

Section 12. Data Collection

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12. Introduction

The purpose of this document is to provide site staff with the information they need to successfully complete and submit MTN-034 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-035 team members, along with their job role and e-mail address, are listed below.

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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-035 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 with specific user permissions access 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-035 Atlas webpage: <https://atlas.scharp.org/cpas/project/MTN/035/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-035 Atlas web page: <https://atlas.scharp.org/cpas/project/MTN/035/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) any time a site has technical questions or problems related to access or use of the Medidata Rave software. Note that the toll-free numbers listed are for use within the US.

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

12.1.1 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, 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 Concomitant Medication Log CRF and coding queries may be placed.
- QCs are listed in the Medidata Rave Task Summary on the study home page of designated site users. Designated site staff members are responsible for routinely checking the Task Summary and correcting/updating study data to resolve any outstanding queries.
- When site staff correct/update study data and/or enter a query response to address a manual or coding query, SCHARP staff review the updated data and/or response, and resolve the query or re-query as needed.

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.**

12.1.2 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. 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 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.
- When direct data entry is not possible due to the nature of the source data - for example, when the source data is a local lab results report - site staff are encouraged to enter study data into the Medidata Rave study database based on the site-specific source document (in this case, the local lab results report).

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

- When completing an eCRF, refer to the CRF Completion Guidelines (CCG) document, posted on ATLAS, for detailed instructions on data collection pertaining to the given form and fields on that form.
- Complete eCRFs as soon as possible once the data is available and has undergone internal QC review, as applicable. Ideally, completion of all required eCRFs for a given visit will occur within 1–2 business days of the visit, though up to 7 days is acceptable.

12.2.2 Screening and Enrollment/Randomization

- Data entry into the study database begins at the Screening Visit. 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-035: data entry is required for the Inclusion/Exclusion Criteria eCRF. Other eCRFs that were completed during the failed screening attempt may remain in the study database and will not undergo QC review.
- For participants who enroll in MTN-035: data entry is required for the Inclusion/Exclusion Criteria eCRF, along with all required Screening and Enrollment Visit CRFs.

Randomization:

Participants will be randomized to study product sequence (Sequence A, B, C, D, E, or F). Randomization to a study product sequence will be done through Medidata. The following steps outline the randomization process for clinic staff:

1. Complete the **Inclusion/Exclusion Criteria CRF**. If all responses indicate that the participant is eligible, you may continue to the Randomization CRF within the Enrollment folder.
2. Navigate to the Enrollment folder and complete the **Randomization CRF**. To randomize a study participant, mark the “Yes” response box (shown in the image below) 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 product sequence and the Randomization Date and Time will appear automatically on the Randomization eCRF.
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.

Page: Randomization - V2.0 - Enrollment

Is the participant ready to be randomized? Yes No

Randomization Date and Time: 02 Jan 2018; 11:11

Replacing Participants

A participant may be replaced if no study product has been administered (e.g. due to non-adherence or permanent discontinuation), or in instances of early termination before Visit 7 (e.g. due to participant voluntarily withdrawing from the study, death, lost to follow-up, relocation, or permanent discontinuation).

The purpose of replacing participants is to compensate for the potential data loss. Replacement decisions will be made on a case-by-case basis by study leadership and the MTN-035 Management Team. Site staff should complete the Participant Replacement Assessment CRF as soon as a participant meets the criteria for replacement. The next participant enrolled will serve as the replacement participant.

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-035 will be assigned an MTN-035 PTID. To do this, site staff will generate in Medidata Rave a participant number (called "Subject ID" in Medidata Rave) within the electronic study and site folder; this number will serve as the participant's PTID. Refer to the "Creating Subjects" section of the Medidata Rave Electronic Data Capture (EDC) Training Manual and the CCG for specific instructions.

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

SCHARP will provide sites with a PTID-Name Linkage file and site staff will maintain this document, which will be used to link a participant's name with his/her assigned PTID. For study purposes, the act of MTN-035 PTID assignment is defined as completion of an entry on the MTN-035 PTID-Name Linkage Log for a given participant.

The MTN-035 PTIDs are nine digits, 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 provides 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 Visit Calendar Tool will be posted on-line at: <https://mtnstopshiv.org/research/studies/mtn-035>.

Screening Attempts (Re-screens)

If a participant's first screening attempt is unsuccessful, they may re-screen once if they choose. If they do re-screen, all screening procedures must be repeated except for PTID assignment. 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 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 the Inclusion/Exclusion Criteria eCRF completed during the failed screening attempt should be updated to reflect the participant's final eligibility status and enrollment into the study.

Follow-Up Visits

For each MTN-035 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 indicated 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 that the participant's Enrollment (i.e., randomization) date be entered. All target visit dates and visit windows are based off of the enrollment date except for visits 4, 6 and 8 as these are based off of when the visit actually occurred. Therefore, an Actual Visit Date for Visits 3, 5, and 7 must be manually entered in addition to the enrollment date to generate the target visit dates and regimen windows for subsequent visits. The calendar can be printed, added to the participant's study notebook, and updated as needed.

Note that the calendar tool was designed to maintain the product use periods and wash out periods. If a visit is not within the windows outlined within the SSP Manual, the visit is technically considered missed. The site records this as a missed visit and can subsequently records data in an interim visit, if applicable. Interim visits are allowed per protocol in these instances.

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. (Refer to SSP Manual Section 5: Study Procedures for more information regarding visit procedures and timing). For example, a participant comes in on their Visit 4 target day and completes most of the required evaluations. They come back the next day and complete 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 within the visit window.

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

MTN-035 Visit Windows

Table 12-1: Visit Timing Requirements

All windows are in days; Enrollment date = Day 0; PUEV=Product Use End Visit

Visit	Visit Code	Target Day	Window Opens	Window Closes
Screening	1.0	NA	45 days prior to Enrollment	
Enrollment Period 1: Study Product Initiation	2.0	0	NA	45 days after Screening Visit
Visit 3: Day 28/Week 4 1st PUEV	3.0	28	28	34
Visit 4 – Day 35/Week 5 Product Switch Visit	4.0	35	35	40
Visit 5 – Day 63/Week 9 2nd PUEV	5.0	63	63	69
Visit 6 – Day 70/Week 10 Product Switch Visit	6.0	70	70	75
Visit 7 – Day 98/Week 14 3rd PUEV	7.0	98	98	104
Visit 8 – Day 105/Week 15 Final Termination Visit	8.0	105	105	112

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 5 until 76 days after enrollment. Per Table 12-1, Visit 5 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 due to an early product discontinuation.

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 12.3.3 below for information on how to assign visit codes to interim visits.

For MTN-035, an Interim Visit Summary CRF is completed for interim visits/contacts as needed.

The following are some examples of interim visits:

1. A participant completes Visit 4 as scheduled. Their Visit 5 visit window opens on November 5, and they are scheduled to complete Visit 5 on November 5. The participant reports to the clinic unexpectedly on November 1 to report new genital AE symptoms.

Why is this an interim visit? The participant is in the Visit 4 visit window and it is too early to conduct their Visit 5 visit. An interim visit code is assigned as new CRFs will be completed (Interim Visit Summary, AE Log, others as needed).

2. A participant completes all required evaluations for Visit 6 on the target day, January 10. The participant returns to the site on January 15 and informs the clinic that they wish to withdraw from the study. As such, early termination visit procedures are conducted as part of the January 15 interim visit.

Why is this an interim visit? On January 15, the participant wishes to withdraw from the study and an early termination visit is conducted. As Visit 6 has been completed, the early termination visit should be assigned an interim visit code. CRFs required at the Visit 8 – Day 105/Week 15/Final Termination 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 Discontinuation of Study Product log CRF, all log forms (i.e., AE Summary and Log, Medical History Log, Concomitant Medications Summary and Log, Protocol Deviations Summary and Log, Social Impact Log, and Product Hold Summary and Log) are housed in the “Ongoing Logs” folder within the study database.

The Discontinuation of Study Product log 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 Product Discontinuation Log CRF is completed for each instance that study product is discontinued.

The Pregnancy Report eCRF and Pregnancy Outcome eCRF are housed within the “Pregnancy” folder. The Pregnancy Report eCRF and Pregnancy Outcome CRF are completed for every pregnancy reported for a participant during the study. The Pregnancy History eCRF is added to a participant casebook via the “Add Event” menu on the participant’s homepage and is completed when the first pregnancy for a participant is reported.

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
Visit 3: Day 28/Week 4 - 1st PUEV	3.0
Visit 4 - Day 35/Week 5 - Product Switch Visit	4.0
Visit 5 – Day 63/Week 9 - 2 nd PUEV	5.0
Visit 6 – Day 70/Week 10 - Product Switch Visit	6.0
Visit 7 – Day 98/Week 14 - 3 rd PUEV	7.0
Visit 8 – Day 105/Week 15 – Final/Early Termination	8.0

Visit codes for Split Visits

See Section 5.5.2 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 his/her Visit 7 – Day 98/Week 14 target day of 21-JUN-19 and completes all required visit evaluations except STI Test Results. They return on 25-JUN-19 (still within the visit window) and his/her STI Test Results are obtained. All CRFs dated 21-JUN-19 and 25-JUN-19 are assigned the same visit code of “7.0” and are housed within the Visit 7 – Day 98/Week 14 visit folder in the study database.

Visit codes for Interim Visits

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

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

- To the left of the decimal point, record the visit code of the most recently required follow-up visit, even if the visit was missed and/or if the participant is within the next visit's window.
- To the right of the decimal point:
 - #.1 = the first interim visit after the most recently-required visit,
 - #.2 = the second interim visit after the most recently-required visit,
 - #.3 = the third interim visit after the most recently-required visit, and so on.

The examples below are from section 11.3.2, where interim visits are defined. These examples now have visit code information added to each example.

1. A participant completes all required evaluations on the Visit 4 – Day 35/Week 5 target day. They then return to the clinic four days later to request additional enema tips.

i. visit code = 4.1

2. A participant completes her Visit 5 – day 63/Week 9 Product Switch Visit as scheduled. Her Visit 6 visit window opens on January 20. The participant reports to the clinic unexpectedly on January 12 to report new genital AE symptoms.

i. visit code = 5.1

3. A participant completes all required evaluations for Visit 6 – Day 70/Week 10 on the target day, March 23. They return to the site on March 25 and inform the clinic that they wish to withdraw from the study. As such, Visit 7 – Day 98/Week 14 3rd PUEV visit procedures are conducted as part of the March 25 interim visit.

i. visit code = 7.1

12.3.4 Form Supply

SCHARP will post a CRF (pdf) file, representing output from the study database eCRFs, on the following MTN-035 Atlas web page:

<https://atlas.scharp.org/cpas/project/MTN/035/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 the need to perform paper CRF completion arise.

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 as source documentation for 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. Table 12-3 below 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 Y/N
	Physical Exam
	Vital Signs
	Anorectal Exam
	Concomitant Medications Y/N
	STI Test Results
	Syphilis Serology
	Pregnancy Test Results
HIV Test Results	
V2 - Enrollment Visit	Randomization
	Enrollment
	Behavioral Assessments Summary, CASI Tracking
	Physical Exam
	Vital Signs
	HIV Test Results
	Anorectal Exam
	Pregnancy Test Results
	Specimen Storage
V3, V5 and V7 – PUEV 1-3	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Discontinuation of Study Product
	Anorectal Exam
	Behavioral Assessments Summary, CASI Tracking
	REQUIRED AT VISIT 7 ONLY
	STI Test Results
	Syphilis Serology
	HIV Test Results
V4 and V6 – Product Switch Visits	Follow-Up Visit Y/N, Follow-Up Visit Summary
Visit 8 – Final / Early Termination Visit	Follow-Up Visit Y/N, Follow-Up Visit Summary
	Pregnancy Test Results
	Behavioral Assessments Summary, CASI Tracking
Pregnancy	Pregnancy Report
	Pregnancy Outcome Log
Pregnancy History	Pregnancy History
As needed	Additional Study Procedures

(Additional Study Procedures/Interim Visit Procedures)	HIV Test Results
	HIV Confirmatory Results
	Physical Exam
	Vital Signs
	STI Test Results
	Genital Exam
	Pelvic Exam
	Syphilis Serology
	Pregnancy Test Results
	Missed Visit
	Participant Replacement Assessment
	Interim Visit Summary
	Behavioral Assessment Summary
	As needed, Ongoing Logs
Protocol Deviation Log	
Adverse Event Log Y/N	
Adverse Event Log	
Concomitant Medications Log Y/N	
Concomitant Medications Log	
Medical History Y/N	
Medical History Log	
Product Hold Y/N	
Product Hold	
Social Impact Log Y/N	
Social Impact Log	
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) prior to their data entry into the study database. While paper CRFs are being reviewed, it is important that they be stored and tracked systematically.

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

MTN-035 QC Review Step #1 (completed during visit)

- Review applicable visit checklist and pelvic or genital exam checklists (if used) to ensure all required procedures were completed
- Review eligibility checklists/worksheets to ensure completeness and verify participant eligibility
- Review LDMS Specimen Tracking Sheet to ensure completeness and accuracy
- Review completed CRFs 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 Assessments Summary, CASI Tracking
 - Follow-up visits, when present: Adverse Event Log

MTN-035 QC Review Step #2 (completed after visit)

General QC #2 procedures for all visits:

- Review visit checklist to ensure all required procedures were completed
- Ensure the PTID is correct, is recorded correctly on all paper source documents (including paper CRFs, if used), and is the same on the paper source documents and the eCRFs for a given participant.
- Ensure that no participant identifiers other than the PTID are present on paper source documents, including paper CRFs (if used).
- Ensure that the assigned visit code is correct, and is consistent between the paper source documents, including paper CRFs (if used), the eCRFs, the LDMS Specimen Tracking Sheet, and LDMS for a given participant visit.

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

- Review the Pelvic Exam, if applicable, Anorectal Exam, Genital Exam, if applicable, Physical Exam, Vital Signs, 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 the Specimen Storage CRF has the correct Specimen Collection Date for plasma archive/storage 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 second screening pelvic exam.
- Review the Specimen Storage eCRF and make sure it matches information documented on the applicable 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 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 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-035 case report forms can be found at the MTN-035 Atlas web page at: <https://atlas.ssharp.org/cpas/project/MTN/035/begin.view?>