CRF Completion Guidelines (CCGs)
Protocol #: MTN-026
V1.3 (28 June 2018)

CONFIDENTIAL DOCUMENT

Table of Contents

Completion Guidelines for Standard CRFs

The following instructions are study-specific data completion instructions intended to assist site staff when completing Case Report Forms (CRFs) for MTN-026 (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 posted on the MTN-026 Atlas web page: https://atlas.scharp.org/cpas/project/MTN/026/begin.view?

General Guidelines – Medidata Rave eCRFs (electronic CRF completion)

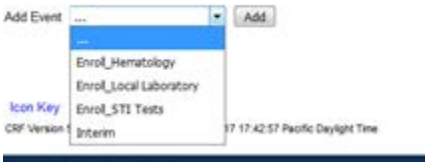
- The Participant ID is automatically assigned by Rave as a 9-digit field, starting with the 3-digit site number followed by a randomly assigned 6-digit participant number.
- All data entered in the eCRF should correspond accurately with the source documents/paper CRFs.
- Complete all required fields on the screens. Please ensure all entries are in English and are accurate, consistent, complete and medically logical.
- Ensure there are no missing data in the eCRF. Where requested to 'specify' for an item, ensure that a specific entry is made.
    - Visit dates should be complete and chronological according to the protocol.
    - All date fields are entered as Day/Month/Year (dd/mmm/yyyy) (e.g., 16 OCT 2017).
- Drop-down menus are available for many fields. Use these menus, when available, to select the appropriate response.
- Avoid using abbreviations and symbols wherever possible. Do not use special characters unless explicitly stated or hit the Return key in text fields.
- If a scheduled visit was missed, do not enter data on any of the eCRF pages for the visit, with the exception of the Follow-up Visit Summary Yes/No and the Missed Visit eCRFs, which should be completed.
- Log (or repeating) forms have been provided. Log forms allow you to enter multiple items on one form, and to switch between portrait and log formats for ease of viewing or data entry. The following are log forms or have the log format within the form for this study: Adverse Events, Concomitant Medications, Protocol Deviations, Pregnancy Outcome, Baseline Medical History, Directly Observed Dosing, and Sexual Lubricant.
    - Click "Add a new Log line" to add a row.
    - Log lines can be inactivated by clicking "Inactivate" and specifying the log line number if needed.
- If corrections are needed: By clicking the "pencil" icon, the field will become editable so that you can then correct the value and give the reason for the change (if needed).
- In case of an incorrect data entry, a system query will fire. System queries will close automatically after saving the form if the data point is entered or corrected (A response to a system query is not required). However, answering a system query prior to updating the data point field will make the query change into a manual query that will need to be closed by SCHARP.
- Data changes can be reviewed in the audit trail. If data is modified inadvertently, the change is also saved in the audit trail.

- The Investigator of Record (IoR) will sign all pages after the participant's data has been reviewed, no further changes or additions to the eCRFs are necessary and the casebook status is frozen. The SCHARP Clinical Data Manager(s) will provide directions for the timing of 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 visits to a participant's casebook.

- The following folders can be added to a participant's casebook:
  - Interim Visits (see section on "Interim Visits" on how to add interim visits to a participant's casebook
- The following forms can be added to the V2.0 – Enrollment folder:
  - STI Tests
  - Hematology
  - Local Laboratory Results



Interim Visits

- Should unscheduled assessments be required for a non-routine visit or procedure, add the visit by clicking on the **Add Event** button. Select "Interim Visit". An Interim Visit folder will appear in the participant's casebook.

- Open the Interim Visit folder to access the "Interim Visit Summary" eCRF. On the Interim Visit Summary eCRF, select "Yes" for each assessment that was performed. The selected forms will be populated automatically within the applicable Interim Visit folder.

- On the Interim Visit Summary eCRF, enter the visit date as the earliest date visit procedures performed at the visit began.

Auto-population of Medidata Rave Forms

- Medidata Rave will dynamically add eCRFs to a visit folder within a participant's casebook based on specified responses on the eCRFs. Below are a few examples:

  - Example 1: Randomization form - Enrollment folder
    - If item "Is the participant ready to be randomized?" is marked "yes", the applicable regular visit folders from V3 – V17 (Termination) will be added to the matrix. Within each visit folder is the Follow-up Y/N eCRF.
  - Example 2: Follow-up Yes/No eCRF
    - If item "Did the participant complete this visit" is 'No', the Missed Visit eCRF will be added to the visit folder and required eCRFs for that visit will not appear in the visit folder.

- Selecting 'Yes' will automatically add the applicable eCRFs that are required to be completed per protocol to the applicable visit folder.

- Example 3: Adverse Event Summary eCRF
  - Selecting 'Yes' for "Has the participant experienced an Adverse Event during the study?" will dynamically add the Adverse Event Log eCRF to the Ongoing Logs folder.

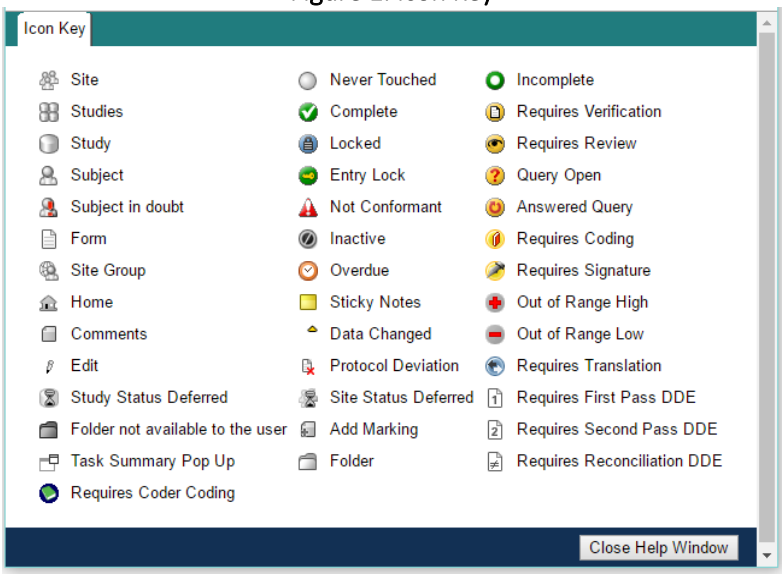
Dynamic Search List Functionality

- Dynamic searchlist functionality is used to look up Adverse Event data *(AE log line, start date, and term, e.g. "1- 05JAN2017-FEVER")*.
- Dynamic searchlist functionality is present on the following eCRFs: Concomitant Medications, Hematology, Local Laboratory Results, Pelvic Exam, Treatment Discontinuation, and Study Discontinuation
- For Example:
  - An AE of '*FEVER*' started on 05JAN2017 and is reported on the Adverse Events eCRF
  - On the Concomitant Medications form, if a listed medication was used for this AE, a dynamic searchlist can be used to select the applicable AE record from the dropdown list.
  - The dynamic search list for 'AE log line, start date, and term' shows records entered on the AE form
  - Your selection can be manually deleted if entered in error
    - **Note:** If the original data (e.g., AE term and/or start date, MH term) changed or the log line was inactivated, the previous selection becomes non-conformant. You will need to correct the item by re-selecting from the search list to correspond with the latest data.

Icon Key

Within Rave, an Icon Key is available. The key contains a description and picture of the commonly used icons. To access the Icon Key, click on the Icon Key hyperlink. The Icon Key will open in a separate pop-up window. Below is a screen shot of the Icon Key.

Figure 1. Icon Key

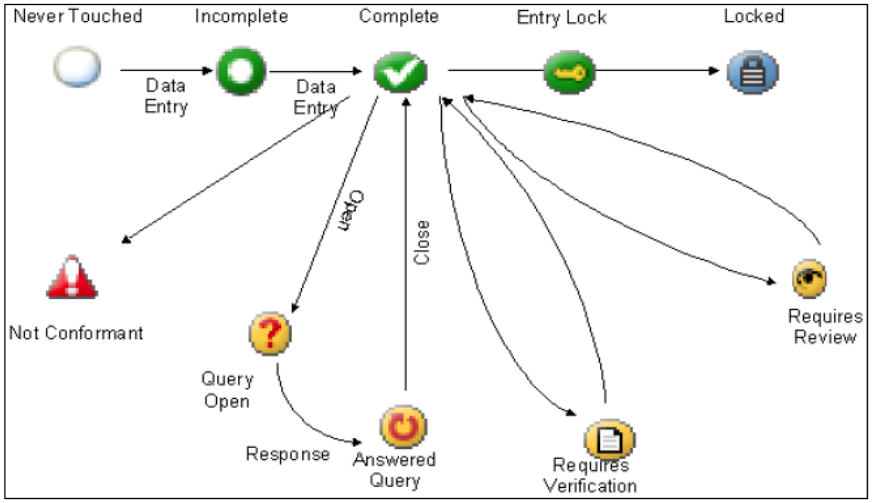


Icon Progressions

The life cycle of folders, forms, fields, etc., follows a logical progression starting with never touched and moving toward complete and locked. Graphical icons are used throughout Rave to visually denote 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 Listing displays all pending tasks for a study. At the Site level, it displays the number of participants within the site that contain the selected item (see Figure 3). For example, 8 participants within the site have open queries. If the "Open Queries task is expanded, the 8 participants are displayed (see Figure 4).

Figure 3. Site-Level Task Summary

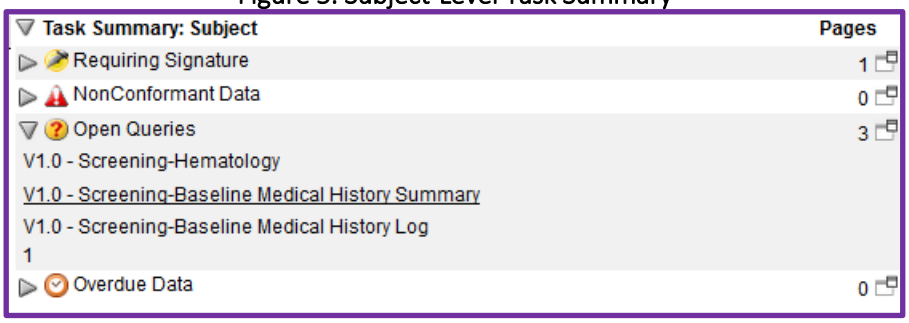
Task Summary: Site	Subjects
Requiring Signature	8
NonConformant Data	0
Open Queries	8
Overdue Data	0

Figure 4. Site-Level Task Summary

Task Summary: Site	Subjects
Requiring Signature	8
NonConformant Data	0
Open Queries	8
998210855	
998238757	
998313907	
998329818	
998423107	
998549894	
998561588	
998672732	
1	
Overdue Data	0

- At the Subject (participant) level, the Task Summary displays the number of pages/forms for the participant that contain the selected item. In Figure 5 below, there are 3 open queries on 3 eCRFs. In the expanded task summary view, if a form name is clicked that form is displayed.

Figure 5. Subject-Level Task Summary



General Guidelines – Paper CRF Completion

When completing a paper CRF, refer to detailed instructions on data collection pertaining to the specific form and fields on that form in this document.

Based on Good Clinical Practices (GCPs), the following guidelines should be used for completing paper CRFs:

- Use a black or dark blue medium ballpoint pen. Do not use any other type of writing tool.
- Press firmly when recording data or writing comments.
- Print all data and comments legibly by hand. Entries that cannot be read may result in incorrect data entry.
- Do not use cursive/script handwriting, as it can be difficult to read.
- Write numbers as large as possible on the line specified.
- Record data on the front of CRFs only.
- If the lines provided for written responses are not long enough, continue in another blank area of the form (within the page margins).
- Mark only one answer except when given the instruction "Mark/Select all that apply."
- A response is required for every item unless instructed otherwise by a skip pattern, as noted in the CCGs.
- **Never** use correction fluid ("white-out") or correction tape on CRFs.

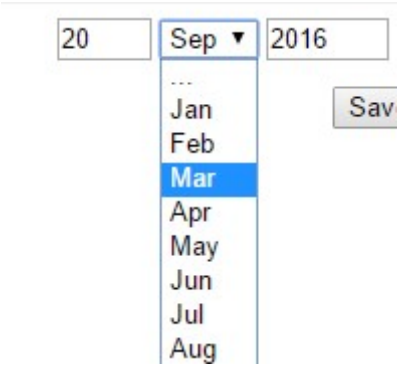
How to Record Dates - Electronic and/or Paper

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.

The month field must be entered with the three-letter abbreviation in English. Abbreviations are shown below. In the study database, these abbreviations will be selected from 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
Unknown	UNK		

For example, September 20, 2016 is recorded as:



Some items allow for partial dates. When recording partial dates, the following guidance applies:

- Enter UN for the day
- Select "UNK" for the month from the drop-down menu.

How to Record Time - Electronic and/or Paper

Time is recorded on CRFs using the 24-hour clock (00:00-23:59), in which hours are designated from 0–23. For example, in the 24-hour clock 2:25 p.m. translates to 14:25 (2 p.m. = 14), which would be recorded as follows:

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

How to Record Numbers (non-dates)

When recording numbers, please enter the whole number without leading zeros. Instead of '00', this should be recorded as '0'. 3 should be recorded as 3, not '03' and so on.

Data Corrections and Additions - Electronic and/or Paper

Sometimes, data on a CRF (paper or electronic) may need to be changed, clarified, or amended. There are many reasons why data may need to be changed, such as in response to a query or as a result of site review.

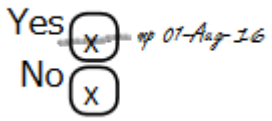
If the electronic CRF is source, it is sufficient to make data updates in the study database itself. If a paper CRF is completed, it is important to make changes to the original CRF first, then enter the updated data into the study database.

Note for paper CRFs: Never write over an entry once it is recorded. Use the standards outlined in the following paragraphs when changing, clarifying, or amending data.
Whenever an entry on a paper CRF is changed, do the following:

- draw a single horizontal line through the incorrect entry (do not obscure the entry or make it un-readable with multiple cross-outs),
- place the correct or clarified answer near the box, and

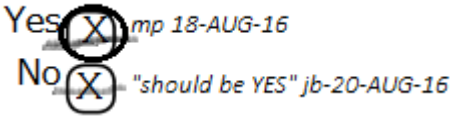
If an X is marked in the wrong response box, correct it by doing the following:

- 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 item,
- write an explanation in the white space near the item, and
- initial and date all corrections as shown below:



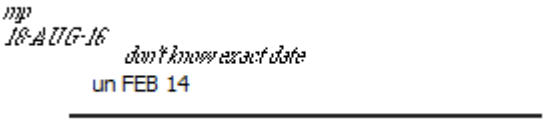
The standards above must ***always*** be followed whenever a paper CRF is changed, clarified, or amended.

How to Handle Missing and Unknown Data

If the answer to an item is not known, is not available, or if the participant refuses to answer for a required item:

- On paper CRFs: draw a single horizontal line through the applicable item and initial and date the item for which the data is unknown. 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 item that is refused, missing, unknown, or not applicable, regardless of whether it is marked as such during the initial paper form completion, or as an update to the form.



- On eCRFs: enter "UN" or select the "UNK" option from the drop-down list of the applicable field for which the data is missing/unknown if applicable. If there is no unknown option and data cannot be obtained, save the form and denote this in response to the system query.

A skip pattern, as noted in the CCGs, is the only valid reason to leave a response blank.

ADMINISTRATIVE FORMS

Participant Identifier

Purpose:
The Participant Identifier page within Medidata Rave will generate each participant's PTID. This page is the first form completed within Medidata Rave for each participant.

General Instructions:
Complete this form for every MTN-026 participant once she has provided written informed consent for study screening and enrollment.

Item-specific Instructions:

<table>
<tr><th>Field</th><th>Instructions</th></tr>
<tr><td>Participant ID</td><td>To add a participant to the study database, select the "Add Subject" link on the MTN-026 site-specific home page. The Participant Identifier page will appear. This is the first page that should be completed for each participant.

No data entry is required by 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 and the home page for the participant's file will appear. The link to refer back to the Participant Identifier page is located at the top of each participant's home page. The participant ID will appear on each eCRF generated in Medidata Rave. The participant ID should be written at the top of each paper CRF completed for a participant.

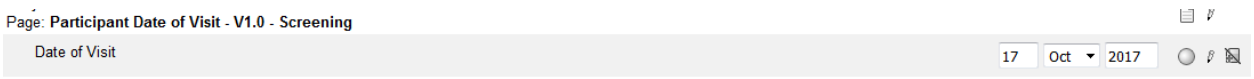
The first three digits of each participant ID will comprise of the Rave site ID. Therefore, each participant ID will begin with the site ID. A list of Rave site IDs is provided in the table below:
<table>
<tr><th>CRS Name</th><th>DAIDS ID</th><th>Rave Site ID</th></tr>
<tr><td>Pittsburgh</td><td>1001</td><td>702</td></tr>
<tr><td>Birmingham</td><td>31788</td><td>821</td></tr>
<tr><td>Bangkok</td><td>31681</td><td>813</td></tr>
</table>
</td></tr>
</table>

Participant Date of Visit

This form is present at the following visit:

- V1.0 – Screening

Please record the visit date by entering the Day and Year and selecting the correct Month from the drop down list in dd MMM yyyy format (for example, 17OCT2017) when entering in the study database.



Note:

- Complete the date on which visit procedures first begin. If the visit reflects data collected across multiple days, enter the date of the earliest collection.

Eligibility Criteria

Purpose:

This form is used to document participant eligibility for enrollment in MTN-026, and if applicable, the reasons for study ineligibility per the inclusion and exclusion criteria per protocol. This form is present in the V1.0 – Screening folder.

General Instructions:

Complete this form for each participant screened in MTN-026. 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).

Item-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.
If eligible but participant did not enroll, 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'.
Select inclusion and/or exclusion criteria that contributed to participant's study ineligibility.	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.

Randomization

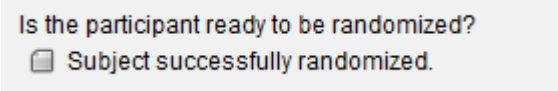
Purpose:

This form is used to officially randomize a participant for MTN-026. 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-026 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 Eligibility Criteria eCRF must be completed before the Randomization eCRF in order for the randomization to be successful.

Item-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).

Enrollment

Purpose:

This form is used to document a participant's study enrollment. 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 is enrolled into MTN-026. This form is present at the V2.0 – Enrollment visit.

Item-specific Instructions:

Field	Instructions
Date the participant marked or signed the study screening and enrollment consent form	A complete date is required.

Field	Instructions
Did the participant consent to long-term specimen storage and future testing?	Select 'Yes' or 'No'. Consent for long-term specimen storage should be updated if the participant changes his/her consent decision after enrollment. Update as needed if the participant changes his/her consent during the study.
Is this a replacement participant?	Select 'Yes' or 'No'.
PTID of participant being replaced	Record the PTID of the participant being replaced as indicated from the Participant Replacement Assessment.
PK, PD and Mucosal Safety Time Assignment	This item will be auto-populated after the Randomization eCRF has been submitted. Based on the participant's time assignment (from Medidata Balance), the field will automatically populate as either '30-60 minutes' or 120 minutes.
PK/PD Sampling Day Assignment	This item will be auto-populated after the Randomization eCRF has been submitted. Based on the participant's day assignment (from Medidata Balance), the field will automatically populate as either '24 hours', '48 hours' or '72 hours'.

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 V17.0 - Termination.

Item-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.

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 V17.0 - Termination.

Item-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 (Visit 4, 5, or 6 and Visit 14, 15, or 16) 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 Treatment 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).
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 not be completed at the scheduled study visit.

Additional Study Procedures

Purpose:

This form is used to record all additional procedures the participant received at his/her scheduled study visit (e.g. clinically indicated physical exam). Do *not* record any procedures required and performed per

protocol on this form. Such procedures should be entered on the relevant CRF within the scheduled visit folder.

General Instructions:
This form appears dynamically when "Were any additional study procedures or forms completed at this visit?" is selected 'Yes' on the Follow-up Visit Summary CRF.

Select the applicable CRFs that will be submitted for the visit. For example, if a physical exam was performed (clinically indicated), select the checkbox corresponding to Physical Exam. Selecting a CRF will dynamically add the applicable form(s) within the associated visit folder.

CASI Summary

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 - Enrollment
- V3.0 - Dosing
- V14.0 – 24 hr PK

Field	Instructions
Was a CASI questionnaire and/or in-depth interview 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. A CASI Tracking CRF does not need to be completed.
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) questionnaires at Enrollment and during follow-up.

General Instructions:
Selecting 'Yes' in the CASI Summary prompt will open up the CASI Tracking CRF. Complete this form at V2.0 - Enrollment, Visit 3.0 - Dosing, and Visit 14.0 – 24 hr PK or early termination visit.

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.
Was an in-depth interview completed?	Select "Yes', 'No', or 'Not required'. Select 'Not required' if an in-depth interview is not required per protocol (e.g. Enrollment).

Protocol Deviations Summary

Purpose:
This form documents if a protocol deviation has occurred.

Generation Instructions:
This form is present within the "Ongoing Logs" folder. Selecting 'Yes' in the Protocol Deviations Summary will add the Protocol Deviation log eCRF.

Item-specific Instructions:

Field	Instructions
Have any protocol deviations occurred? If 'Yes', complete the Protocol Deviation log.	Select 'Yes' or 'No'. If 'Yes' is selected, then the "Protocol Deviation Log" form appears dynamically within the Ongoing Logs folder and can then be completed.

Protocol Deviations Log

Purpose:

This form documents and reports protocol deviations identified for study participants during the implementation of MTN-026.

General Information/Instructions:

Complete this form each time a protocol deviation is identified. Once the Protocol Deviation Log form has been created, complete one log line per protocol deviation when entering in the study database. To add an additional deviation within Medidata Rave, clicking "Add a new Log line" will add an additional page for a new deviation to be completed. Consult the MTN Regulatory Team (mtnregulatory@mtnstopshiv.org) and the Study Management Team if you are unsure if an event requires reporting as a deviation.

Item-specific Instructions:

Field	Instructions
Site awareness date	Record the date the site became aware of the deviation. A complete date is required.
Deviation date	Record the date the deviation occurred (start date). A complete date is required.
Type of deviation	Record the applicable deviation by selecting from the drop down menu. *Please see table below for the types of deviations.* When entering the type of deviation, the first few letters of the description can be entered within the drop-down search list to find the applicable deviation to be entered. Record "Other" if none of the listed categories match.
Description of deviation	Use the text field to briefly describe the specific details of the deviation.
Plans and/or actions to address the deviation	Use the text field to provide a brief description of the plans to address the deviation.
Plans and/or actions to address for future deviations	Use the text field to provide a brief description of the plans to address future deviations.
Deviation reported by	Enter the staff code of the site staff person who completed the form. Sites will need to assign a **four-digit** staff code to each site staff person who will be completing this form. This list is created, maintained and kept at the study site.

PROTOCOL DEVIATION CODE LIST	
Description	Description
Inappropriate enrollment: The participant enrolled and not all eligibility requirements were met.	**Unreported AE**: Site staff become aware of an AE, but do not report it per protocol requirements.
Failure to follow randomization or blinding procedures: Include instances where randomization procedures were not followed by site staff, or product blinding procedures were not followed by pharmacy staff.	**Unreported EAE:** Site staff become aware of an EAE, but do not report it per protocol and DAIDS EAE Manual requirements.
Study product management deviation: The site staff did not instruct the participant to hold, permanently discontinue, or resume study product use per protocol requirements.	**Breach of confidentiality:** Include potential and actual cases where participant confidentiality is breached. For example, a staff member put a participant's name on a case report form.
Study Product dispensing error: The wrong study product was dispensed to a participant, or study product was dispensed to a participant who permanently discontinued study product use. Pharmacy staff must follow up with the MTN Pharmacist separately.	**Physical assessment deviation:** Include missed or incomplete physical/pelvic exam assessments.
Study Product use/non-use deviation: Participant did not use the study product (including refusals) for more than 3 days.	**Lab assessment deviation:** Include missed, or incomplete lab specimen collection
Study product sharing: Participant has shared study product with another person or study participant.	**Mishandled lab specimen:** Include errors in labeling, physical handling, processing, testing, storage, or shipment of collected lab specimens.
Study product not returned: Study product was not returned by the participant per protocol requirements.	**Staff performing duties that they are not qualified to perform:** use for any instance when any study procedure, including clinical and administrative procedures, is completed by a staff member who is not adequately qualified AND delegated to perform the procedure.
Conduct of non-protocol procedure: A clinical or administrative procedure was performed that was not specified in the protocol, and was not covered under local standard of care practice.	**Questionnaire administration deviation:** A required questionnaire was not completed according to protocol requirements. Include instances where the wrong questionnaire was completed.
Improper AE/EAE follow-up: use when an AE or EAE is not followed per protocol. For example, a clinical finding/lab result is not re-assessed as outlined in the protocol.	**Counseling deviation:** Protocol-required counseling was not done and/or not documented correctly.
Use of non-IRB/EC-approved materials: Include use of ANY study-related material that requires IRB or EC approval for use per site requirements.	**Use of excluded concomitant medications, devices, or non-study products.**
Informed consent process deviation: Examples include failure to accurately execute and/or document any part of the informed consent process.	**Visit completed outside of window:** Use when visit procedures for a visit are done within the wrong window or not in a designated visit window. For example, if visit 3.0 procedures are done in the visit 4.0 window.
Other	

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.

Item-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 Treatment 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.

Missed Visit

Purpose:

Complete this form whenever an enrolled participant missed a required visit according to the visit window outlined in the protocol or Study-specific Procedures (SSP) manual.

General Information/Instructions:

A missed visit eCRF will be dynamically added to a visit folder if the response to "Did the participant complete this visit?" on the Follow-up Y/N form is "No". Complete the Missed Visit eCRF only for this visit.

Item-specific Instructions:

Field	Instructions
Target Visit Date:	Record the target date of the visit. A complete date is required.
Reason visit was missed:	Select the reason that the participant missed the visit from the drop down list. If the reason that the participant missed the visit is not included in this list, select 'other', and specify the reason that the reason was missed in the "If other, specify" text field provided.
Steps taken to address the missed visit (corrective action plan)	Record the corrective steps that have been taken or will be taken to address the missed visit and help prevent future missed visits.

Study Discontinuation

Purpose:

This form is used to document a participant's exit from the study (i.e. study termination).

General Instructions:

This form is present within the Discontinuations folder. Complete this form for each enrolled participant at either the scheduled exit/end of study visit or when the participant is no longer participating in the study.

Item-specific Instructions:

Field	Instructions
Date of Study Exit	A complete date is required.
Did the participant complete the study?	Select 'Yes' or 'No'. Select 'Yes' if the participant completed his/her Visit 17.0 Visit. Select 'No' if the participant terminated the study early.
Primary reason for non-completion	Select one reason from the drop-down menu if the participant did not complete the study.
If withdrawal of consent by participant, investigator decision, or other, specify	If the primary reason is 'Withdrawal of consent by participant', 'Investigator decision', or '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.

Was termination associated with an adverse experience?	Select 'Yes', 'No', or 'Don't know'. If 'No' or 'Don't Know', then this is the end of form.
If yes, select applicable Adverse Event	Within Medidata Rave, 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.

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.

Item-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.

STUDY PRODUCT FORMS

Pharmacy Dispensation

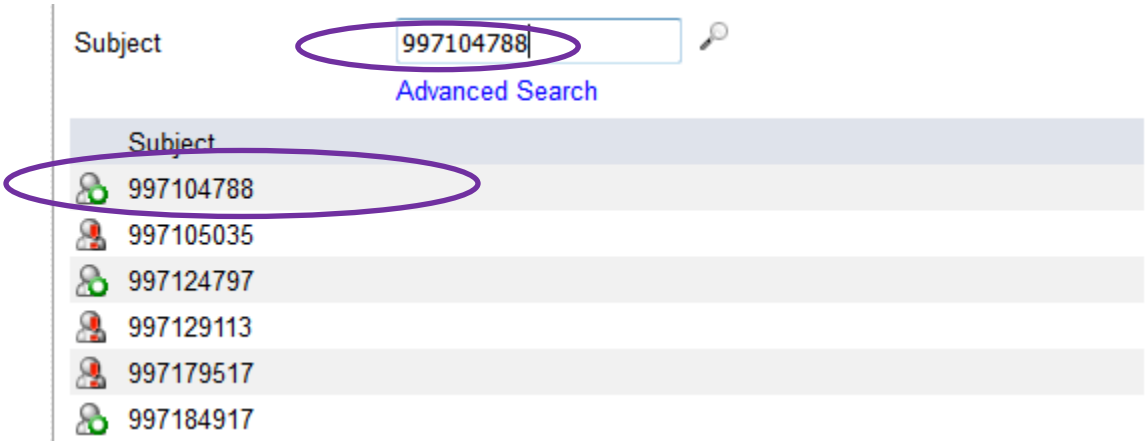
Purpose:

This form is used to collect study product rectal applicator dispensation information.

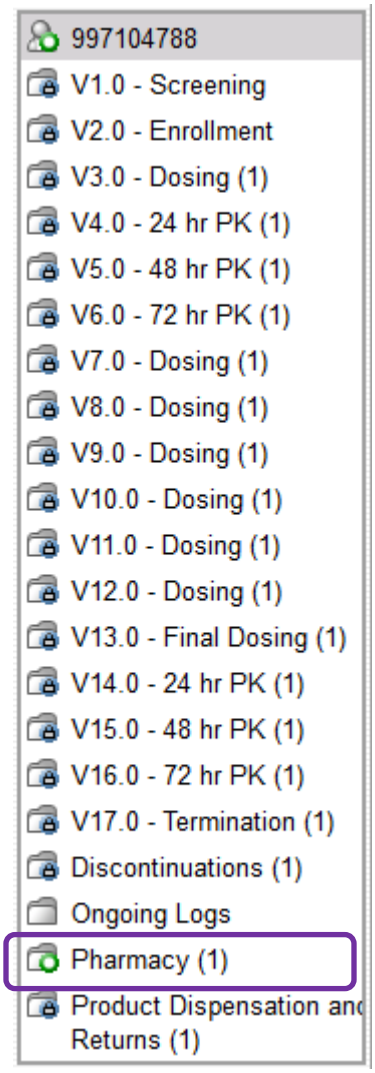
General Instructions:

Complete this form at Visit 3.0 - Dosing. **This form is completed by pharmacy staff only and is not visible to site clinic staff. Only pharmacists who have been granted this role will be able to view and enter data on this eCRF.**

- Select the applicable PTID as documented on the prescription. The search list can be used to find the PTID.



- Navigate to the Pharmacy folder to complete the Pharmacy Dispensation eCRF.



- Complete the Pharmacy Dispensation eCRF and save the form.

Item-specific Instructions:

Field	Instructions
Visit study product dispensed:	Select either 'V3.0 - Dosing' or 'Other'. Per protocol, the first dispensation will occur at the V3.0 – Single Dose Administration Visit. Only select 'Other' if the first dispensation did not occur at this visit.
Date study product dispensed:	Record the exact day, month, and year study product was dispensed to the participant.
Sublot code of first study product dispensed	Record the numeric manufacturing sublot code of the first study product dispensed to the participant. This should match one of three sublot codes the participant was randomized to.
Sublot code participant was randomized to:	The sublot code to which the participant was randomized should appear as an auto-populated, uneditable field on the Pharmacy Dispensation eCRF once a participant is randomized by CRS clinic staff.

Directly Observed Dosing

Purpose:

This log form is used to document observed participant dosing and times for the Single Dose Administration Visit (Visit 3.0) and the 7 daily doses of the Study Product Administration Visits (Visits 7.0 - 13.0).

General Information/Instructions:

This form is present in the Ongoing Logs folder. Complete this form as each dose is observed at the study administration visits each time a dose of study product is administered. Once the first dose has been entered, complete one page (log line) per dose. To add an additional dose, click "Add a new Log line" to complete a new entry for the subsequent dose.

Field	Instructions
Dose number	Select applicable visit /dose number.
Was the gel application observed?	For each dose, select either 'Not done', 'Yes, in clinic', 'No, in home not observed'. - Select 'Yes, in clinic' if the gel application was directly observed at the clinic. - Select 'No, in home not observed' if the gel applicator was inserted at home without observation of clinic staff. If 'Not done', then end form and leave remaining items blank.
Date gel application observed?	Record the exact day, month, and year gel application was observed.
Time gel application observed?	Record the time in the 24-hour clock.
If dose was inserted at home, is this dosing time an estimate?	Complete this field only if dose was administered at home, without observation by staff, and is per **participant report and not documented such as on an appointment card**. Otherwise, this field should be left blank.

Product Dispensation and Returns

Purpose:

This form is used to document when study product designated for non-observed home use is dispensed and returned by the participant during the study.

General Information/Instructions:

This form is present in the Product Dispensation and Returns folder. This first section of this form is completed at Visit 7.0 (Study Product Administration Visit), and updated at Visit 13.0 (Last Study Product Administration Visit) or when the participant returns unused study product.

Field	Instructions
Was product provided for non-observed home use	Select 'Yes' or 'No'. Per protocol, one applicator will be dispensed for at home use in the event he/she is unable to attend a scheduled observed dosing visit at the clinic at Visit 7.0. If 'No', end of form.
Date product provided for non-observed home use	A complete date is required.
Number of applicators provided at this visit for home use.	Record the number of applicators dispensed to the participant in the event that home dosing is needed. Note that per protocol, participants are to receive **one** pre-filled applicator at Visit 7 in the event that they cannot attend one of their seven daily dosing visits.
If provided at a visit other than Visit 7, record reason.	Record reason study product for home use was not provided at Visit 7 (e.g., participant missed visit). If form is being completed at Visit 7.0, this field should be left blank. End of first section.
Was study product (for home use) returned by participant?	This section should be completed when a participant returns unused study product from the Visit 7.0 dispensation. In the event that the participant used his/her study product for home use, select 'No'. If 'No', end of form.
Date study product (for home use) returned by participant.	A complete date is required.
Number of unused applicators returned.	Enter the number of unused applicators returned to the clinic. This number should not be greater than the number provided.

CLINICAL FORMS

Vital Signs

Purpose:

This form is used to document the participant's vital signs.

General Instructions:
Complete this form at V1.0 - Screening, V2.0 - Enrollment, and when clinically indicated during follow-up.

Item-specific Instructions:

Field	Instructions
Date of Assessment	Enter the date the participant's vital signs were measured. A complete date is required.
Height	Enter the participant's height in centimeters. The value can be reported up to one decimal (e.g. 180.1 cm). Per protocol, height is required only at the Screening Visit and this item will be displayed on the Vital Signs eCRF in the V1.0 – Screening Visit only.
Weight	Enter the participant's weight in kilograms. The value can be reported up to one decimal (e.g. 70.1 kg). Per protocol, weight is required only at the Screening Visit.
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).
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).

* In Medidata Rave, the most recent BP reading that is used for clinical management should be recorded on the Vital Signs eCRF. In instances where the BP has already been entered within Medidata Rave, these fields (Systolic BP and Diastolic BP) can be updated within the form and re-saved.

Physical Exam

Purpose:
This form is used to document the participant's physical exam findings.

General Instructions:
Complete this form at V1.0 - Screening, V2.0 - Enrollment, and when clinically indicated during follow-up. If abnormal findings are found for any of the assessments, enter the information on the Baseline Medical History Log or Adverse Event Log eCRF(s) as applicable.

Item-specific Instructions:

Field	Instructions
Exam Date:	Enter the date the physical exam was performed. A complete date is required.

Field	Instructions
Organ Systems or Body Parts Evaluated:	For each organ system or body part evaluated, indicate whether the findings were normal or abnormal. If abnormal, describe the abnormality in the corresponding text field. For any baseline abnormal and clinically significant findings, record the associated condition(s) on the Baseline Medical History Log eCRF. Any post baseline abnormalities or baseline conditions that worsened post baseline should be reported on the Adverse Events Log eCRF. Normal findings may also be described in the text field/space, but it is not required. If not evaluated, select 'Not done'. Additional information may also be provided in the text field for why 'Not done', but this is not required. Per protocol, abdomen, HEENT, oral mucosa, lymph nodes, neck, heart, lungs, extremities, skin, and neurological may be omitted after the Screening Visit.
Other:	If other systems were assessed not covered by the pre-defined assessments, then please specify whether findings were 'Abnormal' or 'Normal' under the "Other" section. If another body system was evaluated and the findings were normal, select 'Normal'. Specify the body system being referenced and describe the findings in the text field provided, regardless of the findings were 'Abnormal' or 'Normal'. If no other components as indicated were assessed, select 'Not Done'.

Pelvic Exam

Purpose:

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

General Instructions:

Complete this form at V1.0 - Screening, V2.0 - Enrollment, PK/PD Sampling Visits (either Visit 4.0, 5.0, or 6.0 and Visit 14.0, 15.0, or 16.0), V13.0 – Last Study Product Administration or Early Termination Visit, and when as clinically indicated at all other study visits. Transcribe information from the **Pelvic Exam Diagrams** form into this form for submission in Medidata Rave.

Item-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 pelvic exam. If 'no abnormal findings' is selected, then skip the "Abnormal findings" section.
Exam Date	A complete date is required.
Abnormal	Select the box to the right of each abnormal finding observed, and check all that

findings	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. If known, specify if the bleed was menstrual or non-menstrual. Assess the blood/bleeding for AE reporting purposes.
Were any new pelvic finding AEs reported at this visit?	Record whether an AE was identified and reported at this visit as part of the pelvic 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. This item should be 'No' prior to participant enrollment in the study (i.e., prior to the AE reporting period).
Cervical Ectopy	Select the percentage of cervical ectopy observed during the pelvic exam assessment by selecting the appropriate drop down option within the eCRF. Select 'Not done' if cervical ectopy was not assessed.

Pelvic Exam Diagrams Form

Purpose:

This form is used to document all variants of normal and all abnormal findings observed during study pelvic exams (screening through termination/study exit).

General Information/Instructions:

This form is completed at V1.0 - Screening, V2.0 - Enrollment, PK/PD Sampling Visits (either Visit 4.0, 5.0, or 6.0 and Visit 14.0, 15.0, or 16.0), V13.0 – Last Study Product Administration or Early Termination Visit, and when as clinically indicated at all other study visits. Transcribe information onto the appropriate Pelvic Exam CRF and store this form in the participant's chart notes. This form is available to download and print on the MTN-026 Atlas webpage under the Case Report Forms section within the "Other Documents" section. Please refer to the back of the form for specific guidelines on completing this form.

Anorectal Exam

Purpose:

This form is used to document the anorectal exam findings identified via perianal visual inspection, digitial rectal examination, anoscopy, and sigmoidoscopy.

General Information/Instructions:

This form is completed at V1.0 - Screening, V2.0 - Enrollment, Visit 3.0 (Single Dose Administration Visit), Visit 7.0 and Visit 8.0 Study Product Administration Visits, the participants assigned PD/PK Sampling Visits (Visit 4.0, 5.0, or 6.0 and Visit 14.0, 15.0, or 16.0),and V13.0 – Last Study Product Administration Visit/Early Termination, and when as clinically indicated at all other study visits. At Screening and Enrollment, evaluate any abnormalities for eligibility. At Enrollment, update the Baseline Medical History Log as applicable. During follow-up, complete or update Adverse Event Log when applicable.

Item-specific Instructions:

Field	Instructions
Exam Date	A complete date is required.
Perianal Examination Findings from the perianal examination	Select 'Not done', 'No abnormal findings', or Abnormal findings'. If 'not done' is selected, then this is the end of this section and all remaining perianal finding items should be left blank. Continue to Digital Rectal Examination section. Select 'abnormal findings' or 'no abnormal findings' to indicate any findings from the perianal exam. If 'no abnormal findings' is selected, then skip the "Abnormal findings" section.
Abnormal perianal findings	Select the box to the right of each abnormal finding observed, and check all that apply. 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.
Digital Rectal Examination Findings from the digital rectal examination	Select 'abnormal findings' or 'no abnormal findings' to indicate any findings from the perianal exam. Describe any abnormal findings from the digital rectal examination in the text field provided. If examination was not done, select 'Not done'.
Anoscopy Rectal mucosa findings from anoscopy	If 'not done' is selected, then this is the end of this section and all remaining anoscopy finding items should be left blank. Continue to Sigmoidoscopy section. Select 'abnormal findings' or 'no abnormal findings' to indicate any findings from the perianal exam. If 'no abnormal findings' is selected, then skip the "Abnormal findings" section.
Abnormal anoscopy findings	Select the box to the right of each abnormal finding observed, and check all that apply. 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.

Sigmoidoscopy Sigmoidoscopy findings	If 'not done' is selected, then this is the end of the form. Select 'abnormal findings' or 'no abnormal findings' to indicate any findings from the perianal exam. If 'no abnormal findings' is selected, then end of form.
Abnormal sigmoidoscopy findings	Select the box to the right of each abnormal finding observed, and check all that apply. 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.

Baseline Medical History Summary

Purpose:

To document any baseline medical history conditions/events reported at the Screening visit or recalled by the participant during follow-up.

General Instructions:

This prompt will be asked at the V1.0 – Screening visit. (Note that this form is not present within the "Ongoing Logs" folder).

Item-specific Instructions:

Field	Instructions
Does the participant have any baseline medical history to report?	Select 'Yes' or 'No'. If 'Yes' is marked, then the "Baseline Medical History" log form appears dynamically within the V1.0 – Screening Visit folder. Complete entries within the Baseline Medical History Log eCRF as needed. If 'No' is selected, no further action is required. If the participant reports any baseline medical history conditions/events after the Screening visit, update the response to this field to 'Yes' and complete the Baseline Medical History Log as needed.

Baseline Medical History Log

Purpose:

This form is used to document information on the participant's baseline medical history, including but not limited to: history of hospitalizations, surgeries, allergies, any condition that required prescription or

chronic medication (that is, more than 2 weeks in duration), and acute conditions ongoing at screening and/or that occur between screening and enrollment.

This form will appear in the V1.0 - Screening folder after the "Baseline Medical History Summary" prompt has been answered as 'Yes'. Use the "Add a new Log line" button to add an additional baseline medical history condition/event in Medidata Rave.

General Instructions:

- At the Screening Visit, record relevant baseline medical history. This includes conditions and symptoms reported by the participant during the baseline medical/menstrual history as well as any conditions identified via pelvic exam, physical exam, or laboratory testing.
- At the Enrollment Visit, review and update as needed. Navigate back to the V1.0 – Screening visit folder to update this log form if needed or add additional entries as needed. Those conditions that are ongoing at the time of enrollment (including ongoing chronic conditions) are considered the participant's pre-existing conditions.
- Do record baseline medical conditions identified during follow-up. Write a chart note to explain why the entry was added after the Enrollment Visit.
- Complete a separate entry (e.g. log line) for each baseline medical history condition/event when entering into the study database.

Item-specific Instructions:

Field	Instructions
Date medical history collected	Record the date the medical history condition/event was reported by the participant. A complete date is required.
Description of medical history condition/event	Whenever possible, provide a diagnosis instead of listing a cluster of symptoms. If no diagnosis is identified, each symptom must be recorded as a separate term. If an abnormal lab value is reported at the Enrollment visit, record the lab assay with the direction (i.e., increased or decreased) of the abnormality. For example, "decreased hematocrit" or "increased ALT". Additional information on the frequency and duration of chronic condition outbreaks can also be provided within this description.
Is condition/event gradable?	If a condition is not gradable (below Grade 1), select 'No'. Review and update as needed for conditions that are ongoing during the study. If a condition is gradable, select 'Yes' and complete the Toxicity (Severity) Grade.

Field	Instructions
Toxicity (Severity) Grade	This item is required if 'Is condition/event gradable?' is 'Yes'. Select from the options provided in the drop-down list. Review and update as needed for conditions ongoing at the Enrollment Visit. The toxicity grade reported in Baseline Medical History should reflect the status at baseline. • If the severity grade has increased or decreased in severity or frequency during the study AE reporting period, then this should be reported as an AE and the Toxicity Grade should remain unchanged on this CRF. However, this should be updated as needed if the severity grade and increased or decreased on or prior to the Enrollment Visit. • If the condition improves in severity or resolves during the study, then the Toxicity Grade should remain unchanged on this CRF. For each condition, grade the severity using the current version of the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events* (including relevant appendices/addendums).
Date medical condition/event started	Record the date the medical condition was first diagnosed or the date the surgery/procedure was performed as applicable. If the participant is unable to recall the exact date, obtain her best estimate. At a minimum, a 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.
Is the condition ongoing?	Select 'Yes' for chronic conditions, as well as any other conditions that are currently ongoing. During each follow-up visit, routinely follow-up on any and all ongoing conditions. If this item is selected 'Yes', then this is the end of form and the "Date medical condition/event ended/resolved" should be left blank.

Field	Instructions
Date medical condition/event ended/resolved	A date is required if 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.

Adverse Event Summary

Purpose:

This form documents if an adverse event was experienced by the participant during the study.

General Instructions:

This form is located within the "Ongoing Logs" folder.

Item-specific Instructions:

Field	Instructions
Has the participant experienced an Adverse Event during the study?	Select 'Yes' or 'No'. Within the "Ongoing Logs" folder, if 'Yes' is selected, then the "Adverse Event" log form appears dynamically and can then be completed. Complete as many Adverse Event eCRFs as needed.

Adverse Event Log

Purpose:

This form is used to document any Adverse Event (AE) reported by the participant or clinically observed as defined by the protocol.

General Instructions:

Complete a separate entry (e.g. log line) for each adverse event when entering into the study database. Use the "Add a new Log line" button to add an additional adverse event in Medidata Rave.

Whenever possible, report a diagnosis instead of listing a cluster of symptoms. If no diagnosis is identified, each symptom must be recorded as a separate AE as separate log entries as applicable. If a cluster of symptoms reported on separate AE Log pages is later attributed to a single diagnosis, change/update the earliest reported symptom page to the diagnosis. In the study database, these other symptoms can be deleted by clicking "Inactivate" and selecting the applicable rows that should be inactivated.

Do not record a condition as an AE if it existed at enrollment as a pre-existing condition, unless it increases in severity or frequency.

If an AE increases in severity/frequency, a new AE should be reported. The original AE should be recorded as "Recovered/resolved" 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.

Item-specific Instructions:

Field	Instructions
Date Reported to Site	Record the date the site became aware of the AE. For lab AEs, record the date the lab result was received. A complete date is required.
Adverse Event (AE)	Use medical terminology to describe the AE. Record a diagnosis if available. Include the anatomical location if applicable. Do not include text on the relationship to study product or timing of AE onset with regard to product use. For lab abnormalities, record the lab name with the direction (i.e., increased or decreased). For example, "increased ALT".
Onset Date	At a minimum, a month and year are required. Record one of the following, as appropriate: the date on which the participant reports first experiencing the AE (onset of first symptom if diagnosis has multiple associated symptoms); date of the study visit/study exam (for physical or pelvic exam findings); specimen collection date (for lab abnormality AEs).
At which visit was this AE first reported?	Choose applicable visit from pull-down menu. If 'Interim Visit' is chosen, then specify interim visit code in next field.
If 'Interim visit' is chosen, provide interim visit code	Enter interim visit code in field. If this was a regularly scheduled visit, this item should be left blank.
Is the AE still ongoing?	Select 'Yes' if the AE is continuing at the time it is first reported. If 'Yes', leave the Outcome Date blank.
If no, outcome date	If the AE is not ongoing, record the outcome date. For the outcome date, a month and year are required, at a minimum. Record one of the following, as appropriate: the date on which the participant reports no longer experiencing the AE or associated symptoms, or the date of the study visit or specimen collection at which it is first noted the AE has resolved or returned to baseline status.
Severity Grade	Record the severity grade using the current version of the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events* (including relevant appendices/addendums).
Relationship to Study Product	Select 'related' if there is a reasonable possibility that the AE may be related to the study agent. Select 'not related' if there is not a reasonable possibility that the AE is related to the study agent. Provide the clinical rationale (the reason) the AE is judged to be 'related' or 'not related' in the applicable Comments section/text field provided for each reported AE.

Field	Instructions
Action Taken with Study Product	*Dose not changed*: Select if there is no change to the participant's planned use of study product as a result of the AE. This option should be selected if the participant is still in the product use period and the AE does not result in a clinician-initiated product hold or permanent discontinuation of study product. *Dose reduced:* This option does not apply and should not be selected in MTN-026. *Dose increased:* This option does not apply and should not be selected in MTN-026. *Drug withdrawn*: Select if the AE results in permanent discontinuation of study product. If multiple AEs are reported at the same visit, mark "drug withdrawn" for each AE contributing to the permanent discontinuation. Ensure a Treatment Discontinuation eCRF is completed with item "Did the participant complete study product use through Visit 13 (Last Study Product Administration Visit)?" selected as 'No'. *Drug interrupted*: Select if the AE results in a clinician-initiated product hold. If multiple AEs are reported at the same visit, select 'drug interrupted' for each AE contributing to the hold. This option does not apply and should not be selected in MTN-026 since per protocol, only permanent discontinuation applies. *Not applicable*: Select if the AE's onset date is on or after the date the participant permanently discontinues study product use.
Other action(s) taken	Select 'None' or check all that apply. *Medication*: Select 'Medication' only if the participant reports taking the medication. Report the medication(s) on the "Concomitant Medications Log" eCRF. If medication is indicated, but not yet used, select 'Other' and describe the medication indicated in the "Other, specify" text field provided; update this item to 'Medication' once the medication has been used and report on the "Concomitant Medications Log". If "New/prolonged hospitalization", "Therapeutic procedure/surgery", or "Diagnostic procedure" is selected, then record applicable details in the Comments section at the bottom of the eCRF. If 'Other', then specify relevant details in the "Other, specify" text field provided.
Outcome	*Recovered/resolved:* AE is no longer present, has returned to baseline severity/frequency, or has increased in severity/frequency. Note that if a participant started taking medication once enrolled to control an AE, the AE is not considered resolved while the medication is still indicated. *Recovering/resolving*: AE is continuing and has not yet resolved or returned to baseline severity/frequency. *Resolved with sequelae:* Participant has recovered from the AE, but with remaining effects or impairment. These remaining effects can be temporary, but are still present at the time of the report. *Not recovered/resolved*: Select this option whenever an AE is continuing at the time of participant termination from the study. *Fatal*: Select only if the severity grade of this AE is Grade 5. Any other AEs continuing at the time of death should be changed to "not recovered/resolved".

Field	Instructions
Has or will this AE be reported as an EAE? If yes, EAE Number	For questions about ICH guidelines and EAE reporting, refer to the current *Manual for Expedited Reporting of Adverse Events to DAIDS.* If this AE was/is reported as an EAE (indicated as 'yes'), provide the EAE number and complete any subsequent updates to this form on the applicable EAE form.
Was this AE a worsening of a baseline medical condition?	Select 'Yes' or 'No'.
Was this AE related to the flexible sigmoidoscopy procedures?	Select 'Yes' or 'No'.
Was this AE related to applicator insertion?	Select 'Yes' or 'No'.
Comments	**This is a required field and should be used to be record the relationship to study product at a minimum.**

Concomitant Medications Summary

Purpose:

This form documents if any concomitant medications were reported the participant during the study.

General Instructions:

This summary eCRF is located within the "Ongoing Logs" folder.

Item-specific Instructions:

Field	Instructions
Is the participant taking any concomitant medications?	Select 'Yes' or 'No'. If 'Yes' is selected, then the "Concomitant Medications" log form appears dynamically within the "Ongoing Logs" folder and complete as many Concomitant Medication eCRFs as needed.

Concomitant Medications Log

Purpose:

This form is used to document all medications taken by the participant starting at the Screening Visit. This includes, but is not limited to: prescription medications, non-prescription (i.e., over-the-counter) medications, contraceptive hormonal medications, preventive medications and treatments (e.g., allergy shorts, flu shots, and other vaccinations), herbal preparations, vitamin supplements, and naturopathic preparations.

General Instructions:

Complete a separate entry (e.g. log line) for each reported concomitant medication when entering into the study database. Use the "Add a new Log line" button to add an additional concomitant medication in Medidata Rave.

Item-specific Instructions:

Field	Instructions
Medication Name	Record the trade or generic name of the medication based on exactly what the participant is taking. If a trade name is not available or not reportable per national guidelines, record the generic name of the medication. A combination medication can be recorded as one entry.
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"). In most instances (excluding nutritional supplements and/or prophylactic treatments), the indication should correspond to an item on the Baseline Medical History and/or Adverse Event eCRF(s).
Date Started	If the participant is unable to recall the exact date of medication initiation, obtain participant's best estimate. At a minimum, the year is required. For injections, record each injection as a separate entry, with the same date used for start and stop date.
Date stopped Or Continuing at end of study	Enter the stop date of this medication if known. At a minimum, the month and year is required. This item can be completed at any time during study participation when the stop date is known. At the participant's Study Exit/Termination Visit, the "Date Stopped" must be recorded for each medication OR the "Continuing at the end of study" box must be checked.
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 a reported AE?	If the concomitant medication was administered to treat a reported AE, select 'Yes'. The relevant AE log form must be completed to link the concomitant medication to the AE log form entered. Choose the applicable AE from the drop-down list. Up to 4 AEs can be selected. If the medication was not administered to treat an AE, select 'No', and end the form.

Sexual Lubricant

Purpose:

This form is used to document all sexual lubricants self-reported by the participant.

General Information/Instructions:

This form is completed at V2.0 - Enrollment, Visit 3.0 (Single Dose Administration Visit), Visit 7.0 Dosing Visit, and V13.0 – Last Study Product Administration/Early Termination.

Complete a separate entry (e.g. log line) for each reported sexual lubricant when entering into the study database. Use the "Add a new Log line" button to add additional sexual lubricants in Medidata Rave.

Item-specific Instructions:

Field	Instructions
Date of completion	A complete date is required.
In the past week, has the participant used a sexual lubricant?	Select 'Yes' or 'No'. If 'No', then end of form and leave remaining items blank.
Date of use	A complete date is required.
Which sexual lubricant(s) were used?	Select the applicable lubricant from the drop-down menu. If the participant reports use of a lubricant that was provided by site staff (e.g. Good Clean Love), select "Study-provided lubricant." Do not record use of study-provided lubricant in any of the other response options, as these are intended to capture use of lubricants that were not provided by site staff. If 'Other' is selected, specify in the corresponding "If other, specify" text field provided.

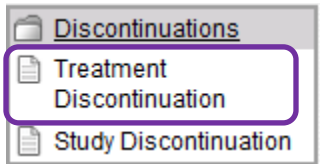
Treatment Discontinuation

Purpose:

This form documents a participant's permanent discontinuation of study product use.

General Instructions:

This form is present within the "Discontinuations" folder. Complete this form for each enrolled participant when study product use is permanently discontinued.



Item-specific Instructions:

Field	Instructions
When was study product use permanently discontinued?	A complete date is required. Record the date when the participant completed or was permanently discontinued from study product.
Date of last study product use	A complete date is required. Enter the exact date the participant had his/her last dose application. If participant completed study product through the last dosing visit (V13.0), this date should be the same as date study product was permanently discontinued.
Did the participant complete study product use through Visit	Select 'Yes' or 'No'. Select 'no' if the participant permanently discontinued study product use *prior* to Visit 13.

13?	If 'yes', then end the form and leave remaining items blank.
Primary reason for ending study product use early	Record the primary reason from the drop-down menu. 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 Treatment Discontinuation eCRF in order for the AE to be available to select with the drop down field. If 'Reported use of prohibited medication' is selected, choose the medication from the CM dynamic drop-down list. Note: If study product is permanently discontinued due to a reported use of prohibited medication, the CM log page must be entered into Rave prior to linking the CM on the Treatment Discontinuation eCRF in order for the CM 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.

Screening Menstrual History

Purpose:

This form is used to document information on the participant's menstrual history, including menstrual-related symptoms and abnormal bleeding patterns.

General Instructions:

Complete this form at the V1.0 - Screening Visit. Please record any baseline abnormalities (e.g. abnormal bleeding patterns such as amenorrhea, menorrhagia, metrorrhagia or menstrual symptoms which contribute to a medical condition (e.g. dysmenorrhea, pre-menstrual syndrome) on the Baseline Medical History Log eCRF.

Item-specific Instructions:

Field	Instructions
Date of assessment	Record the date the medical history condition/event was reported by the participant. A complete date is required.
First day of last menstrual period	Record the first day of the participant's most recent menstrual period. At a minimum, the year is required.
Last day of menstrual period Or Ongoing	Enter the last day of the last menstrual period (last day of bleeding). At a minimum, the year is required. If the participant is currently on her menses, check "Ongoing" and leave the last day of last menstrual period blank. After the Enrollment Visit, this item does not need to be updated with a stop date once known.

Provide additional details as needed to describe the participant's baseline menstrual bleeding pattern	Use this text field to describe, as best as possible, any details on the participant's usual genital bleeding pattern. Include details such as the number of sanitary pads, typically used, any spotting that is experienced, and any additional details on amount/heaviness of flow. Note that up to 400 characters are allowed in this field.

Pregnancy Report and History

Purpose:

Complete this form when reporting a pregnancy of a study participant post enrollment through study discontinuation.

General Instructions:

A Pregnancy Report and History form is required for each new pregnancy that the participant experiences during the study.

To complete a Pregnancy Report and History form within Medidata Rave, complete an Additional Study Procedures form, and check the corresponding Pregnancy Report and History box. This will generate this eCRF in the current visit folder.

Item-specific Instructions:

Field	Instructions
First day of last menstrual period	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 field blank.
Estimated date of delivery	A complete date is required.
What information was used to estimate the date of delivery?	Use drop-down menu to indicate what information was used to estimate the date of delivery. If another method was used which is not covered by the currently listed methods, please select "Other" and describe in the 'If other, specify' text field provided. A physical examination to determine estimated date of delivery includes fundal height, uterine size by pelvic exam, and/or fetal heart rate.
Has the participant ever been pregnant before?	If the participant has never been pregnant before, select "No" and end the form. Leave the remaining items blank.
Is this the participant's first pregnancy since enrollment in this study.	If this pregnancy is not the first reported pregnancy since the participant's enrollment in the study, select 'No' and skip to next item, "Does the participant have a history of pregnancy complications or fetal/infant congenital anomalies?".

Field	Instructions
Does the participant have a history of pregnancy complications or fetal/infant congenital anomalies?	If the participant does not have a history of pregnancy complications, select 'No' and end the form. If "Yes", then include information on pregnancy complications and fetal/infant congenital anomalies experienced prior to enrolling in the study as well as any conditions experienced/reported during the study in the corresponding text field provided.

Pregnancy Outcome Summary

Purpose:

Complete this form when information about a pregnancy outcome becomes available to study staff or when it is determined that the pregnancy outcome is unobtainable. A Pregnancy Outcome Summary prompt must be completed for each pregnancy reported during the study.

General Instructions:

To complete the Pregnancy Outcome form within Medidata Rave, navigate to the Pregnancy Outcome Summary eCRF within the Ongoing Logs folder.

Item-specific Instructions:

Field	Instructions
Was a pregnancy outcome reported?	Select 'Yes' or 'No'. Note that this item should be completed for all female participants, regardless whether a pregnancy outcome was obtainable.
Is the pregnancy outcome data obtainable?	If site staff were able to ascertain an outcome for this pregnancy from the participant, select "Yes". If 'Yes' is selected, then the Pregnancy Outcome Log form appears dynamically within the Ongoing Logs folder, which can then be completed. 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".

Pregnancy Outcome Log

Purpose:

This form is used to report pregnancy outcome information for a pregnancy reported post-enrollment.

General Instructions:

This form will dynamically be added to the participant's visit folder if the Pregnancy Outcome Summary prompt indicates that the outcome is obtainable by study staff. For each pregnancy outcome, complete one log line. To add another outcome, click "Add a new Log line".

Item-specific Instructions:

Field	Instructions
Visit Code that this pregnancy was reported	Select appropriate visit code from pull-down menu. If interim visit is selected, specify visit code in "If interim visit, specify interim visit code" field provided.
Outcome number	A pregnancy outcome can be an infant or fetus. The conception of twins, for example, will result in reporting of two outcomes. For a pregnancy resulting in one outcome, record '1' here. For a pregnancy with multiple outcomes, record the outcome number corresponding to the outcome data recorded on 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", additional Pregnancy Outcome Log lines will be added to the Pregnancy Outcome Log eCRF, as needed. Each Pregnancy Outcome form will have different outcome numbers.
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 still birth/intrauterine fetal demise, 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 discontinuation. On the AE Log 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	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 "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.

LABORATORY FORMS

Please remember to record clinically significant laboratory results on the "Baseline Medical History Log" eCRF or "Adverse Event Log" eCRF as applicable.

- Clinically significant laboratory results do NOT have to be reported as an AE if the lab result is clinically significant due to an indication in the subject's medical history.
- If the clinically significant laboratory result is already recorded in the baseline medical history but has increased in severity, frequency, or character, it should be recorded as an AE.

Hematology

Purpose:

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

General Information/Instructions:

Use this form to report the hematology and differential test results obtained from specimens collected at Visit 1.0 - Screening, and as indicated during the study as they become available. To generate this form at Enrollment, select "Enroll_Local Laboratory" via Add Event. To generate this form at a follow-up visit where tests are not normally required, select 'CBC with differential and platelets' 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 Baseline Medical History Log eCRF, when applicable.

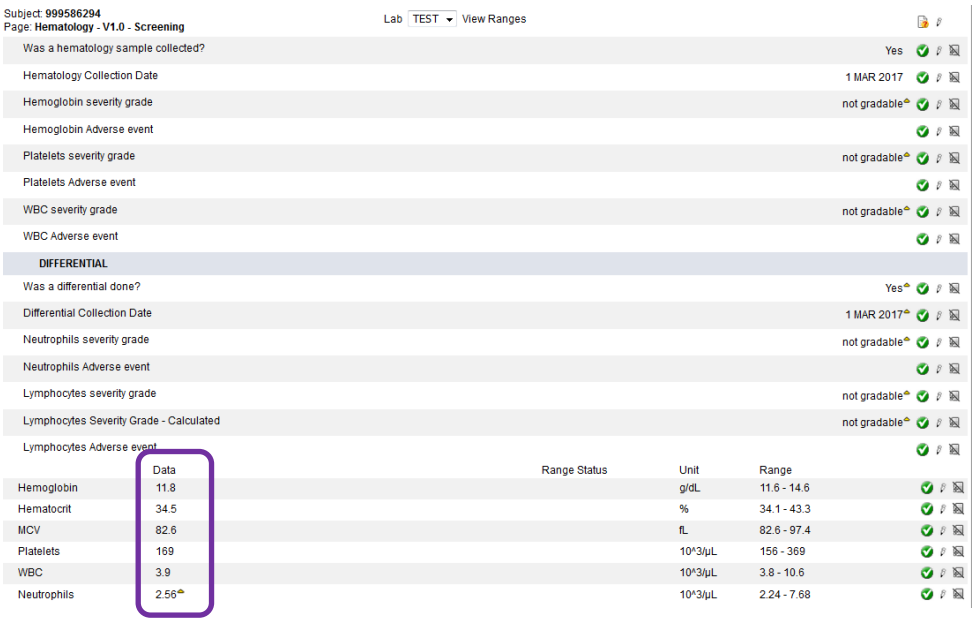
During follow-up, if a test result(s) recorded on this form indicates that the participant has a new (or increased severity) laboratory-confirmed infection or diagnosis, this infection/diagnosis must be recorded as an adverse event on an Adverse Event (AE) Log form.

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 for each result will be populated at the bottom of the form after selecting the appropriate lab.
  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 units.

- 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 Table for Grading the Severity of Adult and Pediatric Adverse Events*. If the units present on the source laboratory results document do not match the units on the CRF 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/mm^3 = 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.

- 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" 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.

Local Laboratory Results

Purpose:

This form is used to provide data on the participant's baseline and follow-up laboratory test results. To generate this form at Enrollment, select "Enroll_Local Laboratory" via Add Event. To generate this form at a follow-up visit where tests are not normally required, select 'Serum Creatinine, AST, or ALT' on the Additional Study Procedures form.

General Instructions:

Use this form to report the serum chemistries from specimens collected at Visit 1.0 - Screening, Visit 16.0, and as indicated during the study. Record results on this form as they become available.

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 Local Laboratory Results form. If the participant enrolls, the updated results should be submitted into the study database.

At Screening, record any applicable diagnoses on the Baseline Medical History Log form, 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 after selecting the appropriate lab.
  Note: The Demographics eCRF needs to be entered prior to entering data on the Local Laboratory Results 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 Table for Grading the Severity of Adult and Pediatric Adverse Events*. If the units present on the source laboratory results document do not match the units on the CRF 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 I/l x 100 = % 10^9/L = 10^3/mm^3 = 10^3/µL

For creatinine, only record the result in the units listed on the source document.

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.

- 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.

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_Local Laboratory" 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 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.

Item-specific Instructions:

Field	Instructions
Was a sample collected for Syphillis testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for Syphilis testing do not need to be completed. Proceed to "Was a urine sample collected for N. gonorrhea 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.
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 a [specimen] sample collected for [STI] testing?	Select 'Yes' or 'No' for each test. If 'No', then the remaining items for that specific test 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.

HIV Tests

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 7.0 – Dosing Visit, Visit 16.0 – 24 Hr PK Visit, and as indicated during follow-up. Record HIV specimen test results on this form as they become available from the local lab.

Item-specific Instructions:

Field	Instructions
Was a Rapid HIV test 1 sample collected?	Select 'Yes' or 'No'. If 'No', proceed to "Was a Rapid HIV test 2 sample collected?".
Rapid HIV test 1 collection date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
Rapid HIV test 1 kit	Select the HIV testing kit that was used from the drop-down list. If 'Other', then specify in the "If Other, specify" text field.
Rapid HIV test 1 result	Select 'Positive/Reactive' or 'Negative/Non-reactive'. If result is 'Positive/Reactive' during follow-up, complete the HIV Confirmatory Results form and Treatment Discontinuation eCRFs as applicable.
Was a Rapid HIV test 2 sample collected?	Select 'Yes' or 'No'. If 'No', proceed to "Was an HIV-EIA test done?".
Rapid HIV test 2 collection date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
Rapid HIV test 2 kit	Select the HIV testing kit that was used from the drop-down list. If 'Other', then specify in the "If Other, specify" text field.
Rapid HIV test 2 result	Select 'Positive/Reactive' or 'Negative/Non-reactive'. If result is 'Positive/Reactive' during follow-up, complete HIV Confirmatory Results form and Treatment Discontinuation eCRFs as applicable.
Was an HIV-EIA test done?	Select 'Yes' or 'No'. If 'No', end of form.
HIV-EIA collection date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
HIV-EIA test result	Select 'Negative', 'Positive', or 'Indeterminate'. If result is 'Positive' or 'Indeterminate' during follow-up, complete HIV Confirmatory Results form and Treatment Discontinuation eCRFs as applicable.

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	Instructions
Was a sample collected for HIV Confirmatory testing?	Select 'Yes' or 'No'. If 'No', proceed to "Was HIV RNA PCR testing performed?".

Field	Instructions
Collection date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
ARCHITECT HIV Ag/Ab Combo	Select 'Nonreactive', 'Reactive', or 'Not done'.
Geenius HIV-1/2	Record the Geenius Confirmatory Assay result as determined by the Geenius reader and software by selecting the appropriate response from the drop-down menu. Record 'Not done' if this assay was not used for confirmatory testing.
Aptima HIV-1 RNA Qualitative assay	Select 'Nonreactive', 'Reactive', 'Invalid', or 'Not done'.
Was HIV RNA PCR testing performed?	Select 'Yes' or 'No'. If 'No', proceed to "Was Absolute CD4+ collected?".
HIV RNA PCR collection date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
HIV RNA PCR symbol	Select '>', '<', or '='. Note that the '>' symbol is 'greater than' and the '<' symbol is 'less than' and '=' is 'equal to' and should be selected from the radio button.
HIV RNA PCR result	Record the participant's HIV RNA PCR result exactly as it appears on the lab report source documentation. If the HIV RNA PCR target is not detected, check 'target not detected' box and leave the HIV RNA PCR field blank.
HIV RNA PCR Kit	Select the HIV RNA PCR testing kit that was used from the drop-down list. If 'Other', then specify in the "If Other, specify" text field.
HIV RNA PCR kit type lower limit of detection	Select '20' or '40' as the lower limit of detection or record the viral copies/mL or record the participant's HIV RNA PCR result exactly as it appears on the lab report source documentation.
Was Absolute CD4+ collected?	Select 'Yes' or 'No'. If 'No', proceed to "Was plasma for confirmatory testing collected?".
Absolute CD4 collection date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
Absolute CD4+	Record the participant's Absolute CD4+ result exactly as it appears on the lab report source documentation. If lab was not able to analyze the Absolute CD4+ result, check 'unable to analyze' box and leave the "Absolute CD4+" field blank.
CD4%	If automatically calculated, record the CD4+ percentage that was reported for the specimen in the "CD4%" field. If the CD4+ percentage is not available (i.e., it was not reported and would have to be manually calculated), mark the "CD4% not available" box.
Was plasma for confirmatory testing collected?	Select 'Yes' or 'No'. If 'No', proceed to "Final HIV status".
Plasma for HIV confirmatory testing collection date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.

Field	Instructions
Was plasma stored for HIV confirmatory testing?	Select 'Stored' or 'Not stored'. If not stored, enter reason in "If not stored, specify reason" field.
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 Treatment Discontinuation as applicable to reflect permanent discontinuation of study product. If the participant status is not clearly negative or clearly positive, select the 'pending' item and update this item once the participant's final HIV status is known.

Pregnancy Test

Purpose:

This form is used to document the pregnancy test result as the result becomes available from the local lab.

General Instructions:

This form is required at Visit 1.0 – Screening, Visit 2.0 – Enrollment, Visit 7.0 – Dosing Visit, and at other visits if indicated. Under Letter of Amendment #01, during follow-up, this form is now also required at Visit 3.0 – Dosing and Visit 13.0 – Final Dosing, and is no longer required at V14.0 – 24 Hr PK Visit.

Item-specific Instructions:

Field	Instructions
Was a pregnancy test done?	Select 'Yes' or 'No'. If 'No' is selected, then end of form and leave remaining items blank. If the sample was collected, then complete "Date of Pregnancy Test", "Time" and "Test result".
Date of Pregnancy Test	Record the date that the pregnancy test was collected and NOT the date the results were reported or recorded within the form for this visit. A complete date is required.
Time	Record the time of sample collection using the 24-hour clock format.
Test Result	Record the result of the pregnancy test - positive (pregnant) or negative (NOT pregnant) by selecting the appropriate radio button. If the result is "Positive" at a follow-up visit, then complete a Treatment Discontinuation eCRF, Study Discontinuation eCRF, and Pregnancy Report and History eCRF. If the result is "Positive" at the Screening or Enrollment visit, then the participant is not eligible and should not be enrolled into MTN-026.

Specimen Storage

Purpose:

This form is used to document collection and storage of plasma specimens and rectal specimens by the local site laboratory during follow-up.

General Instructions:
Complete this form at Visit 2.0 - Enrollment, Visit 4.0, Visit 5.0, Visit 6.0, Visit 7.0, Visit 8.0, Visit 14.0, Visit 15.0, and Visit 16.0.

Item-specific Instructions:

Field	Instructions
Was [specimen] collected?	Select 'Yes' or 'No'. If 'No', then do not complete the date and time of collection and storage item(s).
Collection Date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
Collection Time	Record the time of sample in the 24-hour clock.
Stored/Not Stored	Enter 'Stored' for specimens that are collected and sent to the lab for processing. If the specimen is required to be stored, but for some reason it is not stored, select 'Not stored' and record the reason in the corresponding "If not stored, specify reason" text field provided.

Timed Specimen Storage

Purpose:
This form is used to document collection and storage of timed plasma specimens and rectal specimens by the local site laboratory during first and last study product administration visits.

General Instructions:
Complete this form at Visit 3.0 – Single Dose Administration and Visit 13.0 – Last Study Product Administration/Early Termination Visit.

Field	Instructions
What time group was the participant assigned to for PK/PD/mucosal safety specimen collection?	Select '30-60' minutes' or '120 minutes'. Time group should correspond to "PK, PD, and Mucosal Safety Time Assignment" on Enrollment form.
Was [specimen] collected?	Select 'Yes' or 'No'. If 'No', then do not complete the date and time of collection and storage item(s).
Collection Date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
Collection Time	Record the time of sample in the 24-hour clock.
Stored/Not Stored	Enter 'Stored' for specimens that are collected and sent to the lab for processing. If the specimen is required to be stored, but for some reason it is not stored, select 'Not stored' and record the reason in the corresponding "If not stored, specify reason" text field provided.

Cervical Specimen Storage

Purpose:

This form is used to document collection and storage of plasma specimens and rectal specimens by the local site laboratory during follow-up. This form also documents information about the last menstrual period.

General Instructions:

Complete this form at Visit 2.0 – Enrollment, participant's PK Sampling Visits (Visit 4.0, 5.0 or 6.0 and Visit 14.0, 15.0 or 16.0), and V13.0 – Last Study Product Administration (Early Termination).

Field	Instructions
First day of last menstrual period	Enter the first day of the last menstrual period (first day of bleeding). If the participant has been "amenorrheic for the past 6 months' OR has had 'no menses since participant's last visit', select the applicable option from the drop-down menu. If one of these options is selected, then a first and last date of last menstrual period does not need to be recorded. The month and year are required.
Last day of last menstrual period	Enter the last day of the last menstrual period (last day of bleeding). However, if the participant is currently menstruating, then select the "ongoing" box and the date should be left blank. The month and year are required.
Was [specimen] collected?	Select 'Yes' or 'No'. If 'No', then do not complete the date and time of collection and storage item(s).
Collection Date	Record the date that the first specimen(s) was collected, NOT the date the results were reported or recorded on the form for this visit. A complete date is required.
Collection Time	Record the time of sample in the 24-hour clock.
Stored/Not Stored	Enter 'Stored' for specimens that are collected and sent to the lab for processing. If the specimen is required to be stored, but for some reason it is not stored, select 'Not stored' and record the reason in the corresponding "If not stored, specify reason" text field provided.

BEHAVIORAL FORMS

The behavioral form for MTN-026 is an interviewer-administered form, meaning it is read aloud word-for-word. Please enter the responses directly into Medidata Rave.

Demographics

Purpose:

This form is used to document a participant's demographics and socioeconomic information.

General Instructions:

This form is completed at the Screening Visit. Responses should reflect the participant's status at screening, and should not be changed after screening unless correction is needed.

Item-specific Instructions:

Field	Instructions
What is your date of birth?	Please provide the date of birth. A complete date is required.
Age	This is an automatically derived field based on the participant's date of birth and the date of initial data entry. No data entry is required.
What was your sex at birth?	Select 'male' or 'female'. Note that this response will trigger the applicable forms in the participant's casebook. For example, if male, then the "Pregnancy Test Result" CRF will not appear in the participant's casebook. However, this will be available for completion if this response is selected as 'Female'.
Are you currently married?	Select 'Yes' if the participant is in a legally-binding marriage and has obtained a marriage certificate.
what is your highest level of education?	Select the applicable response from the drop-down list based on the participant's response. If the participant attended or completed a post-secondary diploma or certificate program, select ' attended college or university'.
Do you consider yourself to be Latino/a or of Hispanic origin?	This item is based on self-definition. Per NIH policy, Latino/a or Hispanic includes a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.
What is your race?	Record the participant's race based on self-definition. In the case of mixed race, select all that apply. If a race is other than those listed, select 'Other' and specify in the 'If other, specify' text field provided. Per NIH policy, Latino/a is considered an ethnic group and not a race, and should not be entered as a Race. Note that there are separate sections for **US domestic** and **Bangkok, Thailand** sites. Only one section should be completed based on site location.
Do you earn an income of your own?	Select 'Yes' or 'No'. If 'No' was selected, skip to "How do you identify your gender?"
How do you earn income?	Select the applicable response from the drop-down list.
How do you identify your gender?	Select the applicable response from the drop-down list based on the participant's response. If 'Additional category' is selected, specify in the corresponding "Additional category, specify" text field provided. Site staff is encouraged to document in chart notes if the participant during study participation prefers to be referred to by a specific pronoun or gender.

SUMMARY OF CHANGES

Version		CRF Name	Summary of Changes
Number	Date		
1.3	28 June 2018	Local Laboratory Results Hematology CRF	Clarification was made that results should be documented on the form using the units per the current *DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events*.