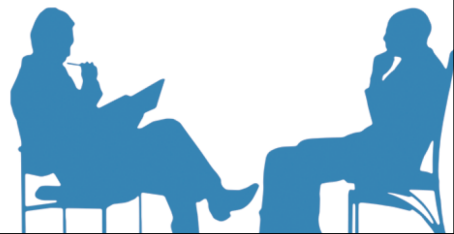




# Final Rule Material: Comprehensive Guide to Informed Consent Changes

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## CITI Program Final Rule Materials

- We invite you to use this presentation as an overview to the Final Rule's changes to informed consent in the Common Rule.
- All CITI Program Final Rule materials are available on the "Resources" tab of the CITI Program website, [www.citiprogram.org/en/resources](http://www.citiprogram.org/en/resources).
- Note: These resources are based on the Final Rule and Interim 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 and 22 January 2018, respectively.

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## Overview

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This presentation provides an overview of the Final Rule's revisions to the informed consent sections (46.116 and 46.117).

The Common Rule numbering scheme and section titles remain largely intact, but with some movement of text and subsection numbering revisions. 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 HHS 45 CFR 46, Subpart A version of the Final Rule.

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## Introduction

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- Final Rule to revise the current regulations at 45 CFR 46, Subpart A (Common Rule) was published by HHS on 19 January 2017 in the *Federal Register*.
- Revisions are 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.*
  - *Revisions to informed consent are effective 19 July 2018.*

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## Understanding 46.116 and 46.117

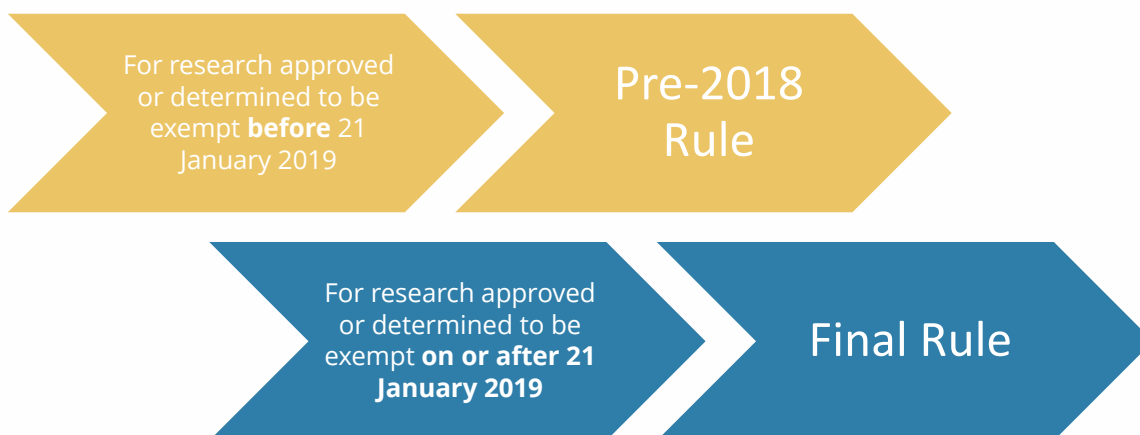
- In the discussion of 46.116, the Final Rule's preamble combines explanations about the requirements for consent (the process) with the requirements for consent forms.
- It is important to remember that, in regulations themselves, 46.117 contains the requirements for forms, while 46.116 still pertains to the consent process and the informational substance contained therein.

46.116  
Requirement  
for  
Consent  
Process

46.116  
Requirement  
for  
Consent  
Process

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## Which Regulation Applies?



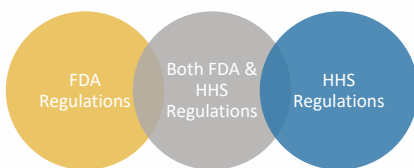
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## Transition Provisions

- Research studies approved via expedited or convened IRB review (or determined to be exempt) **before** the effective date of the Final Rule are “grandfathered;” this means that they will not be required to comply with the changes in the Final Rule.
  - *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.*
  - *If the Final Rule is applied to the grandfathered research, then all Final Rule requirements must be applied (no picking and choosing what to apply from pre-2018 and Final Rule regulations – it is all or none).*

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## FDA Harmonization



- FDA plans to update its regulatory language.
  - *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.*
- Expectation is that FDA will issue its own NPRM for 21 CFR 50 and 56 and eventually a Final Rule.
  - *Different requirements for waivers, consent process, and consent form language.*
- Institutions, IRBs, and investigators must comply with FDA and HHS regulations (pre-2018 or 2018 version as applicable) when both apply.

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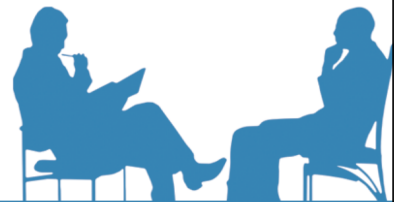
## Key Revisions to Consent

- **New process requirements** for the content, organization, and presentation of information and the process to facilitate a prospective subject's decision about whether to participate in research.
- **New requirements** for the basic and additional elements of consent.
- **Electronic consent is allowed**, but must provide written copy.
- **New broad consent** elements for the storage, maintenance, or secondary research use of identifiable private information and identifiable biospecimens.

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## Key Revisions to Consent, cont.

- **Changes in the waiver and alteration criteria** for consent.
- **New consent provision** that allows IRBs to approve a research proposal without individuals' informed consent for screening, recruiting, or determining eligibility.
- **New requirement to post**, to a federal website, a copy of an IRB-approved version of the consent form that was used for enrollment purposes for each clinical trial conducted or supported by a federal department or agency.



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## Changes to the Consent Process

- The goal of 46.116 (and 46.117) in the Final Rule is to facilitate a prospective subject's or legally authorized representative's understanding of the reasons why an individual might or might not want to participate in the research.
- A new approach to consent is requiring that the "key information" essential to decision making receive priority by appearing at the beginning of the consent form and being presented first in the consent discussion.

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## Easier to Reference Requirements

- In 45 CFR 46.116, the unnumbered list of conditions appearing in the old regulatory "introduction" before the numbered Basic Elements of Consent includes multiple independent and important regulatory requirements.
- In the Final Rule, these requirements have been separated and the previous conditions have been numbered as 46.116(a)(1-3) and (6), and two new conditions have been added.
- The separation and numbering is intended to make it easier to reference these requirements.

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## Updates to 46.116

46.116(a)	General conditions for consent are now numbered, new addition of reasonable person standard, and key information requirement for informed consent presentation
46.116(b)	New additional requirement to basic elements of informed consent if research involves collection of identifiable private information or identifiable biospecimens
46.116(c)	Contains three new additional elements ("when appropriate")
46.116(d)	New broad consent section

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## 46.116(a), General Requirements for Informed Consent

- **General requirements** for informed consent remain essentially intact.
- **Broad consent** may be obtained in place of informed consent obtained in accordance with the basic and additional elements, but only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens. This is not a waiver, but an alternative.
- **Waiver or alteration of consent** in research involving public benefit and service programs conducted by or subject to the approval of state or local officials is described in 46.116(e).
- **General waiver or alteration of informed consent** is described in 46.116(f).

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## 46.116(a)(4) - New Subsection

- Requires that subjects be provided with the information that a “reasonable person” (undefined) would want to have.
- Responsibility remains for the investigator to:
  - *Provide more information when requested by subjects*
  - *Make sufficient time and opportunity to discuss the research*
  - *Answer questions to improve a subject’s understanding*
- For certain types of research (such as, research for which there is reason to believe some subjects will find the research controversial or objectionable), a robust description of the research will be required to meet this reasonable person standard.

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## 46.116(a)(5), Key Information

- This new requirement states that the informed consent process must begin with “key information” and that this part of the informed consent be “organized and presented in a way that facilitates comprehension.”
- Currently, there is no federal (including Office for Human Research Protections [OHRP]) guidance defining these terms. Presumably, further guidance will explain what these terms mean and how to achieve the goal along with what qualifies as a concise and focused presentation.

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## 46.116(a)(5), Key Information, cont.

- According to the preamble of the Final Rule, a brief description of five “factors” (elements) at the beginning of an informed consent process (and consent form) would encompass the key information including a concise explanation of the following (HHS 2017, 7149-274):



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## 46.116(a)(5)(ii), Improving Subject Comprehension

- This new section reminds investigators to present informed consent information in sufficient detail and in a way that helps with subject comprehension, not just running down a list of risks and procedures.
- The Final Rule's preamble discusses both the consent process and consent form somewhat interchangeably, and states that “investigators would first have to present the [relatively short concise] information” and “the final rule replaces [the NPRM differentiation between the ‘body’ of the consent form and appendices] with references to material that must be at the beginning of the consent form, versus material that can appear after that beginning section.”

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## 46.116(b), Basic Elements of Consent

- No changes to the eight previous basic informational elements of consent, but a new requirement was added.

### New Requirement for Informed Consent Form Language

- Added at 46.116(b)(9) is a new requirement to include one of two statements about the collection of private information or identifiable biospecimens for future research:
  - *Identifiers might be removed and the de-identified information or biospecimens used for future research without additional informed consent from the subject; **or***
  - *The subject's information or biospecimens will not be used or distributed for future research studies even if identifiers are removed.*

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## 46.116(c), Additional Elements of Consent

- No changes to the six previous additional informational elements of consent, but three new requirements were added.
  - *46.116(c)(7) - A statement that the 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.*
  - *46.116(c)(8) - A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.*
  - *46.116(c)(9) - 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).*

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## 46.116(d-h) - New Subsections

- 46.116(d), Elements of Broad Consent for the Storage, Maintenance, and Secondary Research Use of Identifiable Private Information or Identifiable Biospecimens
- 46.116(e), Waiver or Alteration of Consent in Research Involving Public Benefit and Service Programs Conducted by or Subject to the Approval of State or Local Officials
- 46.116(f), General Waiver or Alteration of Consent
- 46.116(g), Screening, Recruiting, or Determining Eligibility
- 46.116(h), Posting of Clinical Trial Consent Form

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## 46.116(d), Elements of Broad Consent

- This is a new subsection that addresses broad consent (seeking prospective consent to unspecified future research) for the storage, maintenance, and secondary research use of private information or identifiable biospecimens.
- Broad consent for secondary research use is permitted as an alternative to the standard informed consent requirements for a specific research study.

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## 46.116(e) – New Waiver or Alteration of Consent

- Final Rule added new waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials.
- New and complicated section because:
  - *Research and demonstration projects that are conducted or supported by a federal department or agency are exempt under 46.104(d)(5).*
  - *Restriction that an IRB may not “omit or alter” any of the general requirements (conditions) in 46.116(a).*
  - *Carries an instruction that if an individual was asked to provide broad consent and refused to consent, an IRB cannot waive consent for the use of identifiable private information or identifiable biospecimens.*

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## 46.116(f), General Waiver or Alteration of Consent

- Reflects major revision in content, format, and organization of the general waivers or alterations of informed consent that formerly appeared in 46.116(d).
- Four existing waiver conditions are included unchanged in 46.116(f)(3).
- Additional criterion was added for research that involves accessing or using private information or identifiable biospecimens.
  - *This new requirement is that the research could not practicably be carried out without accessing or using such information or biospecimens in an identifiable format.*
  - *Non-identified information should be used whenever possible to respect subjects' interests in protecting the confidentiality of their information and biospecimens.*

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## 46.116(f), General Waiver or Alteration of Consent, cont.

- IRB cannot waive informed consent under broad consent, or omit or alter any of the required broad consent elements.
- If an individual was asked to provide broad consent and refused to consent, the IRB cannot waive consent.

- Unlike complete waivers at 46.116(f)(1), for alterations at 46.116(f)(2) an IRB may not “omit or alter” any of the general requirements (conditions) in 46.116(a) including the new “format” requirements in 46.116(a)(5). Unless a total waiver under 46.116(f)(1) is granted, single or multiple general conditions cannot be waived/alterd separately.

### General waiver applies to:

- 46.116(a) - General requirements of informed consent
- 46.116(b) - Basic elements of informed consent
- 46.116(c) - Additional Elements of Informed Consent

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## 46.116(g), Screening, Recruiting, or Determining Eligibility

- New addition that addresses privacy issues regarding waivers of informed consent to obtain information or biospecimens for screening, recruiting (contacting), or determining the eligibility of prospective subjects.
  - *The previous requirement for IRBs to waive informed consent was viewed as burdensome and unnecessary for protecting subjects, and is not consistent with FDA regulations.*
- Now in 46.116(g), one of two conditions must be met for an exception:
  - 1) *The information will be obtained by communicating with the prospective subject.*
  - 2) *The information will be obtained by accessing records or stored biospecimens.*
- This is not a waiver of the consent requirement but rather an exception to the requirement.

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## 46.116(h), Posting of Clinical Trial Consent Form



- New requirements for posting clinical trial consent forms on a publicly available federal website that will be established as a repository for clinical trial consent forms.
- The Final Rule's preamble states "ClinicalTrials.gov might be an appropriate choice as the website ... the fact that these trials already have a record in the database will mean that the burden of submission of the informed consent document will be substantially lower."
- Consent forms must meet the requirements of 46.116.
  - *The Final Rule's preamble specifically states that posted consent forms will need to comply with the requirement in 46.116(a)(5), such that a concise presentation of key information is at the beginning of consent forms.*

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## 46.116(h), Posting of Clinical Trial Consent Form, cont.

- 46.116(h)(1) The responsibility for posting is on the awardee or the federal department or agency component conducting the study. The posting can take place any time after the trial is closed to recruitment, so long as the posting is no later than 60 days after the last study visit by any subject (as required by the protocol).
- 46.116(h)(2) The redaction of proprietary or institutionally sensitive information of portions of consent forms is allowed.
- 46.116(h)(3) Only one version (not necessarily the final) of the consent form (absent any signatures) for each clinical trial must be posted on the federal website after the clinical trial is closed to recruitment. In accord with the new "single IRB review" requirement, only one posting is required for each multi-institution study.
- There is no expectation that a version would need to be posted for each study site nor even for each class of subjects in the study (for example, a posting both for adults and for children).

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## 46.116(i), Preemption, and 46.116(j), Emergency Medical Care

- These sections were renumbered and clarified, but otherwise unchanged.

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## 46.117, Consent Forms, Signatures, and Waivers

### Important Changes Include:

Electronic Signatures	Now specifically allows electronic signatures and specifies that a written copy must be given to the person signing the consent form.
Short Form Requirements	Requires that, when using the short form, the consent form must begin with a concise and focused presentation of the key information to assist a prospective subject in making a decision. This subsection requires that this part of the consent form must be organized in a way that facilitates comprehension.
Additional Waiver of Documentation	Allows a waiver of requiring subject's signature on the consent form if the subjects are members of a cultural group or community in which signing forms is not the norm.

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## References

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- [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." Accessed September 30.
- [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.](#)

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