

Section 11. Data Collection

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11 Introduction

The purpose of this document is to provide site staff with the information they need to successfully complete and submit MTN-043 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-043 team members, along with their job role and e-mail address, are listed below.

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11.1 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), or entered into the study database based on other non-CRF source documents (e.g., lab reports, testing logs, chart notes, etc.).

The MTN-043 study database in Medidata Rave may be accessed at www.imedidata.com.

When using Medidata Rave, the internet browser chosen and its 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-043 Atlas webpage: <https://atlas.scharp.org/cpas/project/MTN/043/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-043 Atlas web page: <https://atlas.scharp.org/cpas/project/MTN/043/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	

11.2 Data Entry/Quality Control

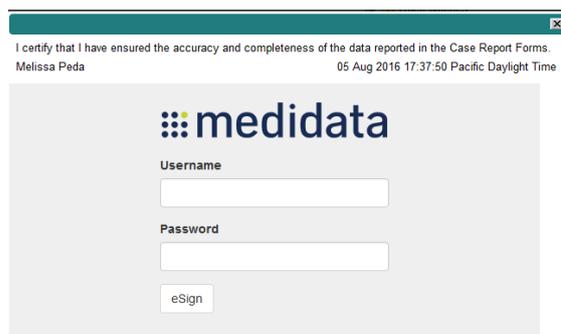
Once an eCRF is completed and saved in the study database, the following may occur:

- 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/or 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 AE Log CRFs, and coding queries may be placed.
- WHO coding will be required for the Concomitant Medication Log CRF 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.
- In the rare event that a site utilizes paper CRFs as source documents, any changes to the paper CRFs **must** be entered into the Medidata Rave study database.

11.3 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. SCHARP will inform site investigators when investigator sign-off of participant data should be completed at the end of the study. 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 Figure 1 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.

Figure 1: Example of Investigator of Record or Designee Sign-off Pop-Up Window



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

11.4 CRF Completion

11.4.1. General Guidelines

- 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 current version of the MTN-043 CRF Completion Guidelines (CCGs) 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.

11.4.2 Subject Identifier and Participant Type

- For both mothers and infants, the Participant Identifier and Participant Type CRFs will be the first two CRFs completed.
- The Participant Identifier CRF is completed to generate a Participant Identifier (see section 11.5.1). This should be completed for mothers and infants at the mother's Screening visit after consent is obtained.
- The Participant Type CRF is completed to indicate if the participant is a mother or an infant. The Screening, Enrollment and Ongoing Logs folders will populate for the participant type (mother or infant) upon completion of the Participant Type CRF.

11.4.3 Mothers: Screening and Enrollment/Randomization

- For mothers, 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 eligibility data should be entered into the study database as follows:
- For participants who screen out of MTN-043: data entry is required for the Participant Type, Inclusion/Exclusion Criteria, and Informed Consent eCRFs. Other eCRFs that were completed with data collected during the failed screening attempt may remain in the study database and will not undergo QC review.
- For participants who enroll in MTN-043: data entry is required for the Participant Type, Inclusion/Exclusion Criteria, and Informed Consent eCRFs., along with all required Screening and Enrollment Visit CRFs. All eCRFs will undergo QC review.

Randomization: Participants will be randomized to study product arm (Dapivirine Vaginal Ring or Truvada Oral Tablet) and purposefully selected to In Depth Interviews (IDI). Randomization to a study product arm will be done through Medidata. Selection to an IDI group will be done outside of the Medidata Rave database. For more information regarding purposeful selection to IDI group, please refer to SSP Section 5 and 14. The following steps outline the study arm randomization process for clinic staff:

1. Complete the **Inclusion/Exclusion Criteria CRF** with all responses indicating that the participant is eligible for study participation.
2. Complete the **Randomization CRF**. To randomize a study participant, mark the “Yes” response box (see Figure 2) for the question “Is the participant ready to be randomized?” Once this response is saved, the database (via the Medidata Balance module) will assign the participant to a study arm and the Randomization Date and Time will appear automatically on the Randomization eCRF.

Note: If a CRS clinic staff attempts to randomize a participant via the Randomization CRF without having indicated that the participant is eligible on the Inclusion/Exclusion Criteria CRF, Medidata Rave will not allow the participant to be randomized, and an error message will appear.

Figure 2: Participant randomization via the Randomization eCRF

Page: Randomization - V2.0 - Enrollment (1)

Is the participant ready to be randomized? Yes No

Randomization date and time

Randomization ID

3. A participant is considered officially enrolled in the study once the Randomization CRF is completed and saved, as evidenced by the appearance of a Randomization Date and Time on the Randomization eCRF.

The treatment arm will be auto-populated on the Enrollment eCRF in the Enrollment Visit folder (see Figure 3). Upon completion of the Randomization eCRF, the clinic staff will navigate to the Enrollment eCRF to view the participant’s randomized arm and complete the MTN-043 Prescription.

Figure 3: Participant randomization via the Enrollment eCRF

MOTHER:

Treatment arm

HIV Status Positive Negative

Pregnancy Status Positive Negative

Was the participant randomized to participate in IDI (In Depth Interview)? Yes No

Was the participant invited to participate in IDI? Yes No

Will this participant participate in IDI? Yes No

11.4.4 Mothers: Follow-up Visits

- The Follow-up Visit Y/N CRF will be auto-populated in every follow-up visit folder (V3 – V7). The only field is “Did the participant complete this visit?”
 - Select “Yes” if the participant completed this visit. Required forms will be added to the visit folder.
 - Select “No – Missed visit” if the participant missed the visit. The Missed Visit CRF will be added to the visit folder.

11.4.5 Infants: Screening and Enrollment

- For Infants, 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 eligibility data should be entered into the study database as follows:
- For participants who screen out of MTN-043: data entry is required for the Participant Type and Inclusion/Exclusion Criteria eCRFs. Other eCRFs that were completed with data collected during the failed screening attempt may remain in the study database and will not undergo QC review.

- For participants who enroll in MTN-043: data entry is required for the Participant Type and Inclusion/Exclusion Criteria eCRFs, along with all required Screening and Enrollment Visit CRFs. All eCRFs will undergo QC review. An infant is considered enrolled in MTN-043 once final determination of infant eligibility has been determined by delegated staff and the mother has been randomized. Complete the Infant section of the Enrollment CRF, with the question “If infant, has this participant enrolled in the study?” answered with “Yes” and date of infant enrollment as the date of maternal randomization. This date will serve as the official enrollment date for the infant. The infant section of the Enrollment eCRF in the Enrollment Visit folder can be seen in Figure 4 below.

Figure 4: Infant Enrollment

Page: Enrollment - V2.0 - Enrollment - Infant (1)

INFANT:

If infant, has this participant enrolled in the study? Yes No

Date of infant enrollment: ...

11.4.6 Site Data Management SOP

As a condition for study activation, each study site must have a site or study-specific SOP for Data Management. A template Data Management SOP is available on the MTN-043 study webpage. 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
- Linking Mother PTIDs with Infant PTIDs
- 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

11.5 Study-specific Data Collection Information

11.5.1 Participant Identification Numbers (PTIDs)

As described in each site’s Data Management SOP, each mother/infant pair who has written informed consent provided to be screened in MTN-043 will have MTN-043 PTIDs for the mother and for her infant assigned. 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. The process for generating maternal PTIDs and infant PTIDs is the same. 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 Log and site staff will maintain this document, which will be used to link a participant's name with her assigned PTID, her infant's assigned PTID and her infant's name. For study purposes, the act of MTN-043 PTID assignment is defined as completion of an entry on the MTN-043 PTID-Name Linkage Log for a given participant. The PTID-name link log is an essential document, and site staff should ensure that each PTID on the link logs is assigned to 1 participant name only. No PTID or name should appear on the logs twice, and no PTID or name should appear on the logs without a corresponding name or PTID, respectively.

The MTN-043 PTIDs are nine digits and formatted as "XXXXYYYYZ". 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.

11.5.2 Study Visit Timing

Screening and Enrollment

The initial screening visit is defined as the day the mother provided written informed consent for herself and her infant to be screened for the study. The Enrollment Visit will be scheduled to take place within 35 days of the initial Screening Visit. The date the mother/infant pair is enrolled is Study Day 0. Mothers are randomized at the Enrollment visit. 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 screening date (i.e., date informed consent provided for the current screening attempt). The tool will be posted online at: <https://mtnstopshiv.org/research/studies/mtn-043/mtn-043-study-implementation-materials>

Screening Attempts (Re-screens)

If a mother/infant first screening attempt is unsuccessful, they may re-screen once per IoR discretion. If the pair does re-screen, all screening procedures must be repeated with the exception of PTID assignments. Once a PTID is assigned to a participant that PTID is used for the re-screening procedures and forms completed for that participant (do not assign a new PTID). If a mother/infant pair re-screens and enrolls, all previously completed eCRFs (from the original, failed screening attempt) must be updated, as needed, to reflect only data from the successful Screening and Enrollment Visit. Note that the Inclusion/Exclusion Criteria eCRF completed during the failed screening attempt must be updated to reflect the participant's final eligibility status and enrollment into the study.

Follow-Up Visits

For each MTN-043 follow-up visit, the visit type, visit code, target visit day, and visit window are listed in Tables 11-1. 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 a spreadsheet tool that may be used to generate individual participant follow-up visit calendars. The spreadsheet requires the mother/infant pair Enrollment date. Once the enrollment date is entered, the target day and visit window will appear for each required follow-up visit.

Because mothers and infants have the same visit schedule, there is only one version of the calendar tool for both mothers and infants. The calendar can be printed, added to each participant's study notebook, and updated as needed.

Seroconversion visit:

Infants of mother who seroconverted will have one additional visit 6 and 12 weeks after maternal seroconversion is confirmed. Sites should use the Seroconversion Scheduling Tool to determine target dates and visit windows for the infant 6-week and 12-week post-seroconversion visits.

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. The Enrollment Visit may not be split with the exception that site's which require a separate IC for enrollment may do this on a different day from the other enrollment visit procedures (see SSP section 5.4.1). Refer to the Study Procedures section of this manual for more information regarding visit procedures and timing. For example, a participant comes in on her V4.0 - Week 2 visit target day and completes most of the required evaluations. She 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 11.3.3 for more information on assigning visit codes to split visits.

Table 11-1: Visit Timing Requirements (mothers and infants)

Visit Code	Visit	Window Opens	Target Day	Window Closes
1.0	Screening	35 days prior to Enrollment	NA	
2.0	Enrollment*	NA	0	35 days after Screening Visit
3.0	Week 1 Visit	5	7	9
4.0	Week 2 Visit	12	14	16
5.0	1 Month Visit	21	28	35
6.0	2 Month Visit	49	56	63
7.0	PUEV/3 Month Visit	77	84	91
8.0	SEV	V7.0+7	V7.0+14	V7.0+28

Missed Visits

In those 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 Visit 4 until 18 days after enrollment. Per Table 11-1, Visit 4 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 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 an Early Termination Visit procedures.

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 eCRF, 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 11.3.3 for information on how to assign visit codes to interim visits.

For MTN-043, an Interim Visit Summary CRF is completed for interim visits/contacts as needed.

The following are some examples of interim visits:

- A participant completes all required evaluations for her on the V4.0 – 2 week visit on the target day. She then returns to the clinic 4 days later to report a Social Impact.

Why is this an interim visit? The participant has already completed all Visit V4.0 – 2 week, and it is too early (and not in the visit window) for Visit 5.0 – 1 Month visit to be conducted. This is an interim visit, conducted between Visits 4.0 and 5.0, and is assigned an interim visit code as new CRFs will be completed.

- A participant completes her Visit 3 – week 1 visit as scheduled. Her Visit 4 – week 2 visit window opens on July 13, and she is scheduled to complete Visit 4 on July 14. 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 Visit 4 visit window, but site staff decide not to conduct Visit 4 visit procedures for this participant on July 13th (e.g., the participant already has Visit 4 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 July 13). An interim visit code is assigned as new CRFs will be completed (Interim Visit Summary, AE Log, others as needed).

- A participant completes all required evaluations for Visit 5.0 – 1 Month visit on September 20. She returns to the site on October 8 and informs the clinic that she wishes to withdraw from the study. As such, Visit 7.0 – PUEV/3 Month Visit procedures are conducted as part of the October 8 interim visit.

Why is this an interim visit? On October 8, the participant wishes to withdraw from the study and an early termination visit is conducted. As Visit 5.0 has been completed, the early termination visit should be assigned an interim visit code. CRFs required at the 7.0 – PUEV/3 Month Visit are completed.

- An infant completes his Visit 4.0 – week 2 visit on the target day. The next day, the infant's mother calls the clinic to report a new mild symptom.

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

11.5.3 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).

11.5.3.1 Mother Visit Folders

With the exception of the Baseline Medical History Log CRF and Pharmacy Dispensation Log CRF, all log forms (i.e., Adverse Event Y/N and Log, Non-Enrolled Infant Adverse Event Y/N and Log,

Concomitant Medications Y/N and Log, Protocol Deviations Y/N and Log, Social Impact Y/N and Log, and Product Hold Y/N and Log) are housed in the “Ongoing Logs” folder within the study database.

The Discontinuation of Study Product eCRF and Study Termination eCRF are housed within the “Discontinuations” folder; The Study Termination form is completed once for each participant to document study termination and the Discontinuation of Study Product eCRF is completed once when the study product is discontinued.

The Pharmacy Dispensation log CRF is housed within the “Pharmacy” folder. This form is completed at each visit when study product is dispensed. The Pharmacy folder is viewable and data can be entered by the Pharmacy role only. The CRC role (i.e., site clinic) cannot view the Pharmacy folder.

11.5.3.2 Infant Visit Folders

All log forms (i.e., Adverse Event Y/N and Log, Concomitant Medications Y/N and Log, and Protocol Deviations Y/N and Log) are housed in the “Ongoing Logs” folder within the study database.

The Study Termination eCRF is housed within the Infant Discontinuations folder; The Study Termination form is completed once for each participant to document study termination.

Tables 11-3 below lists the visit codes assigned to each required follow-up visit.

Visit codes for Split Visits

See Section 11.5.2 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 her Visit 4 - Week 2 visit target day of 23-NOV-19 and completes all required visit evaluations except vital signs. She returns on 24-NOV-19 (still within the visit window) and her vital signs are collected. All CRFs dated 23-NOV-19 and 24-NOV-19 are assigned the same visit code of “4.0” and are housed within the Visit 4 - Week 2 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:
 - #.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.

The examples below are from section 11.5.2, where interim visits are defined. These examples now have visit code information added to each example.

- A participant completes all required evaluations for her on the V3.0 – week 1 visit target day. She then returns to the clinic 4 days later to report a Social Impact.

visit code = 3.01

- A participant completes her Visit 3 – week 1 as scheduled. Her Visit 4 – week 2 visit window opens on July 13, and she is scheduled to complete Visit 4 on July 14. The participant reports to the clinic unexpectedly on July 13 to report new genital AE symptoms.

visit code = 3.01

- A participant completes all required evaluations for Visit 5.0 – 1 Month visit on September 20. She returns to the site on October 8 and informs the clinic that she wishes to withdraw from the study. As such, Visit 7.0 – PUEV/3 Month Visit procedures are conducted as part of the October 8 interim visit.

visit code = 5.01

- An infant completes his Visit 4.0 – week 2 visit on the target day. The next day, the infant’s mother calls the clinic to report a new mild symptom.

visit code = 4.01

11.5.4 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 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 tables (Tables 11-3 and 11-4) 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 11-3: Mothers Schedule of Forms – CRFs Required to be Completed at Each Visit

Visit	CRF
n/a	Participant Identifier
Participant	Participant Type
Visit 1 – Screening Visit	Baseline Medical History Y/N, Baseline Medical History Log
	Chemistry Panel
	Demographics
	Hematology
	Feeding Assessment - Screening and Enrollment
	Inclusion/Exclusion Criteria
	Informed Consent
	Pelvic Exam
	Physical Exam
	Pregnancy History
	Screening Date of Visit
	STI Test Results
	Vaginal Practices
	Vital Signs
Pelvic Exam Diagrams (non- Medidata Rave)	
Visit 2 – Enrollment Visit	Baseline Behavioral Assessment
	Enrollment

	Feeding Assessment - Screening and Enrollment
	Edinburgh Postnatal Depression Scale
	Pelvic Exam
	Physical Exam
	Randomization
	Ring Assessment OR Tablet Assessment
	Ring Insertion and Removal OR PrEP Provisions and Returns
	Specimen Storage
	Vaginal Practices
	Vital Signs
	Pelvic Exam Diagrams (non- Medidata Rave)
Visits 3 and 4 (1 and 2 week visits)	Feeding Assessment – Follow-up, Feeding Inventory
	Follow-up Visit Y/N, Follow-up Visit Summary
	Ring Adherence Y/N, Ring Adherence; OR Tablet Adherence Y/N, Tablet Adherence
	Social Impact
	Specimen Storage
Visits 5 and 6 (1 and 2 month visits)	Behavioral Assessment - Follow Up
	Edinburgh Postnatal Depression Scale (EPDS)
	Feeding Assessment – Follow-up, Feeding Inventory
	Follow-up Visit Y/N, Follow-up Visit Summary
	HIV Test Results
	Ring Adherence Y/N, Ring Adherence; OR Tablet Adherence Y/N, Tablet Adherence
	Ring Assessment OR Tablet Assessment
	Ring Insertion and Removal OR PrEP Provisions and Returns
	Social Impact
	Specimen Storage
Visit 7 - PUEV (3-month visit)	Behavioral Assessment - Month 3 Follow Up
	Chemistry Panel
	Edinburgh Postnatal Depression Scale
	Feeding Assessment - Follow Up, Feeding Inventory
	Follow-up Visit Y/N, Follow-up Visit Summary
	Hematology

	HIV Test Results
	IDI Tracking
	Pelvic Exam
	Physical Exam
	Pregnancy Test Results
	Ring Adherence Y/N, Ring Adherence; OR Tablet Adherence Y/N, Tablet Adherence
	Ring Insertion and Removal OR PrEP Provisions and Returns
	Social Impact
	Specimen Storage
	Vital Signs
	Visit 8 – SEV (2 weeks after PUEV)
Social Impact	
Specimen storage	
Additional study Procedures / Interim Visit Procedures	Additional Study Procedures
	Behavioral Assessment - Follow Up
	Behavioral Assessment – Month 3 Follow Up
	Chemistry Panel
	Edinburgh Postnatal Depression Scale
	Feeding Assessment
	Feeding Inventory
	Hematology
	HIV Confirmatory Results
	HIV Test Results
	IDI Tracking
	Interim Visit Summary
	Missed Visit
	Pelvic Exam
	Physical Exam
	Pregnancy Test Results
	PreP Provision and Return
	Ring Adherence
Ring Assessment	

	Ring Insertion and Removal
	Seroconverter Results
	Social Impact
	Specimen Storage
	STI Test Results
	Tablet Adherence
	Tablet Assessment
	Urine Test Results
	Vaginal Practices
	Vital Signs
	Pelvic Exam Diagrams (non-Medidata Rave)

Ongoing Logs (as needed)	Adverse Event Y/N
	Adverse Event Log
	Concomitant Medications Y/N
	Concomitant Medications Log
	Protocol Deviations Y/N
	Protocol Deviations Log
	Product Hold Y/N
	Product Hold Log
	Social Impact Y/N
	Social Impact Log

Pregnancy	Pregnancy Report
	Pregnancy Outcome

Pharmacy	Pharmacy Dispensation
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Seroconversion Results	Follow-Up Visit Summary
	Seroconversion Results

Discontinuations	Study Termination
	Discontinuation of Study Product

Table 11-4: Infant's Schedule of Forms – CRFs Required to be Completed at Each Visit

Visit	Form Name
n/a	Participant Identifier
Participant	Participant Type
Visit 1 – Screening	Baseline Medical History Y/N, Baseline Medical History Log
	Infant Demographics
	Infant Inclusion/Exclusion Criteria
	Infant Vital Signs
	Informed Consent
	Physical Exam
	Screening Date of Visit
Visit 2 – Enrollment	Enrollment
	Infant Ages and Stages Assessment
	Infant Vital Signs
	Physical Exam
Visits 3 and 4 (1 and 2 week visits)	Follow-up Visit Y/N, Infant Follow-up Visit Summary
	Infant Specimen Storage (V4 only)
Visits 5 and 6 (1 and 2 month visits)	Follow-up Visit Y/N, Infant Follow-up Visit Summary
	Infant Specimen Storage
Visit 7 - PUEV (3-month visit)	Infant Ages and Stages Assessment
	Follow-up Visit Y/N, Infant Follow-up Visit Summary
	Infant Specimen Storage
	Infant Vital Signs
	Physical Exam
Visit 8 – SEV (2 weeks after PUEV)	Follow-up Visit Y/N, Infant Follow-up Visit Summary
	Infant Specimen Storage
As needed	Infant Additional Study Procedures
	Infant Ages and Stages Assessment
	Infant HIV Confirmatory Results
	Infant Interim Visit Summary
	Infant Specimen Storage
	Infant Vital Signs
	Missed Visit
	Physical Exam

	Seroconverter Results
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Ongoing Logs (as needed)	Adverse Event Y/N
	Adverse Event Log
	Concomitant Medications Y/N
	Concomitant Medications Log
	Protocol Deviations Y/N
	Protocol Deviations Log

Seroconversion Results	Follow-Up Visit Summary
	Seroconversion Results

Discontinuations	Study Termination
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11.5.5 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-043 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 for both mothers and infants to ensure completeness and verify participant eligibility
- Review LDMS Specimen Tracking Sheets to ensure completeness and accuracy
- Review mothers completed CRFs based on participant responses to ensure completeness:
 - Screening Visit: Baseline Medical History Log, Demographics, Feeding Assessment - Screening and Enrollment, Inclusion/Exclusion Criteria, Pregnancy History, Vaginal Practices
 - Enrollment Visit: Baseline Behavioral Assessment, Feeding Assessment - Screening and Enrollment, Edinburgh Postnatal Depression Scale, Ring Insertion and Removal or PrEP Provisions and Returns, Ring Assessment or Tablet Assessment, and Vaginal Practices
 - Follow-up visits: Behavioral Assessment - Follow Up, Behavioral Assessment - Month 3 Follow Up, Edinburgh Postnatal Depression Scale (EPDS), Feeding Assessment – Follow-up, Feeding Inventory, Tablet Adherence OR Ring Adherence, Ring Assessment or Tablet Assessment, Social Impact, Vaginal Practices
 - Adverse Event Log, Concomitant Medications Log, Concomitant Medications Log, Protocol Deviations Log, Social Impact Log,
- Review Infant completed CRFs to ensure completeness

- Infant follow-up visits: Infant Inclusion/Exclusion Criteria, Adverse Event Log, Informed Consent, Baseline Medical History Log, Concomitant Medications Log, Infant Ages and Stages Assessment

MTN-043 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 Chemistry Panel, Hematology, Pelvic Exam, Physical Exam, STI Test Results, Vital Signs, Randomization, Ring Assessment OR Tablet Assessment, Ring Insertion and Removal OR PrEP Provisions and Returns, Specimen Storage, and Urine Test Results CRFs (if used), and ensure that medical conditions are recorded appropriately on the Baseline 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).
- Review the Specimen Storage and the Ring Insertion and Removal (if applicable) 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 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 undergo QC review.

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

- Concomitant Medications Log CRF: if a medication is taken for an AE, select the on the Concomitant Medications Log eCRF, and ensure the AE Log CRF for the AE has “Medication(s)” 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 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.

11.6 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.

The current version of the MTN-043 CCGs is located on the MTN-043 ATLAS webpage:

<https://atlas.scharp.org/cpas/project/MTN/042/begin.view?>

11.7 Case Report Forms

SCHARP will post a CRF (pdf) file, representing output from the study database eCRFs, on the following MTN-043 Atlas web page:

<https://atlas.scharp.org/cpas/project/MTN/043/begin.view?>

The pdf file represents the current and complete set of study CRFs, and may be used by site staff for local IRB submission as needed. Should the Medidata Rave study clinical database become unavailable (i.e., offline) during the study, the Rave CRF pdf should be used to perform paper CRF completion.