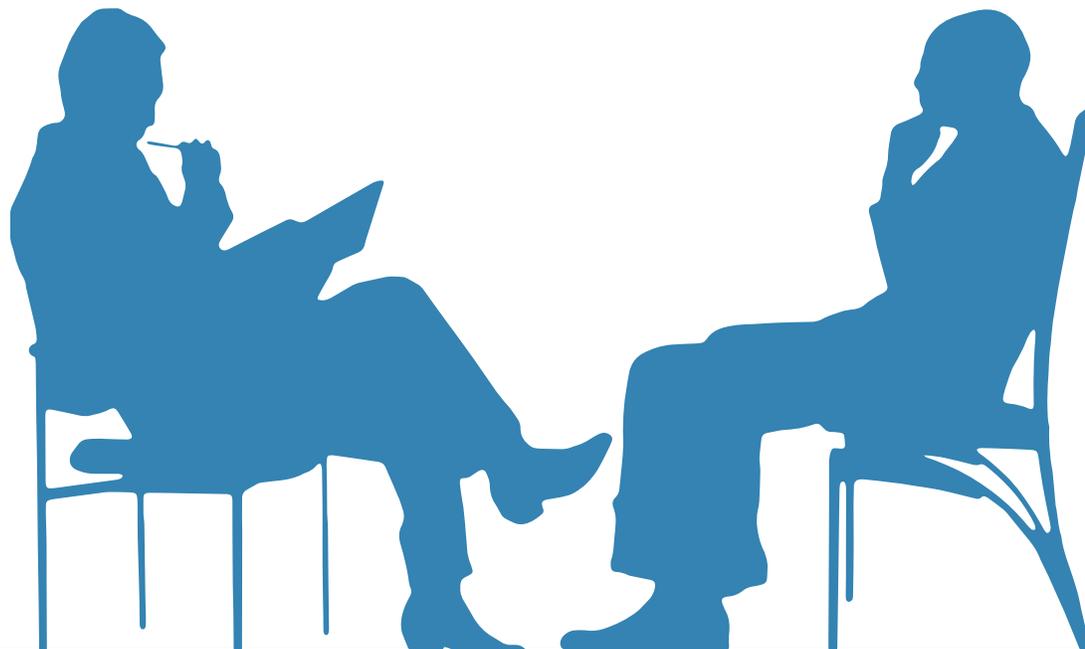




Final Rule Material: Comprehensive Guide to Informed Consent Changes



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The Final Rule changes to the informed consent process, documentation, and waiver regulations are covered in detail in the CITI Program's Final Rule materials. This resource contains the following sections:

- *Overview and Introduction*
- *Changes to the Consent Process*
- *Changes to the Consent Form*

Introduction

On 19 January 2017, the U.S. Department of Health and Human Services (HHS) issued a Final Rule to update the current regulations at 45 CFR 46, Subpart A - "Federal Policy for the Protection of Human Subjects" (the Common Rule) in the *Federal Register*. The Final Rule makes significant changes that affect research institutions, Institutional Review Boards (IRBs), and investigators. The substantive revisions are intended to "modernize, strengthen, and make more effective" the current system of oversight, that has been virtually unchanged since 1991. The revisions are intended to:

- *Better protect human subjects involved in research*
- *Facilitate research*
- *Remove ambiguity*
- *Reduce regulatory burden*

The informed consent section was extensively modified in the Final Rule, primarily due to added regulations for the use of biospecimens in research. New subsections were added and former subsections were modified. The Final Rule adopts, almost verbatim, all the proposals made in the preceding Notice of Proposed Rulemaking (NPRM) to improve and clarify the general requirements for informed consent.

Implementation Date

The changes, as applicable, to the informed consent regulations are effective for all research that is approved on and after 19 January 2018. Research organizations, institutions, IRBs, and investigators will have to revise forms, documents, and practices to comply with the revisions. Consent techniques (presentation) and forms will need to be changed and functional on the compliance date.

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.

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. Such research may continue to completion or closure under the old rules. Institutions and IRBs can voluntarily choose to apply the Final Rule on a study-by-study basis or by formally adding a requirement to its 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).

The intent of the transition phase is to minimize burdens for ongoing research that is conducted over a period of time that extends from before the Final Rule goes into effect until sometime afterwards and to avoid a requirement that such research be regulated by two sets of rules during the life of the research.

U.S. Food and Drug Administration (FDA) Harmonization

The FDA has stated over the past six-year Final Rule gestation (since the Advance Notice of Proposed Rulemaking [ANPRM] published in 2011) that it plans to update its regulatory language at 21 CFR 50 (Protection of Human Subjects) and 21 CFR 56 (Institutional Review Boards) in concert with the government-wide effort to modernize rules governing the use of human subjects in research.

The current expectation is that FDA will issue its own NPRM and eventually a Final Rule to update those regulations that can be harmonized. High on that list will be the changes to informed consent and waivers. Until that time, however, research organizations, institutions, IRBs, and investigators will have to comply with the current FDA regulations, as well as the Common Rule (pre-2018 or Final Rule version per effective dates) when both sets of regulations apply.

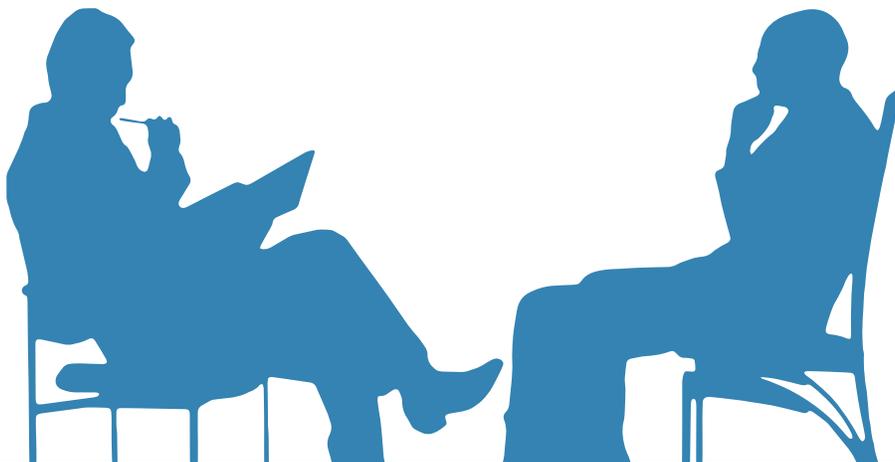


— Overview of the Final Rule’s Informed Consent Revisions —

The Common Rule numbering scheme and section titles remain largely intact, but there is 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 the HHS 45 CFR 46, Subpart A version of the rule. Changes in regulatory wording are shown in **bold**.

Key Revisions

- 1) **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.
- 2) **New requirements** for the basic and additional elements of consent.
- 3) **Electronic consent is allowed**, but must provide written copy.
- 4) **New broad consent** elements for the storage, maintenance, or secondary research use of identifiable private information and identifiable biospecimens.
- 5) **Changes in the waiver and alteration criteria** for consent.
- 6) **New consent provision** that allows IRBs to approve a research proposal for which investigators obtain information or biospecimens without individuals’ informed consent for the purpose of screening, recruiting, or determining the eligibility of prospective human subjects, provided certain conditions are met.
- 7) **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.



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. This new approach to consent requires 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.

In 46.116, the unnumbered list of conditions appearing in the old regulatory "introduction" before the numbered Basic Elements of Consent included multiple independent and important regulatory requirements. In the FDA regulations, these conditions have their own section at 21 CFR 50.25 (Protection of Human Subjects). 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.

Table 1. Updates to 46.116 Sections

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

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.

It is important to note that the 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).

46.116(a)(4)

The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.

This is a new subsection and requires that subjects be provided with the information that a “reasonable person” (undefined) would want to have. The responsibility remains for the investigator to provide more information when requested by subjects, allow sufficient time and opportunity to discuss the research, and 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.

46.116(a)(5)(i)

Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

When broad consent is obtained, the requirements imposed by 46.116(a)(5) for the presenting of information for informed consent and prescribing the order in which consent information is presented, do not apply.

Defining New Terms - “Key Information” and “Organized and Presented”

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.

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):



45 CFR 46.116(a)(5)(ii)

Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

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.”

46.116(a)(6)

The reference to “oral or written consent” was moved to the first sentence of 46.116(a). Otherwise the exculpatory considerations remain unchanged.

46.116(b), Basic Elements of Informed Consent

This subsection makes 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), and described in detail in the next section, 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.

46.116(b)(9)

One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

- A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or**
- A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.**

Preamble Comment on 46.116(b)(9)

"If a specific technology or technique determined to be capable of generating identifiable private information or identifiable biospecimens through [consultation with appropriate experts] described in section 46.102(e)(7)(ii) will be used, that information should be included in the description of the research as required by 46.116(b)(1)."

This is a new subsection that specifically applies to any research that involves the collection of identifiable biospecimens, rather than all biospecimens and collection of identifiable private information. It requires using a brief statement to inform potential subjects about the possible use of their identifiable private information or biospecimens.

46.116(c), Additional Elements of Informed Consent

This subsection makes no changes to the six previous additional informational elements of consent, but three new requirements were added.

46.116(c)(7)

1

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)

2

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)

3

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).

Are investigators required to use broad consent?

Investigators are never required to obtain informed consent through a broad consent process; it is an available optional procedure.

Instead of obtaining broad consent, an investigator may choose the following:

- 1) Conducting the research on non-identified information and non-identified biospecimens, and request that the IRB waive the requirement for informed consent
- 2) Obtaining consent for a specific study

The following are entirely new subsections (46.116 [d] – [h]).

46.116(d), Elements of Broad Consent for the Storage, Maintenance, and Secondary Research Use of Identifiable Private Information or Identifiable Biospecimens

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or non-research purposes) is permitted as an alternative to the informed consent requirements in paragraphs (b) and (c) of this paragraph. If the subject or the legally authorized representative is asked to provide broad consent, the following shall be provided to each subject or the subject’s legally authorized representative:

Preamble Comment on 46.116(d)(1) and (b)(8)

“When appropriate, this element of broad consent will inform subjects that information that has been stripped of identifiers might not be traceable, and thus it might not be feasible to withdraw consent for future use or distribution in this case.

However, if an investigator commits to permitting a subject to discontinue use of the subject’s identifiable private information or identifiable biospecimens, it is expected that the investigator will honor this commitment by not removing identifiers.”

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.

An investigator conducting secondary research with biospecimens will continue to have the options of:

- **Conducting secondary research with non-identifiable biospecimens**
- or**
- **Conducting secondary research with biospecimens that are coded; therefore, allowing the collection of additional information about the subjects over time**

In both of those instances, no additional consent would be required because the research would not involve human subjects as defined by the Final Rule. Even if the investigator wanted to use the biospecimens with identifiers attached, the option still exists of asking an IRB to waive the requirement to obtain additional prospective informed consent.

Highlights of 46.116(d), Broad Consent

46.116(d)(1)	Requires some basic elements, namely: <ul style="list-style-type: none">• <i>Risks</i>• <i>Benefits</i>• <i>Confidentiality</i>• <i>Voluntary statement</i>• <i>Commercial profit (when appropriate)</i>• <i>Whole genome sequencing (when appropriate)</i>
46.116(d)(2)	Requires a general description of the types of research that may be conducted. The IRB must assess whether the description of the research included in the broad consent form is adequate to permit a reasonable person to provide consent for the currently proposed secondary research study.
46.116(d)(3)	Requires a description of the information or biospecimens that might be used in future research; whether sharing might occur; and the types of institutions or researchers that might conduct research.
46.116(d)(4)	Requires a description of the length of time that the information or biospecimens may be stored, maintained, and used.
46.116(d)(5)	Requires a statement whether subjects will or will not be informed of the details of any subsequent research.
46.116(d)(6)	Requires a statement that research results either will or will not be disclosed to subjects.
46.116(d)(7)	Requires contact information to be provided in the broad consent.

46.116(d)(1)

The information required in paragraphs (b)(2), (b)(3), (b)(5), and (b)(8) and, when appropriate, (c)(7) and (c)(9) of this section.

46.116(d)(2)

A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted.

46.116(d)(3)

A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens.

46.116(d)(4)

A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite).

46.116(d)(5)

Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies.

46.116(d)(6)

Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject.

46.116(d)(7)

An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

Broad Consent and Health Insurance Portability and Accountability Act (HIPAA)

In January 2013, the Office for Civil Rights modified its prior interpretation that HIPAA authorizations for research needed to be study-specific, and therefore, that such authorizations could not permit certain future unspecified research.

Under the new interpretation, an authorization now may be obtained from an individual for uses and disclosures of protected health information for future research purposes, so long as the HIPAA authorization adequately describes the future research such that it would be reasonable for the individual to expect that his or her protected health information could be used or disclosed for the future research purposes.

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

Section 46.116(e) is a new and complicated section addressing waiver and alteration of consent in research involving public benefit and service programs that are supported by a state or local government. Research and demonstration projects that are conducted or supported by a federal department or agency are exempt under 46.104(d)(5). The waiver applies to subsections (a), (b), and (c) of 46.116, that is, general requirements, basic elements, and additional elements of consent. Separate paragraphs describe the applicable criteria for waiver of informed consent and the alteration criteria for informed consent (“partial waiver”).

Restrictions

Further complicating matters is the restriction that an IRB may not “omit or alter” any of the general requirements (conditions) in 46.116(a). This implies that unless a total waiver under 46.116(e)(1) is granted, single or multiple general conditions cannot be waived/alterd separately. Because each of the elements of broad consent are considered essential, there is also a restriction for research that uses broad consent, so that IRBs are not permitted to omit or alter any of the required broad consent elements.

Broad Consent Restriction

This new regulation also 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. This rule applies specifically to identifiable private information or biospecimens because the Final Rule does not apply to the research use of nonidentifiable private information or biospecimens. This change is intended to uphold the *Belmont Report* principle of respect for persons, in that, this regulation will prevent an individual’s refusal to consent to additional research use of private information or biospecimens from being overridden.

46.116(e)(1), Waiver

An IRB may waive the requirement to obtain informed consent for research under paragraphs (a), (b) and (c) of this section, provided the IRB satisfies the requirements of paragraph (e)(3) of this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (d) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

46.116(e)(2), Alteration

An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in paragraphs (b) and (c) of this section provided the IRB satisfies the requirements of paragraph (e)(3) of this section. An IRB may not omit or alter any of the requirements described in paragraph (a) of this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under paragraph (d) of this section.

46.116(e)(3), Requirements for Waiver and Alteration

In order for an IRB to waive or alter consent as described in this subsection, the IRB must find and document that:

- i. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
 - a. Public benefit or service programs;
 - b. Procedures for obtaining benefits or services under those programs;
 - c. Possible changes in or alternatives to those programs or procedures; or
 - d. Possible changes in methods or levels of payment for benefits or services under those programs; and
- ii. The research could not practicably be carried out without the waiver or alteration.

46.116(f), General Waiver or Alteration of Consent

This section reflects a major revision in content, format, and organization of the general waivers or alterations of informed consent that formerly appeared in 46.116(d). The format is similar to 46.116(e) above. The four existing waiver conditions are included unchanged in 46.116(f)(3), but an 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.

46.116(e)(1) and (f)(1) do not provide that an IRB may waive informed consent under 46.116(d) (broad consent) because the use of broad consent is not a requirement; it is an option that may be used (permissive not mandated) and a waiver is not necessary.

Like 46.116(e) above, the 46.116(f) general waiver procedure 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*

The waiver carries the same 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.

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/altered separately.

There is also a restriction for research that uses broad consent so that IRBs are not permitted to omit or alter any of the required broad consent elements. This change is intended to uphold the *Belmont Report* principle of respect for persons, by preventing an individual's refusal to consent to additional research use of information or biospecimens from being overridden at a later date by an IRB.

46.116(f)(1), Waiver

An IRB may waive the requirement to obtain informed consent for research under paragraphs (a), (b), and (c) of this section, provided the IRB satisfies the requirements of paragraph (f)(3) of this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (d) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

46.116(f)(2), Alteration

An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in paragraphs (b) and (c) of this section provided the IRB satisfies the requirements of paragraph (f)(3) of this section. An IRB may not omit or alter any of the requirements described in paragraph (a) of this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under paragraph (d) of this section.

46.116(f)(3)

In order for an IRB to waive or alter consent as described in this subsection, the IRB must find and document that:

- i. The research involves no more than minimal risk to the subjects;
- ii. The research could not practicably be carried out without the **requested** waiver or alteration;
- iii. **If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;**
- iv. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
and
- v. Whenever appropriate, the subjects **or legally authorized representatives** will be provided with additional pertinent information after participation.

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

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

- 1) The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
- 2) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

The regulation at 46.116(g) is a 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.

The Final Rule refers to the subject's legally authorized representative to clarify that this exception to informed consent also applies in circumstances in which the prospective subject has a legally authorized representative who will provide information about the prospective subject through oral or written communication with the investigator.

46.116(h), Posting of Clinical Trial Consent Form

46.116(h)(1-3) add 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."

Preamble Comment on 46.116(g) and 46.111

"In approving this exception to informed consent for the purpose of screening, recruiting, or determining the eligibility of prospective subjects, the IRB will be reviewing and approving the entire research proposal. Therefore, all of the IRB approval criteria at [46.111] will need to be satisfied, including that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data [46.111(a)(7)]. Thus, as part of its review and approval of the research, the IRB must determine that there are adequate privacy and confidentiality safeguards for information obtained by investigators for these preparatory-to-research activities."

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)	<p>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.</p> <p>In accord with the new “single IRB review” requirement, only one posting is required for each multi-institution study.</p> <p>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).</p>

NPRM Commenters’ Concern Over Posting of Clinical Trial Consent

The Final Rule’s preamble states that, most of the comments received on posting consent forms on the web “opposed the proposal in whole or in part. Many commenters expressed concern that the proposal represented administrative burden without a corresponding increase in protections to human subjects or benefit to the research community.”

Regardless, HHS stated that “we are not persuaded by the arguments of those commenters who suggest that potential negative consequences of this proposal outweigh its benefits.”

The Final Rule’s preamble states, “The consent form plays a key role in making sure that someone asked to enter a clinical trial receives the information they need to be making an informed decision about whether to enroll in that trial. Accordingly, it also plays a key role in supporting and justifying the public’s trust in the integrity of our clinical trial enterprise. In order to significantly increase the transparency of this portion of our system for protecting subjects, we are finalizing this proposal.”

As required by 46.117(b)(1), consent forms must meet the requirements of 46.116. The Final Rule’s preamble specifically states that posted consent forms must comply with the requirement in 46.116(a)(5), such that a concise presentation of key information is at the beginning of consent forms.

46.116(h)(1)

For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal website that will be established as a repository for such informed consent forms.

This is a new subsection

46.116(h)(2)

If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal website (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

This is a new subsection

46.116(h)(3)

The informed consent form must be posted on the 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.

This is a new subsection

46.116(i), Preemption

The informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws (**including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe**) that require additional information to be disclosed in order for informed consent to be legally effective.

This section was renumbered and clarified, but otherwise unchanged.

46.116(j), Emergency Medical Care

Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law (**including tribal law passed by the official governing body of an American Indian or Alaska Native tribe**).

This section was renumbered and clarified, but otherwise unchanged.

Changes to the Consent Form

This part provides a review of 45 CFR 46.117, Consent Forms, Signatures, and Waivers. This section has a few important changes.

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.

46.117(a)

Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed **(including in an electronic format)** by the subject or the subject's legally authorized representative. A **written** copy shall be given to the person signing the informed consent form.

Specifically allows electronic signatures, but otherwise unchanged.

46.117(b)

Except as provided in paragraph (c) of this section, the **informed** consent form may be either of the following:

This section remains unchanged.

46.117(b)(1)

A written informed consent **form** that **meets the requirements** of section 46.116. The investigator shall give either the subject or the subject's legally authorized representative adequate opportunity to read the informed consent form before it is signed; **alternatively**, this form may be read to the subject or the subject's legally authorized representative.

Reordered and clarified, but otherwise unchanged.

46.117(b)(2)

A short form written informed consent form stating that the elements of informed consent required by section 46.116 have been presented orally to the subject or the subject's legally authorized representative, and that the key information required by section 46.116(a)(5)(i) was presented first to the subject, before other information, if any, was provided. The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the subject or the subject's legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the subject's legally authorized representative, in addition to a copy of the short form. The reference to 46.116(a)(5) was added, but otherwise this section is unchanged.

Re-Contacting Subjects

An additional element of consent that was proposed in the NPRM, but was not included in the Final Rule, would have required providing subjects or their legally authorized representatives with an option to consent, or refuse to consent, to investigators re-contacting the subject to seek additional information or biospecimens or to discuss participation in another research study.

The preamble to the Final Rule states that "for some research studies, it will be desirable to inform prospective subjects about investigators' plan to re-contact subjects for certain purposes, and give them the option to agree or disagree to such re-contact; this information can be included in the consent."

46.117(c)(1)

An IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds **any of the following**:

- i. That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;*
- ii. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context;*
or
- iii. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.* A new [iii] was added, but otherwise this section is unchanged.

46.117(c)(2)

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research. This section was renumbered, but otherwise unchanged.

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." 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.*