Important Changes to Informed Consent: The Regs, the Policies, the Procedures and Forms, Oh My!

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Learning Objectives: Informed Consent Topics

Describe	How the requirements for Informed Consent have changed under the 2018 Common Rule (45 CFR 46)
Describe	Use of the Informed Consent Template(s)
Describe	Changes to Informed Consent procedures for: witnesses, short form consent, documentation of consent, and multisite research

Consent requirements under the 2018 Common Rule (2018 CR)

- The Common Rule at § 45 CFR 46 (effective June 28, 1991) was revised.
- The revised Common Rule, also referred to as the 2018 Common Rule (CR), is applicable to research approved on or after January 21, 2019 (except the Cooperative Research provisions which go into effect January 20, 2020)
- Consent requirements are located at §45 CFR 46.116 and 46.117
- There are new requirements for Broad consent that are not discussed in this presentation

Learning Objectives: Consent requirements under the 2018 Common Rule

Describe	What the Reasonable Person Standard is and what it accomplishes
Describe	What the Key Information section is and why it is required
Describe	The new required elements related to identifiable biospecimens, identifiable data, and genetic research with biospecimens
Describe	The new requirements for posting of consents

2018 CR Consent Requirements: The Problem

Back to basics: Informed consent is one way we operationalize the “Respects for Persons” requirement in the Belmont Report

The Problem: Consents can be complicated…and long… important information can be lost in the detail, and…

Consents are not written from the perspective of the participants. How do we fix the problem?

2018 CR Consent Requirements: Reasonable Person Standard

§46.116(a)(4) states:

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.

2018 CR Consent Requirements: Reasonable Person Standard

- The regulation does not define the Reasonable Person Standard
- Has been interpreted in the context of informed consent as, relevant information that an ordinary person, with average knowledge, skill and judgement would need to decide about whether to participate in the research
- The informed consent should focus on what information the individual deciding to participate would find to be most important and relevant when making a decision to participate in the research

2018 CR Consent Requirements: Reasonable Person Standard

- Investigators should be knowledgeable about their subject population, and:
- Should include information that would be important to their subject population
- Should focus on why an individual might or might not want to participate in the research
- During the consent process, when knowledgeable about the individuals values and goals, should provide additional information tailored to that individual's decision-making process

2018 CR Consent Requirements: Key Information

§46.116(a)(5) states:

(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.

2018 CR Consent Requirements: Key Information

§46.116(a)(5) continued:

(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.

2018 CR Consent Requirements: Key Information

The Key information section:

- Is participant-focused: what is important to the participant or Legally Authorized Representative (LAR) when he/she is deciding whether to participate;
- Puts this information first, in the beginning of the consent;

And;

What information is important will:

1) vary by study, and
2) vary by subject cohort or population

2018 CR Consent Requirements: Key Information

- The preamble to the 2018 Common Rule suggests 5 topics that the Key information section could include:
  - Consent is being sought for research, and participation is voluntary
  - Purpose of the research, how long participation is expected, and what procedures will take place
  - Reasonably foreseeable risks/discomforts
  - Benefits reasonably expected to result from participation
  - Alternative procedures or courses of treatment, if any, that might be advantageous to the participant

2018 CR Consent Requirements: Key Information

- However… the regulation does not specify what Key Information must include, and…
- We know participants have a lot of other considerations that are important to them such as:
  - There is a placebo arm? But, I want the study drug…
  - How many visits do you want me to come to the NIH for?!
  - Will I be paid, how much will I be paid, when will I be paid?
  - What about caregiving for my other family members?
  - Can I still work?
  - Can I still have access to the study drug after participation?

2018 CR Consent New Requirements for Biospecimens and Data: Future Use

In addition to the 8 original required elements at §45 CFR 46.116(b) a new element is added at §46.116(b)(9) that includes:

One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens must be included in the informed consent document:

2018 CR Consent New Requirements for Biospecimens and Data: Future Use

§46.116(b)(9) either:

(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;

2018 CR Consent New Requirements for Biospecimens and Data: No Future Use

§46.116(b)(9) 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.

2018 CR Consent New Requirements for Biospecimens and Data

Three (3) new elements that must be added as appropriate to the research, were added at §45 CFR 46.116(c)(7), (8) and (9)

2018 CR Consent New Requirements for Biospecimens and Data: Commercial Profit

§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;

2018 CR Consent New Requirements for Biospecimens and Data: Commercial Profit

SACHRP* advises:

"The consent also should disclose sponsorship and address issues including (but not limited to) disposition of samples, who will have access, and how samples will be used. Subjects should be informed to what extent, if any, they can expect to control or receive compensation from future commercial uses..."

*SACHRP Updated FAQs on Informed Consent for Use of Biospecimens and Data (March 2018): https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-faqsrecommendations-and-glossary-informed-consent-and-research-use-of-biospecimens-andassociated-data/index.html

2018 CR Consent New Requirements for Biospecimens and Data: Return of Results

§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;

- Are they CLIA certified
- Do you have the right expertise to explain the results?

2018 CR Consent New Requirements for Biospecimens and Data: Genetic Research

§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).

- Be sure to include statements about current *and* future research, if applicable

2018 CR Consent Requirements: Posting Informed Consents

§46.116(h) states:

For each clinical trial conducted or supported by a Federal department or agency: 1) 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.

2018 CR Consent Requirements: Posting Informed Consents

§46.116(h) continued:

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 Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

2018 CR Consent Requirements: Posting Informed Consents

§46.116(h) continued:

3) 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.

2018 CR Consent Requirements: Posting Informed Consents

Definition of Clinical Trial:

"…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."

Implementation at the NIH

Required Elements of informed Consent:

- The NIH required consent template includes required sections or language needed to address: Key Information, and new biospecimen and data requirements, including the genetic testing requirements.
- The IRB can provide guidance about the reasonable person standard when assessing language in the consent

Posting Informed Consents:

- The NIH is a Federal agency, so all NIH clinical trials meeting the definition above, must post at least one (1) IRB-approved informed consent document used to recruit subjects to clinicaltrials.gov.
- At the NIH, the PI is responsible to ensure that the consent is posted within the required timeframes. The PI should work with the IC, if there are questions.

Learning Objectives: NIH Consent Templates

Describe	What consent templates are or will be available
Describe	The key features the templates
Describe	How to use the templates
Describe	When to use the templates

NIH Consent Templates: Availability

- In order to comply with the new consent requirements of the 2018 CR a template was developed and distributed for use in research approved on or after January 21, 2019
- This template is mandatory at the NIH Clinical Center
- Continue to use the existing CC/Site templates for research approved prior to January 21, 2019
- At other NIH sites the template should be fit into the site-specific document until updates to the boilerplate (required NIH language) are complete

NIH Consent Templates: Availability

- An updated legacy template with the new boilerplate is available in IRBO, and consents will be transitioned to this new template as protocols move under review by the NIH IRB
- A Master template for when NIH is the lead site on multisite research is in development
- A template for use when the NIH is relying on an external IRB is in development
- A template is in development for IND expanded access use at the CC
- Updated Short-form consent template is being cleared by OGC and translation will begin upon approval

NIH Consent Templates: Structure

- Pages 1-3 are instructional, remove before use
- Updated Header and Footer are simplified for ease of use, do not modify these section of the document
- Required NIH language (boilerplate) is in bright blue and *may not be edited* unless approved by the IRB, OHSRP and OGC
- *Instructional language is italicized* and should be removed before use
- Bracketed language should be replaced with protocol-specific details. [*PI name here]*
- Required and sample language is provided for use throughout

NIH Consent Templates: Structure

Required NIH language is integrated throughout the document, not just on the first page and next to last page

- Compensation is now in the body of the consent
- Confidentiality, research-related injury, and who to contact are on the next to last page

Expanded signature pages:

- Two parent signature lines
- New Legally Authorized Representative block
- New Assent block for older minors
- Revised witness block and administrative block to document the use of an interpreter

NIH Consent Templates: How to Use

- For new protocols, download the template from the IRBO website under *Forms and Tools*
- Read the instructions carefully and follow them when developing your consents
- Remove instructional pages and language; update bracketed language with protocol-specific language (in footer too)
- Use only applicable sample language

Learning Objectives: Changes to Informed Consent Procedures

Describe	The changes to Witness to Informed Consent requirements at the NIH
Describe	What will happen when I rely on an outside IRB?
Describe	What a Master consent is versus a site-specific consent

Changes to Informed Consent Procedures: Use of a Witness

- Effective January 21, 2019, the use of a witness for long-form consent is no longer required
- Investigators are encouraged to have a second person (who is not obtaining consent) present for the entire consent discussion; document the presence of this person in the medical record
- The witness to the short-form consent is required by regulation [45 CFR 46.117(b)(2)]
  - The same witness must sign both the short and long-form consents
  - Document whether the interpreter was also the witness on the consent and in the medical record

Informed Consent Procedures: Use of a Witness for Short Form Consent

- Where does the subject sign for short form consent?
  - A: The consent in the subject's language, i.e. the short-form
- Where does the investigator sign?
  - A: The long form since generally it is in the language of the investigator
- What if the investigator was the interpreter too?
  - A: A different person must witness the entire consent process and sign both the short and long forms

Informed Consent Procedures: Documentation of Consent in CRIS

- The Office of Research Support and Compliance, working with the IC QA QI staff have developed a new structured note in CRIS for documenting Informed Consent procedures
  - All consents and assents should be documented
  - Fast and easy to use: Who, What, When and Where
  - What type of consent: Short, long, telephone, LAR, etc.

Informed Consent Procedures: Multisite Research

- Are you establishing a new multi-site protocol?
- Who will be your reviewing IRB (NIH or another IRB)? A: Consult with OHSRP
- How you answer that question will help you figure out what type of consent you need:
  - Is the NIH the Reviewing IRB?
    - A: You need a Master Consent
  - Is an outside IRB the Reviewing IRB?
    - A: You need an Site-specific Consent

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Informed Consent Procedures: Master Consent

Master Consent:

- A master consent is developed by the Sponsor or the Lead Site
- Is approved by the Reviewing IRB for use
- Is distributed to each Site as the IRB approves the addition of that site
- When amended and approved by the IRB, must be distributed to all of the approved sites for use

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Informed Consent Procedures: Site-specific Consent

Site-specific Consent:

- A site-specific consent is an IRB-approved Master Consent that incorporates site-specific information, such as: Research-related injury; Conflict of Interest information; Who to contact; Confidentiality protections; and compensation/ remuneration information

- Site-specific amendments, may be permitted
  - Must be cleared by Lead PI/Sponsor
  - Must be approved by the IRB

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Resources

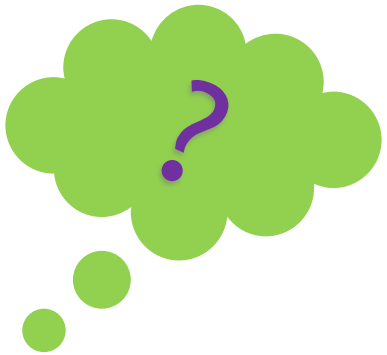
Links:

- The new Office of IRB Operations (IRBO website: https://irbo.nih.gov/confluence/display/IRBO/Home
- Information for PIs and Study Teams: https://irbo.nih.gov/confluence/display/IRBO/For+Study+Teams
- Common Rule Bulletins: https://irbo.nih.gov/confluence/display/IRBO/IRBO+News#IRBONews-CommonRuleBulletins

Email contacts:

- OHSRP: Ohsr_nih_ddir@od.nih.gov
- IRBO: IRB@od.nih.gov

Any Questions?



Thank you