Final Rule Material:
Overview - Introduction

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CITI Program Final Rule Materials

- We invite you to use this presentation to introduce those involved in the research enterprise about the changes to the federal Common Rule made by the Final Rule published by HHS in 2017.
- All CITI Program Final Rule materials are available on the "Resources" tab of the CITI Program website, www.citiprogram.org/en/resources.
- **Note**: These resources are based on the Final Rule issued by the U.S. Department of Health and Human Services (HHS) at 45 CFR 46, Subpart A - "Federal Policy for the Protection of Human Subjects" (the Common Rule) on 19 January 2017. These resources have been updated to reflect the 19 June 2018 Final Rule. The general compliance date is now 21 January 2019.

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Overview - Introduction

This presentation provides a brief introduction and overview of the revised Common Rule, including why it was updated, when it is effective, and which research studies must comply with it.

- **Overview – 46.101-46.115** presentation covers changes to those sections, including the definitions, exempt and expedited research, secondary research, IRB membership, IRB operations, IRB review and records, and cooperative research.
- **Overview – 46.116-46.124** presentation covers changes to those sections, including the informed consent document and process.
- **Overview – Comprehensive** presentation provides a comprehensive review of the revisions to the Common Rule, including describing changes to each regulatory section from 46.101-46.124.

Introduction

- Final Rule to revise the current regulations at 45 CFR 46, Subpart A (Common Rule) was published by U.S. Department of Health and Human Services (HHS) 19 January 2017 in the *Federal Register*.
- Revisions intended to "modernize, strengthen, and make more effective" the current system of oversight under the Federal Policy for the Protection of Human Subjects that has been the federal Common Rule since 1991.
  - *Revisions aim to better protect human subjects involved in research, facilitate research, remove ambiguity, and reduce regulatory burden.*

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Need for Updates

- Large databases, biospecimen repositories, electronic health records, and clinical research networks have spurred new kinds of research
- Final Rule intended to better manage new broader types of research
  - *Specifically including behavioral and social science research*
- Recognizes the evolving technologies including mobile technologies, the Internet, and the growth in computing power that have changed the scale and nature of information collected
- One of the main purposes of the Final Rule is to facilitate the conduct of minimal risk research

Compliance Dates and Transition Provisions

- Final Rule does not immediately go into effect
- Research organizations, IRBs, and investigators will have a some time to revise forms, documents, and practices to comply with the revisions.

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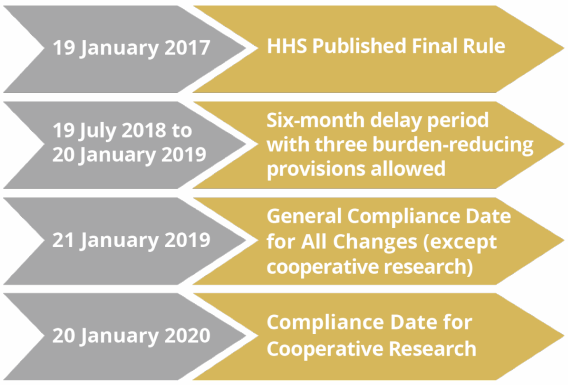
Implementation Dates



The general compliance date for the revised Common Rule is 21 January 2019.

- All regulated parties must be in compliance from that date onward.

One exception is the compliance date for single IRB (sIRB) review of cooperative research.

Final Rule Delay

An Interim Final Rule as published on 22 January 2018 ("Federal Policy for the Protection of Human Subjects: Delay of the Revisions to the Federal Policy for the Protection of Human Subjects") initially delayed the general compliance date to 19 July 2018.

A Final Rule as published on 19 June 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") further delayed the general compliance date of the revised Common Rule until 21 January 2019.

The cooperative research effective date was not revised.

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2018 Final Rule Allows Three Burden-Reducing Provisions

During this delay (19 July 2018 – 20 January 2019), institutions are allowed to employ three provisions from the revised Common Rule (2018 requirements) (HHS 2018) including:

- The definition of "research"
- Elimination of continuing review requirement for no more than minimal risk research
- Elimination of IRB requirement to review grant applications

Institutions that transition ongoing research studies to the 2018 requirements during the delay period must document and date their determination (HHS 2018). The research that is transitioned must also fully comply with all of the 2018 requirements beginning on the general compliance date (21 January 2019).

Transition Provisions – "Grandfathered"

- Actions taken before the compliance dates are "grandfathered."
  - *Ongoing research studies that were initially approved by an IRB or determined to be exempt before the general compliance date will not be required to comply with the changes.*
  - *Such research may continue to completion or closure without change .*
- Institutions and IRBs can voluntarily choose to apply the Final Rule on a study-by-study basis or by formally adding a requirement to their policies.
  - *Further guidance is pending to determine if the IRB must document this per study even if the institution issues an institutional policy applying the Final Rule to all research.*

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Transition Provisions – "Which Rule?"

Research Study Initiation Date	Standards
Research initially approved by an IRB, waived pursuant to [former subsection] 101(i), or determined to be exempt [under former subsection 101(b)] **before** 21 January 2019. (Grandfathered research)	These studies are by default subject to the pre-2018 requirements (the Common Rule as published in the 2016 edition of the CFR). However, an organization engaged in such research may choose to comply with the Final Rule (2018 requirements) for such a study (the grandfathered research) if the organization applies the Final Rule to the study and an IRB documents this determination. Further guidance is pending to determine if the IRB must document this per study even if the institution issues an institutional policy applying the Final Rule to all research.
Research initially approved by an IRB, waived pursuant to [former subsection] 101(i), or determined to be exempt on or **after** 21 January 2019.	These studies are subject to the Final Rule (2018 requirements).

Transition Provisions – "All or None"

- The transition phase is to minimize burdens for ongoing research.
  - *Avoids a requirement for two sets of rules during the life of the research*
  - *Two categories of studies – approved (or determined exempt) before general compliance date or approved (or determined exempt) on or after general compliance date*
  - *Studies are either subject to compliance with pre-2018 rule or Final Rule (not both)*
- After the general compliance date, institutional policy must be in full compliance with either the Final Rule or the pre-2018 Rule (for ongoing research).
- Non-federally funded research is not covered by the Final Rule because the new assurance mechanism eliminates the voluntary extension of the FWA to non-federally funded research.

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FDA Harmonization

- The 21st Century Cures Act (2016) requires the Secretary of HHS to harmonize the differences between 45 CFR 46, Subpart A, and the U.S. Food and Drug Administration (FDA) human subject regulations.
- FDA plans to update 21 CFR 50 and 56 as part of the government-wide effort to modernize rules for the involvement of human subjects in research.
- Until an update is issued by the FDA, research organizations, institutions, IRBs, and investigators must comply with the current FDA regulations, as well as the Final Rule (pre-2018 or 2018 version as applicable) when both sets of FDA and HHS regulations apply.

Guidance Harmonization

- All Common Rule departments and agencies are authorized to issue separate guidance for interpreting and implementing its regulations.
- To promote consistency, the Final Rule creates a requirement that guidance on the protection of human subjects should be issued only after consultation among the Common Rule departments and agencies.
- Guidance may be issued without consultation when varied missions or differences in statutory authority/scope exist.

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Influencing Factors to Revisions

Revisions to the Common Rule were based on a variety of sources, including:

- *Public, stakeholder, and expert comments (for example, SACHRP, individual researchers, and professional organizations)*
- *Advice (including guidance provided by a 2014 National Research Council consensus report, the National Academies of Science, Engineering, and Medicine 2016 report)*
- *Public discussions associated with the President's Precision Medicine Initiative and comments received on the Announced Notice of Proposed Rule Making (ANPRM) and the NPRM*
- *Medicare Access and Children's Health Insurance Program Reauthorization Act of 2015 (Pub. L. 114-10)*
- *Newborn Screening Saves Lives Reauthorization Act of 2014 (Pub. L. 113-240)*
- *National Institutes of Health (NIH) policy on the use of a sIRB for multi-site research*
- *OHRP draft guidance on the required content of consent language for research conducted within the standard of care*
- *FDA's draft guidance on "Use of Electronic Informed Consent in Clinical Investigations"*
- *NIH policy to promote sharing of large-scale human genomic data*

Final Rule Differs from NPRM

The Final Rule differs in significant ways from the 2015 Notice of Proposed Rulemaking (NPRM).

The 2015 NPRM received more than 2,100 public comments. The proposals receiving the most comments were those related to human-derived biospecimens (for example, expanded definition of human subject, requirement for broad consent, and tightened criteria for waiver of consent).

Several NPRM proposals are not being adopted, including:

- *Require that research involving non-identified biospecimens be subject to the Common Rule, and that consent would be needed*
- *Expand the Common Rule to cover clinical trials that are not federally-funded*
- *Concept of "excluded" activities*
- *Standardized privacy and security safeguards for IRB records and identifiable private information and identifiable biospecimens*
- *More restrictive proposed criteria for obtaining a waiver of the consent requirements relating to research with identifiable biospecimens*
- *Require notice to exempt some secondary research including clinical data registries*

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Overview of the Final Rule Revisions

- The Common Rule numbering scheme and section titles remain largely intact, but with some movement of text and subsection numbering revisions.
- The regulations themselves should be read and understood before implementing changes.
  - *Note - the Final Rule's preamble is a good source for further explanation.*

References and Additional Resources

References

- Institutional Review Boards, 21 CFR § 56 (2015).
- National Institutes of Health (NIH). 2016. "Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research."
- Protection of Human Subjects, 21 CFR § 50 (2015).
- 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: Delay of the Revisions to the Federal Policy for the Protection of Human Subjects." *Federal Register* 83(14): 2885-2894.
- 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.

Additional Resources

- FDA's 2006 guidance entitled "Using a Centralized IRB Review Process in Multicenter Clinical Trials" reinforces the FDA's support of centralized IRB review for multi-site research as described in 21 CFR 56.114. It provides researchers and IRB administrators additional clarification regarding roles and responsibilities when relying on an IRB outside the research institution.
- HHS Invesitgator Responsibilities FAQs.

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