Key Changes to the Common Rule Regulations for the Protection of Human Subjects 45 CFR 46

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Final Revisions to the Common Rule

The U.S. Department of Health and Human Services and fifteen other Federal Departments and Agencies have issued final revisions to the Federal Policy for the Protections of Human Subjects (the Common Rule). The Final Rule was published in the Federal Register on January 19. 2017. It implements new steps to better protect human subjects involved in research, while facilitating valuable research and reducing burden, delay, and ambiguity for investigators.

Official version of the 2018 Requirements:

45 CFR 46 of the July 19, 2018 edition of the e-Code of Federal Regulations


Change
Just Ahead

Summary of Transition Dates

- **July 19, 2018:** Effective Date for the 2018 Requirements (i.e. The New Rule)
- **July 19, 2018 – January 20, 2019:** Time period when Institutions may take Advantage of the three-burden reducing Provisions of the 2018 Requirements (optional not required)
- **January 21, 2019:** General Compliance date for the 2018 Requirements (i.e. Revised Common Rule)
- **January 20, 2020:** Compliance Date for the Cooperative Research Provision

What's the Difference?

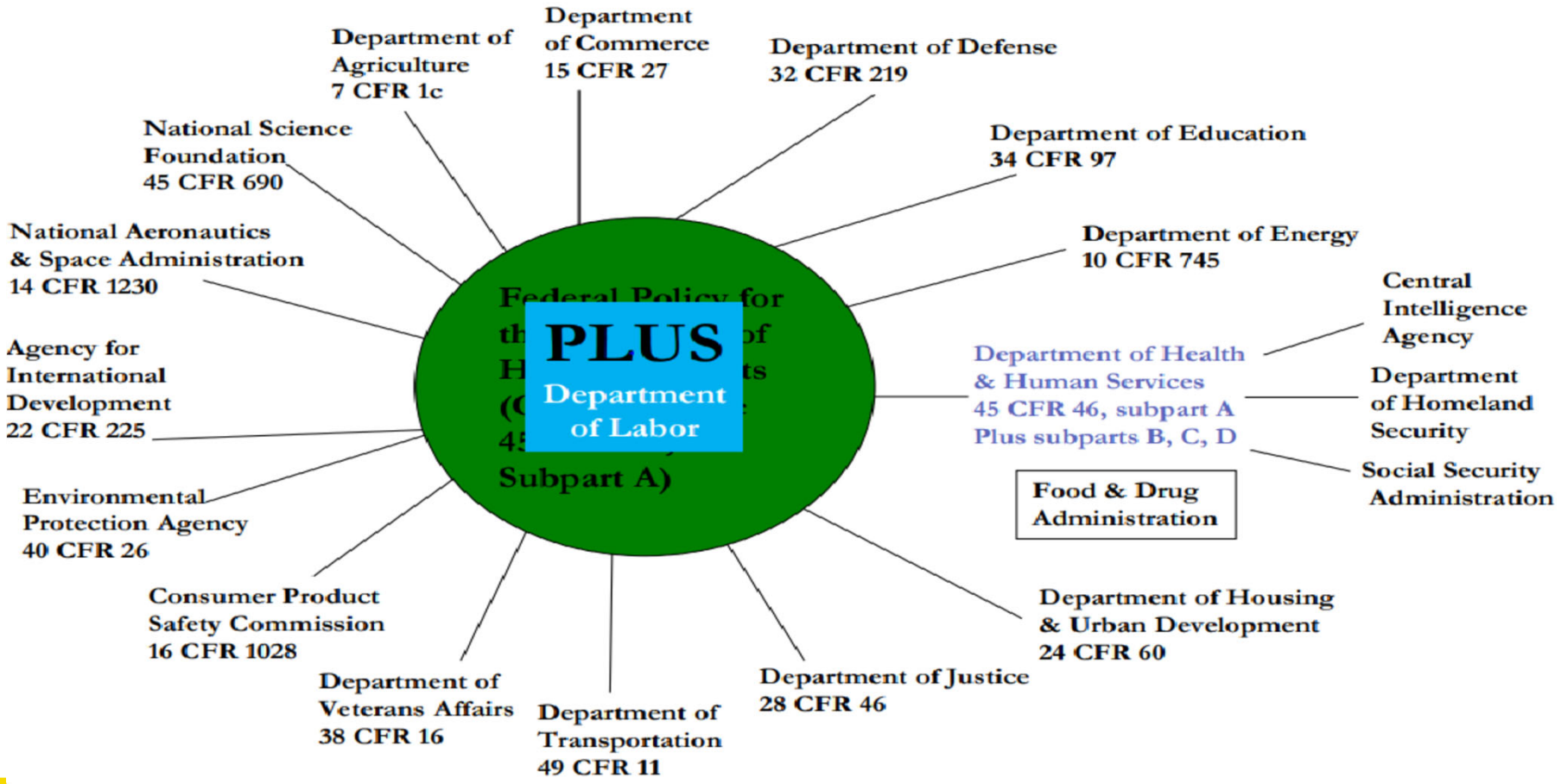
- Verrill Dana Redline of Unofficial Revised Common Rule (January 18, 2017) Against Health and Human Services (HHS) Common Rule at 45 CFR Part 46, Subpart A (2005)

http://www.verrilldana.com/files/uploads/Images/Redline-of-Final-Revised-Common-Rule-FINAL-DRAFT_1-19-2017.pdf

U.S Department of Health and Human Services

OHRP
Office for Human Research Protections

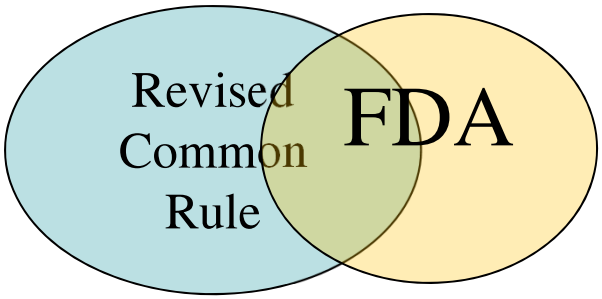
Common Rule Agencies



Common Rule Agencies That Have not Adopted the Common Rule

- Food and Drug Administration (FDA)
- Department of Justice (DOJ)

FDA Guidance on Common Rule



- October 12, 2018: FDA indicated the Revised Common Rule regulations that are not “inconsistent” with FDA’s current policies and guidance can be applied.

Transition Plans at Iowa

- **All existing, IRB approved**, applications will remain under current OHRP Pre-2018 Common Rule regulations – **No Changes required**
- **All Pending IRB application** not approved prior to January 21, 2019 – **Required to transition to Revised Common Rule**
- **All New IRB applications** submitted on or after January 21, 2019 – **Required to comply with Revised Common Rule regulations**

Key Changes

- New & Revised Definitions of Key Terms
- New and Revised Exemption Categories
- Informed Consent Changes
- Use of a Single IRB
- Eliminate Continuing Review for Most Minimal Risk
- Required Posting of the Informed Consent Document for Clinical trials
- Minor changes in IRB Operations
- Limited Scope of the Federal Wide Assurance

What isn't Changing?

- More than minimal risk criteria
- FDA regulated
- Children in research
- Prisoners in research

Key Definitions under 45 CFR46.102

New Terms	Revised Terms
(b) Clinical Trial	(e)(1) Human Subject
(e)(6) Identifiable Specimen	(e)(2) Intervention
(k) Public Health Authority	(e)(3) Interaction
(m) Written or In Writing	(e)(4) Private Information
	(e)(5) Identifiable Private Information
	(i) Legally Authorized Representative
	(l) Research

Human Subject Definition

(e)(1) *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research:

i. **Obtains information or biospecimens** through intervention or interaction with the individual, **and uses, studies, or analyzes the information or biospecimens;** or

ii. **Obtains, uses, studies, analyzes, or generates** identifiable private information or **identifiable biospecimens**.

Terms Defined within “Human Subject” Definition

(e)(2) *Intervention* includes both physical procedures by which information **or biospecimens** are gathered (*e.g.*,venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

(e)(3) *Interaction* includes communication or interpersonal contact between investigator and subject.

Definition of Terms (cont.)

(e)(4) ***Private information*** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (*e.g.* medical record).

(e)(5) ***Identifiable private information*** is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

(e)(6) ***An identifiable biospecimen*** **is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.**

Research Definition

(l) Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. **For purposes of this part, the following activities are deemed not to be research:**

Research Definition (cont)

1. **Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.**

Research Definition (cont.)

2. **Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow 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). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).**

Research Definition (cont.)

3. **Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.**

4. **Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.**

Other Key Definitions

(b) *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.

(i) *Legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. **If there is no applicable law addressing this issue, *legally authorized representative* means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.**

Other Key Definitions (cont.)

(k) *Public health authority* means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate.

(m) *Written,* or *in writing*, for purposes of this part, refers to writing on a tangible medium (*e.g.,* paper) or in an electronic format.

New Categories = Not Human Subjects Research

Scholarly & Journalistic Activities

- e.g. oral history, journalism, biography, literary criticism, legal research, historical scholarship
- Excludes certain activities
  - **Not** entire academic fields
- Focus on specific individuals about whom information is collected
  - Specific Individuals = Not Generalizable

New Categories = Not Human Subjects Research

- Public Surveillance Activities
  - Conducted by **Public Health Authorities**
  - Does not apply to all Public Surveillance Research
- Collection of Information, Biospecimens, or Records for Criminal Justice Investigation or Purpose
- Authorized Operational Activities for National Security Purposes (e.g. Homeland Security, National Defense)

Exemption Categories

- Social\Behavioral Research will significantly benefit from new and revised Exemption categories
- New Exemption categories are much more detailed, and all conditions must apply to be eligible for the exemption
- “New” type of IRB Review (i.e. Limited IRB Review)
- Introduces Broad Consent

Limited IRB Review

- Only Applies to select Exempt Categories
- **Review Must be Conducted by an IRB Member**
- Review does Not Apply All of the Criteria for Approval Outlined in 45CFR46.111
- Continuing Review is Not Required

Limited IRB Review

Can only be applied to the following Exemptions:

- (d)(2)(iii), Educational Tests
- (d)(3)(c), Benign Behavioral Interventions
- (d)(8)(iii), Use of stored identifiable private information and identifiable biospecimens*

*University of Iowa is not adopting Exemption Category 8

Limited IRB Review

Limited IRB Review is:

- .111(a)(7): “When appropriate, the research plan makes adequate provision to protect privacy of subjects and maintain confidentiality of data.”

- Guidance expected from OHRP regarding Limited IRB Review but not likely before the launch of the Revised Common Rule

Exemption Categories

1. Normal Education Setting

2. Educational Tests, Surveys, Interviews, Public Observation

3. Benign Behavioral Intervention

4. Secondary Research of Identifiable Information or Specimens Collected for Other Purpose for which Consent Not Required

Exemption Categories (cont)

5. Public Benefit or Service Program Research conducted or supported by Federal Agency

6. Taste & Food Quality

7. Storage or Maintenance for Which Broad Consent Is Required

8. Secondary research for which Broad Consent Required

Informed Consent – Key Information

- Information provided from a “reasonable person” perspective 45CFR46.116(a)(4)
- Information summarized in a concise and focused presentation 45CFR46.116(a)(5)(i)
- Information presented in sufficient detail 45CFR46.116(a)(5)(ii)
- UI is already doing this now with the **Consent Summary! Will only have minor changes to existing summary.**

Key Information (cont)

- UI is already requiring this now for Clinical Trials and the requirement to use a **Consent Summary!**
  - Minor changes to existing consent summary template.
    - Limited to one page (or less) in length
    - Additional condition added to inform subjects **why they may\may not want to participate** in the research.
- Required for Informed Consent documents 3+ pages in length

New Required Element of Consent 45CFR46.116(b)(9)

Collection of Identifiable Private Information or Biospecimens 45 CFR46.116(b)(9): One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

i. 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

ii. 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.

New Additional Elements of Informed Consent

- **Commercialization 45CFR46.116(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;

- **Clinically Relevant Research Results 45CFR46.116(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; and

- **Whole Genome Sequencing 45CFR46.116(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).

Waiver and Alteration of Informed Consent

New requirement added for waiver and alteration of informed consent. 45CFR46.116(f)(3)(iii)

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

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;

Waiver of Consent (cont.)

Screening, recruiting, or determining eligibility. 45 CFR 46.116(g)
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

Waiver of Documentation of Consent 45 CFR 46.117(c)(1)(iii)

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.

Posting Informed Consent

This requirement (45 CFR 46.116(h)) only applies to research with federal funding.

- 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 Web site that will be established as a repository for such informed consent forms.
- 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 Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.
- The **informed consent form must be posted** on the Federal Web site **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.

Posting Consent (cont.)

- Only applies to Federally funded “clinical trials”
- Sponsor\Coordinating Center responsible
- Post any version of the document
- Two options for posting:
  - ClinicalTrials.gov or Regulations.gov
- New HawkIRB Question - Date (estimate) of last subject visit (VII.B.1.c)
- Redaction
  - Contact information
  - HIPAA section
  - Other redaction discussed on case by case basis

Elimination of Continuing Review for Most Minimal Risk Research

- **Already in place at the University of Iowa for non-federally funded research (Biennial Review)**
  - Will expand to federally funded research on 1/21/19
- Research subject to the FDA regulations are not eligible at this time
- Eliminated for full board once subject interaction is complete
- IRB reserves the right to require a continuing review if there is cause

Biennial Review – UI requirement

- Investigators will receive annual reminders to submit modifications, adverse event reporting, etc.
- Biennial Review required every two years as a “check in”
  - Very brief BR application
  - Does not undergo IRB review, only HRPP screening
- IRB reserves right, with cause, to revoke the biennial review requirement and require annual continuing review

Use of a Single IRB

- Effective January 2020 for all research subject to the Revised Common Rule regulations

Questions?

- Visit the HSO Website https://www.hso.research.uiowa.edu
- Call: (319)335-6564 or Email: irb@uiowa.edu
- Office Hours:
  - Monday 2-4 S108 Lindquist Center
  - Wednesday 2-4 101 HLHS
  - Thursday 10-12 in 101 HLHS