IMPAACT NETWORK ANNUAL MEETING

STUDY COORDINATORS MEETING
13 JUNE 2019
WASHINGTON DC

RECENT UPDATES FROM DAIDS

ANNE COLETTI
IMPAACT OPERATIONS CENTER

IMPAACT
International Maternal Pediatric
Adolescent AIDS Clinical Trials Network

TOPICS COVERED

- Timing of Consent and Re-Consent with Updated IRB/EC/RE-Approved Informed Consent Forms (August 2018)
- Revised Monitoring Process (January 2019)
- DAIDS Protocol Registration Policy and Manual Update (March 2019)
- DAIDS Delegation of Duties Log Policy, Template, and Instructions (March 2019)
- Required Documentation for Pediatric Risk/Benefit Category (April 2019)

TIMING OF CONSENT AND RE-CONSENT WITH UPDATED IRB/EC/RE-APPROVED ICFS

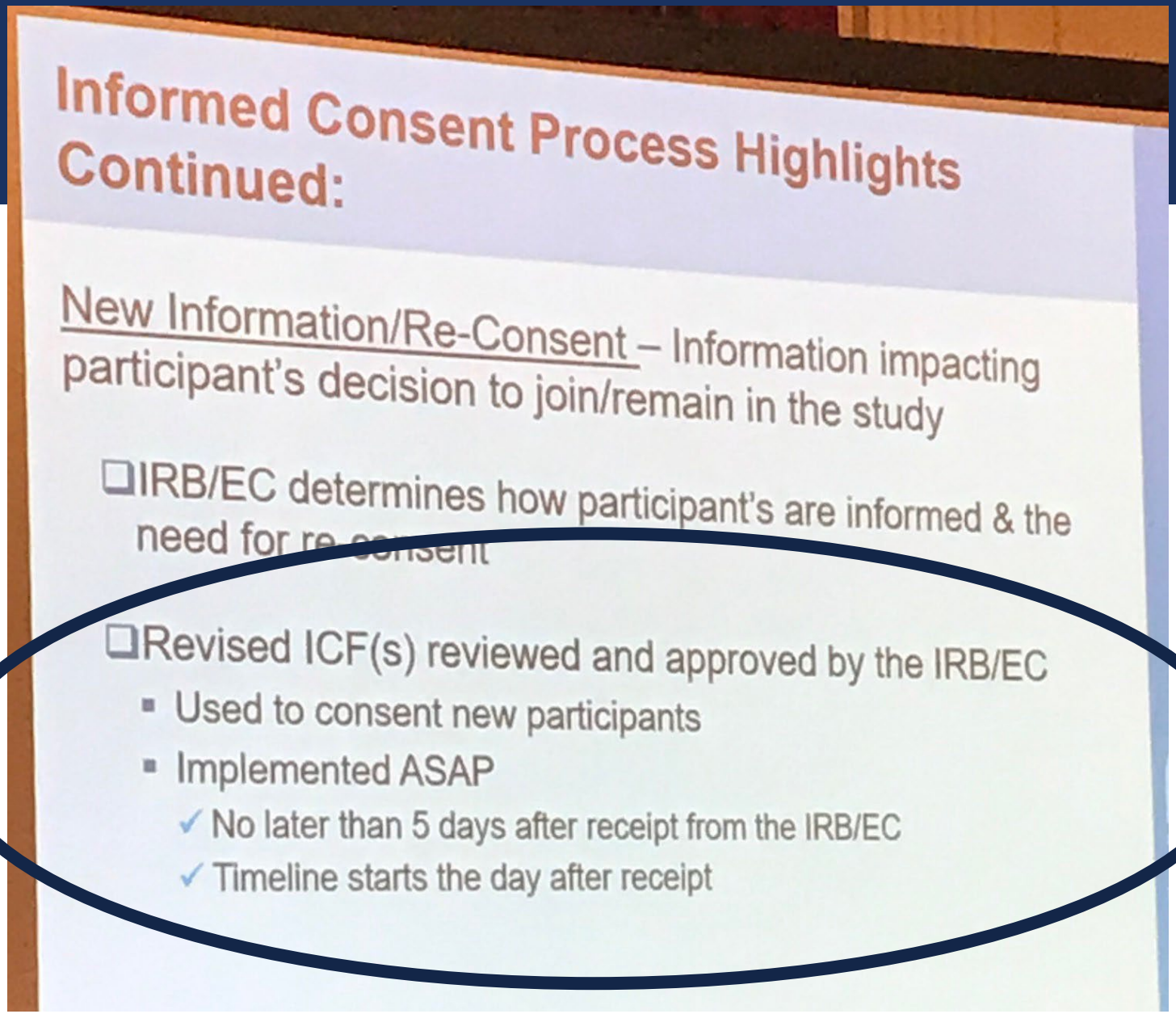
DAIDS OPCRO Memo dated 20 August 2018

It is DAIDS expectation that when there are any changes made to site-specific ICFs, these updated ICFs 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 ICFs. 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 ICFs without delay, usually by or at the participant's next study visit.

TIMING OF CONSENT AND RE-CONSENT WITH UPDATED IRB/EC/RE-APPROVED ICFS

DAIDS OPCRO Memo dated 20 August 2018

- To prevent delays in implementing revised ICFs, preparation for implementation of revised ICFs should begin at the same time as submission of revised ICFs to IRBs/ECs/REs, rather than waiting until after approval
  - Informed consent process SOPs
  - Administrative steps
  - Training
  - Staffing


Informed Consent Process Highlights Continued:
New Information/Re-Consent – Information impacting participant's decision to join/remain in the study
IRB/EC determines how participant's are informed & the need for re-consent
Revised ICF(s) reviewed and approved by the IRB/EC
Used to consent new participants
Implemented ASAP
No later than 5 days after receipt from the IRB/EC
Timeline starts the day after receipt

REVISED MONITORING PROCESS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
And Infectious Diseases
Rockville, MD 20852
5601 Fishers Lane

MEMORANDUM

DATE: January 31, 2019

FROM: Bariatu Smith, Acting Branch Chief, Monitoring Operations Branch (MOB)/Office of Clinical Site Oversight (OCSO)

TO: Clinical Trial Unit (CTU) Principal Investigators
Clinical Research Site (CRS) Leaders
Clinical Trial Unit (CTU) Coordinators
Clinical Research Site (CRS) Coordinators

SUBJECT: Revised Monitoring Process

REVISED MONITORING PROCESS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health

Signatures no longer required on Full Work Orders (FWO) or Record Review Tools (RRT Part B) for each monitoring visit

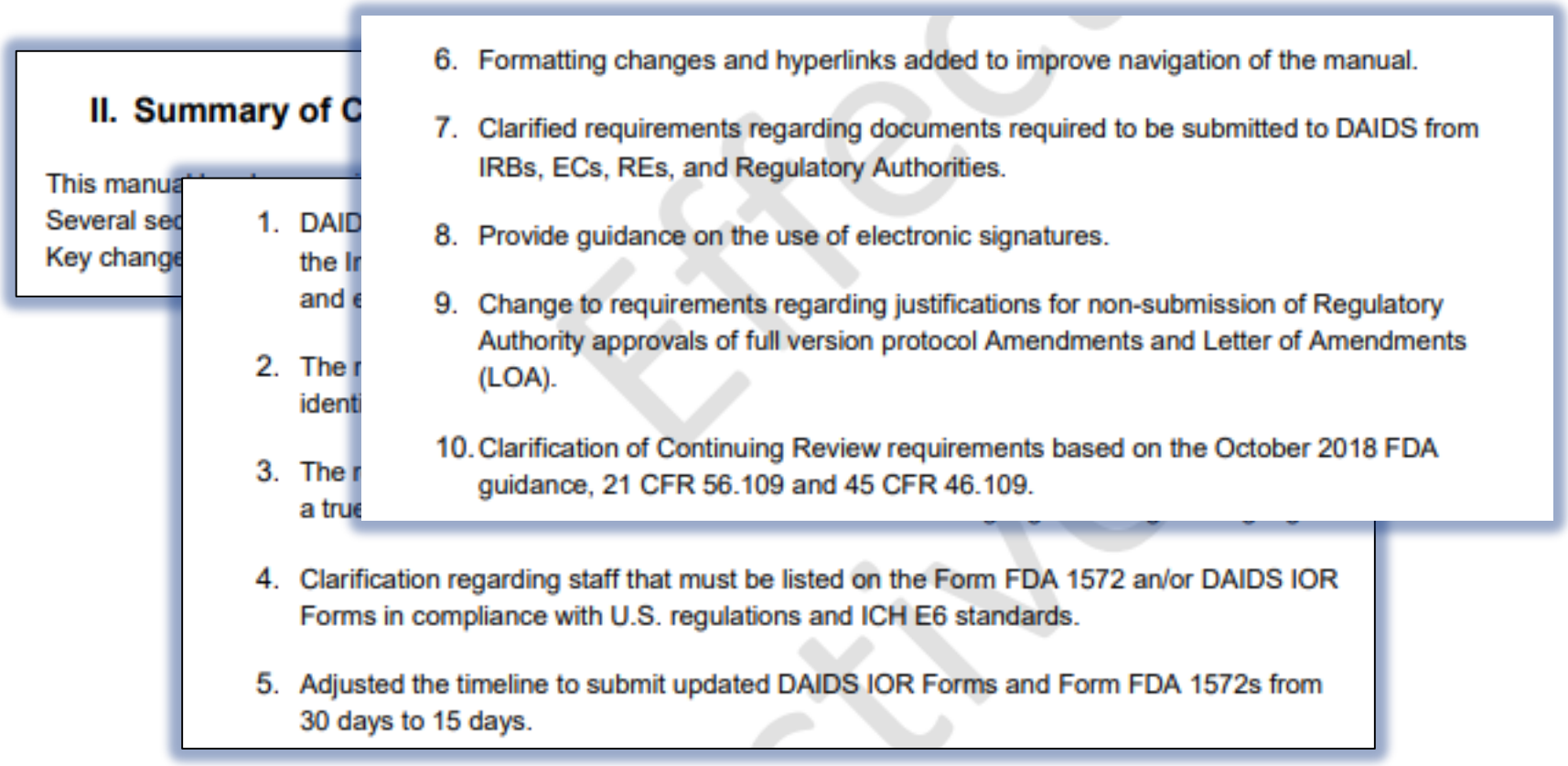
FROM: Bariatu Smith, Acting Branch Chief, Monitoring Operations Branch (MOB)/Office of Clinical Site Oversight (OCSO)

TO: Clinical Trial Unit (CTU) Principal Investigators
Clinical Research Site (CRS) Leaders
Clinical Trial Unit (CTU) Coordinators
Clinical Research Site (CRS) Coordinators

SUBJECT: Revised Monitoring Process

DAIDS PROTOCOL REGISTRATION POLICY AND MANUAL UPDATE

Policy and Manual effective 1 March 2019



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4. Clarification regarding staff that must be listed on the Form FDA 1572 an/or DAIDS IOR Forms in compliance with U.S. regulations and ICH E6 standards.
5. Adjusted the timeline to submit updated DAIDS IOR Forms and Form FDA 1572s from 30 days to 15 days.
6. Formatting changes and hyperlinks added to improve navigation of the manual.
7. Clarified requirements regarding documents required to be submitted to DAIDS from IRBs, ECs, REs, and Regulatory Authorities.
8. Provide guidance on the use of electronic signatures.
9. Change to requirements regarding justifications for non-submission of Regulatory Authority approvals of full version protocol Amendments and Letter of Amendments (LOA).
10. Clarification of Continuing Review requirements based on the October 2018 FDA guidance, 21 CFR 56.109 and 45 CFR 46.109.

DAIDS DELEGATION OF DUTIES LOG POLICY, TEMPLATE, AND INSTRUCTIONS

Policy and Manual effective 14 March 2019

- Applies to studies initiated on or after 14 March 2019 (must use DAIDS DoD Log Template)
- For selected ongoing studies, must switch to DAIDS DoD Log Template by 14 June 2019: IMPAACT 2009, 2010, 2017, 2019 (list will be updated quarterly)

DAIDS DELEGATION OF DUTIES LOG POLICY, TEMPLATE, AND INSTRUCTIONS

Policy and Manual effective 14 March 2019

The IoR is responsible for maintaining a study-specific delegation of duties log, which lists the site staff and other individuals to whom the IoR has delegated significant study-related duties. The IoR must ensure that these staff and others are permitted to perform the delegated duties per local laws, applicable, regulations, and institutional policies.

DAIDS DELEGATION OF DUTIES LOG POLICY, TEMPLATE, AND INSTRUCTIONS

SITE STAFF

Site Staff Information					Start Date and Investigator/IoR Delegation Approval/Date		Stop Date and Investigator/IoR Confirm Delegation End/Date	
Site Staff Full Legal Name	Site Staff Signature	Site Staff Initials	Research Study Role	Key Study Task(s) (choose from list)	Start Date (dd/mm /yyyy)	Investigator /IoR Initials	End Date (dd/mm /yyyy)	Investigator /IoR Initials

DAIDS DELEGATION OF DUTIES LOG POLICY, TEMPLATE, AND INSTRUCTIONS

Investigator/Investigator of Record (IoR)

By signing, I confirm/acknowledge that the tasks listed below will only be delegated to appropriately trained, skilled, and qualified staff. I remain responsible for the overall study conduct and reported data and I will ensure study oversight. Any changes in staff or delegation in staff will be recorded in real time.

Investigator/IoR Name	Investigator/IoR Signature	Initials and Date	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy) (complete only if prior to end of study)

REQUIRED DOCUMENTATION FOR PEDIATRIC RISK/BENEFIT CATEGORY

Memo from DAIDS OPCRO dated 19 April 2019

Per the DAIDS Policy for Enrolling Children (including Adolescents) in Clinical Research, for research studies including children or adolescents, DAIDS requires documentation of the IRB/EC designation of the pediatric risk/benefit category per 45 CFR 46, 404-407 and 21 CFR 50.51-54 and IRB/EC approval for involvement of children based on the determination specified by that pediatric risk/benefit category. This requirement applies to initial and continuing reviews and reviews of protocol amendments involving potential changes to study risks or benefits.

REQUIRED DOCUMENTATION FOR PEDIATRIC RISK/BENEFIT CATEGORY

Memo from DAIDS OPCRO dated 19 April 2019

Effective May 1, 2019, when an IRB/EC determines the pediatric risk/benefit category is 45 CFR 46.407 or 45 CFR 46.406, additional action and documentation will be required by DAIDS.

46.407 = research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

46.406 = research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.

REQUIRED DOCUMENTATION FOR PEDIATRIC RISK/BENEFIT CATEGORY

For Pediatric Risk/Benefit Category 45 CFR 46.407:

If the risk/benefit category indicated on the IRB/EC approval letter for the research study is 45 CFR 46.407, sites will receive a notification from DAIDS Protocol Registration Office (PRO) to **CONFIRM the IRB's/EC's pediatric risk/benefit category designation. The DAIDS PRO review process will be stopped until the site confirms the IRB's/EC's pediatric risk/benefit category designation.**

Upon receipt of a notification from the DAIDS PRO, the CRS Principal Investigator (PI), Study Investigator of Record (IoR), or designee should contact the IRB/EC Chair/Director to either secure documentation of new pediatric risk/benefit category designation (first bullet below), or to confirm that the board/committee intended to select the risk/benefit category 45 CRF 46.407 and that the IRB/EC plans to move forward with the subsequent required steps (second bullet below):

REQUIRED DOCUMENTATION FOR PEDIATRIC RISK/BENEFIT CATEGORY

- *If the risk/benefit category designation 46.407 was mistakenly selected, the site must request written documentation from IRB/EC with the corrected risk/benefit category designation. A copy of the relevant portion of the IRB/EC meeting minutes, signed and dated by the IRB/EC Chair or designee, documenting the IRB's/EC's risk/benefit category discussion and designation can be provided to the DAIDS PRO to meet the written documentation requirement. Sites must provide the documentation with the corrected risk/benefit category designation to DAIDS PRO in-order for the submission process to continue.*

- *If the IRB/EC confirms their decision of the 46.407 risk/benefit category selection, the CRS Principal Investigator (PI), Study Investigator of Record (IoR), or designee should refer to Appendix 1 of the DAIDS Policy for Enrolling Children (including Adolescents) in Clinical Research: Protocol Document Requirements as this risk/benefit category requires a special level of DHHS review beyond that provided by the IRB/EC. Sites can also refer to the DAIDS Policy for Enrolling Children (including Adolescents) in Clinical Research: Clinical Research Site Requirements and to the May 26, 2005 Guidance, "Children as Research Subjects and the HHS "407" Process." The DAIDS PRO review of a CRS's registration submission will be stopped pending a determination from the Secretary, HHS or his/her designee.*

REQUIRED DOCUMENTATION FOR PEDIATRIC RISK/BENEFIT CATEGORY

For Pediatric Risk Category 45 CFR 46.406:

A site must have established written procedures that ensure adequate provisions are in place for:

- Soliciting parents' or guardians' permission, as required in 45 CFR 46.408 (i.e. permission is to be obtained from both parents unless: (1) One parent is deceased, unknown, incompetent, or not reasonably available; or (2) One parent has legal responsibility for the care and custody of the child).
- Soliciting documenting assent, when the IRB/EC requires that assent be obtained.
- Enrolling wards (e.g., orphans) with the appropriate documentation that: (1) recognizes the status of the individual child as a ward; (2) ensures communication of that status to the responsible IRB/EC; and (3) confirms the IRB/EC appointment of an advocate for the child/ward, in addition to any other individual acting as guardian or in loco parentis.

QUESTIONS?