Section 12. Data Collection

12   Introduction

The purpose of this document is to provide site staff with the information they need to successfully complete and submit MTN-038 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-038 team members, along with their job role and e-mail address, are listed below.

Job Role	Name	Email Address
Protocol Statistician	Barbra Richardson	barbrar@uw.edu
Statistical Research Associate	Holly Gundacker	hgundack@scharp.org
Clinical Data Manager	Amanda Brown	abrown@scharp.org
Clinical Programmer	Jackie Fitzpatrick	jackie@scharp.org
Clinical Safety Associate	Christine Thompson	cethomps@scharp.org
Lab Data Coordinator	Sara Aranda	saranda@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-038 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-038 Atlas webpage: https://atlas.scharp.org/cpas/project/MTN/038/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-038 Atlas web page: https://atlas.scharp.org/cpas/project/MTN/038/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	**Direct number**
1-866-MEDIDATA (633-4328)	1-973-659-6780
Toll-free fax	**Direct fax**
1-877-743-2350	1-973-954-5621

Email
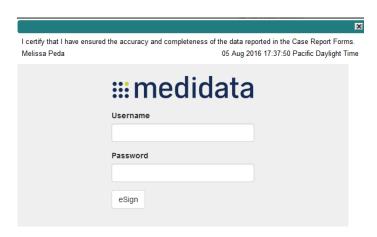helpdesk@mdsol.com

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 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 AE Log CRFs, 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 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 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.
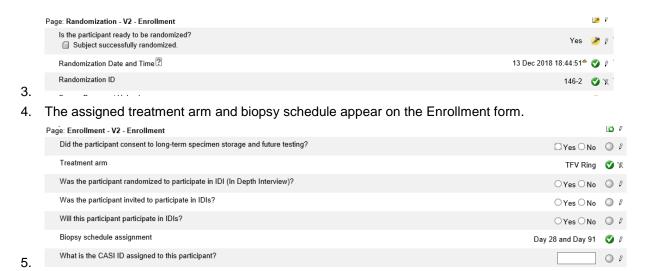
12.2 CRF Completion

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 (ring) 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).

    o 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 MTN-038 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. Adverse events should be reported within three days of site awareness.

12.2.2 Screening and Enrollment/Randomization

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

- For participants who screen out of MTN-038: data entry is required for the Inclusion Exclusion Criteria eCRF. (Other eCRFs that were completed during the failed screening attempt will remain in the study database and will not undergo QC review).

- For participants who enroll in MTN-038: enter data for the Inclusion Exclusion Criteria eCRF, along with all required Screening and Enrollment Visit CRFs.

- **Randomization:** Participants will be randomized to a treatment arm (TFV IVR or placebo IVR), a biopsy schedule, and an IDI group (considered for IDI, not considered for IDI).

    1. Randomization to a treatment arm and biopsy schedule will be done through Medidata:

        1. Complete the Inclusion Exclusion Criteria CRF in the Screening folder, with all responses indicating that the participant is eligible for study participation:

            a. "Did the participant meet all eligibility criteria?" = "Yes"

            b. "Eligibility Status" = "Eligible and Enrolled"

        2. Complete the Randomization form in the Enrollment folder:

            a. "Is the participant ready to be randomized?" = "Yes"

                i. "Randomization Date and Time" and "Randomization ID" will appear automatically on the Randomization eCRF.

3.

Page: **Randomization - V2 - Enrollment**

Is the participant ready to be randomized? ☐ Subject successfully randomized.	Yes
Randomization Date and Time ?	13 Dec 2018 18:44:51
Randomization ID	146-2

4. The assigned treatment arm and biopsy schedule appear on the Enrollment form.

Page: **Enrollment - V2 - Enrollment**

Did the participant consent to long-term specimen storage and future testing?	☐Yes ○No
Treatment arm	TFV Ring
Was the participant randomized to participate in IDI (In Depth Interview)?	○Yes ○No
Was the participant invited to participate in IDIs?	○Yes ○No
Will this participant participate in IDIs?	○Yes ○No
Biopsy schedule assignment	Day 28 and Day 91
What is the CASI ID assigned to this participant?	

5.

2. Randomization to participate in an IDI will be done outside of Medidata:

   1. Download your site IDI Listing from the Atlas website MTN 038 Secure Sections.

   2. Compare the first three digits of the Randomization ID column of the IDI Listing spreadsheet to the Randomization ID assigned on the Randomization form in Rave, and find the match.

      a. On the spreadsheet, if the corresponding value in the "Considered for IDI" column is "No", the participant will not be invited to participate in an IDI.

         i. On the Enrollment CRF, enter "No" for "Was the participant randomized to participate in IDI (In Depth Interview)?".

      b. If the value in the "Considered for IDI" column is "Yes", the participant will be considered for participation in an IDI.

         i. On the Enrollment CRF, enter "Yes" for "Was the participant randomized to participate in IDI (In Depth Interview)?"

   3. Review the Demographics CRF completed at the Screening Visit for this participant:

      a. If the response to "In the past 12 months, what was/were the biological sex(es) of the partner(s) with whom the participant had vaginal sex?" is "Exclusively female partners" or "NA (no sex partners)," then the participant will not be invited to participate in an IDI.

         i. On the Enrollment CRF, enter "No" for "Was the participant invited to participate in IDI?"

      b. If the response to "In the past 12 months, what was/were the biological sex(es) of the partner(s) with whom the participant had vaginal sex?" is "Both male and female partners" or "Exclusively male partners" site staff will invite the participant to participate in an IDI. Sex with a male partner is defined as having penile-vaginal sex, including with a transman with a reconstructed penis.

         i. On the Enrollment CRF, enter "Yes" for "Was the participant invited to participate in IDI?"

   4. If the participant declines the invitation to participate in the IDI or be audio-recorded, enter "no" for "Will this participant participate in IDI?". If the participate agrees to participate in the IDI and be audio-recorded, enter Yes" for "Will this participant participate in IDI?"

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-038 will be assigned an MTN-038 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.

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-038 PTID assignment is defined as completion of an entry on the MTN-038 PTID-Name Linkage Log for a given participant.

The MTN-038 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: https://mtnstopshiv.org/research/studies/mtn-038.

Screening Attempts (Re-screens)
If a participant's first screening attempt is unsuccessful, she may re-screen once if she chooses. If she does re-screen, all screening procedures must be repeated with the exception of PTID assignment. Once a PTID is assigned to a participant that PTID is used for all re-screening 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 Inclusion Exclusion Criteria eCRF completed during the failed screening attempt should be updated to reflect the participant's final eligibility status.

Follow-Up Visits
For each MTN-038 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.

SCHARP will provide sites with an excel tool that may be used to generate individual participant follow-up visit calendars. The spreadsheet requires that the participant's Enrollment (i.e., randomization) date be entered. Once the enrollment date is entered, the target day and visit window for each required follow-up visit up through the Day 91 visit (Visit 9) will appear. The visit window for Visit 10/Final Contact is contingent on the actual visit date of Visit 9/PUEV. The calendar can be printed, added to the participant's study notebook, and updated as needed.

Split Visits
Whenever possible, all required visit evaluations should be completed on the same day. If this is not feasible, it may be possible to conduct a "split" visit (e.g., a participant comes in on her Day 14 target day and completes only some of the required evaluations, so returns the next day to complete the remaining required procedures), A split visit is possible when all required procedures can be conducted within the visit window, **AND** the visit is one of the following:

- Visit 1/Screening
- Visit 4/Day 7
- Visit 5/Day 14
- Visit 6/Day 28
- Visit 7/Day 42
- Visit 8/Day 56
- Visit 9 /Day 91
- Visit 10/Final Contact (24 – 72 hours after PUEV)

The following visits may not be split:

- Visit 2/Enrollment
- Visit 3/Day 1
.
Please refer to the Study Procedures section of this manual for more information regarding visit procedures and timing.

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	Visit Code	Target Day	Window Opens	Window Closes
Screening	1.0	NA	< 45 days prior to Enrollment	
Visit 2 - Enrollment (Day 0)	2.0	0	NA	45 days after Screening Visit
Visit 3 - Day 1	3.0	1	1	1
Visit 4 Day 7/Week 1	4.0	7	6	8
Visit 5 Day 14/Week 2	5.0	14	12	16
Visit 6 Day 28/Week 4	6.0	28	25	31
Visit 7 Day 42/Week 6	7.0	42	39	45
Visit 8 Day 56/Week 8	8.0	56	53	59
Visit 9 Day 91/Week 13	9.0	91	89	93
Visit 10 Day 92/Final Contact	10.0	92	24 - 72 hours after Visit 9	

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 her Day 14 visit until 17 days after enrollment. Per Table 12-1, the Day 14 visit has been missed. The missed visit is documented by completion of a Missed Visit CRF.

Interim Visits
An interim visit is a contact with a study participant 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 if the participant reports a new AE via a phone contact with the site. Required follow-up visit procedures are not done, either because the required follow-up visit has already been completed, or the participant is in between visit windows.
- Required study visit procedures are conducted outside the visit window, either to make up certain procedures from a missed visit, or to conduct Visit 9-Day 91 procedures due to an early termination. For example, if a participant comes to the clinic to withdraw consent for study participation on day 46, she would complete Day 91 visit procedures on Day 46, if she 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, wherein the post-decimal digit is not "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-038, an Interim Visit Summary CRF is completed for interim visits/contacts as needed.

The following are some examples of interim visits:

1. A participant has a family emergency and is unable to come into the clinic to complete her Day 14 visit until Day 17. Per section 5 of this manual (Study Procedures), an interim visit is conducted on Day 17 to make up certain missed Day 7 visit procedures.

   Why is this an interim visit? The Day 14 visit is considered a missed visit, as the visit window has closed. The visit on Day 17 is being conducted outside of the visit window – that is, between when the Day 14 visit window closed and when the Day 28 visit window opens. The interim visit is assigned an interim visit code as new CRFs will be completed (Interim Visit Summary, Cervical Specimen Storage, Pelvic Exam, Specimen Storage, and possibly others, per site consultation with the study management team).

2. A participant completes all required evaluations for her Day 7 visit on the target day. She then returns to the clinic 4 days later to request a new ring.

   Why is this an interim visit? The participant has already completed all Day 7 visit procedures, and it is too early (and not in the visit window) for the Day 14 visit. This is an interim visit, conducted between the Day 7 and Day 14 visits, and is assigned an interim visit code as new CRFs will be completed (Interim Visit Summary, and Ring Insertion and Removal).

3. A participant completes the Day 1 visit as scheduled. Her Day 7 visit window opens on November 15, and she is scheduled to complete the Day 7 visit on November 16. The participant reports to the clinic unexpectedly on November 15 to report new genital AE symptoms.

   Why is this an interim visit? The participant is in the Day 7 visit window, but site staff decide not to conduct Day 7 visit procedures for this participant on November 15 (e.g., the participant already has her Day 7 visit 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 15). An interim visit code is assigned as new CRFs will be completed (Interim Visit Summary, AE Log, possibly others).

4. A participant completes all required evaluations for the Day 42 visit on the target day, October 17. She returns to the site complaining of pregnancy symptoms on October 22. The site clinician requests a pregnancy test and the result is positive. Per protocol, the participant is permanently discontinued from further use of the study vaginal ring and is terminated from the study. Day 91 visit procedures are conducted as part of the October 22 interim visit.

   Why is this an interim visit? On October 22, a pregnancy test is conducted, representing new data collection, the participant is being instructed by study staff to permanently discontinue use of the study vaginal ring, and Day 91 visit procedures are conducted. An interim visit code is assigned, as data collection is occurring between regularly scheduled study visits and outside of the visit windows. CRFs required at the Day 91 visit are completed.

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 Pregnancy Report and Pregnancy Outcome Log eCRFs, which are housed in the Pregnancy folder, and the Medical History Y/N and log, which resides in the Screening folder, all log forms are housed in the "Ongoing Logs":

- Adverse Event Y/N and Log
- Concomitant Medications Y/N and Log
- Protocol Deviations Y/N and Log
- Product Hold Y/N and Log

The Discontinuation of Study Product eCRF and Study Termination eCRF are housed within the "Discontinuation" folder; each of these forms is completed once for each participant to document her permanent product discontinuation and study exit, respectively.

The Pregnancy Report eCRF, Pregnancy History eCRF, and Pregnancy Outcome eCRF are housed within the "PREGNANCY" folder (added through the "Add Event" field on a participant's home page. The Pregnancy Report and Pregnancy Outcome eCRFs are completed for every pregnancy reported for a participant during the study; the Pregnancy History eCRF is completed once for each participant who becomes pregnant during the study.

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
V1 - Screening	1.0
V2 - Enrollment	2.0
V3 - Day 1	3.0
V4 - Day 7 / Week 1	4.0
V5 - Day 14 / Week 2	5.0
V6 - Day 28 / Week 4	6.0
V7 - Day 42 / Week 6	7.0
V8 - Day 56 / Week 8	8.0
V9 - Day 91 / Week 13	9.0
V10 - Final Contact	10.0

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.

> **Example**: A participant comes in on her Day 28 target day of 08 October 2018 and completes all required visit evaluations except pregnancy testing. She returns on 10 October 2018 (still within the visit window) and provides a urine sample for pregnancy testing. All CRFs dated 08-OCT-18 and 20-OCT-18 are assigned the same visit code of "6.0" and are housed within the Day 28 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.

Example #1: A participant completes her Day 7 visit (visit code = 4.0) on the target day. She returns to the site four days later to report a new genital symptom. This interim Visit is assigned a visit code of 4.1.

The examples below are from section 12.3.2, where interim visits are defined. These examples now have visit code information added to each example.

1. A participant has a family emergency and is unable to come into the clinic to complete her Day 7 visit until Day, 9, which is outside the visit window. Per section 5 of this manual (Study Procedures), an interim visit is conducted on Day 9 to make up certain missed Day 7 visit procedures.
   visit code = 4.1

2. A participant completes all required evaluations for her Day 7 visit on the target day. She then returns to the clinic 5 days later to request a new ring.
   visit code = 6.1

3. A participant completes her Day 1 visit as scheduled. Her Day 7 visit window opens on February 4, and she is scheduled to complete the Day 7 visit on that day. The participant reports to the clinic unexpectedly on February 8 to report new genital AE symptoms.
   visit code = 3.1

4. A participant completes all required evaluations for the Visit 8/Day 56 visit on the target day, May 23. She returns to the site complaining of pregnancy symptoms on June 1. The site clinician requests a pregnancy test and the result is positive. Per protocol, the participant is permanently discontinued from further use of the study vaginal ring and is terminated early from the study. Day 91/Final Clinic visit procedures are conducted as part of the June 1 interim visit.
   visit code = 8.1

12.3.4 Form Supply

SCHARP will post a CRF (pdf) file, representing output from the study database eCRFs, on the following MTN-038 Atlas web page:

https://atlas.scharp.org/cpas/project/MTN/038/begin.view??

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 they choose to perform paper CRF completion.

12.3.5 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 tool 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, the ongoing log forms, discontinuation forms, and pregnancy forms.

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

Visit	Form Name
V1 - Screening	Screening Date of Visit
	Inclusion/Exclusion Criteria
	Demographics
	Medical History
	Physical Exam
	Pelvic Exam
	Vital Signs
	STI Test Results
	Hematology
	Chemistry Panel
	HIV Test Results
	Pregnancy Test Results
V2 - Enrollment Visit	Randomization
	Enrollment
	Behavioral Summary, CASI Tracking
	Ring Insertion and Removal
	Physical Exam
	Vital Signs
	Pelvic Exam
	Pregnancy Test Results
	HIV Test Results
	Timed Cervical Specimen Storage
	Specimen Storage
V3 and V4 – Days 1 and 7	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Pelvic Exam
	Specimen Storage
	Cervical Specimen Storage
V5 – Day 14	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Pelvic Exam
	Specimen Storage
	Cervical Specimen Storage

V6 – Day 28	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Behavioral Summary, CASI Tracking
	Ring Adherence YN, Ring Adherence
	Pelvic Exam
	Pregnancy Test Results
	Specimen Storage
	Cervical Specimen Storage
V7 - Day 42	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Pelvic Exam
	Cervical Specimen Storage
V 8 – Day 56	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Pelvic Exam
	Pregnancy Test Results
	Behavioral Summary, CASI Tracking
	Ring Adherence YN, Ring Adherence
	Specimen Storage
	Cervical Specimen Storage
V9 – Day 91 PUEV / Early Discontinuation	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Discontinuation of Study Product
	Pelvic Exam
	Pregnancy Test Results
	Chemistry Panel
	Hematology
	HIV Test Results
	Timed Specimen Storage
	Timed Cervical Specimen Storage
	Ring Insertion and Removal
	Ring Adherence YN, Ring Adherence
	Behavioral Summary, CASI Tracking
V10 – Day 92	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Study Termination
	Specimen Storage
	Cervical Specimen Storage
Pregnancy Folder	Pregnancy Report
	Pregnancy History
	Pregnancy Outcome Log
As needed (Additional Study Procedures/Interim Visits Procedures)	Additional Study Procedures
	HIV Test Results
	HIV Confirmatory Results
	Physical Exam

	Vital Signs
	Pelvic Exam
	Hematology
	Chemistry Panel
	Pregnancy Test Results
	Cervical Specimen Storage
	Specimen Storage
	STI Test Results
	Ring Adherence Y/N
	Ring Insertion & Removal
	Missed Visit
	Interim Visit Summary
	Behavioral Summary, CASI Tracking
As needed, Ongoing Logs	Protocol Deviation Log Y/N
	Protocol Deviation Log
	Adverse Event Log Y/N
	Adverse Event Log
	Concomitant Medications Log Y/N
	Concomitant Medications Log
	Product Hold Y/N
	Product Hold
Pharmacy	Pharmacy Dispensation
Discontinuations	Study Termination
	Discontinuation of Study Product

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 during Medidata outages) 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.

12.3.7 MTN-038 QC Review Step #1 (completed during visit)

- ❑ Review visit checklist and pelvic exam checklist (if used) to ensure all required procedures were completed
- ❑ Review Inclusion Exclusion checklists/worksheets to ensure completeness and verify participant Inclusion Exclusion
- ❑ Review LDMS Specimen Tracking Sheets to ensure completeness and accuracy

□ Review completed CRFs, if needed at those visits, based on participant responses to ensure completeness:

- ○ Screening Visit: Demographics, Medical History log, Concomitant Medications log
- ○ Enrollment Visit: Medical History log, Concomitant Medications log, Behavioral Summary
- ○ Follow-up visits, when present: Ring Adherence, Behavioral Summary, Adverse Event log, Ring Insertion and Removal

12.3.8 MTN-038 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 Ring Insertion and Removal, Pelvic Exam, Physical Exam, Vital Signs, Chemistry Panel, Hematology, Pregnancy Test Results, HIV Tests Results, and STI Test Results, and ensure that medical conditions are recorded appropriately on the Medical History Log. Refer to the CCG 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, Cervical Specimen Storage, Timed Specimen Storage, and Timed Cervical Specimen Storage eCRFs for their respective visits, 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 Inclusion Exclusion 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 will 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 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".

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 MTN-038 CRF Completion Guidelines (CCG) document.

- If a response box with "other", "specify", or "describe" line is present, ensure 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 and consistency. In addition, the database design and system queries ensure skip patterns are followed, per instructions in the CCG.

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 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 MTN-038 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.

12.5 Case Report Forms

The current version of the MTN-038 case report forms can be found at the MTN-038 Atlas web page, link provided below.

https://atlas.scharp.org/cpas/project/MTN/038/begin.view?