# Section 2. Documentation Requirements



## 2. Introduction

Study staff are responsible for proper collection, management, storage, quality control and quality assurance of all study-related documentation. This section contains information on the essential documents that the study site must maintain throughout the study. It also contains information related to establishing adequate and accurate participant research records for MTN-033.

## 2.1 Essential Documents

The DAIDS policy on Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials and E6 Good Clinical Practice: Consolidated Guidance specifies the essential documents the site must maintain. Although all required documentation must be available for inspection at any time, all documents need not be stored together in one location.

A suggested essential document filing structure is available upon request from FHI 360. The study site is not required to adopt the suggested structure, but is encouraged to consider it when developing its filing approach for the study. Further clarifications of the suggested filing structure are as follows:

- Essential documents may be stored in files and/or in binders. The files/binders listed in the essential documents filing structure may be further subdivided, consolidated, and/or re-organized.
- It is recommended that a “contents” sheet be maintained and inserted as the first page(s) of each file/binder. Within each file/binder, it is recommended that documents be filed in ascending date order (most recent documents in front).
- Certain documents related to the investigational study product(s) will be stored in the site pharmacy. A listing of essential documents to be maintained in the pharmacies is provided in Section 2.3.6 below.
- To facilitate routine inspection by study monitors, certain laboratory-related essential documents should be stored in the main study essential documents files/binders. Other lab-related essential documents (e.g., lab SOPs) may be filed in the site laboratory.
- The suggested filing structure assumes that MTN-033 participant research records will be stored separately from the other essential documents listed in the essential documents filing structure. Section 2.2 below provides information on the required contents of these records.

- The MTN-033 PTID-Name Linkage Log and Screening and Enrollment Log **must** be maintained in hard-copy. The suggested filing structure assumes that these logs will be stored in the study clinic or data management area throughout the screening and accrual process and not necessarily with the other essential documents listed.

**Note:** When required documents are modified or updated, the original and all modified or updated versions must be retained.

## 2.2 Participant Research Records

The study site must maintain adequate and accurate participant research records containing all information pertinent to MTN-033 for each study participant. See protocol section 11.2 and 13.6 for further information regarding all participant information which should be stored in locked file cabinets with access limited to authorized study staff. Please note that all records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored separately from study records identified by PTID.

The International Conference on Harmonization Consolidated Guidance for Good Clinical Practice defines the terms source data and source documentation as follows:

The term **source data** refers to all information in original records and certified copies of original records related to clinical findings, observations, or other activities in a clinical study necessary for the reconstruction and evaluation of the trial (including all screening, enrollment and randomization activities). Source data are contained in source documents (e.g., original records or certified copies).

The term **source document** refers to original documents, data, and records (e.g., hospital records; clinical and office charts; laboratory records and notes; memoranda; participants' diaries and/or evaluation checklists; pharmacy dispensing records; recorded data from automated instruments; copies of transcriptions certified after verification for accuracy and completeness; microfiche; photographic negatives; microfilm or magnetic media; x-rays; participant files; and records kept at the pharmacy, laboratories, and medico-technical departments involved in the study).

Source documents are commonly referred to as the documents — paper-based or electronic — upon which source data are first recorded. The study site must comply with the standards of source documentation specified in the DAIDS policy on Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials. The DAIDS policy specifies both requirements and recommendations. The study site must comply with all requirements and are encouraged, but not required, to comply with all recommendations.

## 2.3 Required Source Documentation

For MTN-033, it is expected that participant research records will consist of the following source documents:

- Narrative or chart notes
- Documentation that the participant provided written informed consent to screen for and participate in the study prior to the conduct of any study procedures
- Documentation that the participant met the study's eligibility criteria
- Prescription documentation
- Pharmacy investigational product accountability, dispensing and chain of custody records (maintained in the study site pharmacy), as well as clinic study product accountability documentation (maintained in the study clinic)

- A record of all contacts, and attempted contacts, with the participant
- A record of all procedures performed by study staff during the study (e.g., on visit checklists and/or other site-specific procedural flow sheets or chart notes)
- Local laboratory testing logs and result reports, or another document defined as source for a test result.
- Case report forms (CRFs) and other forms provided by the MTN Statistical and Data Management Center (SDMC).
- Study-related information on the participant's condition before, during, and after the study, including:
  - Data obtained directly from the participant (e.g., interview and/or other self-reported information)
  - Data obtained by study staff (e.g., exam and lab findings)
  - Data obtained from non-study sources (e.g., non-study medical records)
- Other source documents (e.g., site-specific worksheets)

**As a condition for study activation, the study site must establish an SOP for Source Documentation that specifies the source documents for all study procedures.** To establish consistency in source documentation, the source for specific study procedures will be specified in the site Source Documentation SOP. Supplemental information on the use of chart notes, visit checklists, and forms provided by the MTN SDMC or MTN LOC is provided below. Detailed information on proper completion, maintenance, and storage of product dispensing documentation is provided in Section 6 (Study Product Considerations for Non-Pharmacy Staff) of this manual and in the MTN-033 Pharmacy Study Product Management Procedures Manual. Detailed information on proper completion of CRFs is provided in Section 12 (Data Collection) of this manual.

### 2.3.1 Chart Notes

Study staff must document every contact with a study participant in a signed and dated chart note or contact log specifying the following information:

- Visit date at which a contact takes place or at which a particular procedure takes place
- Visit type (scheduled, interim, etc.)
- Purpose of the visit and location of the contact if other than the research clinic
- General status of the participant at the time of the visit

Chart notes should also be used to document the following:

- The informed consent process (if an Informed Consent Coversheet is not used)
- Procedures performed that are not recorded on other source documents (e.g. visit reminder phone calls, emails etc.)
- Additional information related to clinical exam findings to ensure appropriate follow-up
- Study-specific counseling sessions and/or other in-depth discussions with participants (e.g., related to adherence to protocol requirements, if not documented on other worksheets)
- Other pertinent data about the participant that are not recorded on other source documents and/or any clarifications or information needed to supplement data recorded on a CRF
- Reason(s) why protocol-specified procedures were not performed
- Explanation of why procedures in addition to those listed on a checklist were performed
- Contact attempts to follow up on participants who missed a scheduled study visit

### 2.3.2 Visit Checklists

Checklists are convenient tools, which may serve as source documentation if designed and completed appropriately. These checklists alone may not be sufficient for documenting all procedures but can be used to indicate that the procedure was completed. Chart notes may be required to supplement this for any of the reasons mentioned above. Visit Checklist templates are available on the MTN-033 website under Study Implementation Materials.

Instructions for completing visit checklists in accordance with these requirements are as follows:

- Enter the participant identification number (PTID), visit date and code on the top section of each checklist page.

- The “Required at Visits” column indicates when the item is required per-protocol. Complete staff initials next to procedures completed.

- Staff are only to initial beside procedures that they themselves perform; not beside procedures performed by other staff members. If other staff members are not available to initial procedures that they performed, staff completing the checklist can initial and date a note on the checklist documenting who completed the procedure, e.g., “done by {name}” or “done by nurse.”

- If all procedures listed on a checklist are performed on the date entered in the top section of the form, the date need not be entered beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date that each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable.

- If a procedure listed on the checklist is not performed, enter “ND” for “not done” or “NA” for “not applicable” beside the item and record the reason why on the checklist or in chart notes; initial and date this entry.

The sequence of procedures presented on the visit checklists is a suggested ordering. In consultation with the MTN LOC (FHI 360), site staff are encouraged to modify the checklists to maximize the efficiency of site-specific study operations. Sites may alter the sequence of procedures, with the following exceptions:

- Informed consent must be obtained before any study procedures are performed. Study visit procedures are listed in protocol Sections 7.2 – 7.9.

- On the day of enrollment, randomization assignment must take place after final confirmation and verification of eligibility, administration of the Baseline Computer Assisted Self-Interview (CASI) Questionnaire and collection of blood for plasma archive. If a participant is subsequently found to be ineligible and is not randomized, the plasma archive sample should be destroyed.

- Genital and rectal exam procedures must be performed in the sequence shown on the Genital Exam Checklist.

- During follow-up visits, CASI questionnaires should be administered prior to the delivery of HIV and adherence counseling.

Note:

- It is recommended that procedures for determining eligibility for continued product use be conducted early in the visit in the event that the participant needs to abruptly leave the clinic or is short of time.

### 2.3.3 Laboratory

Each lab test must have a defined source document which is the first place the result is recorded or generated. The site laboratory will have a plan for the storage of these documents so that they are easily retrievable.

### 2.3.4 Case Report Forms (CRFs)

See SSP Section 12 (Data Collection) for further details regarding the use of case report forms (CRFs) with the Medidata Rave data management system. CRFs have been designed to be used as source whenever possible. Prior to study activation, **the study site will document the CRFs used as source as well as which CRFs are not used as source (e.g., Specimen Storage CRF) in its SOP for Source Documentation.** The specifications of this SOP must be followed consistently for all study participants. If study staff are not able to record data directly onto forms designated as source documents, the following procedures should be undertaken:

- Record the data onto an alternative source document
- File the alternative source document into the participant's study chart
- Transcribe the data from the alternative source document onto the appropriate form and enter a note on the form stating the alternative source document used
- Write a chart note stating the relevant study visit date and the reason why an alternative source document was used

### 2.3.5 Document Organization and Participant Confidentiality

Study staff must make every effort to store all study records securely and confidentially. Case history records must be stored in the same manner for all participants, in areas with access limited to authorized study staff only. Study staff are responsible for purchasing file folders, binders, storage cabinets, and any other equipment or supplies needed to properly store all records.

Study-related documentation collected during the screening process should be stored in file folder/binders for each potential participant. All screening documentation — for potential participants who eventually enroll in the study as well as for those who do not enroll or "screen out" — must be maintained and available for monitoring throughout the study. This documentation also must be available for reference should participants present to the site for re-screening. For participants who enroll in the study, screening documentation should be transferred to a separate file folder/binder that will serve as the participants' study notebook for the duration of their participation in the study.

All documents contained in participant case history records must bear a participant identifier, which generally will consist of either the participant identification number (PTID) or the participant name. The PTID should be used whenever possible to maximize participant confidentiality. Records that bear names or other personal identifiers, such as locator forms and informed consent forms, should be stored separately from records identified by PTID. Care should also be taken to only refer to participants by PTID in email communication when people outside of the CRS are included.

Regardless of whether the identifier on a particular document consists of the participant name or PTID, the original identifier may not be obliterated or altered in any way, even if another identifier is added. When necessary to maintain confidentiality, identifiers may be obliterated on copies of original source documents. For example, if medical records obtained from a non-study health care provider bear the participant's name, the original documents bearing the name must be stored unaltered with other study documents bearing the name. However, a copy of the original documents could be made, the PTID could be entered onto the copies, and then the participant name could be obliterated from the copies. Copies handled in this way could then be stored in participants' study notebooks and/or transferred or transmitted to non-study site locations.

All on-site databases and CASI questionnaire data must be secured with password protected access systems. Any lists, appointment books, or other documents that link PTIDs to other participant identifiers should be stored securely (locked cabinet/drawer if hard copy; password protected if electronic) and in a location separate from records identified by participant name only and separate from records identified by PTID only. When in use, documents that link PTIDs to other participant identifiers should not be left unattended or otherwise accessible to study participants, other study clinic patients, or any other unauthorized persons.

### 2.3.6 Study Product Accountability, Chain of Custody, and Dispensing Documentation in the Pharmacy

Pharmacy staff will document the receipt and dispensing of each study product, and return/destruction of each unused study product. Separate accountability records must be maintained for each lot of product, per instructions provided in the MTN-033 Pharmacy Study Product Management Procedures Manual available from the MTN Pharmacist.

Study clinic staff will contribute to the documentation of product provision and chain of custody as described in Section 6 (Study Product Considerations for Non-Pharmacy Staff) of this SSP manual.

The specifications related to document security and participant confidentiality described in Section 2.3.5 above also apply to records maintained in the study site pharmacy. All records must be stored securely in the pharmacies with access limited to authorized study pharmacy staff only.

The following essential documents should be maintained in the study site pharmacy:

- Current MTN-033 Protocol
- Investigator Brochure for dapivirine Gel (0.05%): current version and any subsequent updates
- Current FDA Form 1572
- Current list of authorized prescribers and staff authorized to sign Prescriptions, Gel Request Slips (names and signatures)
- Pharmacy Establishment Plan (MTN Director of Pharmacy Affairs Approved)
- MTN-033 Pharmacy Study Product Management Procedures Manual and applicable SOPs for investigational study product management and product Chain of Custody
- MTN-033 product shipping and receipt documentation, product storage temperature logs, and investigational product accountability records
- MTN-033 participant-specific records (including study prescriptions and request slips, study product accountability record, records of receipt of participant study product and documentation of unused product returns)
- MTN-033 monitoring visit reports
- MTN-033 communications with site clinic staff, communications with the MTN Pharmacist, MTN LOC and/or the MTN SDMC or other MTN-033 communications or locally-required administrative, operational, and/or regulatory documentation

## 2.4 Record Retention Requirements

All study records must be maintained for at least two years following the date of marketing approval for the study product for the indication in which they were studied. If no marketing application is filed, or if the application is not approved, records must be retained for two years after the US Food and Drug Administration is notified that the Investigational New Drug application for the product(s) is discontinued.

All records must be retained on-site throughout the study's period of performance, and for at least three years after completion or termination of the study. Study product records must be stored in the site pharmacy. DAIDS will provide further instructions for long-term storage of study records after the study is completed. Study records should not be re-located to an off-site location or destroyed without prior approval from DAIDS.

## 2.5 Protocol Deviations

In addition to the above, DAIDS requires that all protocol deviations be documented in participant records, along with efforts made to correct the deviations, and efforts made to prevent similar deviations in the future. The MTN Manual of Operational Procedures should be referenced for complete guidance on protocol deviations. All protocol deviations are to be reported within 7 days.

For MTN-033 the Protocol Deviation (PD) Log CRF will be used to document each protocol deviation identified. Missed visits are considered protocol deviations per the MTN policy, however, these will *not* be captured on the PD Log CRF for MTN-033 (the Missed Visit CRF will capture this information instead).

Corrective and preventive action plans are required components of protocol deviation documentation. Note that the corrective and preventive action plans documented on the PD Log CRF are not required to be completed in order to report the deviation. The PD Log CRF should be completed, even if all the action plans are pending or in progress. It is important to ensure that documentation includes any associated counseling that was done to address the protocol deviation (e.g., counseling on the importance of retention for missed visit deviations, or reviewing the list of prohibited concomitant medications or other products, etc.).

If there is any question as to whether a deviation has occurred, or how it should be documented, the MTN Regulatory Department (mtnregulatory@mtnstopshiv.org) and MTN-033 Management Team (mtn033mgmt@mtnstopshiv.org) should be contacted. Once the potential protocol deviation has been confirmed, the site will be contacted with this confirmation and the 7-day reporting requirement will begin. Once the CRF is submitted, the MTN Regulatory Department will follow up with the site if any clarifications or additional information on the CRF is needed. The study management team will follow up with the site regarding any next steps as needed.

Note: Some protocol deviations will also be considered critical events. Refer to the DAIDS Critical Event Policy and Critical Event Manual for detailed guidance on the definition of critical events and reporting process. These documents can be accessed on the MTN Website under *Resources and Links* (http://www.mtnstopshiv.org/node/4535*)*. The site OCSO Program Officer should be contacted with any questions related to critical events.

It is recommended that the site report in an expedited manner to IRBs/ECs PDs that pose a potential safety risk to a participant(s) and those that could affect the integrity of the study according to the local IRB's/EC's standard operating procedures and guidelines. It is also recommended that a complete list of all PDs occurring at the site, including PDs not meeting immediate reporting standards noted above, be submitted to the local IRBs/ECs in accordance with their reporting policies. If a local IRB/EC does not have a specific reporting policy, MTN recommends that this be done at the time of IRB renewal submission, annually or semi-annually per local requirements. These listings will be provided to the sites on request. If needed, the site should request these PD listings from SCHARP at least two weeks prior to the planned date of submission to their local IRBs/ECs.