



# Final Rule Material: Final Rule Impact on IRB and Institutional Operations

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## Introduction

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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) and 15 other federal departments and agencies 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 compliance date for cooperative research and use of single Institutional Review Board (IRB) is 20 January 2020 (HHS 2017).

This resource considers ways in which the Final Rule may affect operations for both Institutional Review Boards (IRBs) and institutions.

This material will use the terms "pre-2018 rule" to refer to the current Common Rule and "Final Rule" or "revised Common Rule" when referring to the revised rule. For consistency and clarity (the CITI Program recognizes that each Common Rule agency has different citations for its human subject protection regulations), this material will use citations to the HHS 45 CFR 46, Subpart A version of the Final Rule.

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## Summary of Revisions and Impact on IRB and Institutional Operations

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### *46.101, To What Does This Policy Apply?*

Revisions to the scope and applicability of 46.101 should not have a substantive effect on IRB operations. The following table outlines how changes in this section may potentially affect IRB and institutional operations.

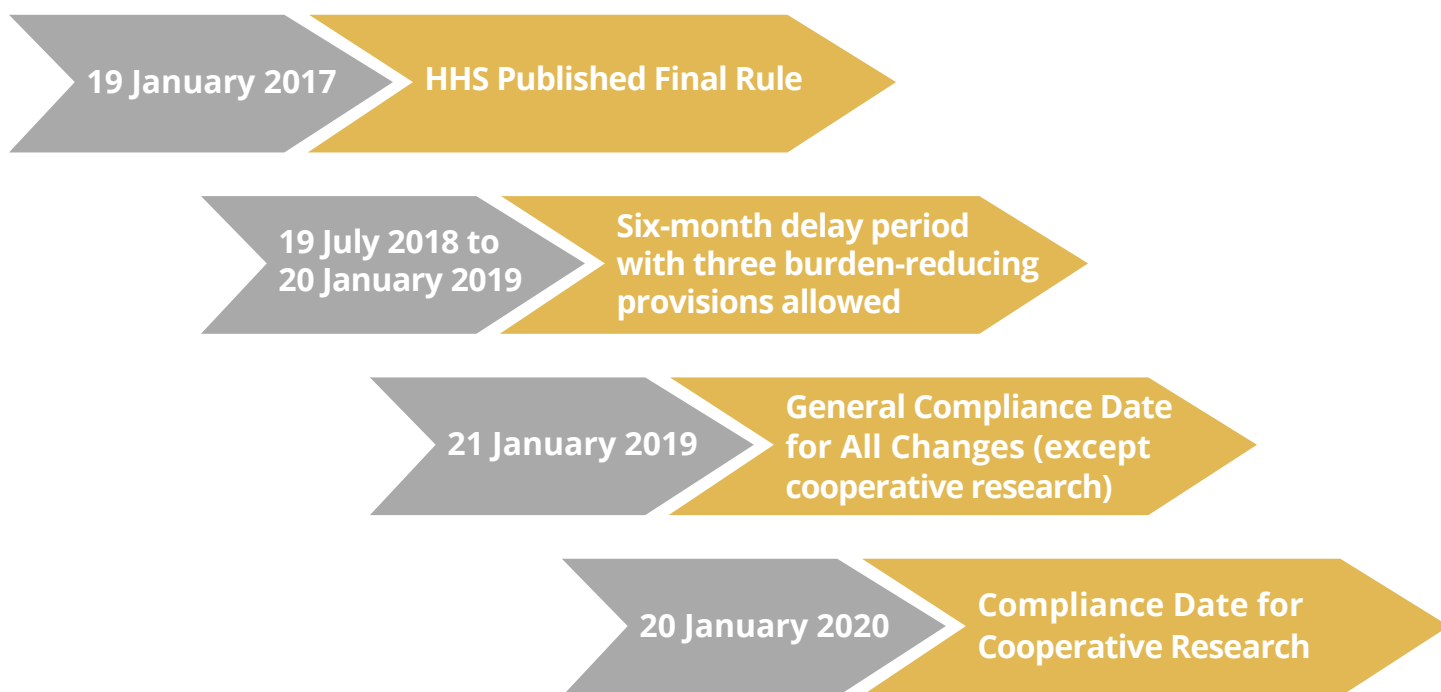
IRBs reviewing research subject to Final Rule (even those not at Federalwide Assurance [FWA]-holding institutions) must comply with the requirements in the Final Rule

A major update that affects institutions and IRBs is the moving of liability from the institution to the external IRB for the external IRB's review. 46.101 states that IRBs that are not part of a FWA-holding organization are subject to the Final Rule.

- Facilitates the use of external IRBs and sIRB review.
- Affects institutional operations, in that, institutions that rely on an external IRB's review are not liable for the external IRB's review (institutions were liable according to the pre-2018 rule).
- Common Rule departments and agencies have the authority to enforce compliance directly with IRBs (that are not part of an FWA-holding institution).

<p>No more “checking the box”</p>	<p>Revisions to 46.101 also removed the ability of institutions to “check the box” and apply the Final Rule to all their research, regardless of funding.</p> <p>Institutions may still do that for their own compliance purposes, but the regulation specifies that FWAs now only apply to federally conducted or federally sponsored research, so externally funded (and unfunded) research is not subject to the assurance.</p> <p>For institutions that do apply the pre-2018 rule to all research, they must revise forms, policies, and procedures to remove the reference to federal oversight and clarify that they are voluntarily complying with the federal regulations (however, federal agencies and departments have no oversight responsibilities). Note: the assurance process has not yet been updated with the change.</p>
<p>Tribal law still applies</p>	<p>IRBs and institutions should already have processes in place that ensure research subject to tribal law is being conducted in accord with those laws.</p>

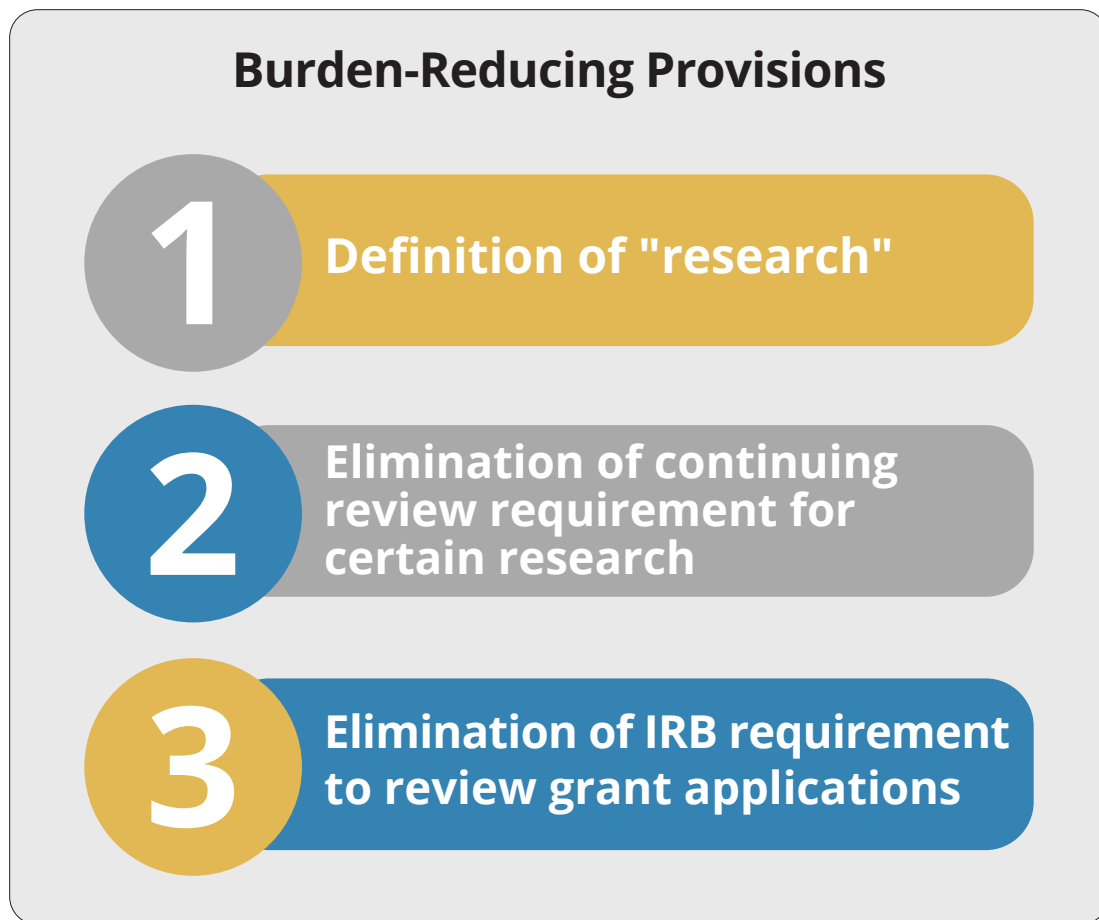
It is also important to note that IRBs and institutions need to understand and comply with the Final Rule by the implementation dates. This includes updating all documents, policies, and practices as applicable. The important dates to know are:



## — Six Month Delay with Three Burden-Reducing Provisions —

There is a six month delay period extending the general compliance date of the revised Common Rule to 21 January 2019. This delay is intended to provide additional time for regulated bodies to prepare for the revised rule.

During the six month delay period (19 July 2018 – 20 January 2019), institutions are allowed (but not required) to employ three burden-reducing provisions from the revised Common Rule's 2018 requirements (HHS 2018).



Institutions that employ the three burden-reducing provisions during the delay period must:

- Document and date the use of the burden-reducing provisions for the research
- Transition the research to comply with all of the 2018 requirements beginning on the general compliance date (21 January 2019)

**Note: Institutions may implement any of the provisions from the revised Common Rule before the general compliance date if they do not conflict with the pre-2018 Common Rule.**

#### 46.102, Definitions for Purposes of this Policy

IRBs and institutions will need to adopt the Final Rule's new and revised definitions.

As such, IRBs will need to update language used on their:

- Websites
- Manuals
- Materials used for education or distribution purposes (such as, guides)
- Checklists and review worksheets
- Approval notices
- Protocol application forms

#### Example

The revised definition of "legally authorized representative" adds specific authorization to use institutional policy when there is no applicable law addressing who can be a legally authorized representative for research.

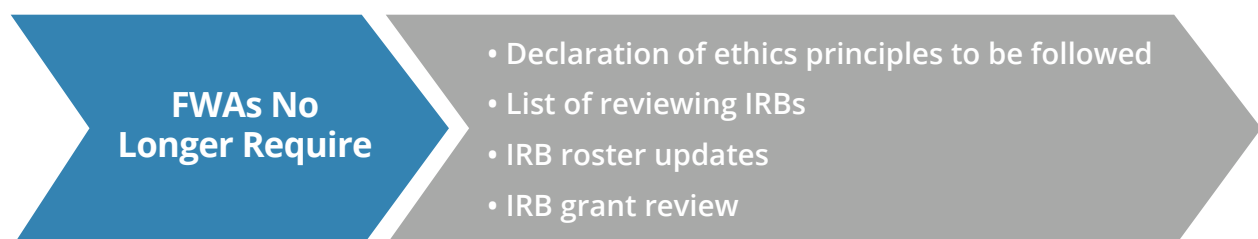
Definitions included in the Final Rule will also necessitate changes to an IRB's standard operating procedures (SOPs).

Of note is the addition of "obtaining, storing, using, studying, analyzing, or generating private information or identifiable biospecimens" to the definition of research with human subjects. Institutions may want to consider internal guidance documents to help staff and reviewers identify activities no longer covered under the revised Common Rule (such as, oral history and most public health surveillance).

It has also been suggested that "institutions will want to find a way to include a placeholder in their SOPs to account for the further federal guidance on the definitions of identifiable private information and identifiable biospecimen due within 1 year of the general compliance date, as well as the list of technologies (also forthcoming within 1 year) deemed to generate individual private information or an identifiable biospecimen" (Verrill Dana 2017). In addition to informed consent and the exempt and expedited review processes, revisions to definitions may require the most modifications to an IRB program's current standard operations.

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

Revisions to the assurances section generally affect IRB operations with respect to the FWA.



Revisions to 46.103 also affect the reliance agreements executed when one institution relies on an external IRB for review.

The Final Rule requires the documentation of the written reliance agreement between the institution and external IRB.

There is flexibility in what the documentation may consist of, including the “implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol” (Final Rule Preamble).

In this way, institutions are now responsible for designing the assurance documentation for these types of reliance agreements. SOPs for the processing and documenting of such assurances may need to be revised. As already noted, the new Final Rule includes no provisions that allow IRB programs to “check the box” when applying the regulations.

#### *46.104, Exempt Research*

For all ongoing exempt research that was determined to be exempt prior to 21 January 2019, the pre-2018 rule applies. For research determined to be exempt on or after 21 January 2019, the Final Rule applies. institutions can choose to comply with the Final Rule for all research, but this must be documented and institutions must allow adequate time to transition to Final Rule compliance.

With the revisions and expansion to the exemption categories, IRBs and institutions should revisit their current processes to determine which procedures currently in place need to be updated to meet the new exemption criteria.

There are new exempt categories, revisions to existing categories, and new concepts like broad consent and limited IRB review.

It is important to note that research with prisoners can now be exempt if the research is aimed at involving a broader subject population that only incidentally includes prisoners.

For secondary research, institutions must identify which existing databases and repositories are governed by the pre-2018 rule or the Final Rule. It must be one or the other. Tracking systems will also be needed for identifying which biospecimens were provided under broad consent, and instances where subjects refused broad consent for future research. The Final Rule allows institutions to elect to comply with the Final Rule for all or some of their existing databases, but this must be documented and the Final Rule is not clear on how an institution may do this.

IRBs will need to develop new processes to document limited IRB review for exemptions. This includes training of IRB members delegated as expedited reviewers on how to perform limited IRB review.

It is likely that revisions will be required to institutional guidance on exemptions, applications requesting review, and reviewer checklists and documentation for approval of exemption research.

### **Institutional Implementation of Final Rule**

It may be helpful to outline the Final Rule by section, and then have IRB staff each take one or more of the sections and check the institution's documents (SOPs, worksheets, and checklists) to determine which require revision and make edits.

Another IRB staff member can review the revisions.

Finally, a director or institutional leader can review each revision and develop the training tools as needed.

Limited IRB review must be conducted by an IRB member (the same requirement for an expedited review). There is no regulatory requirement for who can perform an exempt determination (it may be a non-IRB member like an experienced IRB staff person) though it should be documented in institutional policy.

### *Revised References to Vulnerability in Final Rule*

IRBs and institutions should consider providing training to their IRB members with respect to the new application of vulnerability (specifically, the review of protocol applications). Changes to reviewer checklists and worksheets may be necessary. In addition, language in guidance documents, manuals, and protocol applications with previous language pertaining to coercion and undue influence should be revised to reflect new wording.

The Final Rule refers 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" (Final Rule Preamble).

Additionally, the Final Rule no longer lists pregnant women and handicapped or mentally disabled persons as examples, but does list "individuals with impaired decision-making capacity."

### *46.107, IRB Membership*

This section was only slightly revised, and should not have any major effects. In addition to the revised definition of "vulnerable" as discussed above, the Final Rule removes the specific requirement that IRB membership not consist entirely of one sex (gender) or profession. The preamble explained that the diversity requirement of IRB membership accomplishes the same goal.

### *46.108, IRB Function and Operations*

Any additional changes to IRB programs in respect to the revisions laid out in this section are unlikely. IRB programs should already have processes in place to ensure an accurate list of IRB members, IRB meeting space, and sufficient staff to support the IRB. Workload may be decreased by the elimination of some documentation for assurances, specifically the Final Rule deleted the requirements that institutions designate IRBs on the FWA and that FWA-holders submit roster changes to the Office for Human Research Protections (OHRP).

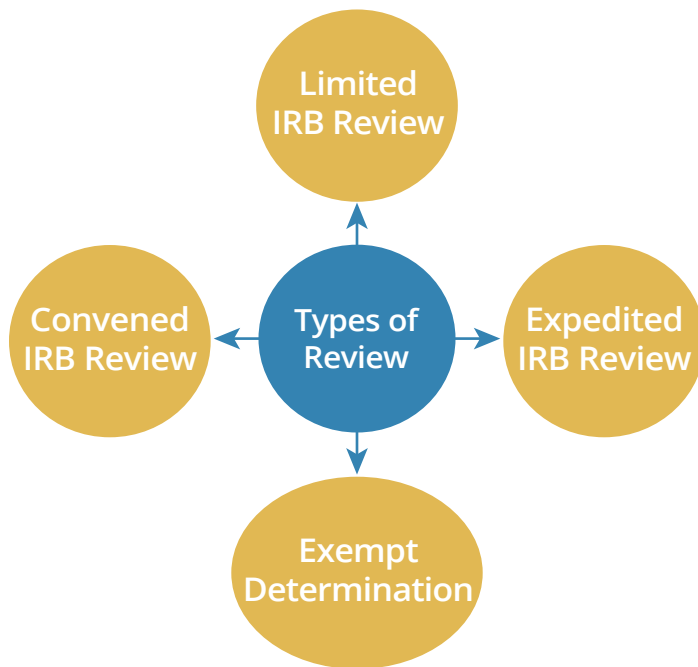




## 46.109, IRB Review of Research

As stated previously, IRBs and institutions will need to modify processes to allow for limited IRB review.

The elimination of the requirement for continuing review of minimal risk studies may not necessarily alter the continuing review process, as it would still be applicable to research studies approved by a convened IRB.



However, IRBs and institutions may want to consider implementing an annual review process for research approved under expedited review that is different from the continuing review reserved for convened (full IRB) review.

Human Research Protection Programs (HRPPs)/IRBs also will need to determine if they will continue to apply the pre-2018 regulations to research approved before the Final Rule's general compliance date (21 January 2019 for all sections except 46.114 [cooperative review] which is 20 January 2020) and how this would be managed, or if they will apply the Final Rule to all research (regardless of approval date).

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

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

There were minor changes to expedited review, including a potential expansion of expedited review which would reduce regulatory burden of review on convened IRBs. An IRB may continue to use the expedited review procedure for research activities appearing on the HHS Secretary's List and that are no more than minimal risk. If it is determined that an activity on the list is more than minimal risk and requires convened IRB review, the rationale for this decision must be documented. This will inform future versions of the HHS Secretary's List. The HHS Secretary's expedited review list will be updated at least every eight years.

The Final Rule further added that expedited review can be used to conduct limited IRB review for research, when limited IRB review is a condition of exemption.

IRBs should review and revise their expedited review policies and provide training to IRB members designated to conduct expedited review to differentiate between the Final Rule and the pre-2018 rule.



#### *46.111, Criteria for IRB Approval of Research*

IRBs and institutions will need to make revisions for the inclusion of limited review and broad consent. As these are two new mechanisms being incorporated into the IRB process, it is advisable for IRB programs to develop new policies, checklists, and training. Institutions will also need to develop processes for tracking of broad consent refusals.

Additionally, revisions to 46.111 include biospecimens in the requirement for IRBs to ensure the adequacy of protections for the privacy of subjects and confidentiality of identifiable private information.

##### **Future Guidance for IRBs on Assessing Privacy and Confidentiality Safeguards**

The HHS Secretary will issue future guidance to assist IRBs in assessing what provisions are adequate to protect the privacy of subjects and confidentiality of information (HHS 2017).

According to the Final Rule's preamble, this future guidance might address the following considerations, such as:

- The extent to which identifiable private information is or has been deidentified and the risk that such deidentified information can be reidentified
- The use of the information
- The extent to which the information will be shared or transferred to a third party or otherwise disclosed or released
- The likely retention period or life of the information
- The security controls that are in place to protect the confidentiality and integrity of the information
- The potential risk of harm to individuals should the information be lost, stolen, compromised, or otherwise used in a way contrary to the contours of the research under the exemption

It is also important to consider the revised wording for “vulnerable populations” when IRB members review research in consideration of equitable selection of subjects, as described in 46.107.

#### *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*

The Final Rule mandates sIRB review for cooperative research. However, 46.116(b)(2)(ii) allows for federal departments or agencies to determine that a sIRB would not be appropriate. It may also be important to note that institutions may still choose to conduct their own review of the research, although the regulations make it clear their review would not have “any regulatory status in terms of compliance with the Common Rule.”

For research subject to the Common Rule, the regulations allow the lead institution to propose which IRB will serve as the IRB of record, but leaves the final decision to the federal department or agency funding the research.

As noted above, revisions requiring the use of a sIRB will take effect 20 January 2020.

IRBs and institutions should update their reliance arrangements with external IRBs to ensure responsibilities of both entities are documented. Institutional policy should also be revised to reflect the cooperative research requirement, as well as new forms to assist in sIRB review.

#### IRB and Institutional Operations Updates for Cooperative Research (Verrill Dana 2017)

IRBs and institutions may want to:

- Create a local information sheet with specific site requirements when the institution relies on an external IRB
- Plan for institutional ancillary reviews (for example, biosafety or departmental)
- Develop an information sheet to collect data about other participating sites if another institution will be relying on the IRB
- Designate an IRB point person to coordinate and track reliance agreements and communication with external IRBs and internal offices (as applicable)
- Assess institutional reliance relationships and look for efficiencies by joining larger networks or master agreements that cover many studies
- Identify IT systems to help manage/track reliance relationships
- Train researchers and staff on processes and policies for working with external IRBs and expectations when serving as the sIRB of record

#### 46.115, IRB Records

Revisions to this section expand the required records IRBs should maintain, such as documenting the rationale for instances that:

- An IRB recommends a research activity for convened IRB review that is listed in the HHS Secretary's list of acceptable expedited review activities.
  - This would require a justification on why the expedited IRB reviewer determined that the research activity was more than minimal risk.
- An IRB conducts continuing review of research that would not otherwise require continuing review per the Final Rule.
  - This would require a justification on why the IRB determined that the research activity required continuing review.




IRBs and institutions will need to revise current SOPs to include collecting and maintaining these records. IRBs could consider creating a standard form or template for these instances, as a way to maintain consistency.

IRBs are also now required to maintain records specifying the responsibilities of each entity when the institution is relying on another IRB for review.

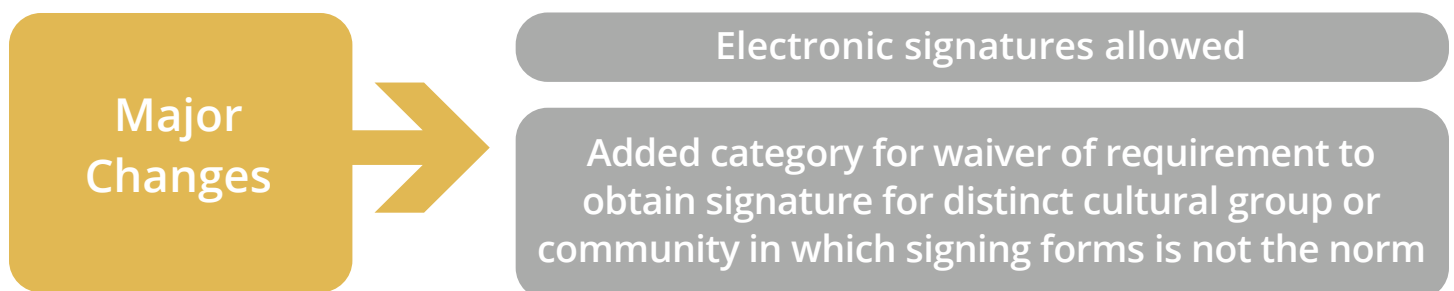
Record retention requirements remain the same (at least three years after the completion of the research), but the Final Rule specifies that the institution or IRB may maintain the records in paper or electronic form.

## 46.116, General Requirements for Informed Consent

The Final Rule provides considerable changes to the informed consent process. This includes informed consent form formatting, consent form discussion, and posting of consent forms.

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- Revising of documents (such as, protocol applications, reviewer checklists, and worksheets)
  - Training for IRB administrators, IRB members, and investigators
  - Creating a variety of new resources (like guides and templates) to help researchers use the new flexibilities allotted (for example, broad consent and traditional informed consent and when and when not to use)
  - Creating new templates for consent forms to include the new regulatory language and organization of the material (key information at the beginning)
  - Creating new broad consent template for future research
  - Creating a procedure for confirming that consent forms for clinical research are added to a federal website as required
  - Updating institutional policy on waiver process to reflect limitation when broad consent is sought and refused (Verrill Dana 2017)
  - Updating institutional policy on returning clinically relevant research results (and under what conditions)
  - Revising screening and recruitment policy to reflect elimination of the requirement for consent (or waiver) for these activities (Verrill Dana 2017)
  - Updating that reading consent forms to subjects is allowed
  - Ensuring that a concise and focused presentation of key information to facilitate comprehension is presented first

Updates to 46.117 affect consent forms documentation and waivers/alterations of documentation. IRBs and institutions will need to revise informed consent language in guidance documents, protocol submission applications, and reviewer checklists and worksheets. Updated documents should include the new requirements to document informed consent. IRB programs may also want to consider training IRB reviewers in applying new waiver criteria per the revisions.



IRBs may or may not have experience in reviewing research with cultural groups or communities for which a signed form is not the norm. For IRBs that do, they may have developed appropriate alternative mechanisms to secure documentation in lieu of a signature.

IRBs and institutions may address these important revisions to informed consent by creating a library of “best practices” to help educate both IRB members and researchers.

Revisions to these sections were made for clarification purposes and should not affect IRB or institutional operations.

## Common Rule Agencies

IRBs and institutions must know which federal departments and agencies conduct or support research subject to the Final Rule. This will help ensure compliance with the regulation. The signatories to the Final Rule are below, but do not reflect all of the pre-2018 Common Rule agencies and departments.

### *Signatories to the Final Rule*

Department of Homeland Security  
Department of Agriculture  
Department of Energy  
National Aeronautics and Space Administration  
Department of Commerce  
Social Security Administration  
Agency for International Development  
Department of Housing and Urban Development

Department of Labor  
Department of Defense  
Department of Education  
Department of Veterans Affairs  
Environmental Protection Agency  
Department of Health and Human Services  
National Science Foundation  
Department of Transportation  
Consumer Product Safety Commission

1

*A new signatory to the Final Rule is the Department of Labor, so this agency's sponsored research would need to comply with the Final Rule on and after the compliance dates.*

2

*The Department of Homeland Security and Social Security Administration formerly applied the rules, but are now codifying the Final Rule into their own agency regulations.*

3

*The Consumer Product Safety Commission (CPSC 2017) adopted the Final Rule through separate rulemaking.*

4

*The Department of Justice (DOJ), a previous signatory to the Common Rule, has not yet signed on to the revised 2018 version of the regulation.*

5

*The U.S. Food and Drug Administration (FDA) is not a signatory, nor are its regulations harmonized yet with the new Final Rule. FDA-regulated research must comply with FDA regulations, which may differ slightly more with the Final Rule than the pre-2018 rule.*

## References

- U.S. Consumer Product Safety Commission (CPSC). 2017. "Protection of Human Subjects." *Federal Register* 82(179):43459–70.
- 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.
- Verrill Dana. 2017. "2018 Common Rule Implementation Checklist." Accessed September 15.