exemption categories to studies that qualify
- ▶ Exempt studies are not subject to continuing review requirements
- ▶ Modifications to exempt studies are only required in specific circumstances
 - ▶ These circumstances are category specific will be outlined in your exemption letter

Previously Approved Studies After January 18, 2018 *DELAYED UNTIL JULY OR ACTIVE DATE*

- ▶ Current protocols reviewed expedited may be eligible for exemption.
- ▶ You don't have to do anything extra.
- ▶ These studies can continue to operate under the old common rule regulations.
- ▶ At the time of your next continuing review or protocol modification, IRB staff will determine if the study can be exempted.
- ▶ A new exemption letter would be issued and the study will be considered exempt from that point forward.
- ▶ This review won't be done for administrative modifications (personnel changes, recruitment flyers, etc.) unless you ask for it directly.

Eliminating Continuing Reviews for Minimal Risk Research: New Applications after January 18, 2018 *DELAYED UNTIL JULY OR ACTIVE DATE*

Continuing Review applications will no longer be required for the following studies initially reviewed and approved after January 18, 2018:

- Research determined to be minimal risk and eligible for expedited review, categories 1-7 and 9
- Greater than Minimal Risk Research that has progressed to the point where it only involves the following activities
 - Data analysis, including analysis of identifiable data and specimens
 - Collecting follow-up clinical data from procedures that subjects would undergo as part of clinical care

For these studies, IRB approval will not expire and continuing review applications are not required. However modifications and reportable events should still be submitted.

Eliminating Continuing Reviews for Minimal Risk Research: Previously Approved Studies After January 18, 2018 *DELAYED UNTIL JULY OR ACTIVE DATE*

- ▶ The IRB can elect to apply the new regulations to active studies and determine that no continuing reviews are required.
- ▶ Active studies should continue to operate under the old common rule regulations.
- ▶ If your approval is set to expire, you should submit a Continuing Review application.
- ▶ At the time of your next continuing review or protocol modification, IRB staff will determine if the new regulations can be applied.
- ▶ Your IRB approval letter will include an expiration date or a notice that continuing review is no longer required.
- ▶ This review won't be done for administrative modifications (personnel changes, recruitment flyers, etc.) unless you ask for it directly.

Examples *DELAYED UNTIL JULY OR ACTIVE DATE*

When will the IRB say my expedited study no longer requires continuing review:

- Minimal risk studies that are closed to enrollment or in data analysis only
- Minimal risk studies that do not include a consent process
- Minimal risk studies that have revised their consent to meet the new common rule regulations.

When won't the IRB say that my study does not require continuing review:

- Minimal risk studies that enroll subjects using a consent form that doesn't meet the new regulatory requirements
- GTMR protocols that have not yet enrolled any subjects
- GTMR protocols that include research procedures in follow up activities

Single IRB Review

- ▶ Multi-site studies conducted within the US must rely on a single IRB for the portion of the research conducted in the United States

Effective Dates of the Policy:

- NIH implementation deadline is 1/25/2018
- Common Rule implementation deadline is 1/18/2020

Note: Policy only applies to research subject to OHRP, DHHS, and FDA oversight.

Penn IRB has guidance available on single IRB review process here:
<https://irb.upenn.edu/reliance-agreements>

What happens next?

- ▶ Waiting...
 - ▶ Last notification states that the revised rule will go into affect on July 19, 2018
- ▶ Informed Consent Changes...
 - ▶ New elements of the revised rule may be put into affect (if they don't contradict the current common rule) as of January 19, 2018
- ▶ Penn IRB Policy Overhaul...
 - ▶ The IRB is currently working on updating our Standard Operating Procedures
 - ▶ Policies and procedures related to expedited review and continuing review will be updated
 - ▶ New guidance will be drafted and additional presentations will be provided as needed
 - ▶ Reliance Agreement Guidance/New Forms were finalized in the Summer 2017