

Section 14. Data Collection

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The purpose of this document is to provide site staff with the information they need to successfully complete and submit MTN-025 case report forms. For questions about this section or about general data collection policies, procedures, or materials, please contact the SCHARP Clinical Data Manager(s) 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-025 team members, along with their job role and e-mail address, are listed below.

MTN-025 Statistical and Data Management Center (SDMC) Staff

Job Role	Name	Email Address
Protocol Statistician	Elizabeth Brown	erbrown@scharp.org

Clinical Data Manager	Melissa Peda	mapeda@scharp.org
Statistical Research Associate	Jason Pan	zpan@scharp.org
Clinical Programmer	Brad Fischer	hfischer@scharp.org
Clinical Safety Associate	Ning Jiang	Njiang2@scharp.org

14.1 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 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-025 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 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 using any of the following browsers will see this banner:

- 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 who are 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, refer to the iMedidata Access Guide, posted on the MTN-025 Atlas webpage: <https://atlas.scharp.org/cpas/project/MTN/025/begin.view?>

To request a new iMedidata user account, access to MTN-025 database for an existing iMedidata account, or to request changes or updates to a user account, complete the Medidata Rave User Request Form available on the MTN-025 Atlas webpage and send the completed form to the SCHARP email alias, sc.access.medidata@scharp.org.

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-025 Atlas web page: <https://atlas.scharp.org/cpas/project/MTN/025/begin.view?>

Site staff should contact the study Clinical Data Manager(s) with any questions related to study data collection and management. A representative from Medidata Solutions may be contacted (see contact information below) anytime a site has technical questions or problems (e.g., account or password issues) related to access or use of the Medidata Rave software. Medidata Help Desk information is also available at: <https://www.mdsol.com/en/contact/>.

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

Emailhelpdesk@mdsol.com**Hours**

24 hours a day, 7 days a week

Data Entry/Quality Control

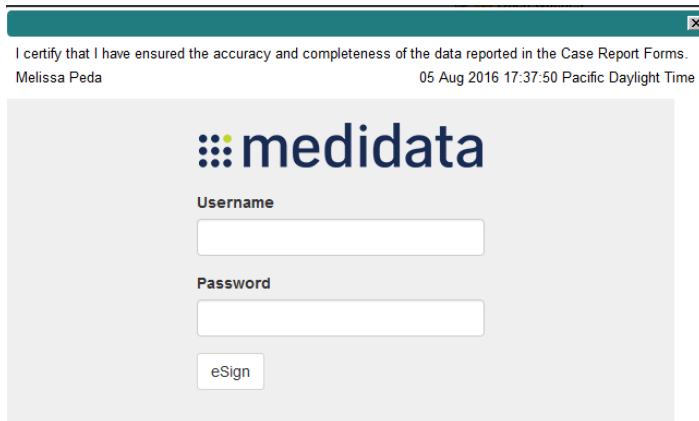
Once an eCRF is completed and saved in the study database, the following may occur:

- 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 Managers 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 manual data queries may be placed.
- MedDRA and WHO coding will be required for AE and Concomitant Medications Log eCRFs, and coding queries may be placed.
- AE-EAE reconciliation will occur, and inconsistency queries may be placed.
- QCs are listed in the Medidata Rave task list on the study home page of designated site users. Designated site staff members are responsible for routinely checking the task list and correcting/updating study data to resolve any outstanding queries.
- When site staff correct/update study data in response to a manual or coding query, SCHARP staff review the updated data and resolve the query or re-query as needed.
- When site staff correct/update study data in response to a monitoring query, the site monitor (i.e., PPD) reviews the updated data 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.

- All queries must be answered and closed prior to any inactivation of forms and/or log lines.

Electronic Signatures by Investigators

Each site investigator or designee will be expected to complete a single sign-off on a casebook level for each participant to attest that the data has been reviewed and is deemed to be accurate. SCHARP will provide additional guidance at the **end of study** and prior to database lock to indicate that investigator sign-off of each participant casebook should take place. Site investigator/designee sign-off for a participant casebook does not need to be completed during the study prior to PPD monitor or SCHARP review of data entered. 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.



I certify that I have ensured the accuracy and completeness of the data reported in the Case Report Forms.
Melissa Peda 05 Aug 2016 17:37:50 Pacific Daylight Time

medidata

Username

Password

eSign

14.2 CRF Completion

14.2.1. Pre-screening, Screening and Enrollment

- Screening data should be recorded on paper CRFs, as specified in each site’s Source Documentation SOP. Once a participant is determined to be ineligible or refuses screening (main MTN-025/HOPE study or decliner population), enrolls, or fails a screening or enrollment attempt, data should be entered into the study database as follows:
 - For ASPIRE participants who do not complete a Screening Visit (e.g., lost to follow-up, not eligible, or not interested in participating), complete and enter the Pre-Screening Outcome CRF only.
 - For ASPIRE participants who screen for but do not enroll in the decliner population, enter the Pre-Screening Outcome CRF and the Eligibility Criteria – Decliner Population CRF only.
 - For ASPIRE participants who enroll in the decliner population, complete and enter the Pre-Screening Outcome CRF and all required forms for the Decliner

Screening/Enrollment Visit (i.e., the Eligibility Criteria –Decliner Population, Enrollment – Decliner population, Demographics, and Baseline Behavior Assessment CRFs).

- For participants who screen but do not enroll in MTN-025/HOPE, enter the Pre-Screening Outcome CRF and Eligibility Criteria CRF only.
- For participants who enroll in MTN-025/HOPE, complete and enter the Pre-Screening Outcome form, as well as all required screening and enrollment CRFs.
 - Data collection for the Screening and Enrollment Visits can occur on paper CRFs first, or via EDC (if a non-CRF paper source is used), or a combination of both, keeping in mind that only data from successful enrollment attempts should be entered into the study database.

14.2.2 General Guidelines – eCRF and Paper 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 (ring) use data.
- When 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 can contribute to database data entry errors.
- When completing a paper CRF or an eCRF, refer to the current version of the CRF Completion Guidelines (CCGs) document, posted on the MTN-025 Atlas webpage, 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 at the site, as applicable. Ideally, completion of all required eCRFs for a given visit will occur no later than 1–2 business days of the visit, though up to 7 days is acceptable.

14.2.3 CRFs Not Requiring Data Entry

In MTN-025, there are two case report forms that are used for data documentation purposes, but are not part of the study database: the Pelvic Exam Diagrams form and the Grade 1 Adverse Experience Log form. These forms ensure consistent and accurate data documentation across study sites for data that is not needed in the study database. Both forms are completed using the general guidelines/instructions located on the back of each form, and completed forms are stored in participant files/binders.

14.2.4 Paper CRF Storage

Specifications for paper form storage are described in the site's Data Management SOP. It is recommended that for each participant, study CRFs be stored in a hard-cover notebook, with a tabbed section for CRFs completed at each study visit.

It is suggested that log forms (i.e., Baseline Medical History Log, Concomitant Medications Log, Family Planning Log, Vaginal Ring Tracking Log, Adverse Experience Log, Grade 1 Adverse Experience Log, Clinical Product Hold/Discontinuation Log, Protocol Deviation Log, Social Benefits Log, and Social Impact Log) be kept in their own tabbed sections within the participant study notebook. This makes page numbering (optional) and updating of these forms easier than if these forms are stored by visit within the participant's study notebook.

14.2.5 Site Data Management SOP

As a condition for study activation, each study site must have an SOP for Data Management that is specific to MTN-025/HOPE or to the MTN. 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 contains information on and outlines site staff responsibilities for 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
- Management of site user account permissions for access to the study database
- Audio Computer Assisted Self Interview (ACASI) study data
- Data storage

14.3 Study-Specific Data Collection Information

14.3.1 Pre-screening Numbers & Participant ID Numbers (PTIDs)

As described in each site's Data Management SOP, each ASPIRE participant will be assigned a MTN-025/HOPE Pre-screening number. 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 Pre-screening number. Refer to the "Creating Subjects" section of the Medidata Rave Electronic Data Capture (EDC) Training Manual for specific instructions and the CCGs for specific instructions.

Once a participant provides written informed consent to be screened for the study, or for the decliner population, she is eligible for PTID assignment. She will not receive a new number; rather, the Pre-screening number becomes her HOPE PTID. Participants who enroll in the Decliner Group and later participate in the main MTN-025 study will retain the same HOPE PTID.

Each Pre-screening Number/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 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 HOPE PTID assignment is defined as completion of an entry on the MTN-025 PTID-Name Linkage Log for a given participant.

On the paper CRFs, space to write the participant's PTID is located at the top of each CRF page. The MTN-025 PTIDs are nine digits, and formatted as "XXX-YYYYYZ" (the hyphen does not appear on the eCRFs). 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 with the participant number, and helps ensure that the correct PTID is recorded/entered.

Participant Transfers: Note that any participant who transfer from one study site to the next will retain her original PTID at the receiving site. All study data collected at the receiving site will be housed in the study database under the original PTID. Refer to Section 6 of the SSP for additional guidance on participant transfers.

14.3.2 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 main MTN-025/HOPE study or the decliner population). The HOPE Enrollment Visit will be scheduled to take place within 56 days of the initial Screening Visit. The date the participant is enrolled is Study Day 0 for the participant.

Screening Attempts (Re-screens)

If a participant's first screening attempt is unsuccessful, she may re-screen if she chooses. If she does re-screen, all screening procedures and forms must be repeated with the exception of PTID assignment and Eligibility Criteria CRF completion (see paragraph below). Once a PTID is assigned to a participant that 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 (main MTN-025/HOPE study or decliner population), only case report forms from the successful Screening and Enrollment Visit are entered into the study database. Note that in this case, the Eligibility Criteria CRF completed during the failed screening attempt should be updated and re-entered along with CRFs from the participant's successful Screening and Enrollment Visits. Do not complete a new Eligibility Criteria CRF for the successful screening attempt.

Follow-Up Visits

For each MTN-025/HOPE follow-up visit, the visit type, visit number, target visit day, and visit window are listed in Table 14-1. Target days and windows are listed in days, with the day of enrollment as study day 0.

Target Days and Visit Windows

Whenever possible, visits should be completed on the target day. If not possible to complete the visit on the target day, the visit should be completed within the visit window. For quarterly follow-up visits, sites should complete the study visit within the target window. However, if needed, it is permitted to complete the study visit within the allowable target windows.

SCHARP will provide sites with a spreadsheet tool that may be used to generate individual participant follow-up visit calendars. The spreadsheet requires that the participant's Enrollment date be entered. Once the enrollment date is entered, the target day and visit window for each required follow-up visit up through the Product Use End Visit (PUEV) will appear. The actual PUEV date is required to be entered within the Calculation of Scheduled Study Exit (SEV) tab in order to generate the SEV target day and visit window. The calendar can then be printed and added to the participant's study notebook.

Split Visits

Refer to the Accrual section of this manual for more information regarding Enrollment Visit procedures and timing.

Whenever possible, all required follow-up visit evaluations should be completed on the same day. In 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. For example, a participant comes in on her Month 3 target day and completes most of the required evaluations. She comes back 7 days later and completes the remaining required procedures. This is allowed, and is referred to as a "split" visit; as 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 "Date of Visit" form within the applicable visit folder is the date of the first part of the split visit. See Section 14.3.3 for more information on assigning visit numbers to split visits.

Table 14-1: Visit Timing Requirements

Visit	Allowable/Target Visit Window Opens	Target Day	Target Visit Window Closes	Allowable Window Closes
V1 - Screening	N/A	No more than 56 days prior to Enrollment	N/A	
V2 - Enrollment	Day after Screening Visit	0	56 days after Screening Visit	
V3 - Monthly Visit Month 1	2 weeks prior to Target Day	28	2 weeks after Target Day	
V4 - Monthly Visit Month 2	2 weeks prior to Target Day	56	2 weeks after Target Day	
V5 - Quarterly Visit Month 3	2 weeks prior to Target Day	84	2 weeks after Target Day	10 weeks after Target Day
V6 - Quarterly Visit Month 6	2 weeks prior to Target Day	168	2 weeks after Target Day	10 weeks after Target Day
V7 - Quarterly Visit Month 9	2 weeks prior to Target Day	252	2 weeks after Target Day	10 weeks after Target Day
V8 - PUEV* (Month 12)	2 weeks prior to Target Day	336	2 weeks after Target Day	Study Completion
V9 - Study Exit/Termination**	2 weeks after actual date of PUEV	364 (28 days after actual date of PUEV)	2 weeks after Target Day	Study Completion

**PUEV must occur prior to completion of SEV.*

***SEV should not occur less than 2 weeks after PUEV.*

Missed Visits

In cases where a participant is not able to complete any part 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 her Month 1 visit until 48 days after enrollment. Per table 14-1, the Month 1 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. For example, an interim visit may occur via a phone contact if the participant reports a new AE requiring reporting on an AE Log CRF, or the participant is instructed by study staff to hold or permanently discontinue study product use.

All interim visits/contacts with the participant should be documented in a chart note. Additionally, if the interim contact results in at least one newly-completed Medidata Rave CRF, the interim visit is assigned an interim visit number (visit number ending in something other than “.00”). All phone contacts that meet interim visit criteria per paragraph above are also assigned interim visit codes. See section 14.3.3 for information on interim visit numbers.

For MTN-025, a Follow-up Visit Summary CRF is completed for interim visits/contacts as needed. The Follow-up Visit Summary CRF will document whether the visit is a required (regular) visit or an interim visit.

The following are some examples of interim visits:

1. A participant comes in 21 days before her scheduled Month 6 visit (scheduled for the target day). She says she is coming back for her scheduled Month 6 visit, but needs more condoms today.

Why is this an interim visit? It is too early to conduct the Month 6 visit, so this is an interim visit. No visit number is assigned since the only study procedure conducted was condom provision, and possibly counseling.

2. A participant completes all required evaluations for her Month 3 visit on the target day. She then returns to the clinic 5 days later to request a new ring.

Why is this an interim visit? The participant has already completed all Month 3 visit procedures, and it is too early (and not in the visit window) for Month 6. This is an interim visit, conducted between Months 3 and 6, and is assigned an interim visit number as new CRFs will be completed (Follow-up Visit Summary, Vaginal Ring Tracking Log, Pharmacy Ring Dispensation (completed by Pharmacy staff) and Ring Collection and Insertion).

3. A participant completes her Month 9 visit as scheduled. Her Month 12 visit window opens on July 12. The participant reports to the clinic unexpectedly on July 13 to report new genital AE symptoms.

Why is this an interim visit? The participant is in the Month 12 window, but site staff determine that it is too early to conduct the Month 12 visit for this participant (e.g., the participant already has her Month 12 visit scheduled on the target date, and has a history of reliably showing up for scheduled study visits). An interim visit number is assigned as new CRFs will be completed (Follow-up Visit Summary, AE Log, possibly others).

4. A participant completes all required evaluations for the Month 3 visit on the target day, July 15. Her labs do not come back until July 18, and she has a grade 4 ALT. The site contacts her by phone on July 18 and instructs her to remove the ring, as she is being placed on clinical product hold due to the ALT result.

Why is this an interim visit? During the phone contact, the participant is being instructed by study staff to hold product use. An interim visit number is assigned, as a new Clinical Product Hold/Discontinuation Log and a new Adverse Experience Log will be completed as well as a Follow-up Visit Summary CRF.

5. A participant completes her Month 9 visit on the target day. The next day, she calls the clinic to report a new genital symptom.

Why is this an interim visit? During the phone contact, the participant reported a new symptom which will result in completion of a new CRF (AE Log). Since new CRFs are completed (AE Log and Follow-up Visit Summary), an interim visit number is assigned.

14.3.3 Visit Numbers

The eCRFs in the study database are set up within pre-defined study visit folders, so the visit name and visit number automatically appear (and do not need to be entered for required study visits. Paper CRFs will include in the header a designated place to record the participant ID, the name of the study visit to which a CRF belongs (e.g., log forms, forms completed at interim visits) as well as the visit date. Record both the visit number and the visit name as they appear in Table 14-1. For example, record the Month 3 visit as “V5.00 – Month 3”.

The table below lists the visit numbers assigned to each required follow-up visit.

Table 14-2: Visit Number Assignments for Required Follow-up Visits

Visit	Visit Number
Screening	1.00
Enrollment	2.00
Month 1	3.00
Month 2	4.00
Month 3	5.00
Month 6	6.00
Month 9	7.00
Scheduled PUEV (Month 12)	8.00
Study Exit/Termination	9.00

The visit numbers for the PUEV and Study Exit for participants who enrolled after the formal accrual period and have a shortened visit schedule will remain 8.00 and 9.00.

Visit Numbers for Split Visits

See Section 14.3.2 for a definition of split visits. When split visits occur, the CRFs completed for the visit are all assigned the same visit number, even though the dates will differ between some of the CRFs. For example, a participant comes in on her Month 6 target day of 23-AUG-16 and completes all required visit evaluations except pregnancy testing. She returns on 26-AUG-16 (still within the visit window) and provides a urine sample for pregnancy testing. All CRFs dated 23-AUG-16 and 26-AUG-16 are assigned the same visit number of "6.00".

Visit Numbers for Interim Visits

Note that interim visit numbers 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 numbers are automatically generated within Rave and is assigned using the following guidelines:

- To the left of the decimal point, the visit number of the most recently required follow-up visit is recorded, 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:

- #.01 = the first interim visit after the most recently-required visit,
- #.02 = the second interim visit after the most recently-required visit,
- #.03 = the third interim visit after the most recently-required visit, and so on.

Example #1: A participant completes her Month 9 visit (visit number = 7.00) on the target day. She returns to the site one day later to report a new genital symptom. This interim visit is assigned a visit number of 7.01.

The examples below are from section 14.3.2, where interim visits are defined. These examples now have visit number information added to each example.

1. A participant comes in 21 days before her scheduled Month 6 visit (scheduled for the target day). She says she is coming back for her scheduled Month 6 visit, but needs more condoms today.

Why is this an interim visit? It is too early to conduct the Month 6 visit, so this is an interim visit. No visit number is assigned since the only study procedure conducted was condom provision, and possibly counseling.

Visit number = not assigned (no new CRFs are completed for this visit – document in chart notes only).

2. A participant completes all required evaluations for her Month 3 visit on the target day. She then returns to the clinic 5 days later to request a new ring.

Why is this an interim visit? The participant has already completed all Month 3 visit procedures, and it is too early (and not in the visit window) for Month 6. This is an interim visit, conducted between Months 3 and 6, and is assigned an interim visit code as new CRFs will be completed (Follow-up Visit Summary, Vaginal Ring Tracking Log, Pharmacy Ring Dispensation (completed by Pharmacy staff) and Ring Collection and Insertion).

Visit number = 5.01

3. A participant completes her Month 9 visit as scheduled. Her Month 12 visit window opens on July 12. The participant reports to the clinic unexpectedly on July 13 to report new genital AE symptoms.

Why is this an interim visit? The participant is in the Month 12 window, but site staff determine that it is too early to conduct the Month 12 visit for this participant (e.g., the participant already has her Month 12 visit scheduled on the target date, and has a history of reliably showing up for scheduled study visits). An interim visit code is assigned as new CRFs will be completed (Follow-up Visit Summary, AE Log, possibly others).

Visit number = 7.01

4. A participant completes all required evaluations for the Month 3 visit on the target day, July 15. Her labs do not come back until July 18, and she has a grade 4 ALT. The site contacts her by phone on July 18 and instructs her to remove the ring, as she is being placed on clinical product hold due to the ALT result.

Why is this an interim visit? During the phone contact, the participant is being instructed by study staff to hold product use. An interim visit number is assigned, as a new Clinical Product Hold/Discontinuation Log and a new Adverse Experience Log will be completed as well as a Follow-up Visit Summary CRF.

Visit number = 5.01

5. A participant completes her Month 9 visit on the target day. The next day, she calls the clinic to report a new genital symptom.

Why is this an interim visit? During the phone contact, the participant reported a new symptom which will result in completion of a new CRF (AE Log). Since new CRFs are completed (AE Log and Follow-up Visit Summary), an interim visit code is assigned.

Visit number = 7.01

14.3.4 Form Supply

Sites are responsible for creating their own supplies of MTN-025 paper case report forms. Sites are encouraged to print CRFs, as needed from pdf files posted on the MTN-025 Atlas web page:

<https://atlas.scharp.org/cpas/project/MTN/025/begin.view?>

The pdf files provide CRFs for Pre-Screening, Decliner Population Screening/Enrollment, Screening, Enrollment, as-needed forms, and an eCRF Rave output. Each CRF packet will contain a cover page and all non-translated CRFs required to be completed for the visit. Any local-language or as needed CRFs needed will be listed on the visit packet cover page, but not included in the packet file. Should sites choose to modify the visit packets according to their Source Document SOP, please notify the SCHARP Clinical Data Manager(s) of these updates.

The “As Needed” CRF pdf file contains CRFs used on an “as needed” basis, such as the Adverse Experience Log form.

A PDF of the study eCRFs print-outs from Medidata Rave are also available on the study ATLAS webpage and can be downloaded and printed as back-up or for other visits during which CRFs are completed via paper (e.g., at the Screening Visit).

14.3.5 Case Report Form Completion Schedule

The SCHARP-provided forms for this study include forms that are completed and entered into the study database, and forms that are completed but not entered into the study database (i.e., Pelvic Exam Diagrams form and Grade 1 Adverse Experience Log form).

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 14-3) lists the forms that are required to be completed at each study visit.

Table 14.3: Schedule of Forms – CRFs Required to be Completed at Each Visit

Visit	Form Name
ASPIRE Participants	
Pre-Screening	Participant Identifier
	Pre-Screening Outcome

DECLINER Population	
Decliner Population Screening/Enrollment	Eligibility Criteria – Decliner Population
	Enrollment – Decliner Population
	Demographics
	Baseline Behavioral Assessment Y/N
	Baseline Behavioral Assessment
HOPE Enrollers	
V1 – Screening Visit	Participant Date of Visit
	*Eligibility Criteria <i>Complete and submit at Screening Visit only if it determined the participant will not enroll in MTN-025</i>
	Demographics
	Concomitant Medications Y/N
	Baseline Medical History Y/N
	Baseline Medical History (Log)
	Laboratory Results
	STI Test Results
	Physical Exam
	Vital Signs
	Pelvic Exam
	Pelvic Exam Diagrams (non MediData Rave)
	V2 - Enrollment Visit
Enrollment	
ACASI Tracking Y/N	
ACASI Tracking	
Pregnancy Test Result	
Specimen Storage	
Concomitant Medications Y/N	
Family Planning (Log)	
Baseline Behavioral Assessment Y/N	
Baseline Behavioral Assessment	
Baseline Vaginal Practices Y/N	

	Baseline Vaginal Practices
	Ring Collection and Insertion
	Additional Study Procedures Y/N
V3, V4 - Months 1, 2	Date of Visit
	Follow-up Visit Summary
	Ring Adherence Y/N
	Ring Adherence
	HIV Test Results
	Pregnancy Test Result
	Specimen Storage
	Concomitant Medications Y/N
	Adverse Experience Y/N
	Ring Collection and Insertion
	Additional Study Procedures Y/N
V5, V6, V7 - Quarterly Visits Months 3, 6, 9	Date of Visit
	Follow-up Visit Summary
	Behavior Assessment Y/N
	Behavior Assessment
	Ring Adherence Y/N
	Ring Adherence
	HIV Test Results
	Pregnancy Test Result
	Specimen Storage
	Concomitant Medications Y/N
	Adverse Experience Y/N
	Ring Collection and Insertion
	ACASI Tracking Y/N <i>(Required at Month 3 only)</i>
	ACASI Tracking <i>(Required at Month 3 only)</i>
Additional Study Procedures Y/N	
V8 - Product Use End Visit (Month 12)	Date of Visit
	Follow-up Visit Summary
	Behavior Assessment Y/N

	Behavior Assessment
	Vaginal Practices Y/N
	Vaginal Practices
	Social Influences Assessment Y/N
	Social Influences Assessment
	Social Influences Supplement Y/N
	Social Influences Supplement
	Ring Adherence Y/N
	Ring Adherence
	ACASI Tracking Y/N
	ACASI Tracking
	HIV Test Results
	Pregnancy Test Result
	Specimen Storage
	Concomitant Medications Y/N
	Adverse Experience Y/N
	Laboratory Results
	STI Test Results
	Physical Exam
	Vital Signs
	Pelvic Exam
	Ring Collection and Insertion
	Additional Study Procedures Y/N
	Pelvic Exam Diagrams (non MediData Rave)
V9 - Study Exit/Termination (Month 13)	Participant Date of Visit
	Follow-up Visit Summary
	Study Exit Assessment Y/N
	Study Exit Assessment
	HIV Test Results
	Pregnancy Test Result
	Specimen Storage
	Concomitant Medications Y/N

	Adverse Experience Y/N
	Termination
	Additional Study Procedures Y/N
<p>Early Termination Visit <i>(Completed in lieu of expected study visit within the visit window)</i></p>	Follow-up Visit Summary
	Concomitant Medications Y/N
	Adverse Experience Y/N
	Pelvic Exam
	Physical Exam
	Vital Signs
	Laboratory Results
	HIV Test Results
	STI Test Results
	Pregnancy Test Result
	Ring Adherence Y/N
	Ring Adherence
	Ring Collection and Insertion
	Specimen Storage
	Behavior Assessment Y/N
	Behavior Assessment
	Vaginal Practices Y/N
	Vaginal Practices
	Social Influences Assessment Y/N
	Social Influences Assessment
	Social Influences Supplement Y/N
	Social Influences Supplement
	ACASI Tracking Y/N
	ACASI Tracking
	Study Exit Assessment Y/N
	Study Exit Assessment
	Termination
	Pelvic Exam Diagrams (non MediData Rave)
As needed	ACASI Tracking

(Additional Study Procedures/Interim Visits Procedures)	Follow-up Visit Summary
	HIV Test Results
	Laboratory Results
	Physical Exam
	Vital Signs
	Pelvic Exam
	Participant Transfer
	Participant Receipt
	Pharmacy Ring Dispensation (completed at site Pharmacy Only)
	Pregnancy Report and History
	Pregnancy Outcome
	Pregnancy Test Result
	Ring Collection and Insertion
	Seroconverter Laboratory Results
	Specimen Storage
	STI Test Results
	Missed Visit
	Pelvic Exam Diagrams (non MediData Rave)
Ongoing Logs	Adverse Experience Log Y/N
	Adverse Experience Log
	Concomitant Medications Log Y/N
	Concomitant Medications Log
	Clinical Product Hold/Discontinuation Log Y/N
	Clinical Product Hold/Discontinuation Log
	Protocol Deviation Log Y/N
	Protocol Deviation Log
	Social Benefits Log Y/N
	Social Benefits Log
	Social Impact Log Y/N
	Social Impact Log
	Vaginal Ring Tracking Log Y/N
	Vaginal Ring Tracking Log
	Grade 1 Adverse Experience Log (non MediData Rave)

14.3.6 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. When administering site-specific translated CRFs, provide participant responses in the indicated space provided on the paper CRF or within Rave in English only.

Site staff are encouraged to practice direct data entry when administering the interviewer-administered forms, 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. Site staff who will conduct the participant interviews and complete the interviewer-administered behavioral and product adherence forms are encouraged to practice conducting the interviews, completing/updating the eCRFs by entering test data, and familiarizing themselves with the eCRF questions, skip patterns, and system queries prior to conducting actual participant interviews.

14.3.7 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 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.

14.3.7.1 MTN-025 QC Review Step #1

- 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 paper CRFs and eCRFs based on participant responses to ensure completeness:
 - Screening Visit: Demographics, Baseline Medical History Log, Pelvic Exam Diagrams, Concomitant Medications Log
 - Enrollment Visit: Baseline Family Planning Log, Baseline Behavioral Assessment, Baseline Vaginal Practices, Baseline Medical History Log,

Concomitant Medications Log, Pregnancy Test Results, Vaginal Ring Tracking Log (if applicable)

- Decliner Population Screening/Enrollment: Demographics, Baseline Behavioral Assessment
- Follow-up visits, when present: Follow-up Visit Summary, Ring Adherence, Behavior Assessment, Vaginal Practices, Social Influences Assessment, Social Benefits Log, Social Impact Log, Study Exit Assessment, Vaginal Ring Tracking Log (if applicable), Pelvic Exam Diagrams, Adverse Experience/Grade 1 Adverse Experience Log CRFs, Physical Exam, Vital Signs, and Pelvic Exam CRFs as indicated.

14.3.7.2 MTN-025 QC Review Step #2

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), 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.
- Ensure that the assigned visit number is correct, and is consistent between the paper source documents, including paper CRFs, 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 Pelvic Exam, Physical Exam, Laboratory Results, Pregnancy Test Results and STI Test Results, and ensure that medical conditions are recorded appropriately on the Baseline Medical History Log. Refer to the CCGs for further guidance.
- Ensure the Laboratory Results form has the correct Specimen Collection Dates recorded. If any labs were repeated, update the original form. If the participant enrolls, enter the updated results into the study database.
- If a second (repeat) full pelvic exam is performed during screening, update the Pelvic Exam Diagrams (non-Medidata Rave) form and Pelvic Exam form to document the 2nd screening pelvic exam. If the participant enrolls in the study, enter the CRF data from the 2nd screening pelvic exam into the study database.
- Review the Enrollment Specimen Storage form and make sure it matches information documented on the visit checklist and Enrollment Visit LDMS Specimen Tracking Sheet (or local lab requisition sheet).
- On the Family Planning CRF: if the contraceptive recorded/entered requires documentation on the Concomitant Medications Log (per CCG instructions), make sure this is done accurately.
- If a participant will not enroll, make sure the Pre-Screening Outcome CRF, Participant Date of Visit, and applicable Eligibility Criteria CRF (Eligibility Criteria CRF for the main MTN-025/HOPE study or Eligibility Criteria – Decliner Population CRF) have been

completed, and enter these three forms into the study database. No other CRFs should be entered into the study database for the participant.

- Wait until a participant enrolls in the study, or the decliner population, before entering any screening or enrollment data into the study database. Once a participant enrolls in the study, complete QC reviews of the Screening and Enrollment Visit CRFs and enter them into the study database.

If an ASPIRE participant does not screen for MTN-025/HOPE or the decliner population (e.g., she is lost to follow-up, not eligible, or not interested in participating), complete and enter the Pre-Screening Outcome CRF only.

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

- If a log CRF is newly completed at a visit that is not an interim visit, make sure the corresponding “Yes/No (Y/N)” CRF is completed for the visit and recorded “yes”. For example, if the AE Log CRF is completed, the Adverse Experience Y/N CRF should be completed and marked “yes”; if the Social Influences Assessment CRF is completed, the Social Influences Assessment Y/N CRF should be completed and marked “yes”, etc.
- Concomitant Medications Log CRF: if “Yes” is marked for “Taken for a reported AE?”, make sure the AE Log page recorded/entered has “Medication(s)” entered, and vice-versa. If the medication is a contraceptive, make sure there is a response marked for the “If contraceptive, was it dispensed at research center?” item.
- Follow-up Visit Summary CRF: if “Yes” is marked for the question, “Is this an interim visit?” ensure there is an interim visit number recorded/entered on the ‘Interim Visit Procedures’ form and at the top of each paper CRF completed.

QC #2 for Paper CRFs

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 and on the front of the forms.
- If a response box with “other”, “specify”, or “describe” line is present, ensure English text is present on this line.
- 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. 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 paper source documents (e.g., data entry of paper CRFs 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 the review.

14.4 Form-Specific Completion Instructions

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

14.5 Case Report Forms

The current version of the MTN-025 paper case report forms can be found at the MTN-025 Atlas web page, link provided below.

<https://atlas.scharp.org/cpas/project/MTN/025/begin.view?>