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MEMORANDUM

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FROM: Judith Brooks, R.N., M.S., Branch Chief, Protection of Participants, Evaluation, and Policy Branch (ProPEP), Office for Policy in Clinical Research Operations (OPCRO), Division of AIDS (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID)

TO: Clinical Trials Unit (CTU) Principal Investigators
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SUBJECT: Timing of consent and re-consent with updated IRB/EC/RE-approved informed consent forms

PURPOSE

The purpose of this memo is to outline DAIDS' expectation regarding the implementation of updated site-specific, institutional review board/ethics committee/regulatory entity (IRB/EC/RE)-approved informed consent forms (ICFs) to obtain consent or re-consent of participants. This memo is in response to recent queries and monitoring findings related to delaying the "immediate" implementation of these consents.

BACKGROUND

Circumstances may arise when it is necessary to revise ICF(s) to include important new information that is relevant for potential participants, as well as for those who are already-enrolled. These circumstances can include:

- New findings that change the risk/benefit profile;
- Procedures have been added, modified, or removed;
- New alternative treatments become available; or
- General study amendments.

Site-initiated revisions can also be made to site-specific ICF(s) due to: IRB/EC/RE stipulations; administrative changes (i.e., contact information), changes made to clarify ICF content, etc. The revised IRB/EC/RE-approved ICF(s) is/are then used to obtain participants consent to join or continue in the study. For already-enrolled participants, sponsors and IRBs/EC/REs will determine if it is necessary to obtain the participant's consent to the changes or information based upon the nature of the change in the research study and information that warranted the change. This process is referred to as "re-consenting" the participant.

The U.S. regulations and guidance and ICH E6 (R2) (section 4.8.2) require that ICF(s) be revised whenever important new information becomes available that may be relevant to the participant's consent. The HHS regulations at 45 CFR 46.116(b)(5) and the FDA regulations at 21 CFR 50.25(b)(5) state:

"A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject."

ICH E6 (R2), section 4.8.10(p) states "that the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial."

However, the U.S. regulations and applicable guidance do not mandate a timeframe within which the new information will be provided to a participant. ICH E6 (R2) uses the phrase "timely manner" but does not quantify this term.

DAIDS' EXPECTATIONS

It is DAIDS expectation that when there are any changes made to site-specific ICF(s), these updated ICF(s) must be reviewed and approved by the IRB/EC/RE, as appropriate, and be implemented "immediately", upon receipt of the IRB/EC/RE-approved revised site-specific ICF(s). This expectation applies to consenting new study participants as well as to re-consenting already-enrolled participants (when re-consent is mandated by the sponsor and/or IRBs/ECs/REs). In this context, DAIDS defines "immediately" and the ICH E6 (R2) language use of "timely manner" as "without delay". Based on this definition, participants should be re-consented using the most recent IRB/EC/RE-approved site-specific ICF(s) without delay, usually by or at the participant's next study visit.

Note: This guidance is consistent with and clarifies the intent of the DAIDS Protocol Registration (PR) Manual Version 3.0, dated April 2015, which states that protocol "amendments, including any revised site-specific ICF(s), must be implemented 'immediately' upon clinical research site receipt of all required IRB/EC/RE approvals unless the amendment specifies otherwise". The PR Manual also outlines the circumstances when delaying implementation of an IRB/EC/RE-approved updated site-specific ICF may be necessary (e.g., delay necessary due to training on new procedures or the IoR has determined that delay is in the participant's best interest), as well as the requisite documentation which must be filed in the site's Essential Documents/regulatory binders to support the delayed implementation of the updated ICF.

Any changes to protocol procedures that are a result of a protocol amendment must not be implemented for an individual participant until after written re-consent is obtained from that that participant.

DAIDS expects that logistical/administrative issues will not delay the consent/re-consent of participants to the most recent IRB/EC/RE-approved ICF(s), as most of these issues can be anticipated and addressed prior to final IRB/EC/RE approval.

SITE CONSIDERATIONS

To prevent delays in implementing the updated site-specific IRB/EC/RE-approved ICF, sites should consider the following actions:

Administrative Steps: Anticipate any administrative matters required to implement the updated site-specific IRB/EC/RE-approved ICF(s). Preparation for implementing the updated ICF(s) should begin at the same time as the IRB/EC/RE submission of the updated ICF to the IRB/EC/RE rather than waiting until after obtaining IRB/EC/RE approval. Consider the following:

- Checking participant visit schedules to be aware of upcoming visits which may occur during the timeline when the updated site-specific IRB/RE/EC-approved ICF(s) is/are available for use
- Making copies of ICF(s) upon receipt of IRB/EC/RE approval
- Efficiently removing the old ICFs from use once the updated ICF is approved by the IRB/EC/RE (e.g., once the e-mail IRB/EC/RE approval is received)
- Performing quality control activities of IRB/EC/RE-approved ICF(s)
- Familiarizing staff with the protocol and ICF changes that do not require additional training
- Ensuring that all relevant site staff are aware that there is a forthcoming updated ICF

Training: Plan for any necessary training based on the IRB/EC/RE-submitted protocol and ICF(s) so as not to delay the consent/re-consent process.

Staffing issues: Ensure coverage/back-up staff to prevent delay in implementing the most recent IRB/EC/RE-approved version of the ICF(s) (e.g., vacations/planned sick leave, unplanned sick leave, emergency back-up staff for each step in the new ICF implementation process, etc.).

Site ICF Process SOPs: The site's written Informed Consent Process SOPs should contain information about re-consenting issues, including any specific IRB/EC/RE directives. These SOPs should be reviewed and approved according to institutional policy (e.g. after IRB/EC/RE review and approval).

Document Maintenance: This guidance as well as any other related communication (e.g., IRB/EC/RE communication, additional DAIDS communication, etc.) should be filed in the site's Essential Documents/regulatory binders.

Contact: We are committed to working with you to successfully implement this guidance. Please contact your OCSO PO with any questions.