

Section 2. Documentation Requirements

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Study staff members are responsible for the 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-029/IPM 039.

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. 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-029/IPM 039 webpage. The suggested filing structure assumes that participant research records will be stored separately from the other essential documents. Section 2.2 below provides information on the required contents of these records. Study sites are not required to adopt this filing 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, which may be 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.
- Certain documents related to the investigational study products 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 standard operating procedures [SOPs]) may be filed in site laboratories.
- The MTN-029/IPM 039 PTID-Name Linkage Log and Screening and Enrollment Log must be maintained in hard copy throughout the duration of the trial. 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

MTN-029/IPM 039 study sites must maintain adequate and accurate participant research records containing all information pertinent to each study participant. See protocol section 13.6 for further information regarding confidentiality of participant information; participant charts should be stored in locked file cabinets with access limited to authorized study staff.

2.2.1 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 and enrollment 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.

2.2.2 Required Source Documentation

For MTN-029/IPM 039, 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
- Documentation that the participant met the study's eligibility criteria
- Prescription documentation
- A record of the participant's use of the investigational study product

- 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 any other document 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, logs)

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 recommended 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 product dispensing documentation is provided in SSP Section 6 and in the MTN-029/IPM 039 Pharmacy Study Product Management Procedures Manual. Detailed information on proper completion of CRFs is provided in SSP Section 11.

2.2.2.1 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 when necessary to document adherence to protocol requirements:

- 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 screening and enrollment informed consent process (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 any associated referrals that are not documented on other source documents
- 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
- Contact attempts to follow up on participants who missed a scheduled study visit

2.2.2.2 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.

2.2.2.3 Case Report Forms (CRFs):

See SSP Section 11 for further details regarding the use of case report forms (CRFs) with the DataFax data management system. 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 is 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

2.2.3 Protocol Deviations

Sites will follow the DAIDS requirements for Protocol Deviations. DAIDS requires that all protocol deviations be documented in participant records, along with efforts made to correct and prevent similar deviations in the future. The MTN Manual of Operational Procedures should be referenced for complete guidance on protocol deviations.

For MTN-029/IPM 039 the Protocol Deviation (PD) Log CRF will be used to document each protocol deviation. Like all CRFs, completed PD Log CRFs are faxed to DF/Net and 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 PD Log CRF. The Missed Visit CRF will capture this information instead.

Protocol deviations related to study product non-adherence will be completed if a participant reports 24 hours or more of non-product use during follow-up. Sites should document when the non-use occurred, in relation to PK sampling visits, in the notes section of the PD Log CRF.

Corrective and preventive action plans are required components of protocol deviation documentation. It is important to ensure that chart notes or other source documents include any associated counseling that was done to address the protocol deviation (e.g. counseling on the importance of retention for missed visit deviations). Note that the corrective and preventive actions must be documented, but are not required to be completed, prior to reporting the deviation to SCHARP. The Protocol Deviation Log page should be transmitted to SCHARP once the CRF is completed, even if all of the actions/plans are still in-progress.

Protocol deviations should be reported within 7 days of site awareness. If there is a question as to whether a deviation has occurred, or how it should be documented, the MTN Regulatory Department and the study Management Team should be contacted at mtnregulatory@mtnstopshiv.org and mtn029mgmt@mtnstopshiv.org. 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 faxed, the MTN Regulatory Department will follow up with the site if any clarifications or additional information on the CRF is needed.

It is recommended that all PDs occurring at the site be submitted to the local IRBs/ECs in accordance with their reporting policies. Some PDs may need to be reported in real time (e.g. those with a potential impact on participant safety) while others can be submitted as part of a summary listing at a later date. If a local IRB/EC does not have a specific reporting policy, the

MTN recommends that a full listing of study protocol deviations be submitted at the time of IRB renewal submission, annually or semi-annually per local requirements. These listings may be provided by the MTN SDMC to the sites upon request.

Note that some protocol deviations may 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.

2.2.4 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 is 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. Any documents transferred or transmitted to a non-study site location — including DataFax forms— must be identified by PTID only. Care should also be taken to only refer to participants by PTID in email communication when people outside of the site 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 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). 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 Study Product Accountability, Chain of Custody, and Dispensing Documentation in the Pharmacy

Pharmacy staff will document the receipt and dispensing of each vaginal ring and the return/destruction of each unused vaginal ring on the MTN-029/IPM 039 Pharmacy Vaginal Ring Accountability Record. Separate accountability records must be maintained for each lot of product, per instructions provided in the MTN-029/IPM 039 Pharmacy Study Product Management Procedures Manual available from the MTN LOC Pharmacist.

Study clinic staff will contribute to the documentation of product provision and chain of custody as described in SSP Section 6.

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-029/IPM 039 Protocol
- Investigator's Brochure for Dapivirine Vaginal Ring: current version and any updates
- Current FDA Form 1572
- Current list of authorized prescribers and staff authorized to sign Prescriptions and Vaginal Ring Request Slips (names and signatures)
- Pharmacy Establishment Plan (DAIDS PAB approved or MTN LOC Pharmacist approved)
- MTN-029/IPM 039 Pharmacy Study Product Management Procedures Manual and applicable SOPs for investigational study product management and Chain of Custody
- MTN-029/IPM 039 product shipping and receipt documentation, product storage temperature logs, and investigational product accountability records
- MTN-029/IPM 039 participant-specific records (including prescriptions and ring request slips, record of receipt of participant study product and documentation of unused product returns)
- MTN-029/IPM 039 monitoring visit reports
- MTN-029/IPM 039 communications with site clinic staff, communications with the MTN Pharmacist, IPM Clinical Supply Coordinator and/or product distributor
- MTN-029/IPM 039 communications with site clinic staff, IPM, the MTN LOC, and/or the MTN SDMC or other 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 site pharmacies, with access limited to authorized study pharmacy staff only. 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.

Section Appendix 2-1: Source Documentation of Study Procedures

<u>Evaluation/Procedure</u>	<u>Source Document(s)</u>
ADMINISTRATIVE AND REGULATORY	
Obtain informed consent	Signed and Dated Informed Consent form Informed Consent Coversheet (or chart note) Informed Consent Comprehension Checklist
Assign a unique Participant Identification (PTID) number	MTN-029/IPM 039 PTID-Name Linkage Log
Collect demographic information	Demographics CRF
Assess and/or confirm eligibility	Eligibility Criteria CRF (item 1) Screening Behavioral Worksheet Enrollment Behavioral Worksheet Eligibility Checklist
Collect/review/update locator information	Site locator document (collect/update) Visit checklist
Provide reimbursement	Visit checklist, site-specific reimbursement log, and/or chart note
Schedule next visit	Visit checklist and/or chart note
BEHAVIORAL	
Protocol adherence counseling	Chart note, site-specific counseling worksheet or Adherence Counseling Worksheet
Breast milk production maintenance counseling	Chart note, site-specific counseling worksheet or Adherence Counseling Worksheet
HIV pre- and post-test counseling	Chart note, site-specific counseling worksheet or HIV Counseling Worksheet
Sexual practices assessment	Sexual Practices Assessment CRF
Product adherence assessment	Participant Ring Use Log CRF Ring Insertion and Removal CRF
Social harms assessment	Chart Note
CLINICAL	
Medical history	Pre-existing Conditions CRF (all baseline conditions including clinical evaluations will be summarized here) Adverse Experience Log CRF (all follow-up conditions including abnormal findings from clinical evaluations) MTN-029/IPM 039 Baseline Medical History Questions, Follow-up Medical History Log, and Chart Notes
Concomitant medications	Concomitant Medications Log CRF
Physical examination	Physical Exam CRF
Pelvic exam	Pelvic Exam Diagrams Pelvic Exam CRF
Breast exam	Breast Exam CRF
Disclose available test results	Chart note and/or visit checklist
Record/update AEs	Adverse Experience Log CRF Chart note
Treat or prescribe treatment for UTIs/RTIs/STIs or refer for other findings	Chart notes, prescription and/or referral documentation
LABORATORY	
hCG	Site-specific lab requisition form Site testing log/results report
Dipstick UA/Urine culture (if indicated)	Site-specific lab requisition form Lab result report
Urine NAAT for GC/CT (if indicated)	Site-specific lab requisition form Lab result report

HIV-1 Serology	Site-specific lab requisition form/ Site testing log/ Lab result report/ Laboratory Results CRF
AST/ALT	Site-specific lab requisition form/Lab results report/ Laboratory Results CRF
Syphilis serology	Site-specific lab requisition form/ Site testing log/ Lab result report
Plasma archive	Enrollment CRF or LDMS Specimen Tracking Sheet
Blood (for PK)	Enrollment PK/PD CRF and Follow-up PK/PD CRF - or site-specific lab requisition - or LDMS Specimen Tracking Sheet
Rapid test or Gen-Probe Aptima test for Trichomonas	Site-specific lab requisition form/ Lab result report Site testing log/ STI Test Results CRF
Cervical NAAT for GC/CT	Site-specific lab requisition form/ Lab result report Site testing log/ STI Test Results CRF
Herpes culture (if indicated)	Site-specific lab requisition form/ Lab result report Site testing log/results report
Vaginal pH (if indicated)	Site testing log/results report, chart note, visit checklist or Pelvic Exam CRF
KOH wet mount for candidiasis (if indicated)	Site testing log/results report/ Lab result report
Saline wet mount for BV (if indicated)	Site-specific lab requisition form/ Lab result report Site testing log/results report
Vaginal quantitative culture	Vaginal Specimen Storage CRF or site-specific lab requisition or LDMS Specimen Tracking Sheet
Gram stain	Vaginal Specimen Storage CRF or site-specific lab requisition or LDMS Specimen Tracking Sheet
Pap smear	Site testing log/results report/ Lab result report
Vaginal fluid (CVF for PK)	Enrollment PK/PD CRF and Follow-up PK/PD CRF - or site-specific lab requisition - or LDMS Specimen Tracking Sheet
Vaginal swab for biomarkers	Vaginal Specimen Storage CRF or site-specific lab requisition or LDMS Specimen Tracking Sheet
Breast milk samples for anti-viral activity, PK, and lipids	At-home Breast Milk Sampling Log CRF; Enrollment PK/PD CRF and Follow-up PK/PD CRF - or site-specific lab requisition - or LDMS Specimen Tracking Sheet
STUDY PRODUCT/ SUPPLIES	
Provision of study VR instructions	Chart notes or visit checklist or site-specific counseling worksheet
Provision of one study VR for insertion with white zip bag	Enrollment CRF, Ring Insertion and Removal CRF Clinic Study Product Accountability Log Chart Note and/or Visit Checklist
Exam(s) by clinician to check VR placement	Chart note or Visit checklist
Collection of used study VR	Vaginal Specimen Storage CRF Clinic Study Product Accountability Log
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
Staff-initiated Study Product Holds and Permanent Discontinuations	Clinical Product Hold/Discontinuation Log CRF and/or chart notes

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

Section Appendix 2-2: DataFax Forms Used as Source Documents

Form Name	Acronym	Is Form Source?	Comments
Adverse Experience Log	AE	Mixed	Follow-up Medical History Log may be source for some items (site to specify which items)
At-home Breast Milk Sampling Log	AHB	No	Participant Breast Milk Collection Log is source for data recorded by participant. Otherwise, data recorded on breast milk collection container labels is source.
Baseline Menstrual History	BMH	Mixed	Baseline Medical History Questions Sheet is source for items 1-3. Form may be source for item 4.
Breast Exam	BE	Yes	
Clinical Product Hold/Discontinuation Log	PH	Yes	
Concomitant Medications	CM	Yes	
Demographics	DEM	Yes	Form is interviewer-administered and all items must be source.
Eligibility Criteria	ECI	Mixed	Form may be source for items 1 and 2. All other items are based on source data recorded on other documents.

Form Name	Acronym	Is Form Source?	Comments
Enrollment	ENR	No	The informed consent form should be source for items 1 and 2. Form may be source for item 3 (or lab requisition or LDMS Tracking Sheet). This form may be source for items 4 and 5.
Enrollment PK/PD	EPK	[Yes]	Form or LDMS Specimen Tracking Sheet may be source.
Follow-up PK/PD	FPK	[Yes]	Form or LDMS Specimen Tracking Sheet may be source.
Follow-up Visit Summary	FVS	No	All items should be completed based on source data recorded on other source documents.
HIV Confirmatory Results	HCR	Mixed	Local laboratory reports are source for items 1 and 2. Form may be source for item 3.
Laboratory Results	LR	No	Local laboratory reports are source.
Missed Visit	MV	Yes	
Participant Ring Use Log	PRU	No	The MTN-029 Participant Ring Use Log completed by the participant is source for all items, if available. Otherwise, items completed based on participant self-report are considered source.
Pelvic Exam	PE	Mixed	Form is source for Item 1. Pelvic Exam Diagrams is source for item 2. The AE Log CRF is source for item 3.
Physical Exam	PX	Yes	

Form Name	Acronym	Is Form Source?	Comments
Pre-existing Conditions	PRE	No	All items should be completed based on source data recorded on other source documents.
Pregnancy and Lactation History	PLH	No	Baseline Medical History Questions Sheet is source.
Pregnancy Outcome, pages 1 and 2	PO-1,2	Mixed	Form may be source for all items or source may be medical records, if available. Supplemental information may also be recorded in chart notes.
Pregnancy Report	PR	Yes	Form is source for all items. Supplemental information also may be recorded in chart notes.
Protocol Deviation Log	PDL	Yes	Form is source for all items. Supplemental information also may be recorded in the chart notes.
Ring Insertion and Removal	RIR	Yes	Form may be source for all items.
Sexual Practices Assessment	SPA	Yes	Form is interviewer-administered and must be source.
STI Test Results	STI	Mixed	Form may be source for item 1. Local laboratory reports are source for items 2-9.
Termination	TM	Yes	
Vaginal Practices	VP	Yes	Form is interviewer-administered. All items must be source.
Vaginal Specimen Storage	SS	Mixed	Form may be source for item 3a. Form or LDMS Specimen Tracking Sheet may be source for all other items.

Section Appendix 2-3: Non-DataFax Forms Used as Source Documents

Form Name	Is Form Source?	Comments
Baseline Medical History Questions	Yes	Form is source for all items.
Eligibility Checklist	No	All items are based on source data recorded on other documents.
Screening Behavioral Eligibility Worksheet	Yes	Form is source for all items.
Enrollment Behavioral Eligibility Worksheet	Yes	Form is source for all items.
LDMS Specimen Tracking Sheet	[Yes]	The LDMS sheet may serve as source to document which specimens were collected, at what time, and on what date. The sheet is also source for specimen weights.
Pelvic Exam Diagrams	Yes	Form is source for all normal and abnormal findings observed during pelvic exams.
Local Site-specific Testing Logs (e.g., HIV, Pregnancy, Urinalysis, Trichomonas, GC/CT, etc.)	Yes	
Local Site-specific Visit and Pelvic Exam Checklists	Yes	Checklists are source to document which procedures were completed
Counseling Checklists (HIV Pre/Post Test and Risk Reduction Counseling worksheet, Breast Milk Production Maintenance Counseling)	Yes	Checklists are source for protocol-specified counseling