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Final Rule Material:
Revisions to Roles - Changes Relevant to HRPP Professionals (IRB Administrators and Staff), IRB Members, and Researchers

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Introduction

The Final Rule to update the current regulations at 45 CFR 46, Subpart A - "Federal Policy for the Protection of Human Subjects" (the Common Rule) was published by the U.S. Department of Health and Human Services (HHS) on 19 January 2017 in the *Federal Register*. The general compliance date of the revised Common Rule is 21 January 2019 (HHS 2018), while the revisions to cooperative research and the use of single Institutional Review Boards (sIRBs) compliance date is 20 January 2020.

What is included in this resource?

1. *Concise table of research roles and which sections of the revised regulation that may affect them*
2. *Brief summaries of revisions to the Common Rule and how the revisions may affect the different research roles*

While CITI Program recognizes that each Common Rule agency has different citations for its human subject protection regulations, for consistency and clarity, this resource will use citations to the HHS 45 CFR 46, Subpart A version of the Common Rule. For the purposes of this resource, the terms "pre-2018 requirements" or "pre-2018 rule" refer to the Common Rule as published in the 2016 edition of the Code of Federal Regulations (CFR); in addition, the terms "Final Rule," "Common Rule," or "revised Common Rule" refer to the 2017 requirements of the Common Rule.

19 January 2017 — **HHS Published Final Rule**

21 January 2019 — **General Compliance Date for All Changes (except cooperative research)**

20 January 2020 — **Compliance Date for Cooperative Research**

Understanding the Affect of the Revised Common Rule on Research Roles

Research Roles and Revised Common Rule Sections	
Researchers and Key Study Personnel	• Exempt research (46.104) • IRB review of research (46.109) • Criteria for IRB approval of research (46.111) • Cooperative research (46.114) • General requirements for informed consent (46.116) • Documentation of informed consent (46.117)
IRB Members and Chairs	• Exempt research (46.104) • IRB review of research (46.109) • Expedited review procedures (46.110) • Criteria for IRB approval of research (46.111) • Cooperative research (46.114) • IRB records (46.115) • General requirements for informed consent (46.116) • Documentation of informed consent (46.117)
HRPP Professionals (IRB Administrators and Staff)	• Definitions for purposes of this policy (46.102) • Assuring compliance with this policy—research conducted or supported by any federal department or agency (46.103) • Exempt research (46.104) • Membership (46.107[a]) • IRB functions and operations (46.108) • IRB review of research (46.109) • Criteria for IRB approval of research (46.111) • Cooperative research (46.114) • IRB records (46.115) • General requirements for informed consent (46.116) • Documentation of informed consent (46.117)
Organizational Leadership	• To what does this policy apply? (46.101) • Cooperative research (46.114) • Federalwide Assurances (FWA) and IRB Registrations (46.103)

Summary of Revisions and Roles Affected

46.101, To What Does This Policy Apply?

This section covers the scope and applicability of the regulation.

Remove "Checking the Box"

FWAs will only apply to federally conducted or supported research. This means that non-federal research will not be part of the FWA and not subject to federal oversight, whereas under the pre-2018 rule an institution could "check the box" to apply the federal regulations and federal oversight to all research, regardless of funding. This "checking the box" will no longer be an option once the FWA process is updated to reflect the revised rule. Institutions may still voluntarily apply the federal regulations to all research, but federal oversight would only apply to federally conducted or supported research.

Use of External IRBs

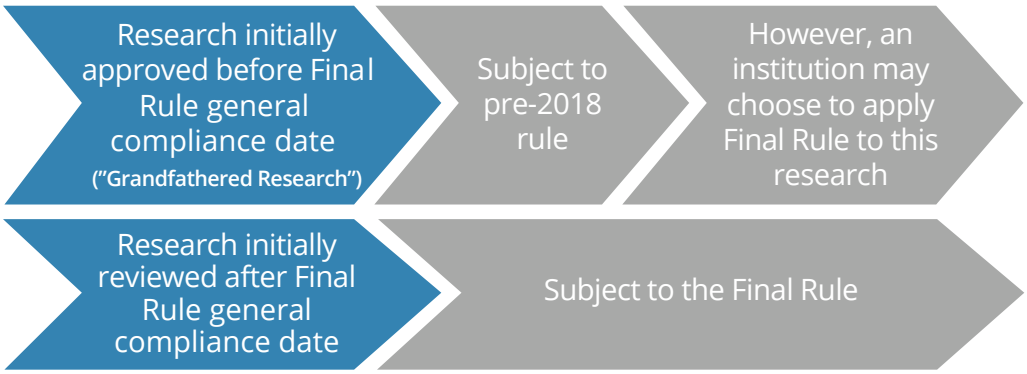
The applicability requirements have a new condition that non-institutionally based IRBs reviewing federally conducted or supported research must comply with the Common Rule. This supports the use of external IRBs and facilitates sIRB use. This also gives the Common Rule departments and agencies the authority to enforce compliance directly with IRBs that are not operated by an assured institution.

Tribal Law

The Final Rule expands language with respect to state and local laws that provide additional protections for human subjects (46.101[f]), to include "tribal law passed by the official governing body of American Indian/Alaskan Native tribe." The revisions in respect to tribal law should not create any additional obligations to researchers, HRPP professionals, or IRB members, but reinforce existing best practices for such research. Researchers should already be designing research by consulting with the tribal elders for advice. IRBs should also have processes in place to ensure that any research subject to tribal law receives the appropriate tribal council approvals.

Transition Provisions

46.101(i) outlines the compliance dates and transition provisions for transitioning from the pre-2018 rule to the revised Common Rule. **Note:** See the "Overview" Final Rule Resource for more information about transition provisions during the six-month regulatory delay period of 19 July 2018-20 January 2019.



Researchers, HRPP professionals, and IRB members should be aware of which regulation the research is approved under for compliance purposes. Institutions should ensure policies are clear as to which regulations apply to which research.

Severability

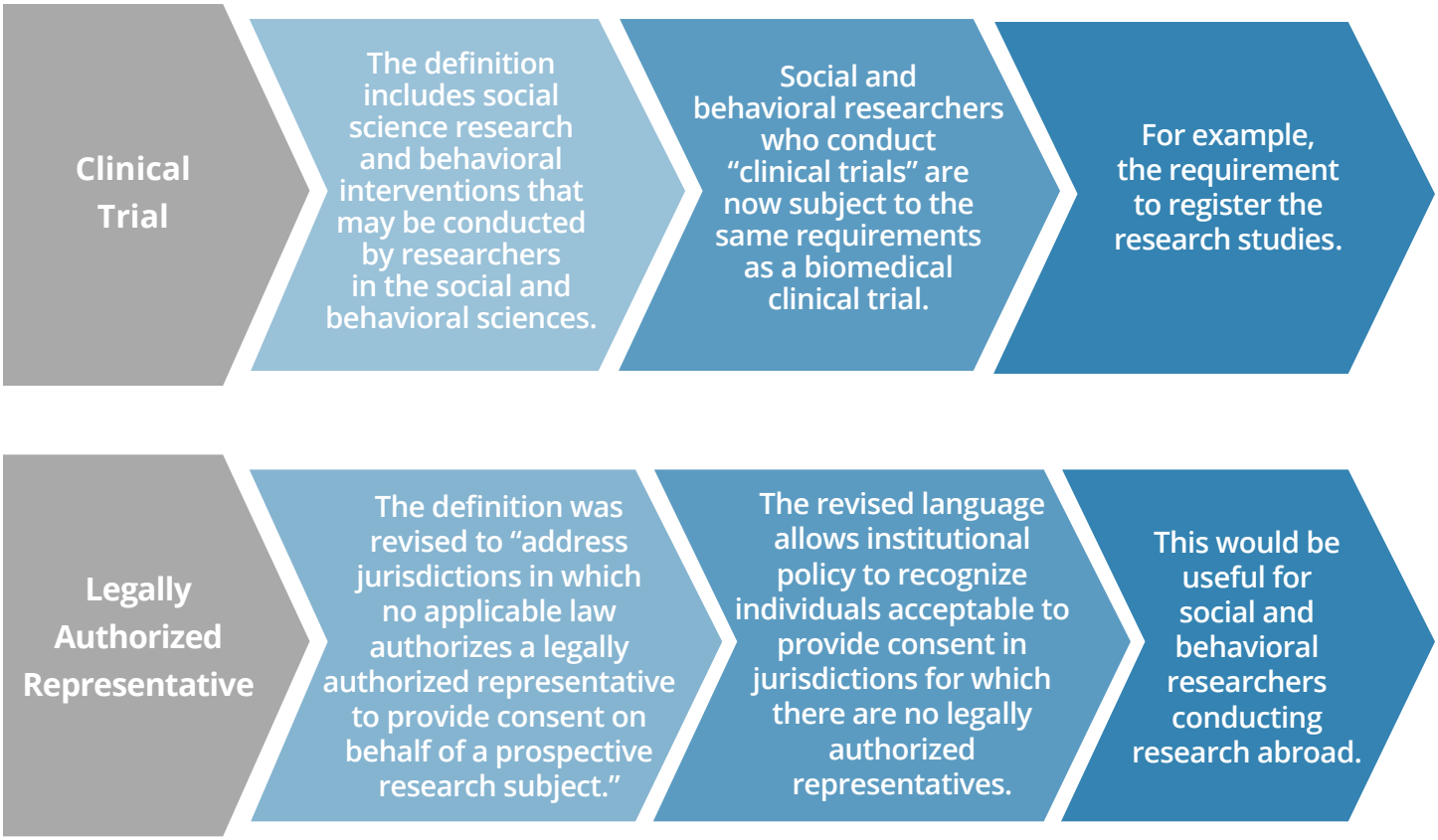
46.101(m) allows any provision of the revised Common Rule that is held to be invalid or unenforceable to be "severed" from the rule. This severed provision would have no effect on the application of the remainder of the rule. Severability is not clearly explained or expanded upon in the Final Rule's preamble. HRPP professionals should carefully monitor any Common Rule agency and department guidance.

46.102, Definitions for the Purposes of this Policy

The Final Rule expands this section to include new and revised definitions of key terms. The revisions to 46.102 will mostly affect HRPP professionals as they assist researchers in determining what projects are considered research and what type of review is appropriate.

HRPP programs may need to update language used on their websites, manuals, materials used for education or distribution purposes (such as, guides), protocol application forms, checklists and review worksheets, approval notices, and standard operating procedures (SOPs).

Two definitions that have bearing for researchers in the social and behavioral sciences are:



46.103, Assuring Compliance with this Policy – Research Conducted or Supported by Any Federal Department or Agency

The Final Rule no longer requires institutions to:

- Provide a statement of ethical principles by which they will abide as part of the assurance process.
- Include an up-to-date list of the IRB members and their qualifications in the institution's assurance. Such a list must be maintained by the HRPP.
- Designate one or more Institutional Review Boards (IRBs) on their FWA.

For IRBs that operate external to an institution (for example, an independent or commercial IRB), the Final Rule requires the institution and organization operating the IRB to document the institution's reliance on the outside IRB. These new provisions allow flexibility in documenting the reliance. For example, institutions and IRBs could document the reliance via IRB Authorization Agreements, institution-wide policy directives stating the division of responsibilities between the institution and the external IRB, or as written in the research plan for a specific study. HRPP professionals must keep documentation of reliance and responsibility allocation as part of the IRB records.

The revisions to the assurances in 46.103 affect HRPP professionals who should ensure their internal processes and documentation reflect the new changes. In respect to revisions pertaining to an institution relying on an external IRB, documents (such as, reliance forms and memoranda of understanding) will need to be modified.

46.104, Exempt Research

Updates to Exemption Categories

- *Category 1 – Revised*
- *Category 2 – Revised*
- *Category 3 – Replaced**
- *Category 4 – Revised*
- *Category 5 – Revised*
- *Category 6 – Unchanged*
- *Category 7 – New*
- *Category 8 – New*

** (Pre-2018 Rule Category Eliminated / New Category Added for Final Rule)*

Exemption categories have been expanded. There are several changes to the existing categories, as well as two new categories.

Additionally, 46.104 specifies provisions for the inclusion of pregnant women and children in exempt research, and the exclusion of prisoners, unless "incidental." This is a major update in that research projects that are "aimed at involving a broader population that only incidentally include prisoners" can be exempt (HHS 2017) and HRPP professionals should update their SOPs.

It is important to note that secondary research for which consent is not required no longer requires the information and biospecimens to be pre-existing ("on the shelf"). Instead, the exemption allows for prospective and ongoing collection for secondary use.

Major changes also include exemption for certain activities with the condition of a "limited IRB review" and activities that require "broad consent."

Revisions to exempt research (46.104) will affect HRPP professionals and researchers. HRPP programs will need to update all materials and procedures related to exempt research, including any SOPs specific to the review and approval of exempt research. Researchers are affected by these revisions, in that, there are more types of research projects that now qualify for exempt categories.

The Final Rule does not restrict or set requirements for how or whom determines if research is exempt by the institution. However, the regulation does state that the IRB chair or a designated reviewer may review research for which limited IRB review is a condition of exemption. Institutions should review their SOPs to identify whether or not changes are required.

References to Vulnerability in 46.107, IRB Membership and 46.111, Criteria for IRB Approval of Research

46.107(a) and 46.111(a)(3) and (b) are identical in the Final Rule and now refer to vulnerability as meaning, "vulnerable to coercion and undue influence, in recognition that coercion or undue influence refers to the ability to make an informed decision about participating in research" (HHS 2017).

Additionally, "pregnant women and handicapped or mentally disabled persons are no longer listed as examples of populations that are potentially vulnerable to coercion or undue influence." The preamble stated that those examples were out of date. Further, the pre-2018 rule language of "handicapped or mentally disabled persons" was revised to "individuals with impaired decision–making ability." However, it is important for HRPP professionals and researchers to note that the additional protections identified in Subpart B were not revised, so when applicable, additional protections are still required for research with pregnant women as a protected population.

The revisions to vulnerability will mostly affect HRPP professionals and IRB reviewers. HRPP programs should update applicable language in reviewer checklists and worksheets. Reviewers will need to be trained to apply the revisions to vulnerability when carrying out reviews.

46.107, IRB Membership

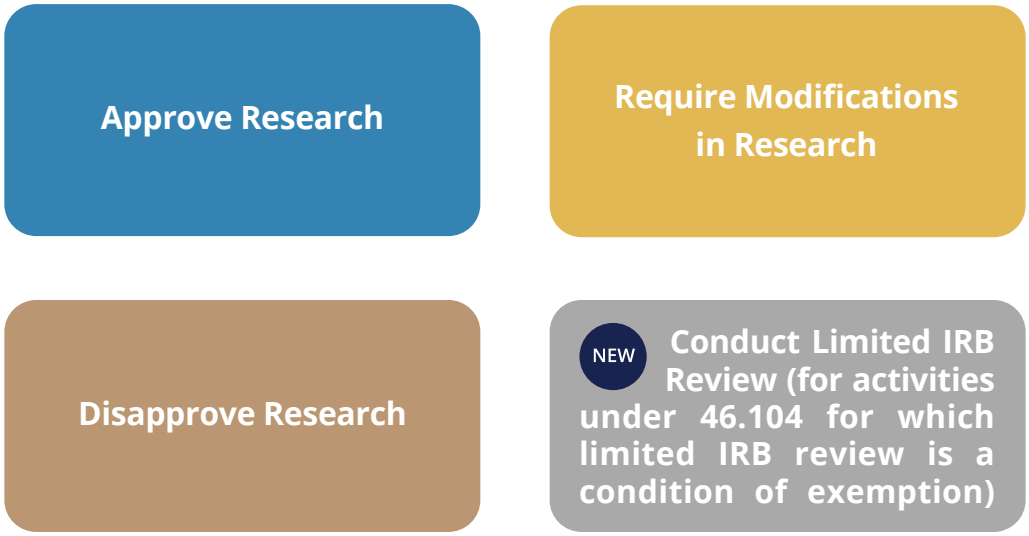
Beyond updating vulnerability references, this section was also revised to remove the stipulation that IRBs cannot consist of members of only one gender. The requirement remains that IRB membership should reflect "diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes," which is meant to accomplish the same thing. HRPP programs should update applicable language in policies or procedures.

46.108, IRB Functions and Operations

IRB functions and operations once described in 46.103 are now described in 46.108. The revisions require that institutions "must maintain an accurate list of IRB members but are not required to submit changes to that roster to the funding department or agency." There were no substantial revisions or added requirements to this section.

46.109, IRB Review of Research

The IRB has the authority to:



The revisions to 46.109 affect HRPP professionals. HRPP professionals will need to learn the limited, exempt, and expedited review conditions for approval, and review and modify processes and SOPs accordingly.

IRB members recommending research studies for approval under expedited review procedures would also need to know which activities no longer require continuing review under the expanded 46.109, as 46.109 eliminates the requirement for continuing review for many minimal risk studies unless an IRB determines otherwise. If an IRB reviewer determines that a minimal risk study requires annual review, the reviewer must explicitly justify why it would enhance the protection of human subjects and document the determination.

46.109 eliminates the requirement for continuing review for many minimal risk studies unless an IRB determines otherwise.

Revisions to 46.109 expanded the IRB authority to include "exempt research activities under .104 for which limited IRB review is a condition of exemption (.104[d][2][iii], .104[d][3][i][C], .104[d][7], and.104[d][8])." The Final Rule allows for the exemption of research collecting identifiable information with the potential to cause harm if disclosed, provided the IRB determined that adequate provisions were in place to protect the privacy of subjects and maintain the confidentiality of data. This review is called a limited IRB review, which is a new concept.

IRB members recommending research studies for approval under expedited review procedures would need to know which expedited activities no longer require continuing review (provided there are no other federal regulations, state laws, or institutional policies that require it).

46.110, Expedited Review Procedures for Certain Kinds of Research Involving No More Than Minimal Risk, and for Minor Changes in Approved Research

Previously, language in 46.110 defined expedited review of research for studies that an IRB determined were no more than minimal risk. This language was revised, so that expedited review may be used for:

- Research appearing to the HHS' Secretary's List (unless determined to be more than minimal risk)
- Minor changes in previously approved research during the approval period
- Limited IRB review for exempt research

The revised Common Rule language allows IRBs to use the expedited review procedure for "some or all of the research appearing on the list of activities" published by the Secretary of HHS, unless the reviewer determines and documents that the research poses more than minimal risk. The Final Rule mandates that the expedited list be reexamined for revisions at least every eight years.

This potentially allows for more studies to be reviewed via expedited review procedures. Shifting the requirements to expedited review, from full board review, was intended to reduce administrative burden on IRBs.

However, the revisions also increase some administrative burden on IRB reviewers by adding required limited review for certain exempt categories of research as a condition of exemption. That is, instead of just determining a research project is exempt from the regulation, now there is requirement for an IRB review (under expedited review) with certain approval criteria that must be met.

The revisions to 46.110 affect HRPP professionals and IRB members designated as expedited reviewers. They will need to understand the new limited IRB review criteria in order to review.

46.111, Criteria for IRB Approval of Research

Revisions to this section include the addition of limited IRB review and broad consent. In addition, as noted above, there were revisions in the definition of vulnerability of subject populations.

Revisions to 46.111 may affect HRPP professionals, researchers, and IRB members. HRPP programs will need to include the provisions for limited IRB review and broad consent in their materials, but specifically in guidance documents, research study submission applications, and reviewer checklists and worksheets. These Common Rule revisions affect researchers by providing additional options in applying for IRB approval and obtaining informed consent. IRB reviewers will need to be trained in the criteria for limited IRB review and broad consent.

46.112, Review by Institution

This section is unchanged.

46.113, Suspension or Termination of IRB Approval of Research

This section is unchanged.

46.114, Cooperative Research

This section was revised to add a requirement that "any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States."

Researchers, HRPP professionals, and IRB reviewers will all be affected when the new requirements for cooperative research go into effect on 20 January 2020. Advance planning to develop or modify current processes will be required. It is important to note that the National Institutes of Health (NIH) policy on "Use of a Single Institutional Review Board for Multi-Site Research" went into effect 25 January 2018 for NIH-funded multi-site research.

46.115, IRB Records

Revisions to 46.115 identify additional documentation requirements, such as the:

Rationale for conducting continuing review of research that otherwise would not require continuing review under the new Final Rule

Rationale for an expedited reviewer's determination that research appearing on the HHS Secretary's expedited review list is more than minimal risk

Revisions to 46.115 will affect IRB members and HRPP professionals. As already mentioned, IRB members will need to be trained in carrying out the revised procedures for expedited reviews. HRPP professionals will need to ensure that rationale for deviating from the new continuing review and expedited review activities, as outlined in the Final Rule, are documented at the time of review.

HRPP professionals will also need to include in the IRB records:

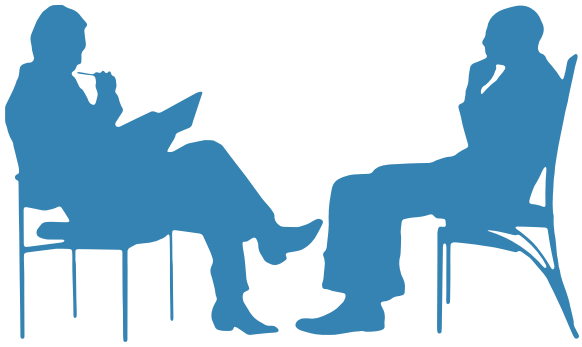
Documentation specifying the responsibilities of both parties when the institution relies on an external IRB for review

An accurate roster of IRB members

It is important to note FWA-holders no longer need to submit roster changes.

46.116, General Requirements for Informed Consent

There are many revisions to 46.116, which addresses the process of obtaining informed consent from subjects. Chief among these changes are revisions and additions to the general requirements and the basic elements, as well additional elements.

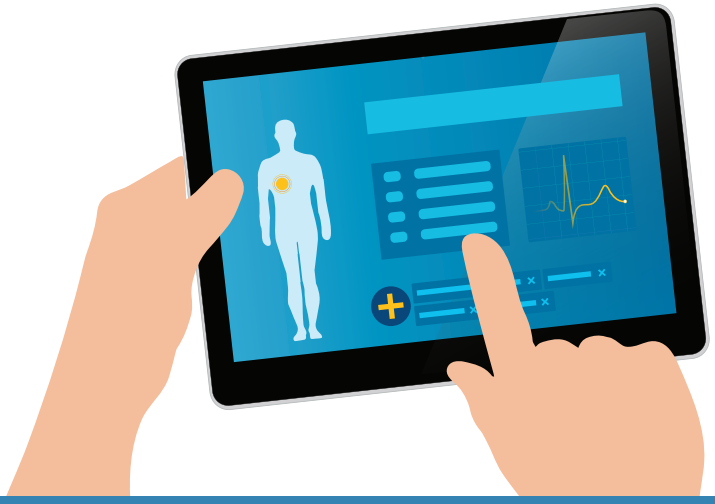


Key Revisions to 46.116 include:

- Updates to the process of obtaining informed consent from subjects.
- Revisions and additions to the general requirements for informed consent, basic elements, and additional elements.
- Modifications to the criteria for waivers and alterations.
- Defined criteria for broad consent.
- Requirements to post consent forms.

Researchers conducting clinical trials are also required to post the consent forms for the trials on a federal website, "after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol." For a multi-site study, only a single consent form from the entire study is required to satisfy the posting requirement (not a consent form from each participanting site). Single site only studies will also require a single consent form.

Revisions to 46.116 will affect HRPP professionals, researchers, and IRB members. Like changes pertaining to broad consent, the new revisions to 46.116 will necessitate changes to informed consent language. This requires updates to guidance documents, research study submission applications, and reviewer checklists and work-sheets. These changes will affect the way in which researchers design informed consent processes and describe their methods for obtaining informed consent or requesting waivers. IRB reviewers will need to be trained to review consent processes and apply the waiver criteria per the new revisions.



46.117, Documentation of Informed Consent

Revisions to 46.117 requirements for the documentation of informed consent now allow for the collection of electronic signatures, and the flexibility in reading aloud consent forms to subjects. Consistent with the addition of including key information at the beginning of consent processes, 46.117 specifies that the "concise and focused presentation of key information" must be included when using short form informed consent.

The Final Rule allows for the waiver of documentation of informed consent when subjects or their legally authorized representatives "are members of a distinct cultural group or community in which signing forms is not the norm," provided that the research "presents no more than minimal risk of harm to subjects" and "an appropriate alternative mechanism" is in place to secure documentation.

Revisions to 46.117 will affect HRPP professionals, researchers, and IRB members. As with the other changes related to informed consent, HRPP programs will need to revise informed consent language in guidance documents, research study submission applications, and reviewer checklists and worksheets. These changes may affect the way in which researchers design and describe obtaining informed consent or requesting a waiver to the requirement to document informed consent. IRB reviewers will need to be trained to review consent processes and apply the waiver criteria per the new revisions.

46.119, Research Undertaken without the Intention of Involving Human Subjects

There were only minor modifications to 46.119. The section now specifies this provision applies only to human subjects research that is nonexempt. Research that adds human subjects to a project must undergo IRB review and certification submitted to the funding agency. The funding agency must approve the change.

These revisions were made for clarification purposes and are not intended to affect researchers, HRPP professionals, or IRB members.

Six Month Delay and Burden-Reducing Provisions

HHS and 16 other agencies published a Final Rule in 2018 to delay the general compliance date of the revised Common Rule until 21 January 2019, but allow for three provisions from the revised Common Rule (2018 requirements) to be available in the delay period.

This delay gives additional time for regulated bodies to prepare for the revised rule. Regulated parties are allowed to implement three specific provisions from the 2018 requirements during the delay period, including (HHS 2018b):

- The definition of "research" at 46.102(l)
- Elimination of continuing review requirement for no more than minimal risk research at 46.109(f)(1)(i) and (iii)
- Elimination of IRB requirement to review grant applications

Note: If an institution chooses to implement any or all of the three burden-reducing provisions for research during the delay period, then the affected research must comply with all of the 2018 requirements after the general compliance date of the revised Common Rule. Institutions or IRBs must also document and date such determinations to transition the ongoing research to the 2018 requirements (HHS 2018b).

During this delay period, some studies may be subject to the pre-2018 requirements and others subject to the revised 2018 requirements. It is important to know which regulation is in effect for each research study. Institutions and/or the reviewing IRBs should provide information to researchers and administrators on which regulations apply to which research.

References

- *U.S. Department of Health and Human Services (HHS). 2017. "Federal Policy for the Protection of Human Subjects." Federal Register 82(12):7149-274.*
- *U.S. Department of Health and Human Services (HHS). 2018. "Federal Policy for the Protection of Human Subjects: Six Month Delay of the General Compliance Date of Revisions While Allowing the Use of Three Burden-Reducing Provisions During the Delay Period." Federal Register 83(118):28497-520.*