Section 12. Data Collection

The purpose of this document is to provide site staff with the information they need to successfully complete and submit MTN-026 case report forms. For questions about this section or about general data collection policies, procedures, or materials, please contact the SCHARP Clinical Data Manager for the study as listed below.

The SDMC (Statistical and Data Management Center) for this study is SCHARP (the Statistical Center for HIV/AIDS Research and Prevention). SCHARP is located in Seattle, USA, and is in the US Pacific Time (PT) time zone. The SCHARP MTN-026 team members, along with their job role and e-mail address, are listed below.

MTN-026 Statistical and Data Management Center (SDMC) Staff

Job Role	Name	Email Address
Protocol Statistician	Elizabeth Brown	erbrown@fredhutch.org
Clinical Data Manager	Melissa Peda	mapeda@scharp.org
Statistical Research Associate	Holly Gundacker	hgundack@scharp.org
Clinical Programmer	Jackie Fitzpatrick	jackie@scharp.org
Clinical Safety Associate	Ning Jiang	njiang2@scharp.org
Laboratory Data Coordinator	Anisa Tracy	actracy@scharp.org

12.1 Medidata Rave Overview

Medidata Rave is the data management system used by SCHARP to receive and manage study data collected at study sites. Each site completes study electronic case report forms (eCRFs) by entering data into the Medidata Rave study database. As specified in each site's Source Documentation SOP, data may be entered directly into the study database (i.e., eCRF is source), collected first on paper CRFs and then entered into the study database, and/or entered into the study database based on other non-CRF source documents (e.g., lab reports, testing logs, chart notes, etc.)

The MTN-026 study database in Medidata Rave may be accessed at www.imedidata.com.

When using Medidata Rave, the internet browser chosen and connectivity quality will be the most critical factors affecting functionality, as Medidata is accessed via a URL using a web browser. Users using outdated browsers will see a new warning banner on the log-in page of iMedidata. This warning will inform them that their browser does not support security features that are being implemented in future iMedidata releases and to upgrade their browser. Users will see this warning banner if they use any of the following browsers:

· Internet Explorer - Versions older than 8.0

· Chrome - Versions older than 30.0

- Firefox - Versions older than 24.0
- Safari - Versions older than 7.0
- Opera - Versions older than 17.0.

Each site's Data Management SOP designates the site staff members responsible for entering data into the study database. SCHARP grants designated site staff access with specific user permissions to the study database. They are required to complete eLearning modules in Medidata, as assigned by SCHARP, before access is granted and data can be entered into the study database. For more detailed information, see the iMedidata Access Guide, posted on the MTN-026 Atlas webpage: https://atlas.scharp.org/cpas/project/MTN/026/begin.view?.

Detailed guidance on data collection, entry, navigation and general use of Medidata Rave is provided in the Medidata Rave Electronic Data Capture (EDC) Training Manual, which is posted on the MTN-026 Atlas web page: https://atlas.scharp.org/cpas/project/MTN/026/begin.view?

Site staff should contact the study Clinical Data Manager with any questions related to study data collection and management. A representative from Medidata Solutions may be contacted (see contact information below) any time a site has technical questions or problems related to access or use of the Medidata Rave software.

For service in English

Toll-free
1-866-MEDIDATA (633-4328)

Direct number
1-973-659-6780

Toll-free fax
1-877-743-2350

Direct fax
1-973-954-5621

Email
helpdesk@mdsol.com

Hours
24 hours a day, 7 days a week

Data Entry/Quality Control
- Once an eCRF is completed and saved in the study database, the following may occur:
  - A system query may be automatically triggered in Medidata Rave (e.g., denoting incomplete or inconsistent data).
  - Review may be required for certain forms and/or fields by the SCHARP Clinical Data Manager and Clinical Safety Associate, and manual data queries may be placed.
  - Review may be required for certain forms and/or fields by the site monitor (i.e., PPD), and data queries may be placed.
  - MedDRA coding will be required for Adverse Event Log CRFs, and coding queries may be placed.

- AE-EAE reconciliation will occur and inconsistency queries may be placed.

- WHO coding will be required for Concomitant Medication Log CRFs, and coding queries may be placed.

- QCs are listed in the Medidata Rave Task Summary on the study home page of designated site users. Designated site staff members are responsible for routinely checking the Task Summary and correcting/updating study data to resolve any outstanding queries.

- When site staff correct/update study data and/or enter a query response to address a manual or coding query, SCHARP staff review the updated data and/or response, and resolve the query or re-query as needed.

- When site staff correct/update study data and/or enter a query response to address a monitoring query, the site monitor (i.e., PPD) reviews the updated data and/or response, and resolves the query or re-queries as needed.

- If a site utilizes paper CRFs as source documents, any changes to the paper CRFs **must** be entered into the Medidata Rave study database.

Electronic Signatures by Investigators

Each site investigator or designee is expected to complete a single sign-off of a participant's study data (one sign-off for each participant at his/her site) once the participant terminates from the study and site staff have resolved all data queries for the given participant. By completing this participant-level sign-off in the Medidata Rave study database, the investigator or designee attests that the data has been reviewed and is deemed to be accurate. iMedidata users will use their login credentials as their electronic signature (see image below). Please refer to the "Electronic Signature" section of the Medidata Rave Electronic Data Capture (EDC) Training Manual and/or the Investigator e-Learning module for specific instructions.

12.2   CRF Completion

12.2.1   General Guidelines – eCRF Completion

- To the extent possible, site staff should utilize direct data entry into the Medidata Rave study database so that the eCRF serves as the source document. Direct data entry is especially encouraged for data collection based on participant self-report, such as behavioral and product use data.

- When direct data entry is not possible due to the nature of the source data - for example, when the source data is a local lab results report - site staff are encouraged to enter study data into the Medidata Rave study database based on the site-specific source document (in this case, the local lab results report).

  - Site staff are encouraged to avoid paper CRF completion, as it represents an additional, intermediate step of data management and QA/QC review into site data management workflows. In addition, paper CRF completion introduces the risk of data transcription errors, and could contribute to database data entry errors.

- When completing an eCRF, refer to the CRF Completion Guidelines (CCG) document, posted on ATLAS, for detailed instructions on data collection pertaining to the given form and fields on that form.

- Complete eCRFs as soon as possible once the data is available and has undergone internal QC review, as applicable. Ideally, completion of all required eCRFs for a given visit will occur within 1–2 business days of the visit, though up to 7 days is acceptable.

12.2.2 Screening and Enrollment/Randomization

- Data entry into the study database begins at the Screening Visit. All screening data should be entered into Medidata Rave, regardless whether the participant enrolls. Once a participant is determined to be eligible, enrolls, or fails a screening attempt, study eligibility data should be entered into the study database as follows:

  - For participants who screen but do not enroll in MTN-026, data entry is required for the Eligibility Criteria eCRF. (Other eCRFs that were completed during the failed screening attempt will remain in the study database).

  - For participants who enroll in MTN-026, enter data for the Eligibility Criteria eCRF, along with all required Enrollment Visit CRFs.

- **Randomization:** The first step in the randomization process is for site staff to complete the Eligibility Criteria CRF with the first two responses indicating that the participant is eligible for study participation. Once these two questions are completed indicating the participant is eligible for study participation and the form is saved, the Randomization form may be completed. To randomize a study participant, site staff should select the "Yes" response option (shown in the image below) for the question "Is the participant ready to be randomized?" on the Randomization eCRF. Once this response is saved, the database (via the Medidata Balance module) will assign the participant to a treatment arm and the Randomization Date and Time will appear automatically on the Randomization eCRF. A participant is considered officially enrolled in the study once this step takes place; that is, a randomization assignment is generated for the participant in Medidata Balance, as evidenced by the appearance of a Randomization Date and Time on the Randomization eCRF.

Page: Randomization - V2.0 - Enrollment

Is the participant ready to be randomized?   ○ Yes ○ No

Randomization Date and Time

Note that the participant's randomly assigned treatment arm will not appear in the study database, since the study is double-blinded. Rather, site pharmacy staff only (in addition to SCHARP staff) will have restricted access to the participant's randomly assigned sublot code, which will appear on the Pharmacy Dispensation eCRF once a participant is randomized, in order to select and dispense the correct study product (i.e., the applicator that contains the study product to which the participant was randomly assigned). Details on this process are specified in each site's
study-specific pharmacy SOP.

Pharmacokinetics, Pharmacodynamics, and Mucosal Safety Assignment: This study has two additional assignments, the time assignment and the day assignment for PK/PD and mucosal sampling which are also assigned via the Medidata Balance module. Once the participant is randomized, the participant's day and time assignment will be auto-populated in Rave on the Enrollment CRF (see image below). The item "PK, PD, and Mucosal Safety Assignment" references the Time assignment (e.g., 30-60 minutes or 120 minutes) for blood and rectal sample collection at Dosing Visits 3 and 13. The item "PK/PD Sampling Day Assignment" refers to if the participant will be assigned to collect samples either at 24, 48, or 72 hours after Dosing Visits 3 and 13.

PK, PD, and Mucosal Safety Time Assignment   ○ 30-60 minutes ○ 120 minutes

PK/PD Sampling Day Assignment   ○ 24 hours ○ 48 hours ○ 72 hours

12.2.3   Site Data Management SOP

As a condition for study activation, each study site must have a site or study-specific SOP for Data Management. This SOP should be reviewed and followed in combination with the information contained in the study protocol, this SSP Manual, and the site's Clinical Quality Management Plan (CQMP).

The Data Management SOP outlines site staff responsibilities and contains information on several data topics, including:

☐ Participant ID (PTID) assignment

☐ Participant study file organization

☐ Participant confidentiality

☐ Site data quality control (QC) processes

☐ Timing of data entry into the study database

☐ Data storage

☐ Data security

☐ Contingency plans in case of interrupted access to the study database.

☐ Management of site user account permissions for access to the study database.

12.3 Study-Specific Data Collection Information

12.3.1   Participant Identification Numbers (PTIDs)

As described in each site's Data Management SOP, each participant who provides written informed consent to be screened in MTN-026 will be assigned an MTN-026 PTID. To do this, site staff will generate in Medidata Rave a participant number (called "Subject ID" in Medidata Rave) within the electronic study and site folder; this number will serve as the participant's PTID. Refer to the "Creating Subjects" section of the Medidata Rave Electronic Data Capture (EDC) Training Manual and the CCG for specific instructions.

Each PTID is unique. It will be assigned to a single participant only at a given site, and not assigned to any other participant at any site or in any study (e.g., MTN, HVTN, HPTN) for which SCHARP is the Statistical and Data Management Center (SDMC).

SCHARP will provide sites with a Microsoft Excel PTID-Name Linkage file and site staff will maintain this document, which will be used to link a participant's name with her assigned PTID. For study purposes, the act of MTN-026 PTID assignment is defined as completion of an entry on the MTN-026 PTID-Name Linkage Log for a given participant.

The MTN-026 PTIDs are nine digits, and formatted as "XXXYYYYYZ". The PTID consists of three parts: the site number (XXX), the participant number (YYYYY), and a numerical check digit (Z). The check digit (Z) is a number generated by SCHARP within the participant number, and helps ensure that the correct PTID is recorded/entered.

12.3.2   Study Visit Timing

Screening and Enrollment
The initial screening visit is defined as the day the participant provided written informed consent to be screened for the study. The Enrollment Visit will be scheduled to take place within 45 days of the initial Screening Visit. The date the participant is enrolled/randomized is Study Day 0 for the participant. SCHARP will provide sites with a visit window calendar tool in Microsoft Excel that can be used to calculate the allowable window for study enrollment based on the participant's screening date (i.e., date informed consent provided for the current screening attempt). The tool will be posted on-line at: http://www.mtnstopshiv.org/node/6908.

Screening Attempts (Re-screens)
Refer to Section 5: Study Procedures of this manual for guidance related to repeat screening attempts (re-screens) by a participant.

If a participant re-screens, all screening procedures and CRFs must be repeated with the exception of PTID assignment. Once a PTID is assigned to a participant, the same PTID is used for the re-screen procedures and forms completed for that participant (do not assign a new PTID).

If a participant re-screens and enrolls, all previously completed eCRFs (from the original, failed screening attempt) must be updated to reflect only data from the successful Screening and Enrollment Visit. Note that in this case, the Eligibility Criteria eCRF completed during the failed screening attempt should be updated to reflect the participant's final eligibility status and enrollment into the study.

Follow-Up Visits

For each MTN-026 follow-up visit, the visit type, visit code, target visit day, and visit window are listed in Table 12-1. Target days and windows are listed in days, with the day of enrollment/randomization as study day 0.

Target Days and Visit Windows

Whenever possible, visits should be completed on the target day. If it is not possible to complete the visit on the target day, the visit should be completed within the visit window. See Table 12-1 for the visit timing requirements.

SCHARP will provide sites with a spreadsheet tool that may be used to generate individual participant follow-up visit calendars based upon the participant's enrollment date. The spreadsheet requires that the participant's Enrollment (i.e., randomization) date be entered. Once the enrollment date is entered, the target days and visit windows for Visit 3 will appear. The target dates for Visits 4 - 6 are contingent on the actual visit date of the Single Dose Administration Visit (Visit 3). In addition, the target dates and visit windows (if applicable) for Visits 8 – 16 are contingent on the actual date of Visit 7: Study Product Administration Visit (Visit 7). Since the visits and visit windows (if applicable) are dependent on the actual date of previous visits, the actual dates of Visit 3, 7, and 16 must be manually entered in order to calculate the visit target date and windows for the remaining visits, including the final Follow-up Safety Contact and Termination Visit. Note that there are no visit windows for Visits 4, 5, and 8 -15. The calendar can then be printed and added to the participant's study notebook.

Split Visits

Whenever possible, all required follow-up visit evaluations should be completed on the same day. In those cases where this is not possible, the participant may come back and complete the remaining evaluations on another day, as long as that day is within the visit window **AND** as long as the visit is Screening, Visit 3, Visit 6, Visit 7, Visit 16, or Visit 17. All other study visits (including Enrollment, Visit 4, Visit 5, and Visits 8 - 15) may not be split. (Refer to the Study Procedures section of this manual for more information regarding visit procedures and timing). For example, a participant comes in on his/her Visit 3 target day and completes most of the required evaluations. S/he comes back the next day and completes the remaining required procedures. While not ideal, this is allowed as needed, and is referred to as a "split" visit; meaning, the participant completed all required visit evaluations on two separate days, both days being in the visit window.

Note that for split visits, the "Visit Date" on the Follow-up Visit Summary form within the applicable visit folder is the date of the first part of the split visit. See Section 12.3.3 for more information on assigning visit codes to split visits.

Table 12-1: Visit Timing Requirements

Visit Code	Visit Type	Target Day	Visit Window
1.0	Visit 1: Screening	No more than 45 days prior to Enrollment	N/A
2.0	Visit 2: Enrollment	**Day 0***	+45 days after Screening Visit
3.0	Visit 3: Single Dose Administration Visit	**Day 7** ~ 7 days after Enrollment	+7-21 days after Enrollment Visit
4.0	Visit 4: Sampling Visit - 24 Hours After Application of Study Product	**Day 8** 24 hours after Visit 3.0	No window (Same as target day)
5.0	Visit 5: Sampling Visit - 48 Hours After Application of Study Product	**Day 9** 48 hours after Visit 3.0	No window (Same as target day)
6.0	Visit 6: Sampling Visit - 72 Hours After Application of Study Product	**Day 10** 72 hours after Visit 3.0	+1-2 days after Visit 5.0
7.0	Visit 7: Study Product Administration Visit	**Day 24** ~ 14 days after Visit 6.0	+14-28 days after Visit 6.0
8.0	Visit 8: Study Product Administration Visit	**Day 25** 1 day after Visit 7.0	No window (Same as target day)
9.0	Visit 9: Study Product Administration Visit	**Day 26** 2 days after Visit 7.0	No window (Same as target day)
10.0	Visit 10: Study Product Administration Visit	**Day 27** 3 days after Visit 7.0	No window (Same as target day)
11.0	Visit 11: Study Product Administration Visit	**Day 28** 4 days after Visit 7.0	No window (Same as target day)
12.0	Visit 12: Study Product Administration Visit	**Day 29** 5 days after Visit 7.0	No window (Same as target day)
13.0	Visit 13: Last Study Product Administration Visit	**Day 30**** 6 days after Visit 7.0	No window (Same as target day)
14.0	Visit 14: Sampling Visit - 24 Hours After Last Application of Study Product	**Day 31** 24 hours after Visit 13.0	No window (Same as target day)
15.0	Visit 15: Sampling Visit - 48 Hours After Last Application of Study Product	**Day 32** 48 hours after Visit 13.0	No window (Same as target day)
16.0	Visit 16: Sampling Visit - 72 Hours After Last Application of Study Product	**Day 33** 72 hours after Visit 13.0	+ 1-2 days after Visit 15.0
17.0	Visit 17: Follow-up Safety Contact and Termination Visit	**Day 40** ~ 7 days after Visit 16.0	+4-14 days after Visit 16.0

Consider the timing of participant menses when scheduling the Enrollment Visit as menses must not coincide with Study Visits 2-6.
**Early Termination Visit Code may vary depending on where participant is in his/her visit schedule.
**If the participant permanently discontinues study product use early (i.e. prior to Visit 13), participants will be asked to complete the Visit 13 – Last Study Product Administration Visit/Early Termination procedures.

Missed Visits

In those cases where a participant is not able to complete <u>any part </u>of a required follow-up visit within the visit window, the visit is considered "missed". For example, an enrolled participant does not report to the clinic for his/her study product administration visit at Visit 9. Per Table 12-1, Visit 9 visit has been missed. The missed visit is documented by completion of a Missed Visit CRF.

Interim Visits

An interim visit occurs when there is contact with the participant, but required follow-up visit procedures are not done, either because the required follow-up visit has already been completed, or it is too early in the visit window to complete the required visit. An interim visit may occur that meets one of the following criteria:

- ☐ Additional study procedures and/or data collection are conducted outside of what is specified in the protocol for a required study visit. For example, an interim visit may occur via a phone contact if the participant reports a new AE. Required follow-up visit procedures are not done, either because the required follow-up visit has already been completed, the participant is in between visit windows, or it is too early in the visit window to complete the required visit.
- ☐ Required study visit procedures are conducted outside the visit window, either to make up certain procedures from a missed visit, or to conduct Visit 13 /Early Termination Visit procedures due to an early product discontinuation. For example, if a participant permanently discontinues study product use after Visit 7, but before the window has opened for Visit 8, s/he would complete Early Termination visit procedures at an interim visit, if s/he is able and willing.

All interim visits/contacts with the participant should be documented in a chart note. Additionally, if the interim contact results in at least one <u>newly-completed eCRF</u>, the interim visit is assigned an interim visit code (visit number ending in something other than ".0"). All phone contacts that meet interim visit criteria as specified above are also assigned interim visit codes. See section 12.3.3 for information on how to assign visit codes to interim visits.

For MTN-026, an Interim Visit Summary CRF is completed for interim visits/contacts as needed.

The following is an example of an interim visit:

A participant completes Visit 6 as scheduled. Her Visit 7 visit window opens on August 15th, and s/he is scheduled to complete Visit 7 on August 16th. The participant reports to the clinic unexpectedly on August 15th to report new genital AE symptoms.

Why is this an interim visit? The participant is in the Visit 7 visit window, but site staff decide not to conduct Visit 7 visit procedures for this participant on August 15th (e.g., the participant already has Visit 7 scheduled for the next day (on the target date) and has a history of reliably showing up for scheduled study visits, and/or there is limited staff time availability on August 15th). An interim visit code is assigned as new CRFs will be completed (Interim Visit Summary, AE Log, possibly others).

12.3.3 Visit Folders and Visit Codes

The eCRFs in the study database are set up within pre-defined study visit folders, so the visit name and visit code automatically appear (and do not need to be entered for required study visits). With the exception of the Baseline Medical History Log eCRF, which is housed in the Screening Visit folder, all log forms (i.e., AE Summary and Log, Concomitant Medications Summary and Log, Protocol Deviations Summary and Log, Pregnancy Outcome Summary and Log, and Directly Observed Dosing) are housed in the "Ongoing Logs" folder within the study database. The Treatment Discontinuation eCRF and Study Discontinuation eCRF are housed

within the "Discontinuations" folder; each of these forms is completed once for each participant to document his/her permanent product discontinuation and study exit, respectively. In addition, the Product Dispensation and Returns eCRF is housed within its own folder.

Table 12-2 below lists the visit codes assigned to each required follow-up visit.

Table 12-2: Visit Code Assignments for Required Follow-up Visits

Visit	Visit Code
Screening	**1.0**
Enrollment	**2.0**
Visit 3 Single Dose Administration Visit	**3.0**
Visit 4 – 24 Hours After Application of Study Product Visit	**4.0**
Visit 5 – 48 Hours After Application of Study Product Visit	**5.0**
Visit 6 – 72 Hours After Application of Study Product Visit	**6.0**
Visit 7 – Study Product Administration Visit	**7.0**
Visit 8 - Study Product Administration Visit	**8.0**
Visit 9 - Study Product Administration Visit	**9.0**
Visit 10 - Study Product Administration Visit	**10.0**
Visit 11 - Study Product Administration Visit	**11.0**
Visit 12 - Study Product Administration Visit	**12.0**
Visit 13 – Last Study Product Administration Visit	**13.0**
Visit 14 - 24 Hours After Application of Study Product Visit	**14.0**
Visit 15 – 48 Hours After Application of Study Product Visit	**15.0**
Day 16 – 72 Hours After Application of Study Product Visit	**16.0**
Day 17 – Follow-up Safety Contact and Termination Visit	**17.0**

Visit codes for Split Visits
See Section 12.3.2 for a definition of split visits. When split visits occur, the CRFs completed for the visit are all assigned the same visit code, even though the dates will differ between some of the CRFs. For example, a participant comes in on his/her Visit 16 target day of 23-AUG-17 and completes all required visit evaluations except chemistry testing. S/he returns on 24-AUG-17 (still within the visit window) and provides a blood sample for chemistry testing. All CRFs dated 23-AUG-17 and 24-AUG-17 are assigned the same visit code of "16.0" and are housed within the Visit 16 visit folder in the study database.

Visit codes for Interim Visits
Note that interim visit codes are not used for visits/contacts between the Screening Visit and Enrollment Visit, as these contacts are considered part of the screening process.

For interim visits occurring after the Enrollment Visit and onwards, interim visit codes are assigned using the following guidelines:

• To the left of the decimal point, record the visit code of the most recently required follow-up visit, *even if the visit was missed and/or if the participant is within the next visit's window.*

• To the right of the decimal point:

  - #.1 = the first interim visit after the most recently-required visit,

  - #.2 = the second interim visit after the most recently-required visit,

  - #.3 = the third interim visit after the most recently-required visit, and so on.

The example below is from section 12.3.2, where interim visits are defined. This example now has a visit code information added to the example.

A participant completes Visit 6 as scheduled. Her Visit 7 visit window opens on August 15th, and s/he is scheduled to complete Visit 7 on August 16th. The participant reports to the clinic unexpectedly on August 15th to report new genital AE symptoms. *Visit code = 6.1*

12.3.4 Case Report Form Completion Schedule

The SCHARP-provided forms for this study include all forms that are completed and entered into the study database, as well as the Pelvic Exam Diagrams, which is an optional form sites may use to source document pelvic exam findings for data entry into the Pelvic Exam eCRF.

Some SCHARP-provided forms are required to be completed at each visit, while other forms are required only at one visit or only when specifically indicated. The following table (Table 12-3) lists the forms that are required to be completed at each study visit, as well as the forms that are completed on an "as needed" basis.

Table 12-3: Schedule of Forms – CRFs Required to be Completed at Each Visit

Visit	Form Name
Visit 1.0 - Screening	Participant Date of Visit
	Eligibility Criteria
	Demographics
	Vital Signs
	Physical Exam
	Anorectal Exam
	Local Laboratory Results
	Hematology
	STI Tests
	HIV Test Results
	Baseline Medical History Summary
	Baseline Medical History
	Screening Menstrual History (female participants only)
	Pregnancy Test (female participants only)
	Pelvic Exam (female participants only)
	Pelvic Exam Diagrams (female participants only)
Visit 2.0 - Enrollment	Randomization
	Enrollment
	Vital Signs
	Physical Exam
	Anorectal Exam
	CASI Summary and CASI Tracking
	Specimen Storage
	HIV Test Results
	Sexual Lubricant
	Cervical Specimen Storage (female participants only)
	Pelvic Exam (female participants only)
	Pregnancy Test (female participants only)
	Pelvic Exam Diagrams (female participants only)
Visit 3.0 - Single Dose Administration Visit	Follow-up Yes/No
	Follow-up Visit Summary
	Sexual Lubricant
	Anorectal Exam

	Timed Specimen Storage
	Directly Observed Dosing (Ongoing Logs)
	CASI Summary and CASI Tracking
	Pregnancy Test (for female participants only) – added via Additional Study Procedures
	Pharmacy Dispensation (completed by and accessible to site pharmacists only)
Visit 4.0 – 24 hour PK Visit Visit 5.0 – 48 hour PK Visit Visit 6.0 – 72 hour PK Visit	Follow-up Yes/No
	Follow-up Visit Summary
	Specimen Storage
Required at participant's assigned sampling group (Visit 4, 5, or 6)	Anorectal Exam
	Cervical Specimen Storage (for female participants only)
	Pelvic Exam (female participants only)
	Pelvic Exam Diagrams (female participants only)
Visit 7.0 – Visit 12.0 - Study Product Administration Visits	Follow-up Yes/No
	Follow-up Visit Summary
	Directly Observed Dosing (Ongoing Logs)
Required at Visit 7 only	Pregnancy Test (female participants only)
	HIV Test Results
	Sexual Lubricant
	Product Dispensation and Returns (Product Dispensation and Returns folder)
Required at Visit 7 and 8	Anorectal Exam
	Specimen Storage
Visit 13.0 - Last Study Product Administration (Early Termination)* *Visit code will vary if Early Term	Follow-up Yes/No
	Follow-up Visit Summary
	Directly Observed Dosing (Ongoing Logs)
	Anorectal Exam
	Sexual Lubricant
	Product Dispensation and Returns (Product Dispensation and Returns folder)
	Timed Specimen Storage
	Treatment Discontinuation (Discontinuations folder)
	Pelvic Exam (female participants only)
	Cervical Specimen Storage (female participants only)
	Pregnancy Test (for female participants only) – added via Additional

	Study Procedures
	CASI Tracking Summary and CASI Tracking (required if Early termination)
	Study Discontinuation (required if early termination; Discontinuations folder)
	Pelvic Exam Diagrams (female participants only)
Visit 14.0 – 24 hour PK Visit Visit 15.0 – 48 hour PK Visit Visit 16.0 – 72 hour PK Visit	Follow-up Yes/No
	Follow-up Visit Summary
	Specimen Storage
Required at Visit 14 only	CASI Summary and CASI Tracking
Required at Visit 16 only	HIV Test Results
	Local Laboratory Results
Required at participant's assigned sampling group (Visit 14, 15, or 16)	Anorectal Exam
	Cervical Specimen Storage (female participants only)
	Pelvic Exam (female participants only)
	Pelvic Exam Diagrams (female participants only)
Visit 17.0 - Follow-up Safety Contact and Termination Visit	Follow-up Yes/No
	Follow-up Visit Summary
	Study Discontinuation (Discontinuations folder)
As needed	Additional Study Procedures
	Anorectal Exam
	CASI Summary and CASI Tracking
	Cervical Specimen Storage (female participants only)
	Interim Visit Summary
	Hematology
	HIV Confirmatory Results
	HIV Test Results
	Local Laboratory Results
	Missed Visit
	Participant Replacement
	Vital Signs
	Pelvic Exam (female participants only)
	Physical Exam
	Pregnancy Report and History (female participants only)
	Pregnancy Test (female participants only)

	Specimen Storage
	STI Tests
	Timed Specimen Storage
	Study Discontinuation
	Treatment Discontinuation
	Pelvic Exam Diagrams (female participants only)
Ongoing Logs	Concomitant Medications Summary
	Concomitant Medications
	Adverse Event Summary
	Adverse Event
	Protocol Deviations Summary
	Protocol Deviations
	Directly Observed Dosing Log
	Pregnancy Outcome Summary (female participants only)
	Pregnancy Outcome (female participants only)
Discontinuations	Study Discontinuation
	Treatment Discontinuation
Pharmacy	Pharmacy Dispensation

12.3.5 Completing Interviewer-administered Forms

In order to standardize interviewer-administered data collection from site to site and to maximize quality, it is critical that participant interviews be conducted with a non-biased, non-judgmental approach. Study staff should help a participant feel comfortable sharing personal information and opinions while asking the study questions in a consistent manner from participant to participant.

Site staff are encouraged to practice direct data entry when administering the interviewer-administered form (i.e. Demographics), to the extent possible, so that the eCRFs serve as the source documents. Skip patterns are documented in the CRF Completion Guidelines (CCG) document, which site staff should reference when administering the forms. The CCG will be posted on the Atlas web site along with the complete set of study CRFs (pdf file
– see above section 11.3.4). The skip patterns are also programmed into the data checks within the study database, and system queries will be generated in real-time, as data is saved within the database, if required items are missed and/or inconsistent responses are entered. This real-time feedback will allow the interviewer to clarify participant responses and update/correct participant self-reported data during the participant interview, yielding accurate, consistent, and complete study data.

12.3.6 Site Review (Quality Control) of CRFs

As described in the site's Data Management SOP [and referenced in the site's Clinical Quality Management Plan, (CQMP)], each site must perform Quality Control (QC) review

steps, especially for paper CRFs (if used) prior to their data entry into the study database. While paper CRFs are being reviewed, it is important that they are stored and tracked systematically.

Below are specific review guidelines that should be followed for these QC review steps.

MTN-026 QC Review Step #1 (completed during visit)

- Review visit checklist and pelvic exam checklist (if used) to ensure all required procedures were completed

- Review eligibility checklists/worksheets to ensure completeness and verify participant eligibility

- Review LDMS Specimen Tracking Sheets to ensure completeness and accuracy

- Review completed CRFs based on participant responses to ensure completeness:

    o Screening Visit: Demographics, Baseline Medical History Log, Screening Menstrual History, Concomitant Medications Log

    o Enrollment Visit: Cervical Specimen Storage, Sexual Lubricant, Concomitant Medications Log

    o Follow-up visits, when present: Cervical Specimen Storage, Sexual Lubricant, Adverse Event Log, Directly Observed Dosing Log (if home dosing reported)

12.3.6.1 MTN-026 QC Review Step #2 (completed after visit)

General QC #2 procedures for all visits:

- Review visit checklist to ensure all required procedures were completed

- Ensure the PTID is correct, is recorded correctly on all paper source documents (including paper CRFs, if used), and is the same on the paper source documents and the eCRFs for a given participant.

- Ensure that no participant identifiers other than the PTID are present on paper source documents, including paper CRFs (if used).

- Ensure that the assigned visit code is correct, and is consistent between the paper source documents, including paper CRFs (if used), the eCRFs, the LDMS Specimen Tracking Sheet, and LDMS for a given participant visit.

Additional QC #2 procedures for Screening and Enrollment Visit documents:

- Review the Pelvic Exam, Physical Exam, Vital Signs, Hematology, Local Laboratory Results, Pregnancy Test, HIV Tests, STI Tests, and Anorectal Exam and Sigmoidoscopy forms, and ensure that medical conditions are recorded appropriately on the Baseline Medical History Log. Refer to the CCGs for further guidance.

- Ensure that all eCRFs used to document lab test results have the correct Specimen Collection Dates entered. If any lab tests were repeated, update the appropriate eCRF(s) to reflect the repeat test result(s).

- If a second (repeat) full pelvic exam is performed during screening, make sure a new pelvic exam source document [e.g., Pelvic Exam Diagrams (non-Medidata Rave)] is completed, and update the Pelvic Exam eCRF in the Screening Visit folder to document the 2nd screening pelvic exam.

- Review the Specimen Storage and Cervical Specimen Storage eCRFs and make sure they match information documented on the visit checklist and Enrollment Visit LDMS Specimen Tracking Sheet (or local lab requisition sheet).
- If a participant screens but does not enroll in the study, make sure the Eligibility Criteria eCRF is completed and entered into the study database. Other eCRFs that were completed as part of the failed screening attempt may remain in the study database, but may not be QC'd.

Additional QC #2 procedures for follow-up visit documents:

- Concomitant Medications Log CRF: if a medication is taken for an AE, make sure the applicable AE is entered on the Concomitant Medications Log eCRF, and make sure the AE Log CRF for the AE has "Medication" entered for "Other action(s) taken".

- Interim Visit Summary CRF: Ensure the correct interim visit number is recorded on the "Interim Visit Summary" eCRF and at the top of each paper CRF and other paper source documents completed

QC #2 for Paper CRFs (if used)

This QC review step should occur before forms are data-entered into the study database. Ideally, this review will happen once all lab results are available, so that all forms for a particular visit can be reviewed for consistency across documents. The goal, as outlined in the site's Data Management SOP, is to correct data inconsistencies/errors prior to entering data into the study database, so that data is accurate, complete, and available at the time of data entry, thus minimizing the likelihood of data queries.

QC #2 procedures for paper CRFs - all visits:

- Make sure a response has been recorded for each item, as required. Make sure skip patterns have been followed correctly, per instructions in the CRF Completion Guidelines (CCGs) document.

- If a response text field with "other", "specify", or "describe" is present, ensure text is present in this field.

- Make sure text responses are clearly recorded.

- For paper CRFs that are not source documents, make sure the data recorded on the paper CRFs matches or is consistent with the source documents.

QC #2 for Electronic CRFs (eCRF)

When data is entered into the study database and an eCRF is saved, system queries are automatically generated in response to inconsistent or incomplete data. Unlike the paper CRFs, which require manual review, eCRFs have the advantage of having the study database itself provide a real-time QC review to ensure data completeness and consistency. In addition, the database design and system queries ensure skip patterns are followed, per instructions in the CCGs.

No additional QC #2 review steps are required for eCRFs that are source (i.e., the data is directly entered into the study database, rather than entered based on a separate paper CRF or other paper source document).

Electronic CRFs that are completed based on other source documents (e.g., paper CRFs, SMS data, or lab reports) should be reviewed to ensure that the data entered matches or is consistent with the source documents. The site's Data Management SOP provides additional details, and specifies which staff members will perform this review.

12.4 Form-Specific Completion Instructions

Detailed form completion instructions for each form are provided in the CRF Completion Guidelines (CCG) document. The instructions document skip patterns and include guidance on completion of eCRFs in the study database. Some items on forms are straightforward and do not require specific instructions. Therefore, you will not see all form items listed in the CCG, but rather only those items needing detailed explanation.

Site staff who will enter data into Medidata Rave are encouraged to practice completing/updating the eCRFs by entering test data, and familiarizing themselves with the eCRF questions, skip patterns, and system queries prior to entering study data.

12.5 Case Report Forms

SCHARP will post a CRF (pdf) file, representing output from the study database eCRFs. The pdf file represents the complete set of study CRFs, and may be used by site staff for local IRB submission as needed, as well as for printing their own paper CRF supplies should paper CRF completion be required (e.g., internet outage).

The current version of the MTN-026 case report forms can be found at the MTN-026 Atlas web page: https://atlas.scharp.org/cpas/project/MTN/026/begin.view?

12.6 Lab Units Conversion Tool

A lab unit conversion tool is available on the following ATLAS page:
https://atlas.scharp.org/cpas/project/Collaborators/Lab%20Unit%20Conversion%20Tool/begin.view
This tool enables sites to convert local laboratory values as needed and enter into Medidata Rave using units reflected in the DAIDS toxicity table. This is an optional tool to be used to facilitate consistent and accurate data entry.