Section 2. Documentation Requirements

Table of Contents

Study staff members 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 each study site must maintain throughout the study. It also contains information related to establishing adequate and accurate participant research records for MTN-017.

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 that study sites must maintain including MTN-017. 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 documents filing structure is available on the MTN-017 Webpage under Study Implementation Materials. Study sites are not required to adopt the suggested structure but are encouraged to consider it when developing their 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 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 site pharmacies. A listing of essential documents to be maintained in the pharmacies is provided in Section 2.3.
- 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 site laboratories.

- The suggested filing structure assumes that MTN-017 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-017 PTID-Name Linkage Log, and Randomization Envelope Tracking Record must be maintained in hard-copy throughout the duration of the trial unless an electronic system is CFR Part 11 compliant. 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

Study sites must maintain adequate and accurate participant research records containing all information pertinent to MTN-017 for each study participant. See protocol section 11.2 for further information regarding all participant information which should be stored in locked file cabinets with access limited to authorized study staff.

2.1.1 Concept of Source Data and Source Documentation

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. All study sites 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. Study sites must comply with all requirements and are encouraged, but not required, to comply with all recommendations. This document can be accessed on the MTN-017 webpage under Study Implementation Materials.

2.1.2 Required Source Documentation

For MTN-017, participant research records should consist of the following source documents:

- Chart notes
- Documentation that the participant provided written informed consent to screen for and participate in the study prior to the conduct of any screening or study procedures, respectively
- Documentation that the participant met the study's eligibility criteria
- Randomization tracking records documenting participants' random assignments

- Prescription documentation
- A record of the participant's use of the investigational study products
- Pharmacy investigational product dispensing and chain of custody records (maintained in the study site pharmacy), as well as 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 other as defined as a source document for a test result.
- DataFax and Non-DataFax 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, each study site must establish an SOP for Source Documentation that specifies the source documents for all study procedures. To establish consistency in source documentation across sites the source for specific study procedures has been specified in Appendix 2-1. Supplemental information on the use of chart notes, visit checklists, and forms provided by the MTN SDMC is provided below. Detailed information on proper completion, maintenance, and storage of participant randomization and product dispensing documentation is provided in Sections 7 of this manual, and the MTN-017 Pharmacist Study Product Management Procedures Manual. Detailed information on proper completion of CRFs is provided in Section 11 of this manual.

2.1.2.1 Chart Notes

Study staff must document every contact with a study participant in a signed and dated chart note or contact log. This is especially important when the following information is necessary to document adherence to protocol requirements:

- Visit date at which a contact takes place or at which a particular procedures 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 also should be used to document the following:

- The informed consent processes (if an Informed Consent Coversheet is not used)
- Procedures performed that are not recorded on other source documents
- 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
- Reason(s) why protocol-specified procedures were not performed

- Explain 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 and/or to retrieve unreturned study product

2.1.2.2 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-017 website under Study Implementation Materials.

2.1.2.3 Laboratory

Each lab test must have a defined source document which is the first place the result is recorded or generated. Site laboratories will have a plan for the storage of these documents so that they are easily retrievable. See SSP Section 10 for more information on source documentation requirements for the lab.

2.1.2.4 Case Report Forms (CRFs)

The case report forms (CRFs) for this study are designed for use with the DataFax data management system described in Section 11 of this manual. As shown in Appendix 2-2, CRFs have been designed to be used as source whenever possible. Prior to study activation, **each study site will document the CRFs used as source as well as which CRFs are not used as source in its SOP for Source Documentation.** The specifications of this SOP must be followed consistently for all study participants. In the event that 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 alternate source document used
- Write a chart note stating the relevant study visit date and the reason why an alternative source document was used

2.1.3 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.

For MTN-017 the Protocol Deviation Log CRF will be used to document each protocol deviation, with the exception of missed visits. The Protocol Deviation Log CRF is completed and faxed to the SDMC for each reportable deviation identified, including deviations related to participant non-adherence to study product use. Like all CRFs, completed Protocol Deviation Log CRFs will be filed in the participant's study binder. Missed visits are considered protocol deviations per the MTN policy, however these will *not* be captured on the Protocol Deviation Log CRF for MTN-017 (the Missed Visit CRF will capture this information instead).

Note: Participant non-adherence to product use is defined in MTN-017 as non-use of study product (no pills taken or applicators used) by the participant between the Initiate and Mid-Period visits or between the Mid- and End-Period visits. Non-use of study product is determined based on conversation with the participant during the Data Convergence Interview. If the interviewer's best estimate of the actual number of doses of study product the participant used since his/her last regularly scheduled visit equals '00', a protocol deviation must be reported.

Note: Partial use of study product, regardless of the amount of study product missed, is NOT considered a protocol deviation but should be discussed with the participant during the product adherence counseling and appropriately documented; see section 6 of this manual for further information. A product hold or permanent discontinuation initiated due to safety concerns is also not considered a protocol deviation.

Corrective and preventive action plans are required components of protocol deviation documentation. 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 and MTN-017 Management Team should be contacted. Once the potential protocol deviation has been confirmed, the site will be contacted with this confirmation and the 3 day reporting requirement will begin. Once the CRF is faxed, 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.

2.1.4 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 a file folder/binder 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 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. As a best practice, 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.

Note: 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.

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.

2.2 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 destruction of each unused study product. Separate accountability records must be maintained for each product, per instructions provided in the MTN-017 Pharmacist Study Product Management Procedures Manual available from the MTN Pharmacist.

Pharmacy staff also will maintain in the study pharmacies a Participant-Specific Pharmacy Dispensing Record for all enrolled study participants, per instructions in the MTN-017 Pharmacist Study Product Management Procedures Manual. Study clinic staff will contribute to the documentation of product dispensation and chain of custody as described in Section 7 of this manual.

The specifications related to document security and participant confidentiality described in Section 2.2.4 also apply to records maintained in the study pharmacies. 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 study site pharmacies:

- Current MTN-017 Protocol
- Investigator's Brochure for Tenofovir Gel (GS-1278): current version and any subsequent updates
- Package Insert for Truvada: current version and any subsequent updates
- Current FDA Form 1572
- Current list of authorized prescribers and staff authorized to sign Study Product Request Slips (names and signatures)
- Pharmacy Establishment Plan (MTN Director of Pharmacy Affairs Approved)
- MTN-017 Pharmacist Study Product Management Procedures Manual and applicable SOPs for investigational study product management and product Chain of Custody
- MTN-017 product shipping and receipt documentation, product storage temperature logs, and investigational product accountability records
- MTN-017 participant-specific records (including study prescriptions and request slips, participant-specific dispensing records, records of receipt of participant study product and documentation of unused product returns)
- MTN-017 monitoring visit reports

- MTN-017 communications with site clinic staff, communications with the MTN Pharmacist, CONRAD, GILEAD and TCG MTN-017 communications with the MTN LOC and/or the MTN SDMC or other MTN-017 communications or locally-required administrative, operational, and/or regulatory documentation

2.2.1 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 site pharmacies. 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.

2.3 Appendices

Section Appendix 2-1- Source Documentation of Study Procedures

Note that items in **bold are required source documents for listed study procedure/evaluation. Other source documents listed are recommended, but site should specify actual source document as needed in the Source Documentation SOP.

Evaluation/Procedure	Source Document(s)
ADMINISTRATIVE AND REGULATORY	
Assess and/or confirm eligibility	**Eligibility Criteria CRF** (item 1)
Assign a unique Participant Identification (PTID) number	**MTN-017 PTID-Name Linkage Log**
Collect/review/update locator information	Site locator documents (collect/update) Visit checklist (review)
Obtain informed consent	**Signed and Dated Informed Consent form** **Informed Consent Coversheet** (or chart note) **Informed Consent Comprehension Checklist**
Provide reimbursement	Visit checklist, site-specific reimbursement log, and/or chart note
Randomization	**MTN-017 Randomization Document**
Schedule next visit	Visit checklist and/or chart note
BEHAVIORAL	
Assessment of product acceptability, sexual behavior, and anorectal/rectal practices	**CASI Baseline and Follow-up Questionnaires** CASI completion documented on: **Enrollment and Follow-up Visit Summary CRFs**
HIV pre- and post-test counseling	Chart note and/or site-specific counseling worksheet
HIV/STI risk reduction counseling	Chart note and/or site-specific counseling worksheet
In-depth phone interview	**Visit checklist**
Product adherence assessment and counseling	**CASI Baseline and Follow-up Questionnaires, SMS diary/calendar, Product Dispensation and Return CRF (product counts as marker of adherence), Data Convergence Interview and PK Data Convergence Interview non-DataFax CRFs**
Product use instructions	Visit checklist, chart note, and/or site-specific counseling worksheet
Protocol adherence counseling	Chart note and/or site-specific counseling worksheet
Rectal biopsy/Fluid procedural counseling (where applicable)	Chart note and/or site-specific counseling worksheet
Social harms assessment	**Social Impact Log CRF** (source for actual event) Chart Note
CLINICAL	
Anal and Rectal exam	**Anorectal Exam CRF** (source for exam completion and documentation of abnormal findings), chart notes, visit checklist
Concomitant medications	**Concomitant Medications Log CRF and Rectal Practices CRF**
Disclose available test results	Chart note and/or visit checklist
Medical history	**Pre-existing Conditions CRF** (all baseline conditions including clinical evaluations will be summarized here) **Adverse Experience Log CRFs**

	Source documentation for participant reported medical history: **MTN-017 Baseline Medical History Questions** Chart Notes
Physical examination	**Abbreviated Physical Exam CRF**
Record/update AEs	**Adverse Experience Log CRFs** and Chart notes
Treat or prescribe treatment for UTIs/RTIs/STIs or refer for other findings	Chart notes , prescription and/or Referral Letter
LABORATORY	
CBC with platelets	Site-specific lab requisition form Lab result report
Chemistries	Site-specific lab requisition form Lab result report
Coagulation (PT/INR)	Site-specific lab requisition form Lab result report
HBsAb	Site-specific lab requisition form Lab result report
HBsAg	Site-specific lab requisition form Lab result report
Hepatitis C antibody	Site-specific lab requisition form Lab result report
HIV-1 Serology	Site-specific lab requisition form Site testing log/results report (rapids) Lab result report (WB/HIV RNA)
HSV 1/2 antibody	Site-specific lab requisition form Lab result report
HSV 1/2 detection – Rectal Swab	Site-specific lab requisition form Lab result report
NAAT for GC/CT – Rectal Swab	Lab requisition form (at sites with capacity) Lab result report
NAAT for GC/CT - Urine	Site-specific lab requisition form Lab result report
Real-time plasma and PBMC PK	Site-specific lab requisition form JHU results spreadsheet
Syphilis rapid plasma reagin (RPR)	Site-specific lab requisition form Lab result report
Urine culture	Site-specific lab requisition form Lab result report
Plasma archive	Enrollment CRF
Plasma for storage	HIV Results CRF
STUDY PRODUCT/ SUPPLIES	
Provision of study-specified condoms	Site-specific counseling worksheets, visit checklist, or chart notes
Provision of study-specified lubricants	Site-specific counseling worksheets, visit checklist, or chart notes
Provision of study tablet or gel instructions	Chart notes or Visit checklist or site-specific counseling worksheet
Provision of study product	Participant-specific Dispensing Record, Product Dispensation and Return CRF, AND visit checklist or chart notes
OTHER	
Protocol Deviations	**Protocol Deviation Log CRF**

A record of all contacts, and attempted contacts, with the participant	Missed Visit CRF Site-specific contact/outreach/retention logs and/or chart notes
A record of all procedures performed by study staff during the study	Visit checklists, chart notes, and/or other site-specific flow sheets
Participant Demographics	**Demographics CRF**
Staff-initiated Study Product Holds and Permanent Discontinuations	**Clinical Product Hold/Discontinuation Log CRF**

Section Appendix 2-2 - CRFs Used as Source Documents

Unless otherwise noted in the Comments column, the CRF may be used as source for all form items.

CRF Name	CRF Acronym	Comments
Abbreviated Physical Exam	APX-1	
Adverse Experience Log	AE-1	
Anorectal Exam	ARE-1	
Clinical Product Hold/Discontinuation Log	PH-1	
Concomitant Medications Log	CM-1	
Data Convergence Interview	N/A	Form is source for items 1a-2 and 7-8. Form may be source for item 6.
Demographics	DEM-1	
Eligibility Criteria	ECI-1	Screening and Enrollment Log may be source for all items except item 1.
Enrollment	ENR-1	Form may be source for items 2c1 and 8-9a.
Enrollment Behavioral Eligibility	N/A	
Follow-up Visit Summary	FVS-1	Form may be source for items 1-3a and 7-7a1.
Follow-up CASI Tracking	FCT-1	
HIV Confirmatory Results	HCR-1	Form may be source for item 5
Missed Visit	MV-1	
Participant Transfer	PT-1	
PK Data Convergence Interview	N/A	Form is source for items 3-4.
Pre-existing Conditions	PRE-1	
Product Dispensation and Return	PDR-1	Form may be source for items 1b-1d, 1f-1i, and 2d.
Protocol Deviation Log	PDL-1	
Rectal Biopsy/Fluid Subset Specimens	RBF-1	Form may be source for items 3-3a.
Rectal Practices	RP-1	
Safety Laboratory Results	SLR-1-2	Form may be source for items 3-3d, and all Severity Grade and AE items.
Screening Behavioral Eligibility	N/A	
Social Impact Log	SIL-1	
Termination	TM-1	

Section Appendix 2-3 - CRFs Not Used as Source Documents

CRF Name	CRF Acronym	Comments
End of Study Inventory	ESI-1	All items are administrative and based on completion of other CRFs.
HIV Results	HIV-1	Site testing logs/lab result reports are source for items 1-3. Visit checklist or lab requisition form is source for items 4-4a.
Participant Receipt	PRC-1	The informed consent form at the receiving site is source for items 1 and 3-4c. The informed consent form at the transferring site and the Participant Transfer CRF are source for item 2.
Specimen Storage	SS-1	Visit checklist or lab requisition form is source.
STI Test Results	STI-1	Site testing logs/lab result reports are source.