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: July 23, 2020

FROM: Manizhe Payton, Director DAIDS Office of Clinical Site Oversight (OCSO)
Bariatu Smith, Acting Branch Chief, DAIDS Monitoring Operations Branch (MOB), OCSO

Manizhe E. Payton -S Digitally signed by Manizhe E. Payton -S Date: 2020.07.23 16:23:57 -04'00'

Smith, Bariatu (NIH/NIAID) [E]

TO: NIAID/DAIDS HIV/AIDS Network Leadership, Operations Center Principal Investigator(s), Clinical Trial Unit (CTU) Principal Investigators, Non-Network Clinical Trial Principal Investigators, Clinical Research Site (CRS) Leaders, CTU Coordinators, CRS Coordinators, Data Management Center Directors

SUBJECT: DAIDS Remote Monitoring Strategy: Implementation of Remote Source Document Verification (rSDV)

As you are aware, DAIDS suspended all onsite monitoring visits as of March 13th, 2020 due to the COVID-19 public health emergency. Unfortunately, due to ongoing travel restrictions, the majority of sites are still unable to accommodate onsite monitoring visits and the environment around in-person monitoring visits is not significantly improving.

Although DAIDS implemented *remote* monitoring visits in mid-April at sites where it was technically feasible and permissible per applicable regulations, the scope of the remote visits was limited. Remote monitoring visits to date consist of quality review of study data available in the Electronic Data Capture (EDC) system without verification to corresponding source documents. Review of source documentation is a critical component of ensuring data integrity. The FDA issued guidance document entitled "FDA Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency", provides the following guidance to sponsors; "*If onsite monitoring visits are no longer possible sponsors should consider optimizing use of central and remote monitoring programs to maintain oversight of clinical sites*". Additional emphasis suggests that the sponsor and monitors may consider multiple options to facilitate rSDV.

Given the volume of study data collected for current and planned studies, DAIDS must implement a mechanism to verify data integrity through source document verification. Therefore, we are now expanding the scope of remote monitoring to include remote Source Document Verification (rSDV) which will allow monitors to access participant source documents to conduct rSDV.

DAIDS is requiring sites that are unable to accommodate onsite monitoring visits to select an option to facilitate remote monitoring including rSDV. More details on timelines and priority studies and sites are described below.

We recognize that clinical research operations at each site varies, including institutional guidelines on confidentiality, privacy, and contractual obligations that may impact rSDV. Therefore, we believe that providing sites with several options to facilitate rSDV is important so that sites can consider which solution may work best in their environment.

DAIDS is proposing 4 options to facilitate rSDV. All systems being offered are HIPAA and 21 CFR Part 11 compliant. However, we are also open to considering existing "telehealth" systems that sites may already have in place which could be leveraged to provide monitors access to source documentation.

Option #1 - Veeva SiteVault Platform- This platform is available for sites to self-subscribe at no cost from Veeva Systems. There is no software to download and the only requirement is internet access. Sites will upload source documents to this secure platform and assign permissions to monitors to access these data for a limited period of time. For sites that are already using this platform in some capacity, they can add specific DAIDS studies to their existing account. In the event that this platform is being used by another entity within the institution, the site can request access to the platform following their internal procedures. However, sites that are not currently using Veeva SiteVault, can obtain additional information by visiting- https://www.veeva.com/products/sitevault/ or sign up to try at sites.veeva.com. Veeva SiteVault may require a signed agreement between the site and Veeva Systems.

Option #2 - Site Controlled SharePoint or Cloud-Based Portal-Your site may already have a platform which allows for sharing of participant source documents, which could be extended to allow monitor's access. This option must be 21CRF 11 and HIPAA compliant as applicable.

Option #3 – Direct Access to Electronic Medical Records (EMRs) by Monitors- This option may be feasible for sites that use EMRs, and whose institutional policy allows for direct access of the site's EMR to monitors for a limited period of time. Please contact your institution's Security Officer for required approvals and any agreements to facilitate remote access to participant source documents.

Option #4 - Medidata Rave Imaging Solution- This electronic platform is hosted by the DAIDS DMCs and made available to sites. It does not require additional purchase of software and sign-on is through your existing single iMedidata account. Sites will upload source documents to this secure platform and monitor permission and access would be assigned by DAIDS DMCs. There is ongoing discussion regarding the implementation timeline for MediData Rave Imaging Solutions, and the DMCs will contact sites regarding demonstration of this solution.

NOTE: There may be delayed implementation of **Medidata Rave Imaging Solution** as DAIDS is working through the agreements and timelines for configuration with all stakeholders for a seamless implementation.

Please start evaluating which option would work in your setting. IRB approval will be required for the option selected. Additionally, institutional policies may require approval by privacy/security officials (as appropriate) and signed agreements to be in place. Our plan is to begin rSDV in mid-late August 2020.

DAIDS is taking a phased approach to initiate rSDV by focusing initially on five (5) priority DAIDS sponsored studies with an estimated database lock dates within the next 1-3 months. The studies indicated in the table below have been designated as priority protocols for rSDV. Although we intend to apply rSDV to all studies that DAIDS sponsors, we will focus only on the 5 studies below initially. If you are a site participating in any of the 5 studies below, DAIDS will be working with you as a priority to identify an option to facilitate rSDV and to schedule rSDV monitoring visits. Please note that the monitors may conduct more frequent remote visits to address the backlog of unmonitored data due to the suspension of onsite monitoring visits. If your CRS is participating in any of these 5 studies, you will receive an additional communication from your OCSO Program Officer in the next week with more details on timelines and process for initiating rSDV.

Study ID	Study Name
HPTN 083	A Phase 2b/3 Double Blind Safety and Efficacy Study of Injectable Cabotegravir Compared to Daily Oral Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC), For Pre-Exposure Prophylaxis in HIV-Uninfected Cisgender Men and Transgender Women who have Sex with Men
IMPAACT P1106	Pharmacokinetic Characteristics of Antiretrovirals and Tuberculosis Medicines in Low Birth Weight Infants
IMPAACT 2007	Phase I Safety and Pharmacokinetic Study of Maraviroc in HIV-1-Exposed Infants at Risk of Acquiring HIV-1 Infection
IMPAACT 2014	Phase I/II Study of the Pharmacokinetics, Safety and Tolerability of Doravirine (MK-1439) and Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (MK-1439A) in HIV-1-infected Children and Adolescents
IMPAACT 2010	Phase III Study of the Virologic Efficacy and Safety of Dolutegravir-Containing versus Efavirenz-Containing Antiretroviral Therapy Regimens in HIV-1-Infected Pregnant Women and Their Infants

We recognize that implementation of rSDV will require more time and effort by site staff, and that each site may have unique challenges. We are committed to working with you to address these challenges, in support of data integrity. Please reach out directly to your PO with any questions about the options we have proposed.

We are grateful for your continuing efforts and dedication during this unprecedented time.