Section 7. Co-Enrollment Considerations

Provided in the remainder of this section is guidance related to the conduct and documentation of MTN-015 relative to parent study visits. This guidance is based on correspondence between the MTN Leadership and Operations Center (LOC) and the DAIDS Office for Policy in Clinical Research Operations (OPCRO); please see Section Appendix 7-1 for a reference copy of this correspondence.

For co-enrolled participants, site staff may conduct MTN-015 study visits and parent study visits on the same day or they may conduct visits on separate days, based on site and participant preferences. At visits when both MTN-015 and parent study procedures are performed, the specimen collection and testing requirements for both studies should be carefully reviewed to avoid duplicate specimen collection while also ensuring adequate blood volumes for the requirements of both studies.

When parent study visits take place within 30 calendar days prior to a MTN-015 visit, certain MTN-015 laboratory and clinical procedures may be omitted. The procedures that may be omitted are listed below:

- Complete blood count with differential and platelets
- Phosphate, creatinine, AST and ALT
- NAAT for Chlamydia and gonorrhea
- Pregnancy testing
- Trichomonas testing
- Vaginal pH assessment
- Syphilis serology
- Physical exams
- Pelvic exams: Note that while a complete MTN-015 pelvic exam is not required, certain MTN-015 pelvic specimens are still required to be collected at the MTN-015 visit. These include vaginal swabs and cervicovaginal lavage (CVL) specimens. A full pelvic exam and other pelvic specimen collection procedures are done if clinically indicated. Contact the MTN-015 Management Team with any questions regarding the above guidance.

NOTE: CD4+ T-Cell Count and Plasma HIV-1 RNA testing must be conducted at MTN-015 visits UNLESS the same specimen/test was collected at the MTN parent study visit within 7 calendar days.

If a laboratory test or clinical procedure is omitted for MTN-015 because it meets the criteria outlined above, a certified copy of the test result and/or other source documentation from the parent study should be filed in the MTN-015 study binder. For test results that must be documented on an MTN-015 Case Report Form (CRF):

- Enter the date of the visit from the parent protocol into the 'Alternate Collection Date' for the MTN-015 CRF
- Transcribe the information from the parent study source document (test result and/or other source documentation) into the MTN-015 CRF
- Lastly, in the comment field, state that the original data was acquired via the parent study.

Using the procedure listings in Section 7 of the MTN-015 protocol as a guide, the remainder of this section provides guidance on the conduct and documentation of MTN-015 procedures for co-enrolled participants. Please contact the MTN-015 Management Team with any questions related to interpretation of, or compliance with, both parent study and MTN-015 protocols. Please also refer to Section 3 of this manual for more information on MTN-015 documentation requirements.

Certified copies from the parent protocol are required on enrollment into MTN-015 to document baseline conditions and eligibility status for MTN-015. These baseline documents are intended to be a snapshot of the participant's medical condition and eligibility at enrollment into MTN-015, and they do not need to be updated if the parent protocol documents are updated at a later time. Throughout study follow-up, certified copies of parent study laboratory results must be made if the testing is being omitted as part of the MTN-015 visit because it was done within 30 or 7 days of the MTN-015 visit, as allowable per protocol. Otherwise, it is generally up to the discretion of the site what system they use for documentation of medical history, counseling, or other events that may occur when a participant is co-enrolled —i.e. sites may opt to maintain two sets of source documents (one for each study) or use certified copies of records from the parent or MTN-015 visit, as needed. Details on source documentation requirements for coenrolled participants is further specified in the table below.

ADMINISTRATIVE PROCEDURES	
Informed consent	This procedure is specific to MTN-015. Conduct and document per the MTN-015 protocol, SSP Manual, and SOPs.
Review parent study records to confirm seroconversion	This procedure is specific to MTN-015. Conduct and document per the MTN-015 protocol, SSP Manual, and SOPs. Prepare certified copies of relevant parent study HIV testing source documents and file the copies in the MTN-015 study record. These records are required source documents for the MTN-015 Enrollment form.
Eligibility determination	This procedure is specific to MTN-015. Conduct and document this procedure per the MTN-015 protocol, SSP Manual, and SOPs.
Assign participant ID	This procedure is specific to MTN-015. Conduct and document per the MTN-015 protocol, SSP Manual, and SOPs. Participants are considered enrolled in MTN-015 when they have been assigned an MTN-015 PTID. Cross-reference enrollment in MTN-015 in chart notes in the parent study record.
Update locator information	Sites may choose to maintain one centralized locator form which is updated for both MTN-015 and the parent protocol during the period that the participant is co-enrolled. Upon exit from the parent protocol, a certified copy of the locator should be made to archive with the parent protocol study records. The centralized locator would then be maintained moving forward as part of MTN-015 follow-up. Alternatively, sites may opt to maintain two locator forms for co-enrolled participants (one for each study) or to prepare certified copies of the parent study locator form and file the copies in the MTN-015 study record. With the latter option, an MTN-015 locator form must be completed after the participant exits the parent study.
Collect demographics	This procedure is specific to MTN-015. Administer the MTN-015 Demographics form per the MTN-015 protocol, SSP Manual, and SOPs.
Schedule next visit	Review the target dates and allowable visit windows for both the

	parent study and MTN-015 when scheduling visit dates with the participant. Schedule visits to minimize duplication of procedures across studies when possible.
Reimbursement	Site SOPs should specify how reimbursement will be handled when MTN-015 visits are conducted on the same day as parent study visits. Reimburse participants per site SOPs and any applicable IRB/EC specifications.
CLINICAL PROCEDURES	
Update medical history	Medical history information is typically collected at parent study visits and MTN-015 visits. When a participant enrolls in MTN-015, prepare a certified copy of her parent study baseline medical history source document and file the copy in her MTN-015 study record. Similarly prepare and file a certified copy of the last interval medical history source document completed for the parent study prior to enrollment in MTN-015. This may be a site-specific medical history tool or chart notes. To document interval history information while the participant is co-enrolled in both studies, sites may opt to maintain two sets of medical history source documents (one for each study) or to prepare certified copies of the parent study medical history source documents and file the copies in the MTN-015 study record. With the latter option, MTN-015 medical history source documents must be completed after the participant exits the parent study. ⚠ If medical history information reported at an MTN-015 visit (on a day when a parent study visit is not also planned to be conducted) identifies any adverse events (AEs) while the participant is co-enrolled in the parent study, document and report the AEs per the parent study protocol, SSP Manual, and SOPs. Cross reference the MTN-015 visit in chart notes in the parent study record, prepare certified copies of the MTN-015 medical history source documents as needed, and file the copies in the parent study record.
Record/update clinical events	This procedure is specific to MTN-015. Complete the MTN-015 HIV/AIDS Associated Events form per the MTN-015 protocol, SSP Manual, and SOPs. See also the guidance above on "update medical history." The MTN-015 HIV/AIDS Associated Events Log form captures medical history data that, for some participants, may have been source documented on parent study medical history documents. For such participants, prepare certified copies of the relevant parent study medical history source documents and file the copies in the MTN-015 study record. ⚠ Clinical events identified in MTN-015 may be considered AEs in the parent study. Document and report AEs per the parent study protocol, SSP Manual, and SOPs. Prepare and file certified copies of MTN-015 source documents as needed to source document the AEs in the parent study record.
Acute seroconversion assessment	This procedure is specific to MTN-015. Complete the MTN-015 Acute Seroconversion Assessment form and the MTN-015

	Seroconversion Symptoms form per the MTN-015 protocol, SSP Manual, and SOPs. Prepare certified copies of relevant parent study HIV testing and medical history source documents and file the copies in the MTN-015 study record.
Concomitant medications assessment	Concomitant medication information is typically collected at parent study visits and MTN-015 visits. Study sites may opt to maintain two sets of concomitant medication source documents (one for each study) or to prepare certified copies of the parent study medical history source documents and file the copies in the MTN-015 study record. With the latter option, MTN-015 concomitant medication source documents must be completed after the participant exits the parent study.
Antiretroviral treatment record	This procedure is specific to MTN-015. Complete the MTN-015 Antiretroviral Treatment Regimen Log form per the MTN-015 protocol, SSP Manual, and SOPs. See also the guidance above on "concomitant medications assessment." The MTN-015 Antiretroviral Treatment Regimen Log form captures medication data that, for some participants, will have been source documented on parent study source documents; for such participants, prepare certified copies of the relevant parent study source documents and file the copies in the MTN-015 study record.
Complete physical exams	These procedures are specific to MTN-015. Perform and document per the MTN-015 protocol, SSP Manual, and SOPs. If a physical exam was conducted for the parent study within 30 days prior of the MTN-015 visit, and there are no new complaints from the participant, then this may be omitted. ⚠ If an exam performed for MTN-015 identifies any AEs while the participant is co-enrolled in the parent study, document and report the AEs per the parent study protocol, SSP Manual, and SOPs. Cross-reference completion of the exam in parent study chart notes, prepare certified copies of the MTN-015 exam source documents as needed, and file the copies in the parent study record.
Gynecologic exam	The gynecologic exams performed for MTN-015 are generally less specific/intensive than parent study exams, but MTN-015 exams require more specimen collection for archive. At visits when an exam is required for both the parent study and MTN-015, perform and document the exam per the parent study protocol, SSP Manual, and SOPs, but add MTN-015 specimen collection in the following order: vaginal swabs for parent study (if required), vaginal swabs for MTN-015, CVL for MTN-015, Pap smear (if applicable). Prepare certified copies of the parent study exam source documents and file the copies in the MTN-015 study record. Complete relevant MTN-015 case report forms using the certified copies as source. At visits when an exam is required for MTN-015 but not for the parent study, perform and document the exam per the MTN-015

	protocol, SSP Manual, and SOPs. If a pelvic exam was conducted for the parent study within 30 days prior of the MTN-015 visit and there are no new complaints from the participant, then the full pelvic exam may be omitted. However, given the additional specimens for archive required for MTN-015, these specimens should still be collected at the MTN-015 visit. ⚠ If an exam performed for MTN-015 identifies any AEs while the participant is co-enrolled in the parent study, document and report the AEs per the parent study protocol, SSP Manual, and SOPs. Cross-reference completion of the exam in parent study chart notes, prepare certified copies of the MTN-015 exam source documents as needed, and file the copies in the parent study record.
Provide test results	Test results provided at any time may be relevant to both the parent study and MTN-015. Provide test results at time points specified in both the parent study protocol and the MTN-015 protocol. Document provision of test results in both study records; use certified copies as appropriate.
Treatment or referral	Treatment and referrals provided at any time may be relevant to both the parent study and MTN-015. Provide treatment and referrals at time points specified in both the parent study protocol and the MTN-015 protocol. Document all treatment and referrals provided in both study records; use certified copies as appropriate.

BEHAVIORAL PROCEDURES	
Baseline and follow-up behavioral questionnaires (ACASI and CRF)	These procedures are specific to MTN-015. Administer the MTN-015 ACASI questionnaires per the MTN-015 ACASI Users Manual.
Adherence questionnaire	This procedure is specific to MTN-015. Administer the MTN-015 Antiretroviral Therapy Adherence form per the MTN-015 protocol, SSP Manual, and SOPs.
Social harms assessment	This procedure is specific to MTN-015. Administer the MTN-015 Social Harms Assessment form per the MTN-015 protocol, SSP Manual, and SOPs. For any social harms that may be reported, probe as needed to determine whether the harm is associated with the parent study, MTN-015, or both, and report the harm accordingly. When reported social harms are associated with both studies, document the harms and all follow-up action taken in both study records; use certified copies as appropriate.
Counseling: HIV secondary prevention, STI risk reduction, contraception	Counseling provided at any time may be relevant to both the parent study and MTN-015. Provide counseling at time points specified in both the parent study protocol and the MTN-015 protocol. Document all counseling provided in both study records; use certified copies as appropriate.
Provision of condoms	Provide condoms at time points specified in both the parent study protocol and the MTN-015 protocol. While the participant is co-enrolled, provide specific brands of condoms per the requirements

	of the parent study. Document all condoms provided in both study records; use certified copies as appropriate.

LABORATORY SAMPLES AND PROCEDURES	
Pregnancy test	Pregnancy testing is typically required at all parent study visits, but is only required for MTN-015 at the Screening and Enrollment Visit, Month 1 and Month 3 non-ART visits, and Final Visit, and when clinically indicated during follow-up. Tests performed for parent studies can be used for purposes of MTN-015. If a pregnancy test was conducted at a parent study visit within 30 days of an MTN-015 visit, perform and document the test per the parent study protocol, SSP Manual, and SOPs. Prepare certified copies of the parent study testing source documents and file the copies in the MTN-015 study record. Complete relevant MTN-015 case report forms using the certified copies as source. For participants identified as pregnant, pregnancy history data and pregnancy outcomes must be reported on both parent study case report forms and MTN-015 case report forms. File source documents relevant to these case report forms in the parent study record; prepare and file certified copies in the MTN-015 study record.
Chlamydia, gonorrhea, and syphilis tests, complete blood count, liver and renal function tests	Tests performed for parent studies can be used for purposes of MTN-015. If these laboratory tests were conducted at a parent study visit within 30 days of an MTN-015 visit, perform and document the test per the parent study protocol, SSP Manual, and SOPs. Prepare certified copies of the parent study testing source documents and file the copies in the MTN-015 study record. Complete relevant MTN-015 case report forms using the certified copies as source. At visits when a test is required for MTN-015 but not for the parent study, or if any laboratory tests for the parent study are discontinued after a participant seroconverts, perform and document the exam per the MTN-015 protocol, SSP Manual, and SOPs. ⚠ If a test performed for MTN-015 identifies any AEs while the participant is co-enrolled in the parent study, document and report the AEs per the parent study protocol, SSP Manual, and SOPs. Cross-reference completion of the test in parent study chart notes, prepare certified copies of the MTN-015 testing source documents as needed, and file the copies in the parent study record.
CD4+ cell count and HIV RNA (viral load)	Perform and document per the MTN-015 protocol, SSP Manual, and SOPs, unless the same specimen/test was collected at the MTN parent study visit within **7 calendar days**. If the parent study test results is used, prepare certified copies of the parent study testing source documents and file the copies in the MTN-015 study record. Complete relevant MTN-015 case report forms using the certified copies as source.

	At visits when a test is required for MTN-015 but not for the parent study, or if any laboratory tests for the parent study are discontinued after a participant seroconverts, perform and document the exam per the MTN-015 protocol, SSP Manual, and SOPs.
Specimens for storage	These specimens are specific to MTN-015. Collect, store, and document per the MTN-015 protocol, SSP Manual, and SOPs. If applicable, separately collect, store, and archive specimens for the parent study per the parent study protocol, SSP Manual, and SOPs.

Section Appendix 7-1
Copy of Email Correspondence with DAIDS Related to Documentation Requirements for Participants Co-Enrolled in MTN-015 and HPTN 035

From: Reese, Karen (NIH/NIAID) [E] [mailto:KReese@niaid.nih.gov]
Sent: Wed 1/16/2008 10:53 AM
To: Anne Coletti
Cc: Humphries, MJ (NIH/NIAID) [C]
Subject: RE: Source Documentation Question

Anne,

I think the plan you have outlined below is fine. You may want to put a Note to File in the study regulatory files to clearly define the process you are using or to reference the section in the study procedure manual that outlines the plan in detail. I think the plan is well thought out and certainly makes sense from a participant burden and risk standpoint.

Karen Reese, MS, CCRA
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kreese@niaid.nih.gov

From: Brooks, Judy (NIH/NIAID) [E]
Sent: Tuesday, January 15, 2008 10:14 AM
To: 'Anne Coletti'
Cc: Humphries, MJ (NIH/NIAID) [C]; Reese, Karen (NIH/NIAID) [E]
Subject: RE: Source Documentation Question

Ann, I have limited access to my computer so I have asked Karen Reese or MJ Humphries to respond to you question.
Judy

Judith Brooks
Chief, Policy, Training, and Quality Assurance Branch
OPCRO/DAIDS/NIAID/NIH
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From: Anne Coletti [mailto:AColetti@fhi.org]
Sent: Friday, January 11, 2008 10:24 PM
To: Brooks, Judy (NIH/NIAID) [E]
Subject: Source Documentation Question

Dear Judy --

I hope this message finds you well and enjoying the New Year.

I am writing with a question related to source documentation for an upcoming Microbicide Trials Network (MTN) study. You may recall from the MTN regional meeting last May that MTN-015 is an observational follow-up study for women who become infected with HIV while taking part in an HPTN or MTN microbicide trial. The MTN-015 protocol has been finalized and the study team is now working on the study procedures manual, site SOPs, etc. Some of the participants who enroll in MTN-015 will also continue follow-up in the microbicide study in which they were originally enrolled, and my question about source documentation relates to that situation. First I will give you a more concrete example, and then I will ask my question:

Let's say a participant in HPTN 035 becomes infected with HIV after approximately 9 months of follow-up in that study. She decides to continue follow-up in HPTN 035, and also agrees to join MTN-015. On the day when she returns to the clinic for her Month 12 visit for HPTN 035, she is eligible to complete her Month 3 visit for MTN-015. According to the two study protocols, a pelvic exam and complete blood count is required at this visit for both studies. In this situation, to minimize participant burden and risk, the study staff would conduct one pelvic exam and collect one blood sample for testing, and use the exam and test results for both studies.

My question relates to documentation requirements in this type of situation, in which there is one original source document for data collected for two studies. Upon doing some brainstorming and consulting with others on how to approach this situation, a suggestion has been made to retain the original source documents in the participant's file for the "parent" microbicide study and to prepare certified copies of these documents for filing in the participant's file for MTN-015. With this approach, a valid source document is contained in both files, such that the MTN-015 file can "stand alone" for purposes of monitoring and/or auditing. Having a "stand alone" MTN-015 file also helps protect the confidentiality of information in the parent study file that is not relevant to MTN-015.

If this type of approach were to be adopted for MTN-015, the study procedures manual would specify which parent study procedures can be utilized for MTN-015, and study SOPs would list all documents -- original or certified copy -- that are intended to serve as source for MTN-015 study data.

Could you please advise as to whether this approach would be considered compliant with DAIDS' documentation policies? We also would be grateful for any other guidance or recommendations that you think would benefit the MTN-015 study team.

Thank you in advance,
Anne