Final Rule Material:
Overview - 46.116-46.124

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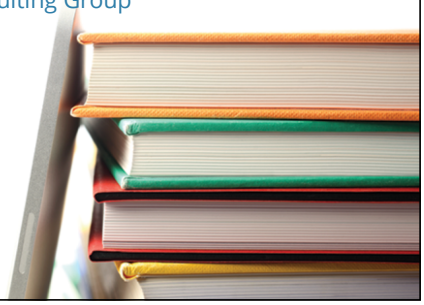

CITI Program Final Rule Materials

- We invite you to use this presentation to introduce those involved in the research enterprise to 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 - 46.116-46.124

This presentation reviews Final Rule regulatory sections 46.116-46.124 and covers changes to the following:

- *Informed Consent*

Other presentations available for the **Final Rule Materials: Overview** material are**:**

- **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.
- **Overview – Introduction** 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.

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.*

45 CFR 46.116, Informed Consent Process

- The informed consent section was extensively modified, primarily due to added regulations for the use of biospecimens in research.
- New subsections are added.

Goal of 45 CFR 46.116 and 45 CFR 46.117

- Facilitate subjects' understanding of the reasons to participate (or not) in the research.
- Requires that "key information" essential to decision-making receive priority by:
  - *Being presented first in the consent discussion.*
  - *Appearing at the beginning of the consent document.*

45 CFR 46.116, Informed Consent Changes

- The unnumbered list of conditions appearing in the pre-2018 rule "introduction" before basic elements of consent have been separated and the conditions renumbered as 46.116(a)(1-3) and (6).
- Subsections 46.116(a)(4) and (5) are new, and deal with the amount and presentation of information in the consent process.

45 CFR 46.116(a)(4), "Reasonable Person" Standard

- The prospective subject (or LAR) 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 be given an opportunity to discuss that information.
  - *Investigators remain responsible for providing more information when requested by subjects or to improve a particular subject's understanding.*
  - *Controversial research (if some subjects will find the research objectionable) need a substantial description of the future research in order to meet the "reasonable person" standard.*

45 CFR 46.116(a)(5)(i)

- Informed consent must begin with a "concise and focused" presentation of "key information."
  - *Information most likely to assist in understanding why to participate (or not) in the research.*
- Informed consent must be organized and presented in a way that facilitates comprehension.

"Key Information"

- The preamble lists five elements that cover "key information:"
  - *The fact that consent is being sought for research and that participation is voluntary.*
  - *The purposes, the expected duration of participation, and the procedures to be followed.*
  - *The reasonably foreseeable risks or discomforts to the prospective subject.*
  - *The benefits to subjects or others that may reasonably be expected.*
  - *Appropriate alternatives, if any, that might be advantageous.*
- Essentially, the first four basic elements of consent plus "#8."

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

- Investigators must present informed consent information in sufficient detail and organize and present the information in a way that does not "merely provide lists of isolated facts, but rather facilitates the prospective subject's ... understanding."

45 CFR 46.116(a), Caution

- "Broad consent" may be obtained in lieu of informed consent obtained in accordance with paragraphs (b) and (c) only for storage, maintenance, and secondary research uses of private information and identifiable biospecimens.
- This is an optional/alternative avenue for consent.

45 CFR 46.116, "Down-shift"

- Inserting a new 46.116(a) means that subsection 46.116(b) now contains the basic informational elements of consent.
  - *Added is a requirement to include one of two statements about the collection of private information or identifiable biospecimens for future research.*
- 46.116(c) now contains the **additional** applicable elements.
  - *Three new additions: biospecimen use, commercial profit, and return of results.*
- 46.116(d) adds broad consent for future research as an alternative.
  - *Replaces old 46.116-d waiver (moved to [f]).*
- Waiver for state/local public benefit/service programs is in 46.116(e).

45 CFR 46.116(f)

- General waiver or alteration of informed consent is now 46.116(f).
  - *Old 116 (d).*
  - *New criterion added to require that the research could not practicably be carried out without accessing or using the information or biospecimens in an identifiable format.*
- Caution: If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use and **refused** to consent, an IRB **cannot waive** consent for the use of identifiable private information or identifiable biospecimens, nor can they be de-identified and used.
  - *Is asking again permissible? This has not been addressed in guidance or regulation.*

45 CFR 46.116(g) and (h)

- 46.116(g) allows waivers of informed consent to obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects.
- 46.116(h) adds new requirements for posting "clinical trial" consent forms on a publicly available federal website.

45 CFR 46.117, Consent Forms, Signatures, and Waivers

- Electronic signatures are specifically allowed.
- Reading consent forms to subjects is allowed.
- A **written** copy must be given to the person signing the consent form.
- Short form consent forms must begin with a "concise and focused" presentation of "key information."
- Consent forms must be organized to facilitate comprehension.
- Added a third signature waiver category:
  - *Members of a distinct cultural group in which signing forms is not the norm and the research is minimal risk.*

"Documentation" in Section 46.117

- Means obtaining the **signature** of subjects (or LAR) on consent forms.
- It **does not** mean recording that the process has taken place.
  - *This term has caused confusion at research sites.*
- "Waivers of documentation" only mean that no signature is obtained.
  - *Still good practice to:*
    - *Document (record) occurrence of the consent process.*
    - *Document (record) the fact that the subject agreed to participate.*
- Waivers of documentation (signature) must be documented (recorded) in IRB records.

45 CFR 46.118 through 45 CFR 46.124

- These sections have remained essentially unchanged except for some minor clarifying wording.

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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