The following list encompasses the most significant changes to the Common Rule (45 CFR 46 Part A) as indicated in the Notice of Proposed Rule Making (NPRM):

1. **Informed Consent - General**
   Improve informed consent by increasing transparency and by imposing stricter new requirements regarding the information that must be given to prospective subjects, and the manner in which it is given to them, to better assure that subjects are appropriately informed before they decide to enroll in a research study.

   - **Consent document should include only required elements.**
     - Other information would be presented in an appendix _._116.

   - **New required elements**
     - Statement that deidentified data may be used for future research or shared with another investigator or that deidentified data will not be used for future research _._116(a)(9)

   - **Additional required elements (if applicable)**
     - Statement that biospecimens may be used for commercial profit and whether subject will share profit _._116(b)(7)
     - Statement regarding whether clinically relevant research results will be disclosed (or not) and under what conditions _._116(8)
     - Option for subject or representative to consent (or not) to recontact for additional information or for future research _._116(b)(9)

**Research Impact**
These changes would require a new structural organization of written informed consent material along with an expansion of elements that must be included or must be considered for inclusion, if applicable.

Prior to the effective date, study teams, sponsors, and IRBs will need to adjust existing templates and local guidance materials.

2. **Expanded Definition of Human Subjects - Informed Consent - Biospecimen Research**
   The regulatory definition of human subjects would expand to include all biospecimens in federally funded research or in clinical trials at a federally supported institution whether the biospecimens are deidentified or identifiable and regardless of whether they were collected for clinical or research purposes.

   Informed consent will be required for the use of stored biospecimens in secondary research (for example, part of a blood sample that is left over after being drawn for clinical purposes), even if the investigator is not being given information that would enable him or her to identify whose biospecimen it is. That consent would generally be obtained by means of broad consent (i.e., consent for future, unspecified research studies) to the storage and eventual research use of biospecimens.

   Waivers of consent will be rare.

   The NPRM offers two alternative proposals to limit the definition of human subject: a) only to those instances where whole genome sequencing will be utilized on the
specimen; b) any technology would be applied that produces “bio-unique” information

• **Broad consent for future use and sharing**
  Provides required new required elements of informed consent for storage, maintenance and secondary research use of specimens and identified data .116(c).
  o Considered as part of limited IRB review now required for exemptions .104(f).
  o HHS will publish consent templates (not yet provided) .116(d)(1)
  o Oral consent permitted for exempt studies .116 (d)(3)
  o Must document/track if consent is not given .116(d)(4)
  o Reconsent required every 10 years to permit broad future use for new research studies involving clinical specimens (that were not collected under a specific research project)

• **Waiver of Consent**
  Changes the conditions and requirements for waiver or alteration of consent such that waiver of consent for research involving biospecimens (regardless of identifiability) will occur only in very rare circumstances.
  o New consent waiver criteria for research involving access to identified data or biospecimens, that the research could not be carried out without accessing or using identifiers .116(f)(1)(iii)
  o Informed consent cannot be waived for use of biospecimens unless there is a compelling scientific reason .116(f)(2)
  o Cannot waive informed consent for use of data/specimens from subjects who have denied permission for future use .116(f)(3)

**Research Impact**
These changes extend the definition of human subjects to include deidentified biospecimens and limit the ability of IRBs to issue waivers of informed consent where explicit participant consent was not previously obtained.

These changes will have a significant impact on the ability of institutions to conduct research with fully deidentified biospecimens that become available after all clinical uses are complete.

• Such uses would not be permitted without the explicit consent of individuals. Who will do consent patients, when will this be done, and where will it be recorded?
• Use of specimens collected from individuals admitted in emergency circumstances (the patient is not capable of providing consent) may not be permitted unless the IRB can approve a waiver of consent under new, stringent criteria
• All institutions working with U-M would need to comply otherwise U-M could not accept samples from elsewhere, including partnering community hospitals
• Re-consent must be obtained every 10 years to continue to utilize clinical specimens for any new research utilization; tracking and re-contact of individuals is necessary.
• All researchers must ascertain who permitted or declined utilization of their excess clinical (including deidentified) specimens for research purposes. This
means they must also ascertain the identity of patients before use their otherwise deidentified specimens for research – this significantly diminishes the privacy of patients by requiring that they first be named prior to assessment of a database documenting their intentions.

- IRBs currently assess these circumstances and issue waivers – this will be only rarely permitted.

3. Research Excluded from the Common Rule

Exclude from coverage under the Common Rule certain categories of activities that should be deemed not to be research, are inherently low risk, or where protections similar to those usually provided by IRB review are separately mandated.

- Exclusions
  The IRBs currently make decisions regarding the requirement for IRB review based upon the regulatory definitions of research and human subjects. This new category of “excluded” includes some research that is currently considered to be exempt.

- Not research \(\_101(b)(1)\)
  Defines certain types of projects excluded from IRB oversight because they do not meet the regulatory definition of research (currently considered by U-M IRBs to be “not regulated” activities)
  - Data collection for institutional evaluation \(\_101(b)(1)(i)\)
  - Oral history, journalism, biography, historical scholarship \(\_101(b)(1)(ii)\)
  - QA/QI (implementation of an accepted practice not the evaluation of a new practice) \(\_101(b)(1)(iv)\)

- Low risk \(\_101(b)(2)\)
  Defines certain types of human subjects research that is considered to be low risk and now not subject to regulation
  - Research that involves the use of educational tests, survey procedures, interview procedures, or observation of public behavior (unless identifiable or disclosure of responses to could reasonably put subjects at risk) (similar to current federal exemption 2). Does not include interventions \(\_101(b)(2)(i)\)
  - Research involving the collection or study of information that has been acquired for solely for non-research or for other research studies (similar to current federal exemption 4). Does not permit research with biospecimens. \(\_101(b)(2)(ii)\)
  - Research involving only collection and analysis of Protected Health Information (already covered by HIPAA) \(\_101(b)(2)(iv)\)
  - Secondary research use of biospecimens designed to generate info already known about the individual \(\_101(b)(3)(i)\)

Research Impact

The definition of QA/QI activities is more limited than the current interpretation used by most institutions in the new definition of excluded research. Research activities that are currently not regulated (excluded) by the IRB are limited those that do not meet the definition of human subjects research. The excluded categories include research that currently would qualify for an exempt determination. These new categories of excluded research will require subjective determinations by investigators.
4. Develop New Categories of Exempt Research

Adds additional categories of exempt research to accommodate changes in the scientific landscape and to better calibrate the level of review to the level of risk involved in the research. A new process would allow some studies to be determined to be exempt without requiring any administrative or IRB review. Certain exempt and all non-exempt research would be required to provide privacy safeguards for biospecimens and identifiable private information. Some of the proposed exemptions require limited IRB review.

New categories include:

• Certain research involving benign interventions with adult subjects
• Research involving educational tests, surveys, interviews or observations of public behavior when sensitive [identifiable] information may be collected, provided that data security and information privacy protections policies are followed;
• Secondary research use of identifiable private information originally collected as part of a non-research activity, where notice of such possible use was given;
• Storing or maintaining biospecimens and identifiable private information for future, unspecified secondary research studies, or conducting such studies, when a broad consent template to be promulgated by the Secretary of HHS is used, information and biospecimen privacy safeguards are followed, and limited IRB approval of the consent process used is obtained.

Exemptions are now grouped into 3 categories, each requiring differing levels of review.

• Low risk _.104(d)
  o Research in standard educational settings involving normal educational practices (no risk to student learning or teacher evaluation) (similar to current federal exemption 1) _.104(d)(1)
  o Federal research and demonstration projects (current exempt 5) _.104(d)(2)
  o Research involving benign interventions with adults and data collection via verbal or written responses (similar to current U-M exemption 2a) _.104(d)(3). No deception without notice to subjects permitted.
  o Taste and food quality evaluation (current federal exemption 6) _.104(d)(4)

• Exempt if new data security requirements in _.105 are met (data security requirements not yet defined) _.104(e)
  o Research, not including interventions, involving the use of educational tests, survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if the information is recorded in such a manner that human subject can be identified directly or through identifiers linked to subjects. _.104(e)(1)
    ▪ Permits collection of sensitive, identifiable data.
    ▪ Limited to research with adults (except educational tests or observation without interaction)
  o Secondary use of identifiable private information that has been or will be acquired for non-research purposes, if notice has been given regarding possible research use and data is used only for the specific proposed study _.104(e)(2).
• **Exempt if new data security requirements met and after limited IRB review** §104(f)
  o Storage of identifiable data and/or biospecimens for future research use.
    ▪ Biospecimens and data must be obtained under broad consent for future use and sharing §104(f)(1).
  o Secondary use of identifiable data and/or biospecimens, if consent for future use was obtained §104(f)(2).
  o Not exempt if individual research results will be returned to participants (e.g. genetic analyses)

• **New exempt review process §104(c)**
  o OHRP will develop decision tool to allow investigators to self-determine exemptions (not yet developed). Each federal agency may develop its own decision tool.
  - Institutions must track exempt studies.
  - Institutions may continue to have the IRB make exemption determinations.

**Research Impact**

Current exemptions require only one type of assessment – whether the research activity meets the criteria for exemption. The new exemptions are more complex and require differing levels of IRB review. IRB review is no longer required for a number of research activities that are currently subject to expedited or full committee review, such as surveys that collect sensitive, identifiable data that may pose some risks to participants beyond the risk of breach of confidentiality.

5. **Mandated Single IRB of Record for Cooperative Research Studies**

The provision mandates that U.S. institutions engaged in cooperative research rely on a single IRB for that portion of the research that takes place within the United States, with certain exceptions. To encourage the use of IRBs that are otherwise not affiliated with or operated by an assurance-holding institution (“unaffiliated IRBs”), this NPRM also includes a proposal that would hold such IRBs directly responsible for compliance with the Common Rule.

• **Requirement for single IRB review of multi-site research §114**
  o The IRB of Record will be identified at time of grant submission
  o Significant financial and administrative burden to designated institution/IRB
  o May not be appropriate for all types of research

**Research Impact**

This provision will mandate the development of single IRB of Record mechanisms – particularly among large, well-funded institutions (such as U-M) who receive federal awards for multi-site research. This will place significant infrastructure and financial demands on the institution such as:

• New policy and procedure developments which are likely to be variable among these IRB of Record institutions
• Addition of IRB and study personnel to manage the flow of materials in and out of the IRB and study team
• Liability obligations incurred by institution for determinations made by the IRB of Record
• Development of new electronic tracking mechanisms
6. **Eliminate Continuing Review for Certain Aspects of Minimal Risk Research**

   Eliminate the continuing review requirement for studies that undergo expedited review and for studies that have completed study interventions and are merely analyzing data or involve only observational follow-up in conjunction with standard clinical care.

   - Elimination of continuing review for minimal risk research including all expedited research and all research once the project has moved to analysis of identified data \( \_109(f)(1) \)
   - Must confirm annually that research is ongoing and not changes have been made \( \_109(f)(2) \)

**Research Impact**

This would reduce regulatory burden for research investigators and IRBs to undergo full continuing review procedures as now defined. There is still a regulatory requirement to provide confirmation of the ongoing nature of the research, which must be tracked by the institution.

7. **Extend the scope of Federal Policy to Cover all Clinical Trials**

   Extends the scope of the policy to cover all clinical trials, regardless of funding source, conducted at U.S. institutions that receive federal funding for non-exempt human subjects research.

   - OHRP oversight required for all clinical trials conducted at an institution receiving federal funds regardless of funding source \( \_101(a)(2) \)
     - Clinical trial definition - a 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 \( \_102(b) \)
   - Extends federal oversight to minimal risk behavioral interventions, including student research, regardless of funding source and may extend the requirement for use of a single IRB of record (above) to such projects.

**Research Impact**

Generally, all clinical trials, as currently defined, at the U-M are already fully reviewed under federal human subject protection standards to offer the same protections to all participants. This regulatory change would permit OHRP to exercise its federal regulatory authority over the clinical trial (including evaluating the study’s records and suspending its conduct) even when the trial is not federally sponsored. Currently, this is not permitted under existing regulatory flexibility.