CRF Completion Guidelines

MTN-039

Version 1.0

CRF Completion Guidelines

Protocol Name:	A Phase 1 Open Label Safety and Pharmacokinetic Study of Rectal Administration of a Tenofovir Alafenamide/Elvitegravir Insert at Two Dose Levels
Protocol Number:	MTN-039
Author:	Julie Ngo
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Approvals

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CRF Completion Guidelines

The following instructions are study-specific data completion instructions intended to assist site staff when completing electronic case report forms (eCRFs) and paper case report forms (CRFs). Detailed guidance on general data collection, entry, navigation and general use of Medidata Rave is provided in the Medidata Rave Electronic Data Capture (EDC) Training Manual, which is found on the MTN-039 Protocol page: https://atlas.scharp.org/cpas/project/MTN/039/begin.view?

General Guidelines

- The Participant ID is automatically assigned by Rave EDC as a 9-digit field, starting with the 3-digit site number followed by a randomly assigned 5-digit participant number, and 1-digit check number.
- All data entered in Rave must match the data on any source documents/paper CRFs.
- Complete all required data fields. Ensure that all entries are in English and are accurate, consistent, complete and medically logical.
- If “Other” is chosen as a response, further details must be provided by responding to the “If ‘Other’, specify” field.
- Text box fields have character limits. Text exceeding the limit will not be saved and a “Non-conformant” icon will appear.
- Visit dates must be complete and in chronological order according to the protocol.
- Most date fields must be entered as Day/Month/Year (dd/mmm/yyyy) (e.g., 01 NOV 2017). Exceptions are detailed in specific form sections where applicable.
- Drop-down menus are available for many fields. Use these menus, when available, to select the appropriate response.
- Avoid using abbreviations, symbols or special characters.
- Avoid hitting the return or enter key in text fields.
- If a scheduled visit is missed, do not enter data on the forms required for the visit, except for the Date of Visit form. Marking “no” on the Date of Visit form will add the Missed Visit form to the visit folder for completion.
- Log forms allow you to make multiple entries over the course of the study. All entries at the same time in ‘Complete View’ and View individual entries in portrait view.
- The following log forms for this study are available in the Ongoing logs folder at the bottom of the sidebar on the Participant’s home page:
    - Adverse Event
    - Concomitant Medications
    - Medical History
    - Protocol Deviations
    - Product Hold
- Correct/update data fields by clicking the pencil icon at the far right of the field, correct/update the value and give the reason for the change, if applicable. Save the form to apply the changes.

- If an incorrect data entry is made, a system query will fire. Correct the error and save the form.
    - System generated queries with no query response will automatically close with a form correction.
    - System generated queries with a query response will change into a manual query that will need to be closed by the data management team.
- All actions performed on a data field are tracked in the audit trail. If data is modified inadvertently, the change is also shown in the audit trail for that field.
- The Investigator of Record (IoR) will sign all forms after the participant's data has been reviewed. After the signature is applied, no further changes or additions to the forms are expected.
- Any modifications that are made to forms after the IoR has signed off will remove the signature. Once the data has been reviewed, the signature will need to be applied again.
- The SCHARP Clinical Data Manager will provide direction for when the Investigator should perform the final review and sign the eCRF pages.

Add Event

- The **Add Event** drop-down menu can add select forms and visit folders to a participant's casebook.

Interim Visits

- Add an Interim Visit folder to a participant's casebook by clicking on the **Add Event** button on the PTID (Subject)-level page and selecting "Interim Visit", then clicking "Add". An Interim Visit folder will appear in the participant's casebook.
- Open the Interim Visit folder to access the Interim Visit form. On the Interim Visit form, select the forms that were completed at the interim visit. The selected forms will then load in the folder.
- On the Interim Visit form, enter the visit date as the earliest date visit procedures were performed for that interim visit.

Loading of Forms in Visit Folder

- Medidata Rave will add forms to a visit folder in a participant's casebook based on specified responses on forms. Below are a few key examples.
    - **Example 1**: Follow-up Visit Y/N form
        - If question "Did the participant complete this visit" is marked "No", the Missed Visit form will add to the visit folder and the required forms for that visit will not appear in the visit folder.
        - Most forms under "Additional Procedures/Forms" on the Follow-up Visit Summary form that are checked will be added to the visit folder. If a checked form does not load, please contact the study clinical data manager, who will load the form manually.
    - **Example 2**: Interim Visit form
        - Forms under "Forms Completed at Interim Visit" on the Interim Visit form that are checked will be added to the Interim Visit folder.
        - Any "Procedures completed at Interim Visit" on the Interim Visit form that are marked will be added to the Interim Visit folder.

Loading of Folders in Participant Casebook

- Medidata Rave will add folders to a participant's casebook based on how certain forms are completed. See Table 1 for actions required to add folders to a participant's casebook.

Table 1. Folder Dynamics

Folder	Action Required to Add Folder
V1.0 – Screening V2.0 – Day 0/Enrollment Ongoing Logs Discontinuation	Save Participant Identifier form.
V3.0	Select "Yes" for "Is the participant ready to be randomized?" on the Randomization form in V2.0 folder.
V4.0-V11.0	• Select "Yes" for "Did the participant complete this visit?" on the Follow-up Visit Y/N form in the visit folder. • Select "No" for "Did the participant exit/terminate the study at this visit?" on the Follow-up Visit Summary form in the visit folder.

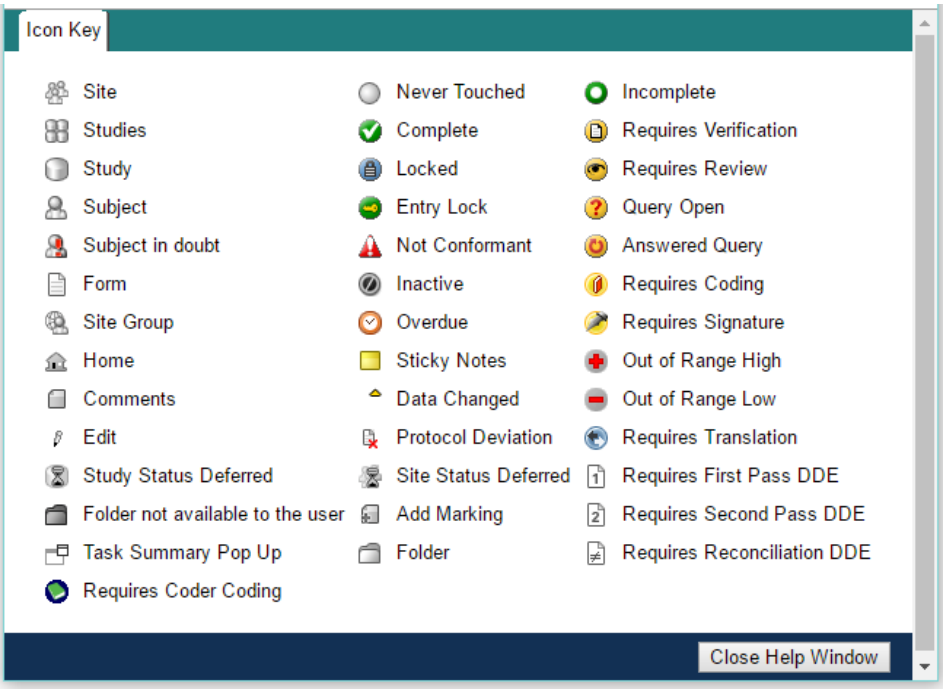
Dynamic Search Lists

- Some forms have data fields with 'dynamic' drop-down lists of available options. Options are populated by corresponding log form entries.
- Dynamic drop-down lists will be blank until entries are made and saved in the corresponding log form.
- Your selection in the dynamic search list can be deleted if entered in error.
- Changing the original log data or inactivating a log form entry that has been selected for a dynamic search list field, will make that field non-conformant and it will need to be updated.
- For Example:
    - An AE of '*FEVER*' started on 05DEC2017 and is reported on the Adverse Events log form
    - On the Concomitant Medications log form, if a listed medication was used for this AE, a dynamic search list can be used to select the applicable AE record from the dropdown list.
    - The start date for AE *'FEVER'* is corrected to 06DEC2017 on the Adverse Events log form.
    - The selection on the Concomitant Medication log form becomes non-conformant.
    - To resolve the non-conformant data, re-select the AE '*FEVER'* from the dynamic search list with the corrected start date.

Icon Key

A link to an Icon Key is available on the PTID (Subject)-level page. The key contains pictures and descriptions of the icons used in Rave. Below is a screen shot of the Icon Key.

Figure 1. Icon Key

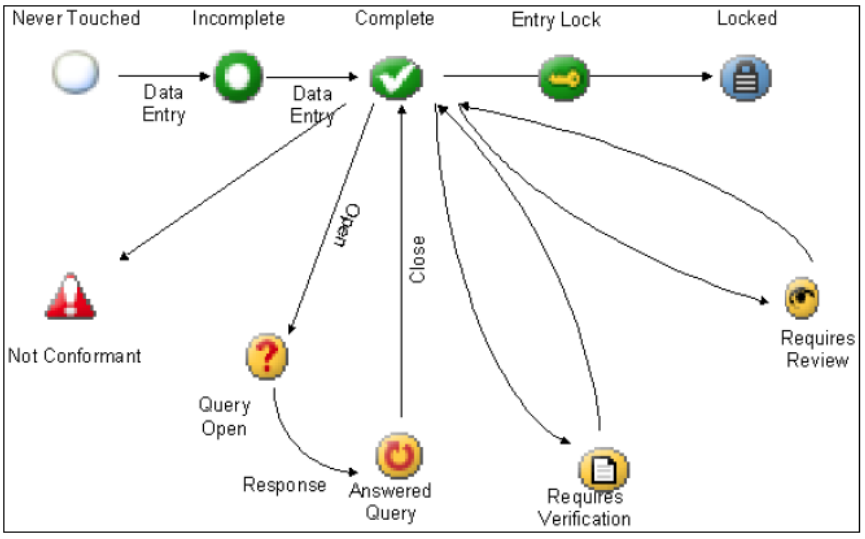


Icon Progression

The life cycle of participants, folders, forms, and fields follows a logical progression starting with “never touched” and moving toward “complete” and “locked”. Graphical icons are used throughout Rave to show status.

The following figure illustrates the status represented by each icon and the progression of icons through the life cycle.

Figure 2. Icon Progression



Task Summary

The Task Summary displays all pending tasks for the study. It displays the number of participants with outstanding tasks that need site review (see Figure 3); for example, open queries. Clicking on the arrow next to the task expands it to show the specific participants with open queries (see Figure 4). Clicking on a PTID will open the participant's casebook.

Figure 3. Site-Level Task Summary

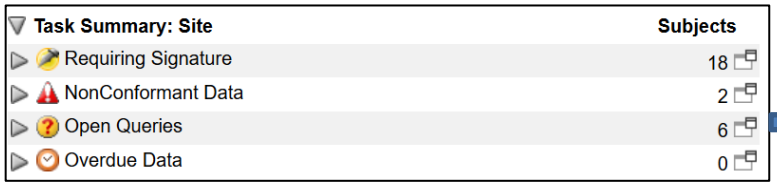
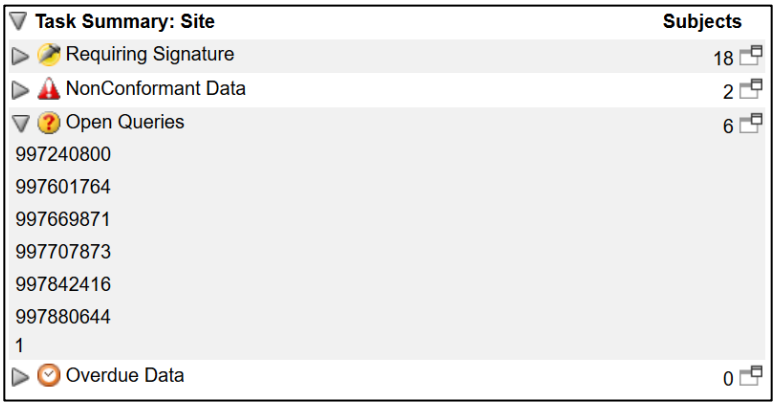
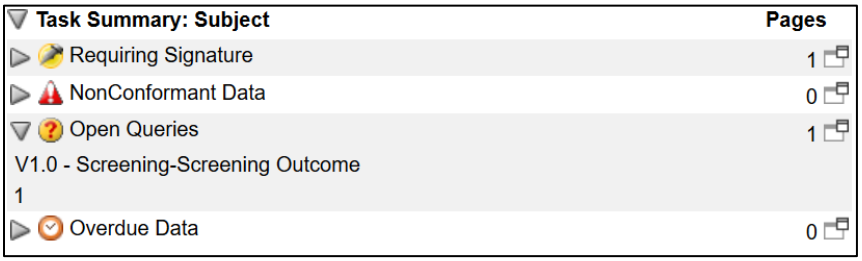


Figure 4. Site-Level Task Summary



At the Subject level, the Task Summary displays the number of pages for that participant that need site review. In Figure 5 below, there is one open query on the Screening Outcome form at V1.0 – Screening. In the expanded task summary view, clicking on this form link will open the form.

Figure 5. Subject-Level Task Summary



General Guidelines – Paper CRF Completion

CRF PDFs are generated from Rave and posted on the protocol webpage. When completing a paper CRF, refer to detailed instructions for data collection pertaining to the specific form and fields on that form in this document.

- Based on Good Clinical Practices (GCPs), refer to the following guidelines to complete paper CRFs:
  - Use a black or dark blue medium ballpoint pen. Do not use any other type of writing tool.
  - Print all data and comments legibly by hand. Do not use cursive/script handwriting.
  - Record data on the front side of the paper only.
  - If the spaces/lines provided for a response are not large enough, continue in another blank area of the paper CRF.
  - Mark only one answer unless instructions state to mark or select all that apply.
  - A response is required for every data field unless skip instructions are provided.
  - Do not use correction fluid ("White-Out") or correction tape on paper CRFs.

Recording Dates – Rave Form and/or Paper CRF

- Dates are entered using the "dd MMM yyyy" format, where "dd" represents the two-digit day, "MMM" represents the three-letter abbreviation of the month (in capital letters), and "yyyy" represents the four digits of the year.
- Month abbreviations are shown below. In Rave EDC, these abbreviations are in a drop-down list in the month field.

Month	Abbreviation	Month	Abbreviation
January	JAN	July	JUL
February	FEB	August	AUG
March	MAR	September	SEP
April	APR	October	OCT
May	MAY	November	NOV
June	JUN	December	DEC

For example, record September 20, 2016 as:

Recording Time - Rave Form and/or Paper CRF

- Use a 24-hour clock (00:00-23:59), where hours are designated from 0–23.
- Midnight is recorded as 00:00, not 24:00.

The following chart shows equivalencies between the 12- and 24-hour clocks:

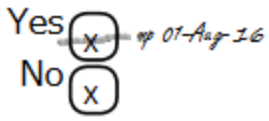
12-hour clock (a.m.)	24-hour clock	12-hour clock (p.m.)	24-hour clock
Midnight	00:00	Noon	12:00
1:00 a.m.	01:00	1:00 p.m.	13:00
2:00 a.m.	02:00	2:00 p.m.	14:00
3:00 a.m.	03:00	3:00 p.m.	15:00
4:00 a.m.	04:00	4:00 p.m.	16:00
5:00 a.m.	05:00	5:00 p.m.	17:00
6:00 a.m.	06:00	6:00 p.m.	18:00
7:00 a.m.	07:00	7:00 p.m.	19:00
8:00 a.m.	08:00	8:00 p.m.	20:00
9:00 a.m.	09:00	9:00 p.m.	21:00
10:00 a.m.	10:00	10:00 p.m.	22:00
11:00 a.m.	11:00	11:00 p.m.	23:00

For example, record 2:25 p.m. as: 14 25 24-hour clock

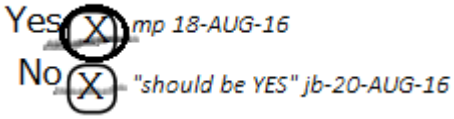
Data Corrections and Additions - Rave Form and/or Paper CRF

- Data fields may need to be updated or corrected, such as in response to a query or after site review.
- If the source document is non-CRF in nature (i.e., lab report), it is sufficient to make data updates in the study database itself. If a paper CRF was completed, make changes to the paper CRF first and then enter the updated data into Rave.
- Use the standards below when changing, clarifying, or amending data:
  - Draw a single horizontal line through the incorrect entry. Do not obscure the entry or make it unreadable with multiple cross-outs.
  - Place the correct or clarified answer near the previous response.

- If an **X** is marked in the wrong response box, correct it by doing the following:
  - draw a single horizontal line through the incorrectly marked box,
  - mark the correct box, and
  - initial and date the correction as shown below:



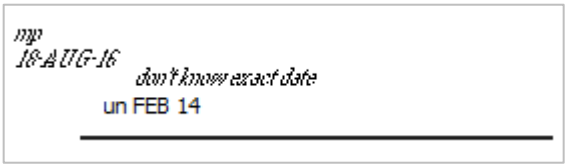
- If the correct answer has previously been crossed out, do the following:
  - circle the correct response,
  - write an explanation in the white space near the response, and
  - initial and date all corrections as shown below:



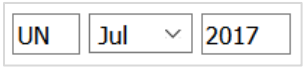
Missing and Unknown Data - Rave Form and/or Paper CRF

On paper CRF, if the answer to a required question is unknown, unavailable, or if the participant refuses to answer, draw a single horizontal line through the applicable question and initial and date. It is helpful to write “don’t know,” “refuses to answer,” “UNK” (unknown), “N/A” (not applicable), or “REF” (refused) near the fields.

- For example, when recording a date, if the exact day is not known, write “un” to designate the “dd” (or date) and write “don’t know” next to the response, as shown below. Initials and date are required for any data that are refused, missing, unknown, or not applicable, regardless of whether they are marked as such during the initial form completion, or as an update to the form.



- In Rave, where the data are missing or unknown, enter “UN” for the day and/or select ‘UNK’ from the drop-down list for the month.



Form-Specific Instructions

Adverse Event Y/N

Purpose:
This form is used to trigger the Adverse Event log.

General Instructions:
This form is in the "Ongoing Logs" folder and is only completed once, at the time the first adverse event is reported or at the end of the study if no adverse events are reported.

Field-specific Instructions:

Field	Instructions
Has the participant experienced an adverse event during the study?	• If "Yes" is selected, the **Adverse Event** log loads in the Ongoing Logs folder. • At the end of study participation, mark "No" if no adverse events have occurred.

Adverse Event

Purpose:
This form documents Adverse Events (AEs) reported by the participant or clinically observed as defined by the protocol.

General Instructions:
- Complete one log line for each adverse event (AE).
- Add additional log lines by clicking "Add a new Log line".
- Only list conditions that start on or after enrollment date, otherwise record as medical history.
- Record increases in severity/frequency as new events with corresponding start/stop dates. The original AE should be recorded as "Severity/frequency increased" and have an Outcome Date equal to the Onset Date of the new AE.
- Note that decreases in severity (AE improvements) are not recorded as new AEs.

Field-specific Instructions:

Field	Instructions
Adverse event (AE)	• Describe the AE using medical terminology. • Record a diagnosis/anatomical location if available. • For lab abnormalities, format is (increased/decreased [test name]).

Field	Instructions
Onset date	At minimum, month and year are required. Record one of the following, as appropriate: • The date on which the participant reports first experiencing the AE. • If the AE is discovered during a study visit, record the date of the study visit. • If the AE is an abnormal lab result, record the date on which the specimen was collected.
Severity grade	Record the severity grade using the most current version of the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events* (including relevant appendices/addendums) • Grade 1 (Mild) • Grade 2 (Moderate) • Grade 3 (Severe) • Grade 4 (Potentially life-threatening) • Grade 5 (Death)
Relationship to study product	Mark the assessment of the relationship between the AE and the study product. • "Related" - reasonable possibility that the AE may be related to the study product. • "Not related" - not a reasonable possibility that the AE is related to the study product. Record pertinent details for relationship assessment in comments. For more information, refer to the *Manual for Expedited Reporting of Adverse Events to DAIDS,* most current version.
If "No", outcome date	At minimum, month and year are required. Record one of the following as appropriate: • The date on which the participant no longer experienced the AE. • The date of the study visit or specimen collection at which the change in status/outcome is first noted.

Field	Instructions

Action taken with study product	• ***Dose not changed:***
	  ○ Mark if the participant is expected to continue to use study product and the AE does NOT result in a study product hold or permanent discontinuation.
	• ***Dose reduced:***
	  ○ Not applicable
	• ***Dose increased:***
	  ○ Not applicable
	• ***Drug withdrawn:***
	  ○ Mark if the AE results in permanent study product discontinuation.
	  ○ If multiple AEs are reported at the same visit, mark "withdrawn" for the AE(s) that contributed to the permanent discontinuation.
	  ○ *Complete a Discontinuation of Study Product form*
	• ***Drug interrupted:***
	  ○ Mark if the AE results in a study product hold.
	  ○ If multiple AEs are reported at the same visit, mark "interrupted" for the AE(s) that contributed to the hold. Ensure the Product Hold Summary, Product Hold/Discontinuation forms are completed.
	• ***Not applicable:***
	  ○ Mark if the AE occurred after the participant had completed all administration of the study product.
	  ○ Mark if the study product is held or permanently discontinued for a different reason.
	  ○ Mark if the AE is grade 5-death.

Field	Instructions

Status/Outcome	• ***Recovered/Resolved:*** AE is no longer present or returned to the pre-enrollment severity/frequency. If a participant is taking a medication to control an AE that arose during study participation, it is not considered resolved.
	• ***Recovering/resolving:*** AE is continuing and has not yet resolved or returned to baseline severity/frequency.
	• ***Recovered/resolved with sequelae:*** Participant has recovered from the AE, but with remaining effects or impairment.
	• ***Fatal:*** Severity of this AE is grade 5. Update any other AEs continuing at the time of death to "Not Recovered/Not Resolved."
	• ***Severity/frequency increased:*** AE increases in severity or frequency after it has been reported on the AE Log:
	  ○ On the original AE log line, update the "Status/outcome" field to "severity/frequency increased." Record the date of increase in the outcome field data.
	  ○ Report the increase in severity or frequency of the AE on a new log line. For this new AE, the "onset date" will be the date that the severity or frequency increased. Update SAE form if applicable.
	  ○ Note that decreases in severity should not be recorded as new AEs,
	• ***Not recovered/not resolved***: Whenever an AE is continuing at the time of participant termination from the study.

Is this a serious adverse event according to ICH/GCP or protocol guidelines? Has or will this AE be reported as an EAE?	If the AE is a Serious Adverse Event (SAE), complete the subsequent SAE criteria questions. Mark all of the SAE criteria that apply. If the AE is not an SAE, skip to "Has or will this AE be reported as an EAE?". For questions about ICH/GCP guidelines and EAE reporting, refer to current *Manual for Expedited Reporting of Adverse Events to DAIDS.*
Has or will this AE be reported as an EAE? EAE number	If reported as an EAE (indicated as "Yes"), provide the EAE number and complete any subsequent updates to this form on the applicable EAE form. Refer to form instructions for EAE format.
Study agent	Not applicable for this study.
Comments	Comments are required for every AE. • Record pertinent details for relationship assessments. • Record pertinent clinical information.

Anorectal Exam

Purpose:

This form documents anorectal exam findings.

General Instructions
Complete at all required study visits as specified in the protocol and schedule of forms.

Field-specific Instructions:

Field	Instructions
Was an anorectal exam performed? Body System	If an anorectal exam is performed: • For each portion of the exam, mark “Normal”, “Abnormal” or “Not done”. • If “Abnormal” describe findings in corresponding “If "Abnormal", specify:” box.
Other abnormal findings If “Other abnormal findings”, specify	• If there is an abnormal finding not listed on the form, enter it in the “If "Other abnormal finding", specify:” box.
Were any new anorectal AE findings reported at this visit?	• If there are new AE findings to report, select the adverse event from the dynamic search list fields.

Behavioral Assessment

Purpose:
This form is used to document participant completion of the Computer-assisted Self Interview (CASI) questionnaires at Enrollment and during follow-up.

General Instructions:
This prompt is present at the following visits:

- V2.0 – Baseline
- V4.0 – Follow-up
- V8.0 – Follow-up
- V10 – Visit 10

Field-specific Instructions:

Field	Instructions
Was a CASI questionnaire completed at this visit?	Select ‘Yes’ or ‘No’. If ‘Yes’ is selected, then the CASI Tracking form appears dynamically. Complete “CASI Tracking” CRF. If a CASI questionnaire was completed by a participant, this item should be marked ‘Yes’ regardless of whether the questionnaire was uploaded to SCHARP.

	If 'No' is selected, then record the reason why it was not done in the text field below.
If no, please explain:	Record the reason why a CASI questionnaire was not completed in the text field.

CASI Tracking

Purpose:
This form is used to document information about the Computer-Assisted Self Interview (CASI) or In-depth Interview (IDI) questionnaires at Enrollment and during follow-up.

General Instructions:
Selecting 'Yes' in the Behavioral Assessment prompt will open up the CASI Tracking CRF. Complete this form at V2.0 - Enrollment, Visit 4.0, Visit 8.0, and Visit 10.0.

Field-specific Instructions:

Field	Instructions
CASI collection date	A complete date is required.
CASI ID	Enter the corresponding 6-digit CASI ID.
Which questionnaire was completed?	Select the applicable questionnaire from the drop down list that was completed for the participant.
Were there any problems or issues related to the administration or completion of the questionnaire?	Select 'Yes' or 'No'.
If yes, please describe:	Use the text field space to describe when and why multiple CASI questionnaires are completed for a participant at a visit or if the incorrect CASI questionnaire is completed at a visit. Use this text field to indicate any technical errors that took place in the administration, storing, or uploading of a CASI questionnaire. If there are any unusual details related to the CASI questionnaire administration or completion, describe them in this field.

Chemistry Panel

Purpose: This form is used to provide data on the participant's baseline and follow-up laboratory test results. To generate this form at a follow-up visit where tests are not normally required, select "Chemistry Panel" on the Additional Study Procedures form.

General Instructions:

- The lab that collected the specimens used for these tests will automatically be selected from the Lab dropdown list at the top of the form. The units and lab ranges for each result will be populated at the bottom of the form.

Note: The Demographics eCRF needs to be entered prior to entering data on the Chemistry Panel eCRF because the derived age from the Date of Birth on the Demographics eCRF is used to populate the reference ranges.

- For each lab test (e.g. Serum Chemistries), enter the specimen collection date at the top of the form for that specific test each time this form is completed unless it was not collected.
- For each individual lab result (e.g. AST, ALT, Creatinine), record the numeric results in the appropriate field at the bottom of the form.
- Enter the severity grade at the top of the form for that specific result. The following results require entry of the severity grade (if applicable):
    - SERUM CHEMISTRIES: AST (SGOT), ALT (SGPT), Creatinine

  See the Severity Grade section for further instructions on completing the severity grade.

Lab Result Units and Rounding

- Results should be documented on the form using the units used in the current version of the DAIDS AE Grading Table. If the units present on your source results report do not match the units on the form and in the DAIDS Toxicity Table, results will need to be converted using the Lab Conversion Tool on Atlas before entry into the eCRF.

- Note that the following units are equivalent:

  IU/L = U/L I/l x 100 = % 10^9/L = 10^3/mm3 = 10^3/µL

All analytes should be recorded using the same level of precision according to the source laboratory results document.

Reporting Severity Grade

- Record the severity grade at the top of the form by selecting from the drop-down menu for each corresponding lab analyte when applicable. If the analyte does not meet criteria for severity grade 1 or greater per the DAIDS Toxicity table (Corrected Version 2.1), select the 'Not gradable' option.
- Enter the severity grade for each specific result:
    - AST (SGOT)
    - ALT (SGPT)
    - Creatinine
-

- The severity grade options are as follows:
    - Grade 1 – Mild
    - Grade 2 – Moderate
    - Grade 3 – Severe
    - Grade 4 – Potentially life-threatening
    - Not gradable

- If any values meet the criteria for severity grade 1 or greater, according to the appropriate DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, record the grade. If the value is below Grade 1, select the option 'not gradable'.

- Always compare the severity grade range to the value that was recorded on the form (not the lab-reported value).
- When working with calculated severity grade ranges (e.g., 1.1–1.5 times the site lab upper limit of normal), the calculated range may have more significant digits than the lab result.
    - Treat all missing digits in the lab value as zeros.
    - If the lab value falls between two calculated severity grade ranges, assign it the higher grade.
- Record any Grade 1 or higher lab values on the "Baseline Medical History" log or "Adverse Event" log as applicable.
- If an abnormal lab finding meets AE reporting criteria, select the corresponding AE within the drop-down menu. Please note that the AE must be entered within the Ongoing Logs folder prior to completing this form in order to link the associated AE.

Field-specific Instructions:

Field	Instructions
Specimen collection date	Record the date that the specimen was *collected*, not the date results were reported or recorded on the form.
Severity grade	• Select laboratory value severity grade according to the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events*, most current version. • Select 'Not gradable' for a value that does not meet grading criteria.
Adverse event	Select the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form to be visible in the drop-down list.

Concomitant Medications Y/N

Purpose:
This form is used to trigger the Concomitant Medication log in Rave.

General Instructions:
This form is present in the "Ongoing Logs" folder in Rave and is only completed once, at the time the first concomitant medication is reported.

Field-specific Instructions:

Field	Instructions
Is the participant taking any concomitant medications?	• If "Yes" is selected, then the **Concomitant Medications** log appears dynamically in the "Ongoing Logs" folder. • At the end of study participation, mark "No" if no concomitant medications were reported.

Concomitant Medications

Purpose:
This form documents all medication(s) that are used by the participant during the study (including the protocol-defined screening period), other than study product, [study specific] must be documented on this form. This includes, but is not limited to, prescription and non-prescription drugs, vitamins, topical products, alternative/complimentary medicines (e.g., herbal and health food supplements), recreational drugs, vaccinations, and allergy shots.

General Instructions:

- Complete one log line for each reported concomitant medication.
- Add additional log lines by clicking “Add a new Log line”.

Field-specific Instructions:

Field	Instructions
Medication name	Record the medication name as reported by the participant. For example, if the participant reports taking a trade name medication report the trade name. If a trade name is not available or not reportable per national guidelines, record the generic name of the medication.
Indication	• For health supplements, such as multivitamins, record “general health”. • For preventive medications, record “prevention of [insert condition]” (e.g., for flu shot, record “prevention of influenza”). • For recreational drugs, record “recreation”.

Date started	• If the participant is unable to recall the exact date, obtain participant’s best estimate. At a minimum, the year is required.
	  ○ If the exact day is unknown, enter ‘UN’ for the day field.
	  ○ If the exact month is unknown, then select ‘UNK’ for the month field.
	  ○ For example, a partial date may be recorded as: UN-Jan-2010 or UN-UNK-2010
	• For injections
	  ○ If it is a one-time injection (including contraception), record each injection as a separate entry, with the same date used for date started and stopped.
	  ○ If it is a series of injections, record the date of the first injection as date started and the date of the last injection as the date stopped.

Date stopped *Or* Ongoing	At the participant’s Termination visit, the “Date Stopped” must be recorded for each medication OR the “Ongoing” must be checked. At a minimum, the month and year are required.

Frequency	Select the frequency from options provided in the drop-down list. Below is a list of common frequency abbreviations: PRN: as needed QD: every day BID: twice daily TID: three times daily QID: four times daily QHS: at bedtime ONCE: one time Other: alternative dosing schedule or unknown If 'Other' is selected, specify in the corresponding "If other frequency, specify" text field provided. For injections, frequency should be 'Once', with same date used for start and stop dates.
Route	Select the route from options provided in the drop-down list. If 'Other' is selected, specify in the corresponding "If other route, specify" text field provided.
Dose	Record the dose. If the participant does not know the exact dose units (e.g., "250 mg"), record an estimate (e.g., "1 tablet"). For multivitamin tablets or liquids, record the number of tablets or liquid measurement (e.g. "1" pill or "1" tablespoon") if the exact dosage is unknown. If the dose is unknown, check "Unknown" and leave the dose field blank. When documenting medical devices with no active medication, such as an IUCD, enter the dose as "1". For topical applications, if exact quantity is not known, record the number of applications instead (e.g. 'one application').

Dose Units	Select/record the applicable dose units provided in the drop-down list. If the participant does not know the exact dose units (e.g., "250 mg"), record an estimate (e.g., "1 tablet"). If no information on units is known, select the 'Unknown' option. When documenting medical devices with no active medication, such as an IUCD, mark the Dose Unit as 'Other' and specify "device" in the "If other dose units, specify" text field provided. For topical applications, if exact quantity is not known, record the number of applications instead (e.g. 'one application'). If 'Other' is selected, specify in the corresponding "If other dose units, specify" text field provided.
Taken for Reported Adverse Event Y/N If "Yes", select adverse event.	If "Yes", choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.

Demographics

Purpose:
This form documents a participant's demographic and socioeconomic information.

General Instructions:
Complete and submit this form for participants who have signed a study-specific consent form, regardless of if they enroll in the study or not. This form is completed at the [insert relevant visits]. If the participant does not understand the question, read the categories to the participant. Responses should reflect the participant's status at screening and should not be changed after screening unless correction is needed. If the participant is found to be ineligible prior to the collection of all demographic data, enter all available data and respond to system queries with "Not Collected".

Field-specific Instructions:

Field	Instructions
Date of birth	If the entire date of birth is unknown, record participant's best estimate. At a minimum year is required.
Age	The age field is calculated automatically based on the "Date of birth" field and the "Informed consent date" field on the Inclusion/Exclusion Criteria form. No data entry is required.
Sex at birth	This is the sex that the participant was assigned at birth.

Field	Instructions
Ethnicity Race	Record the participant's ethnicity and race based on self-definition.
Gender	• This response must be self-reported by the participant. • Site staff are encouraged to document in chart notes if the participant, during study participation, prefers to be referred to by a specific pronoun or gender. • Gender is the social part of being male or female and related to self-identity. Below are descriptions of each gender category: o Male: Any person who identifies their gender as male. o Female: Any person who identifies their gender as female. o Transgender male (also known as trans male) refers to a person assigned female at birth, but whose gender identity is male or trans*male. o Transgender female (also known as trans female) refers to a person assigned male at birth, but whose gender identity is female or trans*female. o Gender nonconforming/Gender variant: A person whose gender expression is different than gender norms and does "fit" the male/female categories, regardless of their gender identity or sexual orientation. o Self-identify: Any other gender reported by the participant. Record what the participant reports in the "If 'Self-identify', specify:" field.
How do you define your sexual orientation?	Below are descriptions of each sexual orientation: • Gay/Lesbian/Homosexual: Attracted to the same sex as yourself • Bisexual: Attracted to both the same and different sex than yourself • Queer • Two spirit • Straight/Heterosexual: Attracted to a different sex than yourself • Additional category: Any other sexual orientation reported by the participant. Record what the participant reports in the "If 'Additional category', specify:" field. • Not sure • Prefer not to answer

Discontinuation of Study Product

Purpose:
This form documents permanent discontinuation of study product.

General Instructions:
Complete this form at the time of **permanent** study product discontinuation, including a scheduled end of product use. This form is located in the "Discontinuations" folder.

Field-specific Instructions:

Field	Instructions
Date that study product use ended	A complete date is required. Record the date when the participant completed or was permanently discontinued from study product.
Primary reason for ending study product use	If more than one reason applies, mark only the primary reason for discontinuing study product. If 'Scheduled study product use period completed', then end the form If 'Adverse Event' is selected, choose the AE from the AE dynamic drop-down list. Note: If study product is permanently discontinued due to an AE, the AE log page must be entered into Rave prior to linking the AE on the Product Discontinuation eCRF in order for the AE to be available to select with the drop down field. If the primary reason is "Other", provide additional details in the "If other, specify" text field provided.

Dose Administration

Purpose:
This form documents dosage and administration of study product.

General Instructions:
The form must be completed at all dosing visits.

Field-specific Instructions:

Field	Instructions
Visit Number	Select the visit from the dropdown menu.
Date insert administered Time insert administered	Enter the date and time of insert administration. A complete date and time is required.
Dosage Administered	Select the dosage amount from the dropdown menu.

Follow-up Visit Summary

Purpose:
This form is used to summarize information from each participant follow-up study visit.

General Instructions:

This form is completed for each scheduled visit and is present in each follow-up visit folder if 'Yes' is entered on the Follow-up Yes/No eCRF, starting at V3.0 – Dosing Visit through V11.0 - Termination.

Field-specific Instructions:

Field	Instructions
Visit Date	A complete date is required.
Was this a PK/PD Sampling visit?	Select 'Yes' if this is the participant's assigned sampling visit or 'No' if this is not a participant's assigned sampling visit.
Was study product use permanently discontinued (scheduled or early) at this visit?	Select 'Yes' or 'No'. If 'Yes', then complete a Discontinuation of Study Product eCRF within the Discontinuations folder.
Did the participant exit/terminate the study at this visit?	Select 'Yes' or 'No'. If 'Yes', then complete a Study Termination eCRF within the Discontinuations folder.
Were any new adverse events (AEs) reported at this visit? If yes, complete the AE Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one Adverse Event (AE) was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable AE(s).
Is the participant taking any concomitant medications that have not been previously reported? If yes, complete the Concomitant Medications Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one concomitant medication was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable CM(s).
Have any protocol deviations been reported at this visit? If yes, complete the Protocol Deviations Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one protocol deviation was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable PD(s).

Were any additional study procedures or forms completed outside of the study visit per protocol?	Select 'Yes' or 'No'. Select 'Yes' if any additional procedures at this study visit were completed (e.g. clinically indicated exam). The Additional Study Procedures eCRF will then be added to the participant's visit folder. Select 'No' if only required procedures were completed at this visit per protocol. That is, it is determined that no additional study procedures (and thus CRFs) will be completed at the scheduled study visit.

Follow-up Visit Yes/No

Purpose:

This form is used to document whether a regular study visit was completed.

General Instructions:

This form is completed for each scheduled visit, even if the visit was missed. This eCRF is present in each follow-up visit folder, starting at V3.0 – Dosing Visit through V11.0 - Termination.

Field-specific Instructions:

Field	Instructions
Did the participant complete this visit?	Select 'Yes' or 'No'. If 'No', a Missed Visit eCRF appears dynamically and can then be completed. The remaining forms associated with this visit will not be present in the applicable visit folder. If 'Yes, then the Follow-up Visit Summary and other forms required at this visit appear dynamically and can then be completed.

Hematology

Purpose: This form is used to provide data on the participant's laboratory test results, specifically CBC with differential and platelets.

General Instructions:

Use this form to report the hematology and differential test results obtained from specimens collected. To generate this form at a follow-up visit where tests are not normally required, select 'Hematology' on the Additional Study Procedures form.

If any or all of the lab tests listed on this form are repeated (re-drawn) between the Screening and Enrollment Visit, document the repeated results on the same Hematology form. If the participant enrolls, the updated results should be submitted into the study database.

At Screening, record any applicable diagnoses on the Medical History Log eCRF, when applicable.

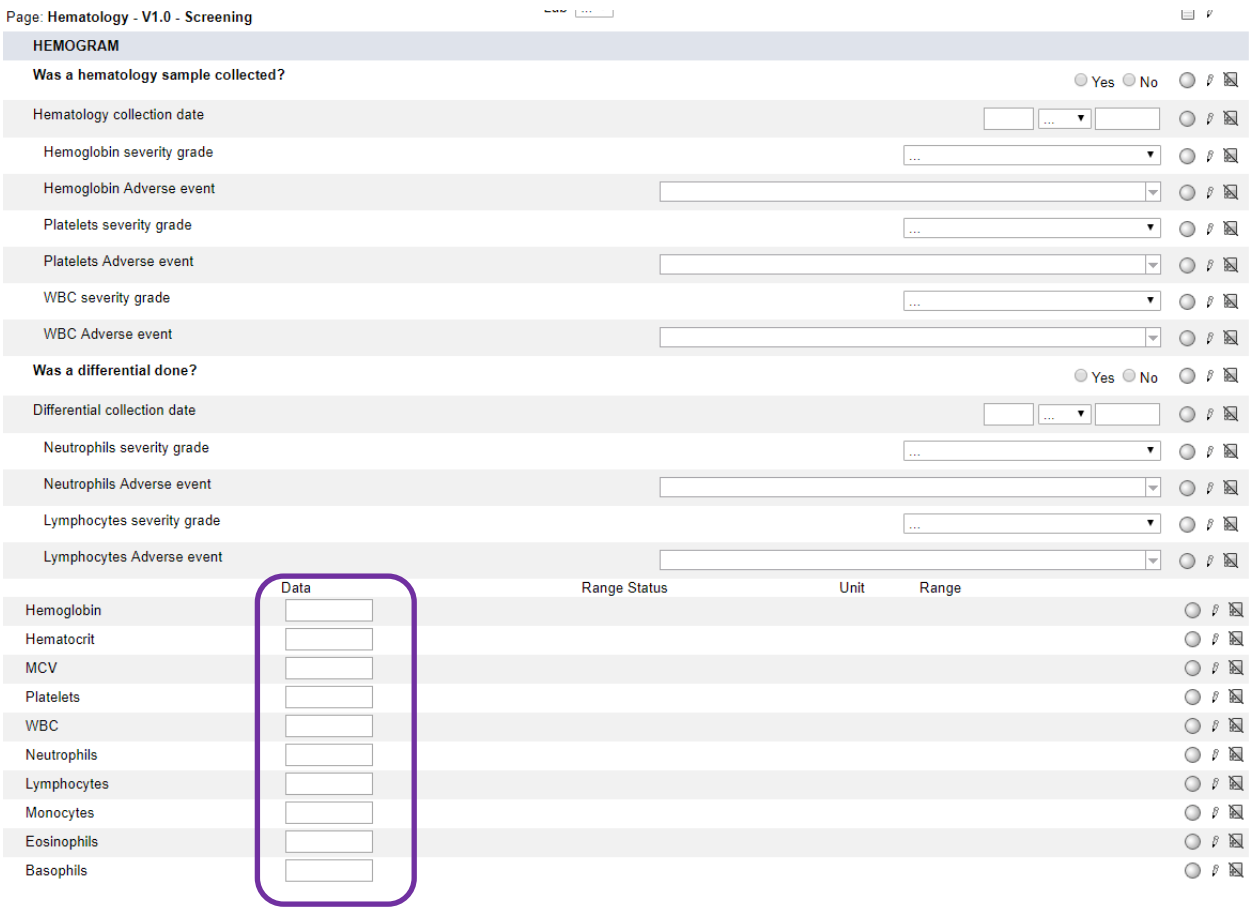
During follow-up, if a test result(s) recorded on this form indicates that the participant has a new (or increased severity) laboratory-confirmed infection or diagnosis, this infection/diagnosis must be recorded as an adverse event on an Adverse Event (AE) Log form.

Entering Laboratory Results

- The lab that collected the specimens used for these tests will automatically be selected from the Lab dropdown list at the top of the form. The units and lab ranges for each result will be populated at the bottom of the form.
  Note: The Demographics eCRF needs to be entered prior to entering data on the Hematology eCRF because the derived age from the Date of Birth on the Demographics eCRF is used to populate the reference ranges.

- For each lab test (e.g. Hematology and Differential), enter the specimen collection date at the top of the form for that specific test each time this form is completed unless it was not collected.

- For each individual lab result (e.g. Hemoglobin, Hematocrit, MCV Platelets, WBC, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils), record the numeric results in the appropriate field at the bottom of the form.



- Enter the severity grade at the top of the form for that specific result. The following results require entry of the severity grade (if applicable):

    - HEMATOLOGY: Hemoglobin, Platelets, WBC
    - DIFFERENTIAL: Neutrophils, Lymphocytes

    See the Severity Grade section for further instructions on completing the severity grade.

Lab Result Units and Rounding

- Results should be documented on the form using the units used in the current version of the DAIDS AE Grading Table. If the units present on your source results report do not match the units on the form and in the DAIDS Toxicity Table, results must be converted before entry into the eCRF. An optional lab units conversion tool is available on Atlas: https://atlas.scharp.org/cpas/project/Collaborators/Lab%20Unit%20Conversion%20Tool/begin.view

- Note that the following units are equivalent:

    IU/L = U/L l/l x 100 = % 10^9/L = 10^3/mm3 = 10^3/µL

Reporting Severity Grade

- Record the severity grade at the top of the form by selecting from the drop-down menu for each corresponding lab analyte when applicable. If the analyte does not meet criteria for severity grade 1 or greater per the DAIDS Toxicity table (Corrected Version 2.1), select the 'Not gradable' option.

- The severity grade options are as follows:
  - Grade 1 – Mild
  - Grade 2 – Moderate
  - Grade 3 – Severe
  - Grade 4 – Potentially life-threatening
  - Not gradable

- If any values meet the criteria for severity grade 1 or greater, according to the appropriate DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, record the grade. If the value is below Grade 1, select the option 'not gradable'.

- Always compare the severity grade range to the value that was recorded on the form (not the lab-reported value).

- When working with calculated severity grade ranges (e.g., 1.1–1.5 times the site lab upper limit of normal), the calculated range may have more significant digits than the lab result.

  - Treat all missing digits in the lab value as zeros.
  - If the lab value falls between two calculated severity grade ranges, assign it the higher grade.

- Record any Grade 1 or higher lab values on the "Medical History Log" or "Adverse Event Log" eCRF(s) as applicable.

- If an abnormal lab finding meets AE reporting criteria, select the corresponding AE within the drop-down menu. Please note that the AE must be entered within the Ongoing Logs folder prior to completing this form in order to link the associated AE.

NOTE: The fields for lab analyte values (for example: WBC) are located at the bottom of form.

Field-specific Instructions:

Field	Instructions
Collection date	Record the date that the specimen was *collected*, not the date results were reported or recorded on the form.
Severity grade	• Select laboratory value severity grade according to the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events*, most current version. • Select 'Not gradable' for a value that does not meet grading criteria.
Adverse event	Select the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form to be visible in the drop-down list.

HIV Confirmatory Results

Purpose:
This form is used to document HIV confirmatory results from local lab confirmatory HIV testing once a participant has a newly positive or indeterminate HIV test result.

General Instructions:
Complete this form any time when a participant has a newly positive or indeterminate HIV test result. Record HIV specimen test results on this form as they become available from the local lab. Select 'Not done' for any applicable tests in the event that a specimen was not collected, or if the specimen was collected, but a result is not available due to specimen loss or damage.

Field-specific Instructions:

Field	Instructions
Geenius HIV-1/2 confirmatory test	Record the Geenius Confirmatory Assay results as determined by the Geenius reader and software.
Was plasma stored for HIV confirmatory testing?	If plasma was not stored or was not required to be stored, skip to the HIV RNA PCR item. If plasma was stored for confirmatory testing, complete the Specimen Collection and Storage CRF to document that "Plasma for archive" was collected and stored.
Plasma for HIV confirmatory testing collection date:	A complete date is required if plasma for HIV confirmatory testing was stored.
HIV RNA PCR	Note that the ">" symbol is "greater than", the "<" symbol is "less than" and the "=" is "equal to" the result provided. When completing this item on the form within Rave, select the "greater than", "equal to", or "less than" from the drop down menu.
HIV RNA PCR	Record the participant's HIV RNA PCR result exactly as it appears on the lab report source documentation, regardless of whether the result is more or less than the limit of detection for the assay. If the HIV RNA PCR target is not detected, mark the "target not detected" box and leave the HIV RNA PCR field blank. If the HIV RNA PCR result is below the limit of detection, indicate that the results is "less than" the value provided. If HIV RNA PCR testing is not done/not collected, skip to the Seroconverter Plasma Storage items.
HIV RNA PCR Kit	Select the HIV RNA PCR testing kit that was used. If completing a paper form mark the kit from the response options provided. When completing the form within Rave, select the kit from the drop-down field.

Field	Instructions
HIV RNA PCR Kit Lower limit of detection	Select “20” or “40” as the lower limit of detection or record the viral copies/mL
CD4%	If automatically calculated, record the CD4+ percentage that was reported for the specimen in the item, “Absolute CD4”. If the CD4+ percentage is not available (i.e., it was not reported and would have to be manually calculated), mark the “not available” box.
Final HIV Status	Once a participant’s HIV status has been determined, record the final HIV status. If the participant’s final HIV status is determined to be positive (according to the protocol testing algorithm), update the Clinical Product Hold/Discontinuation Log to reflect permanent discontinuation of study product. If the participant status is not clearly negative or clearly positive, mark the “pending” box and updated this item once the participant’s final HIV status is known. When completing the paper form, mark the participant’s final HIV status from the list of outcomes provided. When completing the form, select the participant’s HIV status from the drop-down field.

HIV Test Results

Purpose:
This form is used to document HIV rapid test results from local lab.

General Instructions:
Complete this form at V1.0 – Screening, V2.0 – Enrollment, Visit 10, and as indicated during follow-up.
Record HIV specimen test results on this form as they become available from the local lab.

Field-specific Instructions:

Field	Instructions
HIV test 1 Kit	Select the kit name that was used from the drop-down field. If “Other” is selected, then specify the test kit in “If “Other, specify”.
HIV test results 1	If “Antibody positive”, “Antigen positive”, or “Antibody and antigen positive” is selected, complete a Product Hold Log line and Discontinuation of Study Product form, if applicable.
HIV test 2 Kit	Select the kit name that was used from the drop-down field. If “Other” is selected, then specify the test kit in “If “Other, specify”.
HIV test results 2	If the HIV test 2 results is “Antibody positive”, “Antigen positive”, or “Antibody and antigen positive” complete a Product Hold Log line and Discontinuation of Study Product form, if applicable. If HIV test 1 and test 2 are both “Negative”, end the form.

Inclusion/Exclusion Criteria

Purpose:
This form documents a participant's enrollment status at the Screening Visit.

General Instructions:
Complete this form for each participant screened in MTN-039. Complete this form when it is determined whether the participant will enroll in the study. If the participant has a second screening attempt, update this form with data from the second screening attempt (do not complete a new form).

Field-specific Instructions:

Field	Instructions
Did the participant meet all eligibility criteria?	Select 'Yes' or "No' to indicate if the participant met all eligibility criteria.
Eligibility Status	Record the applicable eligibility status by selecting from the drop down menu. If participant met all eligibility criteria, and Eligibility Status is 'Eligible and enrolled', then end of form.
Select reason(s) why participant is ineligible.	If participant is deemed ineligible per inclusion or exclusion criteria, use the drop-down menu to select a reason and save. Note that it may be necessary to scroll to the right to access drop down menu. Alternatively, the first few characters of each criterion can be keyed in to bring up a more selective list. If there is more than one reason for ineligibility per inclusion or exclusion criteria, click on the "Add a new Log line" and select another reason. Add all applicable reasons as appropriate.
If other reason, including investigator decision, specify	If "Has any other condition that, in the opinion of the IoR/designee, could preclude informed consent…" was selected, record reason in the specify text box. If any other response was selected, leave this field blank.
If eligible but participant declined enrollment, specify reason.	Record the reason an eligible participant did not enroll. This text field should only be completed if "Eligibility status" is 'Eligible, but participant did not enroll'.

Interim Visit Summary

Purpose:
This form is used to summarize information from each participant at an interim visit and to record all procedures or assessments the participant received at any interim study visit (e.g., clinically indicated physical exam) that is completed during the study.

General Information/Instructions:

This form is required for each interim visit completed for a participant. Use the “Add Event” feature to dynamically create the Interim Visit folder, which will add an Interim Visit Summary eCRF to the participant’s casebook within the applicable Interim Visit folder.

Field-specific Instructions:

Field	Instructions
Visit Date	A complete date is required.
Interim Visit code	Enter the applicable interim visit code. Refer to the Data Collection SSP for more information on visit codes.
Was study product use permanently discontinued (scheduled or early) at this visit?	Select 'Yes' or 'No'. If 'Yes', then complete a Product Discontinuation eCRF within the Discontinuations folder.
Did the participant exit/terminate the study at this visit?	Select 'Yes' or 'No'. If 'Yes', then complete a Study Discontinuation eCRF within the Discontinuations folder.
Were any new adverse events (AEs) reported at this visit? If yes, complete the AE Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one Adverse Event (AE) was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable AE(s).
Is the participant taking any concomitant medications that have not been previously reported? If yes, complete the Concomitant Medications Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one concomitant medication was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable CM(s).
Have any protocol deviations been reported at this visit? If yes, complete the Protocol Deviations Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one protocol deviation was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable PD(s).
Reason for interim visit	Select all that apply.
If completion of missed visit procedures, for which visit are procedures being made up?	If "Completion of missed visit procedures" is selected, then select the applicable visit from the drop-down menu for which procedures are being made up.

If other, specify	If "Other" is selected for reason for interim visit, then specify the reason in the text field provided.
What study procedures were completed at this visit:	Select the applicable procedures that were completed at the study visit. The applicable eCRF(s) will then be added to the participant's visit folder. For example, if a physical exam was performed, select the checkbox corresponding to **Physical Exam**.

Medical History Y/N

Purpose:
This form is used to trigger the Medical History log.

General Instructions:
This form is in the "Ongoing Logs" folder and is only completed once, at the time the first medical history condition/event is reported or at the end of the study if no medical history condition/events are reported.

Field-specific Instructions:

Field	Instructions
Does the participant have any medical history to report?	• If "Yes" is selected, then the **Medical History** log loads in the "Ongoing Logs" folder. • Select "No" at the end of the study if the participant has not reported a medical history condition/event.

Medical History

Purpose:
This form documents a snapshot of the participant's medical history at enrollment.

General Instructions:
- Record only medical conditions/events experienced up to study product initiation unless otherwise specified in the protocol or Study Specific Procedures (SSPs).
- Include current medical conditions/events and any ongoing conditions such as mental illness, alcoholism, drug abuse, and chronic conditions (controlled or not controlled by medication).
- Complete one log line for each medical history condition/event.
- Add additional log lines by clicking "Add a new Log line".
- If a participant recalls additional medical history after enrollment, update the **Medical History** log by adding a new log line.
- Do not update existing log lines after the Enrollment Visit.

Field-specific Instructions:

Field	Instructions
Description of medical history condition/event	Whenever possible, provide a diagnosis instead of listing a cluster of symptoms. If no diagnosis is identified, record each symptom as a separate entry on the **Medical History** log. If an abnormal lab value is reported, record the lab assay with the direction (i.e., increased or decreased) of the abnormality. For example, "decreased hematocrit" or "increased ALT."
Is condition/event gradable?	Mark "No" for a condition/event that does not meet grading criteria per *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events*, most current version.
Severity grade	• Grade the severity according to the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events*. • Record the severity grade of the condition/event at the time of enrollment. ○ Example: left ankle sprain that was initially grade 3 (severe) during screening, but grade 1 (mild) upon enrollment, to be reported as grade 1 (mild). • If the severity grade has increased in severity or frequency during the study AE reporting period, then report the change as an AE. The Severity Grade should remain unchanged on the **Medical History** log. • If the severity grade increased or decreased **on or prior to** Enrollment, this should be updated on the **Medical History** log as needed. • If the condition/event improves in severity or resolves during the study, the Severity Grade should remain unchanged on the **Medical History** log.

Start date of medical history condition/event	• If the participant is unable to recall the date, obtain participant's best estimate.
	• At a minimum, the year is required. If the date is within the same year as study enrollment, the month and year are both required.
	  ○ If the exact day is unknown, enter 'UN' for the day field.
	  ○ If the exact month is unknown, then select 'UNK' for the month field.
	  ○ Example: UN-Jan-2010 or UN-UNK-2010.
	• If the condition is diagnosed due to an abnormal lab result, record the date on which the specimen was collected. If a diagnosis is not available, record the date of onset of condition.

Is the condition ongoing?	Review and update conditions marked "ongoing" only prior to and including the Enrollment Visit.
Date medical condition/event ended/resolved	A date is required if 'Is the condition ongoing?' is 'No'. If the exact day is unknown, enter 'UN' for the day field. If the exact month is unknown, then select 'UNK' for the month field. At a minimum, a year is required. Record the date the medical condition was considered resolved. For surgeries/procedures, record the date the surgery/procedure was completed.

Missed Visit

General Instructions:
Complete whenever an enrolled participant misses a required visit according to the Study-specific Procedures (SSP). A Missed Visit form will be added to the visit folder if the response to "Did the participant complete this visit?" is "No" on the Date of Visit form.

Field-specific Instructions:

Field	Instructions
Target visit date	Record the target date of the visit that was missed.

Participant Identifier

Purpose:
This form generates a PTID for the participant. Complete this form first for each participant.

Field-specific Instructions:

Field	Instructions
Participant ID	• To add a participant to the study database, select the 'Add Subject' link on the study home page. The Participant Identifier form will load. • No data are required from the site on this form. Click the "Save" button at the bottom of the form. A pop-up box will appear to indicate that a participant has been added to the database. The participant's home page will appear. • The link for the Participant Identifier form is at the top of each participant's home page. PTID will appear on each form in participant's casebook. • The PTID must be written at the top of each CRF PDF completed for a participant. • The first three digits of each PTID is the Rave site ID number.

Participant Replacement Assessment

Purpose:
This form is used to assess whether a participant meets criteria for replacement in the study.

General Instructions:
Complete this form on an as-needed basis. It is required for each participant who will be replaced in the study. To dynamically add this eCRF to visit folder, select 'Participant replacement assessment' on the Additional Study Procedures form.

Field-specific Instructions:

Field	Instructions
Date of assessment	A complete date is required.
Does this participant meet protocol-specified criteria for replacement?	Select 'Yes' or 'No'. If the response is 'No', then end the form and leave remaining items blank.
Which replacement criteria were met?	Select the replacement criteria from the drop-down menu. If replacement criteria is other than what is listed, select 'Other' and record the reason in the "If Other, specify" text field provided.

Pelvic Exam

Purpose:

This form is used to document the participant's pelvic exam assessment.

General Instructions:
Complete this form as clinically indicated at all study visits for female participants only.

Field-specific Instructions:

Field	Instructions
Pelvic exam assessment	If 'not done' is selected, then this is the end of form and all remaining items should be left blank. Select 'abnormal findings' or 'no abnormal findings' to indicate any findings from the genital exam. If 'no abnormal findings' is selected, then skip the "Abnormal findings" section.
Exam Date	A complete date is required.
Abnormal findings	Select the box to the right of each abnormal finding observed, and check all that apply. Specify additional details in the text field provided where applicable. If an observed abnormal finding is not listed, select "Other abnormal findings" and specify/describe the abnormal findings in the text field provided, including the anatomical location. Please record any baseline abnormalities on the Baseline Medical History Log eCRF. Any post baseline abnormalities or baseline conditions that worsened post baseline should be reported on the Adverse Event eCRF. In general, for abnormal findings reported as adverse events on an AE Log, use the abnormal finding text provided on this form as the AE descriptive text Abnormal blood or bleeding, describe: If unexpected blood or bleeding is observed, briefly describe the color, amount, and location of the blood/bleeding. Assess the blood/bleeding for AE reporting purposes.
Vaginal Abnormalities	Select the box to the right of each abnormal finding observed, and check all that apply. Specify additional details in the text field provided where applicable. If an observed abnormal finding is not listed, select "Other abnormal findings" and specify/describe the abnormal findings in the text field provided, including the anatomical location. Please record any baseline abnormalities on the Baseline Medical History Log eCRF. Any post baseline abnormalities or baseline conditions that worsened post baseline should be reported on the Adverse Event eCRF. In general, for abnormal findings reported as adverse events on an AE Log, use the abnormal finding text provided on this form as the AE descriptive text Abnormal vaginal discharge, select "slight", "moderate", or "pooling" from the dropdown menu.
Were any new pelvic finding	Record whether an AE was identified and reported at this visit as part of the genital exam assessment by selecting 'Yes' or 'No'. If an AE was reported at the study visit, select the corresponding AE log form within the dynamic searchlist function on the eCRF. Up to 3 AEs can be selected.

AEs reported at this visit?	This item should be 'No' prior to participant enrollment in the study (i.e., prior to the AE reporting period).

Physical Exam

Purpose:
This form documents physical exam findings.

General Instructions
Complete at all required study visits as specified in the protocol and schedule of forms.

Field-specific Instructions

Field	Instructions
Was a physical exam performed? Body System Exam Date	If a physical exam is performed: • For each organ or body system, mark "Normal", "Abnormal" or "Not done". • If "Abnormal" describe findings in corresponding "If "Abnormal", specify:" box. • Enter the date the physical exam was performed. A complete date is required.
Other system finding	• If no additional body system is evaluated, select "Not done". • If a body system is evaluated that is not listed on the form, enter body system in the "If "Other system finding", specify:" box. • If "Abnormal" enter findings in the "If "Abnormal", specify:" box.

Pregnancy History

Purpose:
This form is used to document the participant's pregnancy history.

General Instructions:
- Complete this form if a participant becomes pregnant during the study, and it is the participant's first pregnancy since enrollment in the study.
- Complete this form only once during the study.
- This form will load into the participant's pregnancy folder if the last question on the Pregnancy Report form is answered "Yes".

Field-specific Instructions:

Field	Instructions
Has the participant ever been pregnant before?	• Select "No" If the participant has never been pregnant before and end the form. • Select "Yes" if the participant has ever been pregnant. ○ An entry is required for each pregnancy outcome. (e.g. "Number of full term live births")

	○ Enter '00' for any that do not apply.
Does the participant have a history of pregnancy complications or fetal/infant congenital anomalies?	• Select "No" if the participant does not have a history of pregnancy complications and end the form. • If "Yes", include information on pregnancy complications and fetal/infant congenital anomalies experienced prior to enrolling in the study.

Pregnancy Outcome

Purpose:
This form documents a pregnancy outcome.

General Instructions:
This form loads in the "Pregnancy" folder when a Pregnancy Report form is submitted.

Field-specific Instructions:

Field	Instructions
Is the outcome of this pregnancy obtainable?	If site staff were able to ascertain an outcome for this pregnancy from the participant, select "Yes". If site staff were not able to ascertain an outcome for this pregnancy from the participant (i.e. the participant refuses further contact), select "No" and end the form.
How many pregnancy outcomes resulted from this reported pregnancy?	If the pregnancy results in two or more outcomes, complete a Pregnancy Outcome Log eCRF (new log line) for each outcome. If the item is completed as greater than "1", add additional Pregnancy Outcome Log lines to the Pregnancy Outcome Log eCRF, as needed.
Outcome Date	A complete date is required.
Place of delivery/outcome	Enter the place of delivery/outcome from the drop-down menu. If 'Other' is selected, specify in the corresponding "Other, specify" text field.
Specify Outcome	Specify the outcome from the drop-down menu. If the outcome is spontaneous fetal death, still birth, spontaneous abortion, therapeutic/elective abortion, or ectopic pregnancy, the outcome itself is not an adverse event (AE). If a therapeutic/elective abortion is performed due to a pregnancy complication, the pregnancy complication should be reported on an Adverse Event (AE) Log, if prior to termination, with 'therapeutic procedure/surgery' checked for item "Other action(s) taken". If there are any maternal complications as a result of the pregnancy outcome, refer to the protocol, Study-specific Procedures (SSP) manual, and Manual for Expedited Reporting of Adverse Events to DAIDS, Version 2 for guidance on AE and expedited AE reporting requirements. If 'other' is selected, specify in the corresponding "If Other, specify" text field.
Method	Select the method from the drop-down menu only if the outcome is 'full term live birth (≥37 weeks)' or 'premature term live birth (< 37 weeks)'. "Operative Vaginal" delivery includes delivery with forceps and/or vacuum. If the outcome is 'full term live birth', skip to "Were there any complications related to the pregnancy outcome?"

Field	Instructions
Provide a brief narrative of the circumstances	Include information on medical conditions associated with the outcome, including early contractions, rupture of membranes, and cramping, along with actions taken as a result of these conditions. This item is only required if not a full term live birth.
Were there any complications related to the pregnancy outcome?	Select 'yes' or 'no' to indicate if there were any complications related to the pregnancy outcome. If 'no', then items "Delivery-related complications" and "Non-delivery related complications" are not required.
Delivery-related complications	Select 'None' or check all that apply. If 'other' is selected, specify in the corresponding "If Other, specify" text field.
Non-delivery related complications	Select 'None' or check all that apply. If 'other' is selected, specify in the corresponding "Other, specify" text field.
Were any fetal/infant congenital anomalies identified?	Record if any fetal/infant congenital anomalies were identified. If "No" or "Unknown", go to statement "Complete the infant items below for live births only" above "Infant Gender".
Congenital anomalies identified.	If there were fetal/infant congenital anomalies identified, then check all that apply. If a woman on study has a baby with a congenital anomaly, report the event on an Adverse Event (AE) Log eCRF, if prior to study termination. On the Adverse Event eCRF, record "Congenital Anomaly in Offspring" in the AE description, record the Outcome Date as the Onset Date, and record the specific anomaly in the Comment Section. Submit an Expedited Adverse Event (EAE) Reporting form.
Describe the congenital anomaly/defect	Describe the congenital anomaly/defect in the text field provided.
Infant items	Complete the infant items for live births only. Otherwise, end the form.
Infant Gender, Infant birth weight, Infant birth length, Infant birth head circumference, Infant birth abdominal circumference	Complete these items for live births only. Record the information as documented in medical records. If no medical record documentation of the information is available, complete this item based on participant report. Check the "unavailable" box if no medical record documentation is available and the participant does not know the information.
Infant Gestational age by examination in weeks; Infant gestational age by examination in days; Or Infant gestational age by examination unavailable If other, specify	Record the infant's gestational age at birth. If the infant's gestational age is determined using the Ballard method, record "0" in the "days" box. Check the "Infant gestational age by examination unavailable" box if no medical record documentation of the infant's gestational age is available, and end the form. If an 'other' method is selected for "Method used to determine gestational age", specify in the corresponding "If other, specify" text field.

Pregnancy Report

Purpose:
This form is used to document pregnancies that occur between study enrollment and termination.

General Instructions:

- Complete this form for each new pregnancy that the participant experiences during the study.
- This form will load into the participant's "pregnancy" folder if a positive pregnancy test result is submitted.

Field-specific Instructions:

Field	Instructions
Date pregnancy reported to site	A complete date is required.
Visit at which this pregnancy was reported	Record the visit at which the pregnancy was reported. A complete date is required.
If interim	If relevant, add the appropriate Interim Visit code.
Date of onset of last menstrual period OR Amenorrheic for past 6 months	A complete date is required. Record best estimate if date not known. If the participant is amenorrheic, select the checkbox for item 'Amenorrheic for past 6 months' and leave the First day of last menstrual period date fields blank.
Estimated date of delivery	A complete date is required.
What primary information was used to estimate the date of delivery?	Choose the primary method that was used to estimate the date of delivery. If another method was used which are not covered by the currently listed methods, please select 'Yes' for "Other" and describe them in the 'If "Other, specify' text field.
Is this the participant's first pregnancy since enrollment in this study?	Select "Yes" or "No". If "Yes", complete the Pregnancy History form.

Pregnancy Test Results

Purpose:
This form documents pregnancy test results.

General Instructions:
The pregnancy test must be done at the Screening and Enrollment visits and as indicated for follow-up visits.

Field-specific Instructions:

Field	Instructions
Was a pregnancy test done?	If "No" end of form.
Collection date	Record the date that the pregnancy test was collected and NOT the date the results were reported or recorded. A complete date is required.
Pregnancy test result	If participant is pregnant (tests positive): • DO NOT ADMINISTER STUDY PRODUCT if on planned study product administration date. Complete Product Hold Log, Discontinuation of study product and Study termination forms • Complete **Pregnancy Report** form • Complete **Pregnancy History** form

Specimen Collection and Storage (All, Group 1, and Group 2)

General Instructions:
Refer to the SSP for the number and type of tube(s) required at each visit.

The Specimen Collection and Storage CRF will auto-populate at each required visit, but it can also be added through the Additional Study Procedures CRF. On each form, the specimen type fields are auto-populated depending on which group the participant was randomly assigned to.

Do not use this form to document any local lab specimens. Use this form only to document the collection of research blood specimens that will be sent to the site processing lab.

Field-specific Instructions:

Field	Instructions
Was specimen collected?	Select "Yes" or "No"
Was sample stored? If "No", record why sample was not stored	Select "Yes" or "No" If a sample was not stored, record the reason.

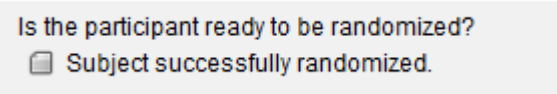
Randomization

Purpose:
This form is used to officially randomize a participant for MTN-039. This form is completed at Enrollment for participants who have provided informed consent and who are eligible to participate in the study.

General Instructions:
Complete this form for each participant who will enroll in MTN-039 indicating the participant is ready to be randomized. The Randomization Date and Time will be auto-populated from Medidata Balance into Medidata Rave. This eCRF is use in Rave to generate the participant's treatment assignment and day

and time sampling assignments in Medidata Balance. It is located in the Enrollment Visit folder. The item "Did the participant meet all eligibility criteria?" on the Inclusion Exclusion Criteria eCRF must be completed before the Randomization eCRF in order for the randomization to be successful.

Field-specific Instructions:

Field	Instructions
Is the participant ready to be randomized?	Select 'Yes' and Save the form. If the participant is successfully randomized, a note will appear under this item as shown below:  If randomization was not successful, this message will not appear and the Randomization Date and Time will not automatically populate. If successful, the participant will be assigned to a treatment arm in the Medidata Balance module.
Randomization Date and Time	Once "Is the participant ready to be randomized?" is saved as 'Yes', then the randomization Date and Time will automatically populate. The Randomization Time will be auto-populated in Coordinated Universal Time (UTC).

STI Tests
Purpose:
This form is used to document STI test results performed by the local site laboratory.

General Instructions:
Complete this form at the V1.0 - Screening Visit and as indicated during the study. To generate this form at Enrollment, select "Enroll – STI Test Results" via Add Event.
If any or all of the lab tests listed on this form are repeated (re-drawn) between the Screening and Enrollment Visit, document the repeated results on the same STI Test Results form. If the participant enrolls, the updated results should be submitted into the study database.

At Screening, record STI diagnoses on the Baseline Medical History Log form when applicable. During follow-up, if a test result(s) recorded within this form indicates that the participant has a new (or increased severity) laboratory-confirmed infection or diagnosis, this infection/diagnosis must be recorded as an adverse event in the Adverse Event Log eCRF as applicable.

Field-specific Instructions:

Field	Instructions
Was a pharyngeal sample collected for N. gonorrhea and C. trachomatis testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for pharyngeal N. gonorrhea and C trachomatis testing do not need to be completed. Proceed to "Was a pelvic sample collected for N. gonorrhea and C. trachomatis testing?"
Collection Date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
N. gonorrhea – Pharyngeal test result	Select "Positive" or "Negative".
C. trachomatis – Pharyngeal test result	Select "Positive" or "Negative".
Was a pelvic sample collected for N. gonorrhea and C. trachomatis testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for pelvic N. gonorrhea and C trachomatis testing do not need to be completed. Proceed to the next question
Collection Date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
N. gonorrhea – pelvic test result	Select "Positive" or "Negative".
C. trachomatis – pelvic test result	Select "Positive" or "Negative".
Was a urine sample collected for N. gonorrhea or C. trachomatis testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for urine N. gonorrhea and C trachomatis testing do not need to be completed. Proceed to the next question.
Collection Date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
N. gonorrhea – URINE test result	Select "Positive" or "Negative".
C. trachomatis – URINE test result	Select "Positive" or "Negative".
Was a rectal swab sample collected for N. gonorrhea or C. trachomatis testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for rectal swab N. gonorrhea and C trachomatis testing do not need to be completed. Proceed to "Was a sample collected for Syphilis testing?"
Collection Date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.

Field	Instructions
N. gonorrhea – rectal swab test result	Select “Positive” or “Negative”.
C. trachomatis – rectal swab test result	Select “Positive” or “Negative”.
Was a sample collected for Syphilis testing?	Select ‘Yes’ or ‘No’. If ‘No’, then the remaining items for Syphilis testing do not need to be completed.
Collection date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
Syphilis screening test	If the result of the Syphilis screening test is ‘Reactive,’ complete the Syphilis confirmatory test results. Enter ‘Not reported’ in the event that a specimen was collected, but the result is not available due to specimen loss or damage.
Syphilis titer	Record the titer in the format 1: XXXX. When completing this form in Medidata Rave, please include the “1:” in the same field for the syphilis titer.
Syphilis confirmatory test	If the result of the Syphilis screening test is ‘Reactive,’ complete the Syphilis confirmatory test results (either ‘Negative,’ ‘Positive,’ or ‘Indeterminate’ or ‘Not done’).
Was the participant diagnosed with asymptomatic BV	Select “Yes” or “No”.
Was the participant diagnosed with asymptomatic candida	Select “Yes” or “No”.
Was a sample collected for Hepatitis B Surface Antigen (HBsAG) testing?	Select ‘Yes’ or ‘No’. If ‘No’, then the remaining items for Hepatitis B Surface Antigen testing do not need to be completed.
Collection Date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
Hepatitis B Surface Antigen (HBsAG)	Select “Positive” or “Negative”.

Study Termination

Purpose:

This form documents participant's termination from the study.

General Instructions:

- Complete once for every participant at the time of early study termination or at visit 11.0.
- This form is in the Discontinuations folder.

Field-specific Instructions:

Field	Instructions
Date of Study Exit	A complete date is required.
Primary reason for completion/discontinuation	Select one reason for study termination from the drop-down menu.
If "Other", specify	If the primary reason is Other', then provide additional details in the text field provided.
If death, enter date of death	If the primary reason for study non-completion is 'death', provide the date of death. A complete date is required.
If "Adverse Event", select applicable adverse event	Select the applicable Adverse Event from the list of AE's in the drop down menu. In situations where more than one AE is associated with termination, record the AE that most strongly influenced the decision to terminate.

Vital Signs

Purpose:
These forms document vital signs.

General Instructions:
The form must be completed at screening and enrollment and as needed at all other visits.

Field-specific Instructions:

Field	Instructions
Were vital signs done?	Select 'Yes' or 'No'.
Date of Assessment	Enter the date the participant's vital signs were measured. A complete date is required.
Height (may be omitted after Enrollment)	Enter the participant's height in centimeters. The value must be reported in whole numbers (e.g. 180 cm).
Weight (may be omitted after Enrollment)	Enter the participant's weight in kilograms. The value can be reported up to one decimal (e.g. 70.1 kg).
Body Temperature	Enter the participant's temperature in Celsius. The value can be reported up to one decimal (e.g. 37.2˚ C).
Systolic BP	Enter the participant's systolic blood pressure in mmHg (e.g., 120 mmHg).

Field	Instructions
Diastolic BP	Enter the participant's diastolic blood pressure in mmHg (e.g., 60 mmHg).
Pulse	Enter the participant's pulse in beats per minute (e.g., 60 beats/min).
Rate of respiration	Enter the participant's respiratory rate in breaths per minute (e.g., 14 breaths/min).

Change History

Summary of Changes to Study DMP

Version		Affected Section(s) or Form(s)	Summary of Revisions
Number	Date		