Final Rule Material:
New and Revised Definitions

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CITI Program Final Rule Materials

- We invite you to use this presentation as an introduction to the Final Rule's changes to the definitions 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.
- **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.

Overview

This presentation provides an overview of the Final Rule's revisions to the Definitions section (46.102).

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.

Introduction

- 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.*

Unchanged Definitions

- Minimal Risk
  - *Concept of minimal risk is key to numerous Common Rule provisions.*
  - *Affects the type of review required, the frequency of review, considerations for IRBs in the review process, and the permissibility of waiver of informed consent.*
- IRB
- IRB Approval

Revisions to Definitions

- Definitions have been reordered alphabetically in 46.102.
- Three new terms added to 46.102.
  - *Clinical Trial*
  - *Public Health Authority*
  - *Written* or *in Writing*
- Additionally, revisions were made to existing terms in 46.102.
- Outside of 46.102, definitions and new terms were provided throughout the revised regulation and in the Final Rule's preamble.

New Term Added, 46.102(b)

Clinical Trial

"Clinical trial" means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

- This definition should be used for determining which studies require posting of the IRB-approved consent form (Final Rule preamble).

New Term Added, 46.102(k)

Public Health Authority

"Public health authority" means an agency or authority that is responsible for public health matters as part of its official mandate.

- Certain public health surveillance activities are now **excluded** from the definition of research.
  - *Exclusions limited to activities necessary for a public health authority to "identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products)."*

New Term Added, 46.102(m)

Written or In Writing → Writing on a tangible medium (e.g., paper) or in an electronic format.

- New definition of "written or in writing" is included in the Final Rule to clarify that these terms include electronic formats.
  - *Aligns the Common Rule with U.S. Food and Drug Administration (FDA) and the International Council for Harmonization (ICH) initiatives to promote electronic consent.*

Importance of Definitions

- It is important to take note of terms used in the Final Rule that are not defined, as word selection and usage are extremely important in regulations.
- It can be challenging to determine how the federal regulation is using a term and what the significance or meaning is, and how it is applicable to research practice.
  - *Look for clues in the context of the regulation -- when the term is used, how it is used, and sometimes an explanation is provided.*
  - *Federal guidance can help provide direction on how to understand and comply with undefined terms in research practice.*

Terms Not Added to Definitions, 46.102

- **Vulnerable (to Coercion or Undue Influence)**
  - *Not added to 46.102, but updated in both 46.107 (IRB membership requirements) and 46.111 (criteria for approval of research).*
  - *"Vulnerability" of the subjects in research studies should be considered as a function of the possibility of coercion or undue influence.*
- **Deception**
  - *Not added to 46.102, but it is specified in 46.104(d)(3)(iii).*
  - *"Authorized deception would be prospective agreement by the subject to participate in research where the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research" (Final Rule preamble).*

Terms Not Added to Definitions, 46.102

- **Generalizable Knowledge**
  - *Remains undefined and unaddressed in the Final Rule.*
- **Single IRB (sIRB) Review and Cooperative Research**
  - *Not added to 46.102, but it is specified in 46.114.*
  - *Cooperative research is explained within the regulation as research "involving more than one institution" (in other words, essentially all federal multi-site research).*
  - *Federal agencies can determine that some multi-site research does not require sIRB review.*

Terms Not Added to Definitions, 46.102

- **Key Information**
  - *Undefined, but important, regulatory term added in 46.116.*
  - *"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."*
- **Practicably**
  - *Appears in the consent waiver and alteration sections; is intentionally left undefined.*

Terms Not Added to Definitions, 46.102

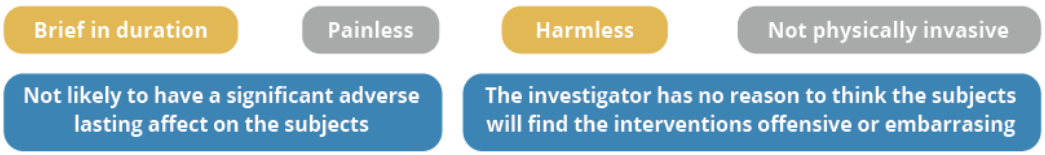
- **Broad Consent**
  - *New term in 46.116(a) and (d), which addresses elements of consent for the storage, maintenance, and secondary research use of private information or identifiable biospecimens.*
  - *"Seeking prospective consent to unspecified future research." (Final Rule preamble)*
- **Secondary Research Use**
  - *Not defined in regulations.*
  - *"Re-using identifiable and non-identifiable information and biospecimens that are collected for some other 'primary' or 'initial' activity" (Final Rule preamble).*

Terms Not Added to Definitions, 46.102

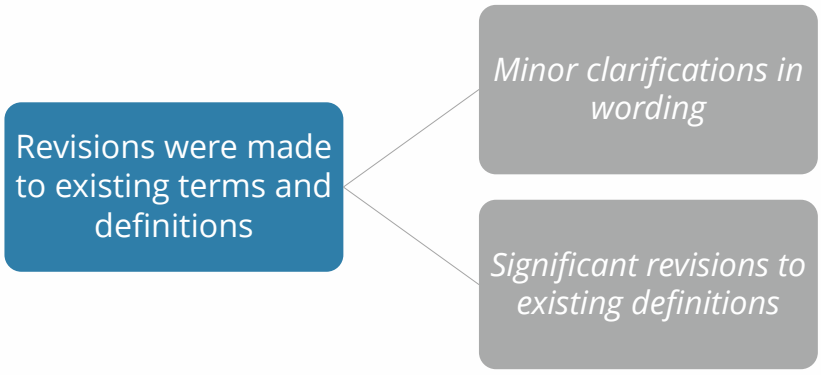
- **Limited IRB Review**
  - *Not added to 46.102.*
  - *"Limited IRB review is making and documenting the determination required by 46.111(a)(7), to ensure that there are adequate privacy safeguards for identifiable private information and identifiable biospecimens in the proposed research" (Final Rule preamble).*

Terms Not Added to Definitions, 46.102

- **Benign Behavioral Intervention**
  - *Not added to 46.102, but described in 46.104 (d)(3).*
  - *"Low risk behavioral [not biomedical] interventions in conjunction with collecting information from an adult subject through oral or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and certain conditions are met."*
  - *Regulations add that benign behavioral interventions are:*



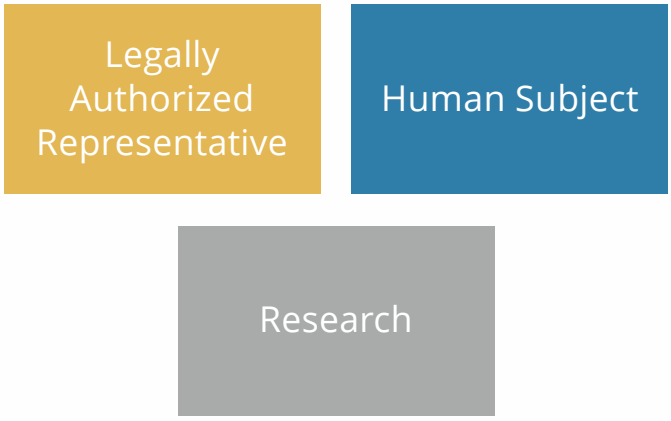
Revisions of Existing Terms and Definitions



Minor Clarifications to Wording

- "Intervention," "interaction," "private information," and "identifiable private information" were elevated to get their own subsection numbers and have been changed only to clarify wording.

Significant Revisions to Existing Definitions



Significant Revision - Legally Authorized Representative

- Definition of legally authorized representative now adds specific authorization to use institutional policy when there is no applicable law (state statute or regulation, case law, or an opinion of a state Attorney General) that addresses this issue.
- This change is intended to bring consistency to the consent process and it allows institutional policies in either the clinical context or other non-research contexts to authorize who may serve as a legally authorized representative in that institution.

Significant Revision – Human Subject

- The definition of "human subject" now references "information and biospecimens" (replacing "data") and adds obtaining, storing, using, studying, analyzing, or generating identifiable private information or identifiable biospecimens as trigger events.
- The human subject definition is triggered if the information and biospecimens are obtained through intervention or interaction with the living individual, regardless of whether the information or biospecimen has identifiers attached (for example, anonymous surveys or collections of samples using a swab).

Significant Revision - Research

- The definition of research has been expanded.
  - *Lists activities that are specifically deemed **not** to be research, including:*
    - *Scholarly and journalistic activities*
    - *Public health surveillance activities*
    - *Collection and analysis for criminal justice purposes*
    - *Authorized activities in support of intelligence, homeland security, defense*
- The Final Rule specifies that the collection of information is permitted under public health surveillance, but subsequent research using information collected from public health surveillance activities would fall under the definition of research as secondary use.

Definition of "Research" During Delay

- Institutions are allowed (but not required) to employ three specific burden-reducing provisions from the revised Common Rule during the six month delay period of 19 July 2018 – 20 January 2019.
  - *One of the burden-reducing provisions is the definition of "research"*

References

References

- 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). 2018a. "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). 2018b. "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.