National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Bethesda, MD 20892

MEMORANDUM

Date: June 18, 2019

From: Protection of Participants, Evaluation and Policy Branch, OPCRO, DAIDS, NIAID, NIH

To: CRS Leaders, CTU PIs

Subject: Revised Common Rule and Implementation

Background:

The revised Common Rule (45 CFR 46 Subpart A), which is a regulation, became effective on January 21, 2019. This regulation applies to all research conducted or supported by any Common Rule Agency, including HHS. The revised Common Rule has three major areas of changes in comparison to the prior Common Rule requirements [in effect from June 18, 1991 through January 20, 2019] – elements of Informed Consent Forms (ICFs) including use of identifiable biospecimens/private information, Institutional Review Boards (IRBs), and other changes [such as, updated and new definitions, requirement to post an IRB-approved ICF used to enroll participants in a clinical trial to a publicly-available federal website, and the upcoming (January 20, 2020) single IRB (sIRB) requirement for any portion of a multisite study that is conducted in the U.S.].

Application of the Revised Common Rule

The revised Common Rule requirements apply to any clinical research study that receives initial IRB approval on or after January 21, 2019. The trigger for when the revised Common Rule requirements are applied is the date of initial IRB approval at the site, and not sponsor approval, of a study. Therefore, it is possible that for a given study, sites that received initial IRB approval on or after January 21, 2019 fall under the revised Common Rule requirements, and sites that received initial IRB approval before January 21, 2019 will fall under the previous Common Rule requirements, unless the institution decides to transition the study to comply with the revised Common Rule.

Transition of studies that received IRB approval prior to January 21, 2019

The clinical research institution (not study sponsor) may determine that a clinical research study which received initial IRB approval prior to January 21, 2019 will transition to comply with the revised Common Rule requirements. For a clinical research institution that chooses to transition a study to the revised Common Rule, please note that the revised Common Rule applies in its entirety – this includes ICFs with content and format that meet the new Common Rule requirements, and the posting of an IRB-approved ICF used to enroll participants in a clinical trial to a publicly-available federal website. In addition, any portion of a multisite clinical research study that is conducted in the U.S. must comply with the sIRB requirement beginning on January 20, 2020.

Requirements for compliance with the revised Common Rule

Please note that for compliance with the revised Common Rule:

1. All HIV/AIDS networks must ensure that their ICF templates are compliant with the requirements of the revised Common Rule.
2. In addition, all networks and non-network multisite clinical trials with one or more clinical research sites that fall under the revised Common Rule, must have a plan in place to post one version of an IRB-approved ICF used to enroll participants to a public website (i.e., clinicaltrials.gov or regulations.gov). The posting of an IRB-approved ICF to a publicly-available federal website must occur after the clinical trial is closed to recruitment (i.e., enrollment is complete), and no later than 60 days after the last study visit by any participant. NOTE: www.clinicaltrials.gov only accepts English language consents, while www.regulations.gov accepts non-English consents as well. Additional information can be found at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-110.html.
3. Additionally, when any portion of a multisite clinical research study is conducted in the U.S. where one or more of the U.S. sites received initial IRB approval on or after January 21, 2019, the awardee must identify a sIRB to review the study on or after January 20, 2020, on behalf of the institutions that fall under the revised Common Rule. Please note that this sIRB requirement is a regulatory requirement and is different from the NIH policy for sIRB.

Status of DAIDS' Sample Informed Consent Forms

DAIDS' Sample Informed Consent forms (SICs) have been taken down from the DAIDS RSC website (https://rsc.niaid.nih.gov/networks-protocol-teams/protocol-templates), and are being updated to reflect the revised Common Rule updates. DAIDS will notify you when the updated SICs are available.

DAIDS plans to have 3 SICs (see list below):

a. General Use,
b. Broad Consent [Optional consent for future use of stored samples], and
c. Consent with Tiers.

In the interim, to assist you in complying with the new requirements, we provide the following:

1. Three (3) tables showing the required changes to ICs and the requirement of the revised Common Rule from which those changes derive. The tables below (See Tables 1-3) delineate the elements that should be included in these consent forms.
2. A short summary table showing only the newly added (Basic and Additional) elements to the existing General Use and Broad Consent (Table 4).

ACTION

Please share this memo with your staff/grantees/collaborators, as appropriate, for use as a guide to ensure compliance of IC templates with the revised Common Rule.

Table 1: General Use Template

This table lists the new Basic and Additional Elements that will be included in the DAIDS General Use template per the revised Common Rule[1].

Element	Requirement	ICF Question	Change Emphasis
Revised Common Rule 45 CFR 46.116(a)(5)(i) New Basic Element.	Informed consent must begin with a concise and focused presentation of the key information needed by a "reasonable person" (prospective participant or legally authorized representative) to decide on participation in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.	Question 2: What key information should you know about this study?	The prospective participant or the legally authorized representative (LAR) must be provided with the information that a reasonable person would want to have to make an informed decision about whether to participate in the study. The participant or their LAR must be given an opportunity to discuss that information.
Revised Common Rule 45 CFR 46.116(b)(9)(i) & (ii) New Basic Element.	For research involving collection of identifiable biospecimens or identifiable private information (IPI) for future use.	Question 15: What will happen to your samples at end of this study?	One of the following statements (as appropriate): Identifiers may be removed and identifiable biospecimens or IPI and used for future research without additional consent. OR IPI or biospecimens will not be used for future research, even if identifiers are removed.

Element	Requirement	ICF Question	Change Emphasis
Revised Common Rule 45 CFR 46.116(c)(7) New Additional Element	For research involving collection of identifiable biospecimens or identifiable private information (IPI) for future use.	Question 15: What will happen to your samples at the end of the study?	A statement that the participant's biospecimens (even if identifiers are removed) will or will not be used for commercial profit and whether the participant will or will not share in this commercial profit. For a study where there is no intent to use the samples for commercial profit, a statement such as, "The NIH has no plans to use participant's samples for commercial gain."
Revised Common Rule 45 CFR 46.116(c)(8) New Additional Element	A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to participants, and if so, under what conditions.	Question 14: What will happen at the end of the study?	Add language to notify participants whether or not this type of information will be shared with them, and if information will be shared, how the study will share this information.
Revised Common Rule 45 CFR 46.116(c)(9) New Additional Element	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).	Question 15: What will happen to your samples at end of this study?	Explain what will happen to samples at study completion – for example, samples will be stored for future use, or discarded. Explain whether limited genetic testing or more complete whole genome sequencing (WGS) will be conducted on participant samples.

Table 2: Broad Consent (Optional)

A template is in development for the new option of "Broad Consent" now available under the revised Common Rule[1](see definition in Table 4 below). This Broad Consent may be used in concert with the general use consent for a study where samples will be stored for future use. There is a restriction with Broad Consent, where if an individual was asked to provide Broad Consent and refused to consent, an IRB cannot at a later time waive consent for the use of identifiable private information or identifiable biospecimens. This rule applies specifically to identifiable private information or identifiable biospecimens because the revised Common 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. Investigators, ICF developers and CRSs should be made aware of this change to ensure the appropriate informed consent template is used.

The following table lists the various sections of the Broad Consent and the requirements addressed under the specific informed consent form questions.

Element	Broad Consent Requirement	ICF Question	Change Emphasis
45 CRF 46.116(d)(1) Element of Broad Consent	The information required per 46.116(b)(2), (b)(3), (b)(5), and (b)(8) and, when appropriate, (c)(7) and (c)(9)		Consent should cover the following: 1. Description of any reasonably foreseeable risks or discomforts to the participant; 2. Foreseeable benefits to the participant or to others; 3. Description of the extent, if any, to which confidentiality of records identifying the participant will be maintained; 4. Statement that participation is voluntary, no penalty or loss of benefits for refusal to participate and no penalty or loss of benefits for withdrawal; 5. What will happen to the data and samples if consent is withdrawn (e.g. destroyed or de-identified). However, if research is already underway, researchers will not be able to destroy samples or information; 6. If the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit; and 7. Whether the research will (if known) or might include whole genome sequencing (WGS).

Element	Broad Consent Requirement	ICF Question	Change Emphasis
45 CFR 46.116(d)(2) Element of Broad Consent	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.	Question 3: What are researchers asking you to do?	Requires a general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens.

Element	Broad Consent Requirement	ICF Question	Change Emphasis
45 CFR 46.116(d)(3) Element of Broad Consent	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.	Question 4: What identifiable samples and identifiable information will researchers collect and store? Question 5: Where will researchers store your identifiable information and identifiable samples? Question 7: How will researchers use your identifiable information and identifiable samples? Question 19: Will researchers be able to use your stored samples and information for other types of future research?	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.

Element	Broad Consent Requirement	ICF Question	Change Emphasis
45CFR 46.116(d)(4) Element of Broad Consent	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).	Question 6: How long will researchers store and use your identifiable information and identifiable samples for future research?	Requires a description of the length of time that the information or biospecimens may be stored, maintained, and used.
45 CFR 116 (c)(9) Element of Broad Consent	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).	Question 8: What genetic testing will researchers do with your identifiable samples?	Notify participants as to whether the research will (if known) or might include whole genome sequencing (WGS).

Element	Broad Consent Requirement	ICF Question	Change Emphasis
45 CFR 46.116(d)(5) & 45 CFR 46.116(d)(6) Elements of Broad Consent	Unless the participant 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 participant'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. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the participant in all circumstances, a statement that such results may not be disclosed to the participant.	Question 9: What other research could researchers do with your identifiable information? Question 20: Will researchers contact you if they find something important about your health?	Requires a statement whether participants will not be informed of the details of any specific research studies that might be conducted using their identifiable private information or identifiable biospecimens. Requires a statement that clinically relevant research results either will or will not be disclosed to participants.

Element	Broad Consent Requirement	ICF Question	Change Emphasis
Basic Element	Risks	Question 10: What are the risks of storing your identifiable samples and identifiable information for future research?	NO CHANGE
Basic Element	Benefits	Question 11: What are the benefits of storing your identifiable samples and identifiable information for future research?	NO CHANGE
Basic Element	Confidentiality	Question 12: How will researchers keep your information confidential?	NO CHANGE
Basic Elements	Voluntariness and Choices	Question 13: What other choices do you have? Question 14: Can you change your mind about the storage and use of your identifiable samples and identifiable information?	NO CHANGE

Element	Broad Consent Requirement	ICF Question	Change Emphasis
Additional Element	Costs	Question 15: What are the costs to you?	NO CHANGE
45 CFR 46.116(c)(7) New Additional Element	A statement that the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit.	Question 16: Will you receive any payment, or share in any potential commercial profit?	If the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit. For a study where there is no intent to use the samples for commercial profit, a statement such as, "The NIH has no plans to use participant's samples for commercial gain."
Basic Element	Contact Information	Question 17: Who should you contact if you think you are injured during the collection of extra samples?	NO CHANGE
45 CFR 46.116(d)(7) Element of Broad Consent	An explanation of whom to contact for answers to questions about the participant's rights and about storage and use of the participant's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.	Question 18: What are your rights and who should you contact if you have questions about storage or future research using my identifiable samples and identifiable information?	Requires contact information to be provided in the Broad Consent. In case participants want to change their permissions to testing with identifiable samples. As well as other contact for any reason related to Broad Consent.

Element	Broad Consent Requirement	ICF Question	Change Emphasis
Requirement	Signatures	Question 21: How do you confirm my permission to collect, store and use my identifiable samples and identifiable information in future research?	NO CHANGE

Table 3: Consent with Tiers

The intended use of this template will be as a standalone consent for specimen-only studies. This template has various levels (tiers) of consent to allow participants to choose the specific areas of research where he/she will allow investigators to use their identifiable private information and/or identifiable samples. The concept of "tiers" will be described at the beginning of the template.

Element	Requirement	ICF Question	Change Emphasis
45 CFR 46.116 General requirements for informed consent. New Basic Required Element	Informed consent must begin with a concise and focused presentation of the key information needed by a "reasonable person" (prospective participant or legally authorized representative) to decide on participation in the research.	Question 1: Key information Question 2: What is "consent with tiers (choices)"?	The prospective participant or the legally authorized representative (LAR) must be provided with the information that a reasonable person would want to have to make an informed decision about whether to participate in the study. The participant or their LAR must be given an opportunity to discuss that information. This information must be organized and presented in a way that facilitates comprehension. Explains the concept of tiers or choices up front.

Element	Requirement	ICF Question	Change Emphasis
45 CRF 46.116(d)(1) (b)(2), (b)(3), (b)(5), and (b)(8) and, when appropriate, (c)(7) and (c)(9)	Basic Consent Elements	Question 3: What are researchers asking you to do?	Consent should cover the following: 1. Description of any reasonably foreseeable risks or discomforts to the participant; 2. Foreseeable benefits to the participant or to others; 3. Description of the extent, if any, to which confidentiality of records identifying the participant will be maintained; 4. Statement that participation is voluntary, no penalty or loss of benefits for refusal to participate and no penalty or loss of benefits for withdrawal; 5. What will happen to the data and samples if consent is withdrawn (e.g., destroyed or de-identified). However, if research is already underway, researchers will not be able to destroy samples or information; 6. If the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit. For a study where there is no intent to use the samples for commercial profit, a statement such as, "The NIH has no plans to use participant's samples for commercial gain"; and 7. Whether the research will (if known) or might include Whole Genome Sequencing (WGS).

Element	Requirement	ICF Question	Change Emphasis
45 CFR 46.116(d)(3) Element of Broad Consent	Sharing of Data or Biospecimens	Question 4: What samples will researchers collect and store? Question 5: Where will researchers store your information and samples? Question 6: How will researchers use your information and samples?	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.
45 CFR 116 (c)(9) New Additional Element	Genetic Testing	Question 7: What genetic testing will researchers do with your samples?	State whether the research will (if known) or might include Whole genome sequencing (when appropriate). Additionally, at the end of the IC where participant makes choices this element should be emphasized.
45 CFR 46.116(d)(5) Element of Broad Consent	Future Research Use	Question 8: What other research could researchers do with your information?	Requires a statement whether participants will or will not be informed of the details of any subsequent research studies that might be conducted using their identifiable private information or identifiable biospecimens.
45 CFR 46.116(d)(4) Element of Broad Consent	Duration and Storage	Question 9: How long will researchers store your samples for future research?	Requires a description of the length of time that the identifiable private information or identifiable biospecimens may be stored, maintained, and used for research.
Basic Element	Risks	Question 10: What are the risks of storing your samples and information for future research?	NO CHANGE

Element	Requirement	ICF Question	Change Emphasis
Basic Element	Benefits	Question 11: What are the benefits of storing your samples and information for future research?	NO CHANGE
Basic Element:	Confidentiality	Question 12: How will researchers keep your information confidential?	NO CHANGE
Basic Elements	Voluntariness and Choices	Question 13: What other choices do you have? Question 14: Can you change your mind about the storage and use of my samples and information?	NO CHANGE
Additional Element:	Costs	Question 15: What are the costs to you?	NO CHANGE
45 CFR 46.116(c)(7) New Additional Element	Commercial profit	Question 16: Will you receive any payment?	A statement that the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit.
Basic Element	Contact Information	Question 17: Who should you contact if you think you are injured during the collection of extra samples?	NO CHANGE

Element	Requirement	ICF Question	Change Emphasis
45 CFR 46.116(d)(7) Element of Broad Consent	Requires contact information to be provided.	Question 18: What are your rights and who should you contact if you have questions about future research using your samples and information?	NO CHANGE
Tiers	Choices regarding specific areas of research	Question 19: Can I choose the types of future research ("tiers")?	Restating participant's choices for the storage and testing of his/her samples for future research.
45 CFR 46.116(d)(5) Element of Broad Consent	Requires a statement whether participants will or will not be informed of the details of any subsequent research.	Question 20: Will researchers be able to use your stored samples and information for other types of future research?	NO CHANGE
45 CFR 46.116(d)(6) Element of Broad Consent	Requires a statement that research results either will or will not be disclosed to participants.	Question 21: Do you want researchers to contact you if they find something important about your health?	Include information to account for new requirements of informing participants when results of any type from future research are to be shared.
Tiers	Specific Choices	Question 22: How do you confirm your permission to collect, store and use your samples and information in future research?	NO CHANGE

[1]See Revised Common Rule and Revised Common Rule Q&As
[1]See Revised Common Rule Educational Materials
[1]See Electronic Code of Federal Regulations

Table 4: Tools highlighting key changes to ICs per the revised Common Rule

A: General Consent

General IC Requirements [46.116(a)(5)]
The IC must begin with a concise and focused presentation of the key information including: • The project is research • Participation is voluntary • Summary of research, including the purpose, duration, and procedures • Summary of common risks as well as rare and significant risks that may affect willingness to participate • Direct benefit of intervention including possibility of no direct benefit (e.g., Phase 1 studies) • Any alternative procedures or course of treatment The key information section must also satisfy the elements of informed consent under 46.116(b) and (c), this information does not need to be repeated in the body of the consent. Short ICs must also begin with the "key information" and be organized in a way that facilitates comprehension. [46.117(b)(2)]
The information included in the consent must be: • Presented in enough detail to facilitate the decision-making process • Organized and presented in clear, simple, and concise language • Not merely provide lists of isolated facts
The IC should provide the participant with information that a reasonable person would want to know in order to make an informed decision

Basic Element 9 - Future Use of Information or Biospecimens [46.116(b)(9)]
The IC must address how biological specimens may be used in future study-related and/or unspecified future research including one of the following scenarios: 1. That identifiers might be removed from the identifiable private information or biospecimens and that, after such removal, the information or biospecimens could be used for future research studies without additional informed consent (if this might be a possibility) **-OR-** 2. That the participant's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research

Additional Element 7 - Commercial Profit of biospecimens [46.116(c)(7)]
The IC must clarify whether the participant's biospecimens (even if identifiers are removed) may be used for commercial profit and if so, further clarify whether the participant will or will not share in this commercial profit. Proposed language is below (with OHRP concurrence): The NIH has no plans to use participant's samples for commercial gain.

Additional Element 8 - Research Results [46.116(c)(8)]
The IC must state whether clinically relevant research results, including individual research results, will be disclosed to the participant and if so, under what conditions.

Additional Element 9 - Whole Genome Sequencing [46.116(c)(9)]
The IC must state whether the research will (if known) or might include whole genome sequencing (WGS).

B: Broad Consent

The regulations now provide (optional) requirements for "Broad Consent" as described below.

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.

Please note, 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 participants over time.

DAIDS already has an informed consent template for storage of samples (currently under revision) and the only addition to that template language is the section below.

Additional Broad Consent Information
1. Waiver [46.116(e)(1) & (f)(1)]: If an individual previously refused to provide Broad Consent for the storage, maintenance, and secondary research use of their identifiable private information or identifiable biospecimens, an IRB/EC cannot waive informed consent. 2. Alteration [46.116(e)(2) & (f)(2)]: If Broad Consent is used, none of the elements described in 46.116(a) can be omitted or altered for the storage, maintenance and use of identifiable private information or identifiable biospecimens.

Excerpts from the revised Common Rule re: sIRB

§__.114 Cooperative research.
(a) Cooperative research projects are those projects covered by this policy that involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy.
(b)(1) Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.
(2) The following research is not subject to this provision:

(i) Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or
(ii) Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for that particular context.
(c) For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort.