CRF Completion Guidelines (CCGs)
Protocol #: MTN-036/IPM 047
Version 4.0 (31 Oct 2018)

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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-036/IPM 047 (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-036 Atlas web page: https://atlas.scharp.org/cpas/project/MTN/036/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 APR 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 Y/N, 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 for this study: Adverse Events Log, Concomitant Medications Log, Protocol Deviations Log, Pregnancy Outcome Log, Baseline Medical History Log, and Product Hold Log. Some forms have log fields. The following are forms with log fields: Cervical Specimen Storage, Eligibility Criteria, Ring Adherence, Ring Insertion and Removal, and Specimen Storage
    - 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 the 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
  - Pregnancy
- The following forms can be added to the Enrollment folder in a participant's casebook:
  - Hematology
  - Local Laboratory Results
  - STI Test 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 folders and 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 eCRF - Enrollment folder
    - If "Yes" is selected for "Is the participant ready to be randomized", folders will be added for visits 3.0 – 11.0, Discontinuations and Pharmacy (for Pharmacists only to complete).
  - Example 2: Follow up Visit Summary eCRF
    - If item "Was this visit completed" is marked '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' for various study procedures completed at this visit will dynamically add the applicable forms to the applicable visit folder.
  - Example 3: Adverse Events Summary eCRF
    - Selecting 'Yes' for "Has the participant experienced an Adverse Event during the study?" will dynamically add the Adverse Events Log eCRF to the Ongoing Logs folder.

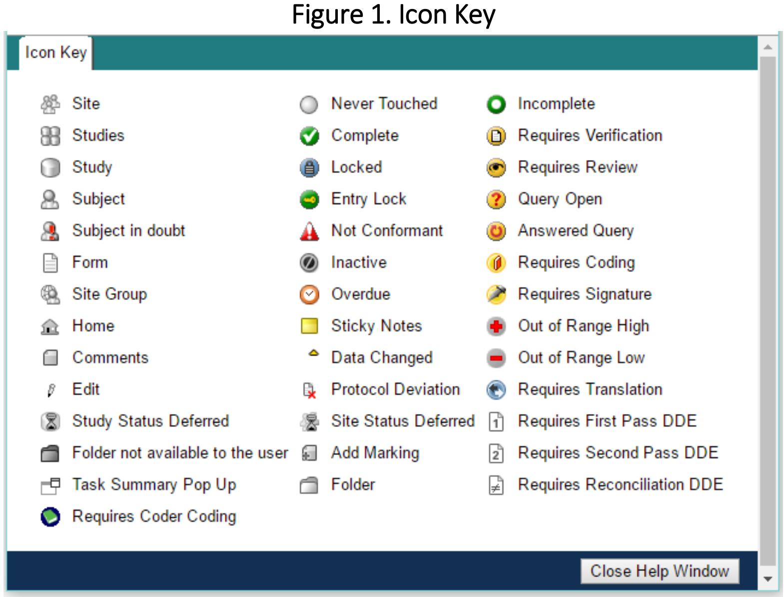
Dynamic Search List Functionality

- Dynamic searchlist functionality is used to look up Adverse Events data *(AE log line, start date, and term, e.g. "#001 05JAN2017-FEVER")*.
- Dynamic searchlist functionality is present on the following eCRFs: Concomitant Medications, Hematology, Local Laboratory Results, Pelvic ExaFm, Pregnancy Outcome Log, Product Discontinuation, Product Hold Log, 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 taken for this AE, a dynamic searchlist should 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.

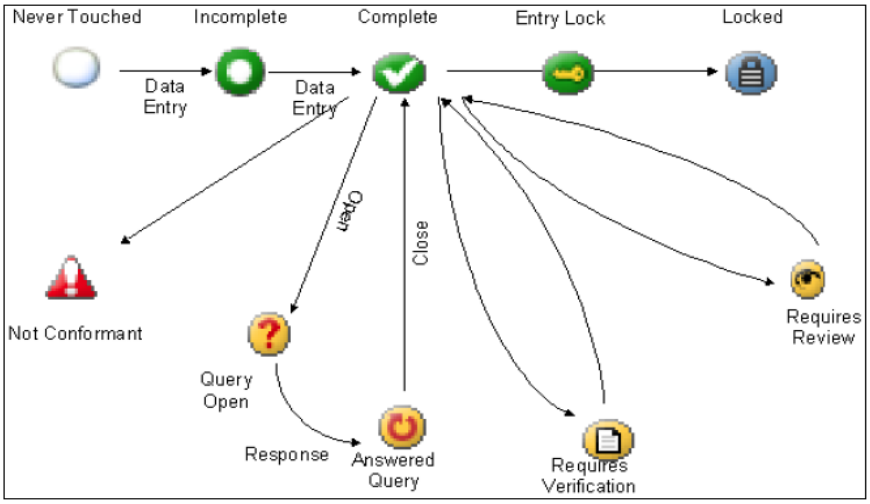
Figure 1. Icon Key



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

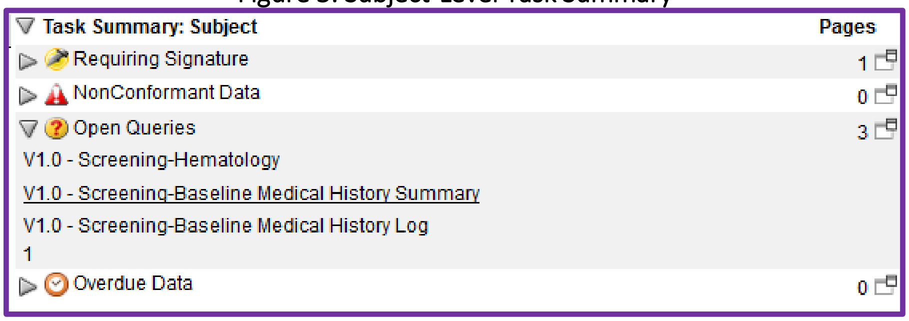
Task Summary: Site	Subjects
Requiring Signature	8
NonConformant Data	0
Open Queries	8
Overdue Data	0

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

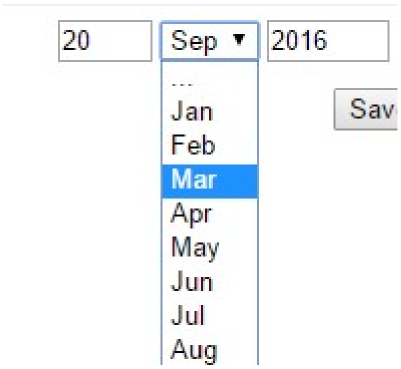
Dates are entered using the “dd MMM yyyy” format, where “dd” represents the two-digit day, “MMM” represents the three-letter abbreviation of the month (in capital letters), and “yyyy” represents the four digits of the year.

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

Documentation of Numbered responses (non-dates)

When recording numbered responses, 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. For example, if the participant’s rate of respiration is 9 breaths per minute, the response to this question on Vital Signs eCRF should be recorded as “9”.

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.

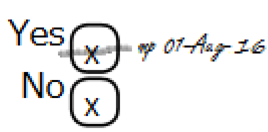
If the electronic CRF is source, it is sufficient to make data updates in the study database itself. If a paper CRF is completed, it is important to make changes to the original CRF first, then enter the updated data into the study database.

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

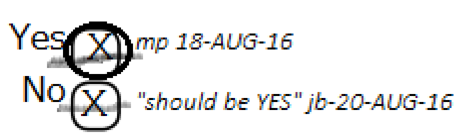
If an **X** is marked in the wrong response box, correct it by doing the following:

- 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:



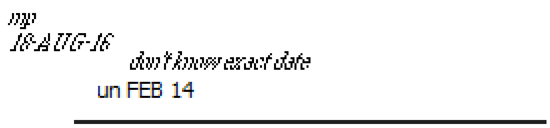
The standards above must ***always*** be followed whenever a paper CRF is changed, clarified, or amended.

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.

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-036 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-036 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>San Francisco</td><td>30305</td><td>764</td></tr><tr><td>Birmingham</td><td>31788</td><td>821</td></tr></table></td></tr>
</table>

Screening Date of Visit

Purpose:
This form is used to document the date of the participant's Screening Visit.

General Instructions:

If screening procedures are conducted across multiple days, this date should correspond to the first day on which screening procedures are done. If a participant has a second screening attempt, update this form with the date from the second screening attempt. Do not complete a new form.

Eligibility Criteria

Purpose:
This form is used to document participant eligibility for enrollment in MTN-036, and if applicable, type of ineligibility and reasons for study ineligibility per the inclusion and exclusion criteria per protocol.

General Instructions:
Complete this form for each participant screened in MTN-036 when it is determined whether the participant will enroll in the study. If a 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’.
Eligibility Status	Select ‘Ineligible’, ‘Eligible, but participant did not enroll’, ‘Eligible, enrolled’, or ‘Incomplete screening’ from the drop-down list. If ‘Eligible, enrolled’, or “Incomplete Screening”, end the form.
If eligible, but participant did not enroll, specify reason	Complete this item only if the response to the item ‘Eligibility Status’ is ‘Eligible, but participant did not enroll’ and specify in the text field provided.
Select inclusion and/or exclusion criteria that contributed to participant's study ineligibility	Complete this item only if the response to ‘Did the participant meet all eligibility criteria?’ is ‘No’. Select all Inclusion or Exclusion criteria that were not met from the drop-down list. Add a new log line for each criterion, as needed.
If other reason, including investigator decision, specify	Complete this item if the participant was deemed ineligible for a reason other than those listed in the exclusion and inclusion criteria, use this text field to explain.

Randomization

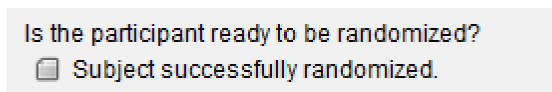
Purpose:
This form is used to officially randomize eligible participants to a ring strength for MTN-036 and to confirm that those participants who do not enroll in the study will not be randomized.
NOTE: This form is not used to randomize a participant to an IDI group. IDI randomization will be done outside of Rave and will be documented on the Enrollment CRF.

General Instructions:
The Randomization CRF is completed for each screened MTN-036 participant.

For participants who screen fail and will not be re-screened: Complete this form after the Eligibility form is completed and it is determined that the participant will not enroll.

For participants who will enroll in MTN-036: Complete this form for each participant who will enroll in MTN-036 at the Enrollment Visit. The Randomization Date and Time will be auto-populated from Medidata Balance into Medidata Rave. (NOTE: The time zone is GMT, not the time zone where data is being entered.) Completion of this eCRF will generate the participant's treatment assignment in Medidata Balance. 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?	If the participant is eligible to be enrolled, 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. If the participant will not be enrolled, select 'No' and save the form. End of form. The remaining fields will not be auto-populated.
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).
Randomization ID	Once "Is the participant ready to be randomized?" is saved as 'Yes', then the randomization ID will automatically populate.

Demographics

Purpose:
This form is used to document a participant's demographic 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 the participant's date of birth?	Please provide the participant's date of birth. A complete date is required.
Age	This is an automatically derived, locked data field based on the participant's date of birth and the date of initial data entry. No data entry is required.
What was the participant's sex at birth?	This is a locked data field pre-specified with "Female".
What is the participant's current gender identity?	This item is based on self-definition.
Ethnicity	This item is based on self-definition. Per NIH policy, Latina or Hispanic includes a person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.
Race	Record the participant's race based on self-definition. In the case of mixed race, mark all that apply. If a race is other than those listed, select 'Other race' and specify in the 'Other race, specify' text field provided. Per NIH policy, Latina is considered an ethnic group and not a race, and should not be entered as a Race.
In the past 12 months, with whom did the participant have vaginal sex?	Record with whom the participant has had sex in the last 12 months. Sex with a male partner is defined as having penile-vaginal sex, including with a trans man with a reconstructed penis.

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-036. 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.
Did the participant consent to long-term specimen storage and future testing?	Select 'Yes' or 'No'. Consent for long-term specimen storage can be changed if the participant changes her consent decision after enrollment. Update as needed if the participant changes her consent during the study.

Field	Instructions
Was the participant randomized to participate in IDI (in-depth-interview)?	Select 'Yes' or 'No'. Refer to SSP section 12.3.1 for instructions on IDI randomization. If 'Yes', complete the next field. If 'No', then leave remaining items blank and save the form.
Was the participant invited to participate in IDI?	Select 'Invited' or 'Not invited'. Refer to SSP section 12.3.1 for instructions on IDI randomization.
Will this participant participate in IDI?	Select 'Yes' or 'No'. If the participant agrees to participate in the IDI and agrees to audio recording of the interview, select 'Yes'.

Follow-up Visit Y/N

Purpose:
This form documents if a scheduled follow-up visit was completed.

General Instructions:
This form is completed for each scheduled visit and is present in each follow-up visit folder, starting at V3.0 – Day 1 through V11.0 – Day 92/93/94. Selecting 'Yes' will add the 'Follow-up Visit Summary' eCRF to the visit folder. Selecting 'No' will add the 'Missed Visit' eCRF to the visit folder.

Item-specific Instructions:

Field	Instructions
Did the participant complete this visit?	Select 'Yes' or 'No'. If 'Yes' is selected, the 'Follow-up Visit Summary' form will be added to the visit folder and can then be completed. If 'No' is selected, the 'Missed Visit' form will be added to the visit folder 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, starting at V3.0 – Day 1 through V11.0 – Day 92/93/94.

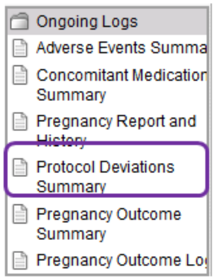
Item Specific Instructions:

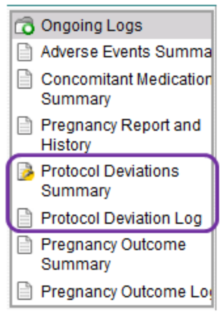
Field	Instructions
Visit Date	A complete date is required.
Was study product use permanently discontinued (scheduled or early) at this visit?	Select ‘Yes’ or ‘No’. If ‘Yes’, then complete a Product Discontinuation eCRF within the Discontinuations folder.
Did the participant exit/terminate the study at this visit?	Select ‘Yes’ or ‘No’. If ‘Yes’, then complete a Study Discontinuation eCRF within the Discontinuations folder.
Were any new adverse events (AEs) reported at this visit? If yes, complete the AE Log.	Select ‘Yes’ or ‘No’. Select ‘Yes’ if at least one Adverse Event (AE) was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable AE(s).
Is the participant taking any concomitant medications that have not been previously reported? If yes, complete the Concomitant Medications Log.	Select ‘Yes’ or ‘No’. Select ‘Yes’ if at least one concomitant medication was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable CM(s).
Were any protocol deviations been reported at this visit?	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 scheduled study visit per protocol?	Select ‘Yes’ or ‘No’. Select ‘Yes’ if additional procedures were completed at this visit. Navigate to the Additional Study Procedures from to select the applicable study procedures. If “No” is selected, the Additional Study Procedures CRF will be removed from the visit folder.

Protocol Deviation 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?	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 Deviation Log

Purpose:
This form documents and reports protocol deviations identified for study participants during the implementation of MTN-036.

General Information/Instructions:
Complete this form each time a protocol deviation is identified. Once the Protocol Deviation Log form has been created, complete one page 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.

Field	Instructions
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 prevent future occurrences of the deviation	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	

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 in each follow-up visit folder. The form is removed dynamically when “Were any additional study procedures or forms completed outside of the schedule study visit per protocol?” is selected ‘No’ on the Follow-up Visit Summary CRF.

Item-specific Instructions:

Field	Instructions
CASI and/or IDI	Select this field to add the Behavioral Assessment form
Vital Signs	Select this field to add the Vital Signs form
Physical Exam	Select this field to add the Physical Exam form
Pelvic Exam	Select this field to add the Pelvic Exam form
Pregnancy Test	Select this field to add the Pregnancy Test Results form
STI Tests	Select this field to add the STI Test Results form
HIV Tests	Select this field to add the HIV Test Results form
CBC with differential and platelets	Select this field to add the Hematology form
AST or ALT	Select this field to add the Local Laboratory Results form
Specimen collection	Select this field to add the Specimen Storage form
Ring Insertion or Removal	Select this field to add the Cervical Specimen Storage form
HIV Confirmatory Test Results	Select this field to add the HIV Confirmatory Test Results form

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.

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).
Were any protocol deviations 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.)	Select all that apply. Mark the checkbox for each reason for the interim visit. Leave the checkbox unmarked for reasons that were not applicable.
If completion of missed visit procedures, for which visit are procedures being made up?	Select the Visit for which procedures are being made up.
If yes, for which visit are procedures being made up?	If "Completion of missed visit procedures" is 'Yes', 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 all that apply. Mark the checkbox for 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, mark the checkbox for **Physical Exam**. Leave the checkbox unmarked for procedures that were not completed at the study visit.

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 (SS) manual.

General Information/Instructions:
A missed visit form will be dynamically added to a visit folder if the response to "Was this visit completed?" on the Follow-up Visit Summary from 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 based on the participant's Enrollment date. 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 her Visit 11.0 Final Contact Visit. Select 'No' if the participant terminated the study early. If 'Yes', end of form.
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 event?	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	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.

RING FORMS

Pharmacy Dispensation

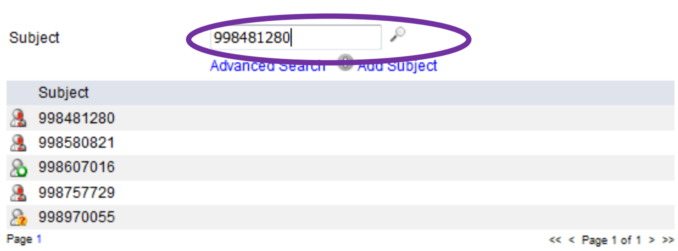
Purpose:

This log form is used to collect vaginal ring dispensation information at the site Pharmacy.

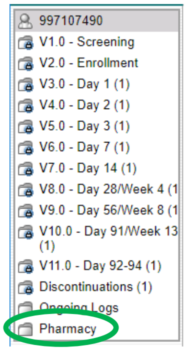
General Instructions:

Complete this form at the Enrollment Visit for participants randomized to the 100 or 200 mg ring; complete this form at Enrollment, and add new log lines at Visit 8 and Visit 9 for participants randomized to the 25 mg ring. **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 enter the PTID and locate the participant's casebook.



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



- Complete the Pharmacy Ring Dispensation eCRF and save the form.

Item-specific Instructions:

Field	Instructions
Date study product dispensed	Record the day, month, and year study product was dispensed to the participant. A complete date is required. At enrollment, the date should match the randomization/enrollment date on the Randomization eCRF.
Ring strength participant was given	Use the drop-down menu to select the ring strength the participant was given.
Ring strength participant was randomized to	This field is read-only. The ring strength will be auto-populated by Medidata Balance once the form is saved for QC purposes.
Manufacturer's lot number	Use the drop-down menu to select the manufacturer's lot number of the ring given to the participant.

Ring Insertion and Removal

Purpose:

This form is used to document participant ring use, as well as any ring insertions or removals that occur during follow-up visits (regularly scheduled or interim).

General Instructions:

Complete this form at enrollment and each follow-up visit (regularly scheduled or interim) when a ring is inserted of removed during the visit.

Item-specific Instructions:

Field	Instructions
Date of assessment	A complete date is required.
Did the participant have a ring in place at the start of the visit?	Select 'Yes' or 'No'. If 'No', and a ring was not brought into the clinic, then skip to "Was a ring inserted at this visit?" If 'No', but a used ring was brought into the clinic not inserted (for example, removed at home and brought to the clinic in a bag), the ring removal items below should be completed.

Was the ring removed at this visit?	Select 'Yes' or 'No'. If 'No', and a ring was not brought into the clinic, then skip to "Was a ring inserted at this visit?" If 'No', but a used ring was brought into the clinic not inserted (for example, removed at home and brought to the clinic in a bag), the ring removal items below should be completed.
Date ring was removed	A complete date is required.
Time ring was removed	Record the time in the 24-hour clock.
Who removed the ring?	Select 'Participant' or 'Study staff'.
Reason ring was removed	Select the primary reason the ring was removed from the drop-down menu. If 'Participant declined study ring use' or 'other' is selected as the primary reason, then specify details in the specify text field provided.
Ring Storage	Select 'Stored' or 'Not stored'. If 'Not stored' is selected, then specify reason in the text field provided.
Was a ring inserted at this visit?	Select the applicable response from the drop-down menu. If a ring was not inserted at this visit (i.e. "Was a ring inserted at this visit?" = 'No'), then end the form.
Date ring was inserted	A complete date is required.
Time ring was inserted	Record the time in the 24-hour clock.
Did the participant attempt to insert the ring herself?	Select 'Yes' or 'No, inserted by study staff' If 'No, inserted by study staff' is selected, end of form.
Based on your assessment and her feedback, how easy or difficult was it for the participant to insert the ring?	Based on study staff's assessment and the participant's feedback, select one of the following: • Select 'Very Difficult' if insertion required 3+ attempts and/or caused pain and/or sever discomfort • Select 'Difficult' if insertion required 2 attempts and/or caused moderate discomfort • Select 'Easy' if insertion required 1 attempt with some repositioning and/or cause mild discomfort • Select 'Very Easy' if smooth insertion and positioning in one attempt with no discomfort

Ring Adherence Summary

Purpose:

This form is used to document if the participant has used a vaginal ring since the last study visit.

General Instructions:

This form is completed at Visit 8.0 – 28 days, Visit 9.0 – 56 days, and Visit 10.0 – 91 days.

Item-specific Instructions:

Field	Instructions
Since the participant's last study visit, has she ever used a vaginal ring?	Select 'Yes' or 'No'. If 'Yes', then complete the Ring Adherence eCRF.

Ring Adherence

Purpose:

This form is used to document **participant-reported** vaginal ring removals and expulsions that occur during the study follow-up period. This includes all instances when the ring has not been used, regardless of the reason(s) for non-use.

General Instructions:

Complete this form at Visit 8.0 – 28 days, Visit 9.0 – 56 days, and Visit 10.0 – 91 days. Ring removals that occur during study visits (either by site staff or participant) should **not** be recorded on this form; rather, they should be recorded on the Ring Insertion and Removal eCRF.

Item-specific Instructions:

Field	Instructions
Since her last study visit (or since the ring was inserted if Visit 8/Day 28), how many times in total has the participant had a vaginal ring out, excluding expected instances when a ring was briefly removed and replaced with a new ring?	Record the number of separate times the participant reports having the ring out since her last scheduled visit (or since the ring was inserted if Visit 8 – Day 28). If '0', then end the form.
How many of these times since the participant's last study visit was a vaginal ring out for more than 12 hours continuously?	Record the number of separate times the participant reports having the ring out for more than 12 hours continuously since her last scheduled visit (or since the ring was inserted if Visit 8 – Day 28). If '0', skip to "Was the ring removed?"
Since the participant's last study visit, what is the longest number of days in a row the vaginal ring was out?	Record the longest number of days the participant reports having the ring out since her last scheduled visit (or since the ring was inserted if Visit 8 – Day 28).
Was the ring removed?	Select 'Yes' or 'No'. Select 'No' if the vaginal ring was out due to it coming out on its own. If 'No', then skip to "Did the ring come out on its own?"
What are the reason(s) why the vaginal ring was removed?	Select the reason(s) why the participant reports the vaginal ring was removed by the participant or clinician. If 'Other', then specify in the "Other, specify" text field provided.

	Click 'Add a new Log line' to complete additional rows as needed.
Did the ring come out on its own?	Select 'Yes' or 'No'. Select 'No' if the vaginal ring was out due to it was intentionally removed. If 'No', then end of form
What are the reason(s) why the vaginal ring came out on its own?	Select the reason(s) why the participant reports the vaginal ring came out on its own. If 'Other', then specify in the "Other, specify" text field provided. Click 'Add a new Log line' to complete additional rows as needed

CLINICAL FORMS

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** at follow-up visits) as applicable.

Item-specific Instructions:

Field	Instructions
Exam Date:	Enter the date the physical exam was performed. A complete date is required.
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. Any abnormalities or baseline conditions that worsened during follow-up should be reported on the Adverse Events Log. Normal findings may also be described in the text field/space, but it is not required. If an organ system or body part is 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, lymph nodes, abdomen, neck, heart, lungs, extremities, skin, and neurological may be omitted after the Enrollment Visit.

Field	Instructions
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. The body system can be specified in the text field provided. If no other abnormal findings are identified, select 'Not Done'.

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).
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).
Respirations	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.

Pelvic Exam

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

General Instructions:

Complete this form at Screening, Enrollment, Visit 3.0 – Day 1, Visit 4.0 – Day 2, Visit 5.0 – Day 3, Visit 6.0 – Day 7, Visit 7.0 – Day 14, Visit 8.0 – Day 28, Visit 9.0 – Day 56, and Visit 10 – Day 91. Transcribe information from the MTN-036 **Pelvic Exam Diagrams** form or other local site-specific source document into this form for submission in Medidata Rave.

Item-specific Instructions:

Field	Instructions
Pelvic exam assessment	If 'not done' is selected, then end of form. 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 findings	Select the box to the right of each abnormal finding observed, and check all that apply. Specify additional details in the text field provided where applicable. If an observed abnormal finding is not listed, select "Other abnormal findings" and specify/describe the abnormal findings in the text field provided, including the anatomical location. Record any baseline abnormalities on the Baseline Medical History Log. Any baseline abnormalities that worsened during follow-up should be reported on an 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.
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 search list function on the eCRF. Up to three AEs can be selected. This item should be marked '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 assessed' 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 Screening, Enrollment, Visit 5.0 – Day 3, Visit 6.0 – Day 7, Visit 7.0 – Day 14, 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-036 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.

Baseline Medical History Summary

Purpose:
To document any baseline medical history conditions/events reported at the Screening visit or recalled by the participant at Enrollment.

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 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 at the Enrollment 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.

- If a medical condition increases in severity or frequency during follow-up and is captured as an AE, the medical history **should not** be updated to include an End Date.
- 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 item improves 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 the condition resolves during follow-up, this item should not be updated. 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. If a condition resolves during the study, the Baseline Medical History form should <u>not</u> be updated with a resolution or end date for the medical condition.

Adverse Events Summary

Purpose:

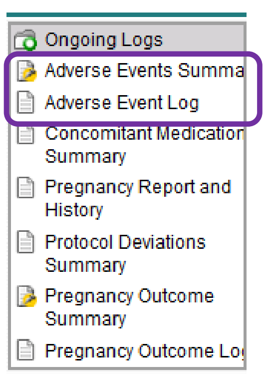
This form documents if an adverse event was experienced by the participant during the study.

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 one Adverse Event eCRF for each AE reported during the AE reporting period .



Adverse Event Log

Purpose:

To document any Adverse Event (AE) reported by the participant or clinically observed as defined by the protocol.

General Instructions:
Complete a separate AE log form 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 log page as applicable. If a cluster of symptoms reported on separate AE Log pages is later attributed to a single diagnosis, update the earliest reported symptom page to the diagnosis. In the study database, the remaining symptoms can be deleted by clicking "Inactivate" and selecting the applicable rows that should be inactivated.

A baseline medical condition should only be recorded as an AE during follow if the condition increases in frequency and/or severity.

If an AE increases in severity/frequency, a new AE should be reported. The original AE should be marked "Recovered/resolved" with 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 regarding 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?	Select the visit at which the AE was first reported from the drop down menu. If the AE was reported at an interim visit, select "interim visit" and enter the interim visit code in the text field provided.
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.
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.

Field	Instructions
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 Comments section/text field provided.
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 marked 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-036. *Dose increased:* This option does not apply and should not be selected in MTN-036. *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. *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. Complete a Product Hold log form for each AE that results in a clinician-initiated product hold. *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. Select ‘Medication’ only if the participant reports taking the medication. Report the medication(s) on the Concomitant Medications Log . If a 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 “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.

Field	Instructions
Status/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".
Is this a Serious Adverse Event according to ICH/GCP or protocol guidelines? If "No", go to "Has or will this AE be reported as an EAE?". If "Yes", check all that apply.	If "Yes", select all that apply: "Results in death", "Is life-threatening", "Requires inpatient hospitalization or prolongation of existing hospitalization", "Results in persistent or significant disability/incapacity", "Is a congenital anomaly/birth defect", and/or "Is another serious important medical event that may jeopardize the patient or require intervention to prevent one of the other outcomes listed above".
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'.
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 log form for each reported concomitant medication. 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	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 "Or, continuing at 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 unknownIf ‘Other’ is selected, specify in the corresponding “If other frequency, specify” text field provided.
Route	Select the route from options provided in the drop-down list. Below is a list of common route abbreviations: PO: oral IM: intramuscular IV: intravenous TOP: topical IHL: inhaled VAG: vaginal REC: rectal SC: subcutaneous Other: alternative routes or unknown 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”). If the dose of each ingredient of a combination drug is provided separately, document each active ingredient as a separate log entry. For example, record the use of hydrocodone/acetaminophen 5/500 as two separate log entries – one log form for the hydrocodone and a second log form for acetaminophen. 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 select the “Dose Unknown” checkbox and heave the Dose field blank. When documenting medical devices with no active medication, such as an IUCD, enter the dose as “1”.

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.
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 four AEs can be selected. If the medication was not administered to treat an AE, select ‘No’, and end the form.

Product Hold Summary

Purpose:
This form documents if a clinician-initiated product hold was applied during the study.

General Instructions:
This form is present within the “Ongoing Logs” folder. Selecting ‘Yes’ in the “Does the participant have any clinical product holds to be applied?” prompt will add the “Clinical Product Hold” log to the “Ongoing Logs” folder.

Product Hold Log

Purpose:
This form is used to document temporary clinical holds of study product use as instructed by study site staff.

General Instructions:
This form is completed each time a participant is instructed by study staff to temporarily stop (hold) study product use. If, at the same visit, a product hold is initiated for more than one reason, complete one Product Hold log line for each reason. To add an additional Clinical Product Hold log line within Medidata Rave, click “Add a new Log line” to add an additional log line for a new product hold to be completed.

Complete this form for any clinical reason that warrants a product hold regardless of whether participants choose to use the ring or who choose to not use study product during the study. Do not complete this form in cases where a participant has decided herself to not use the study vaginal ring.

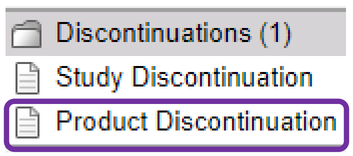
Item-specific Instructions:

Field	Instructions
Date when study product hold was initiated:	Record the date when the product hold was initiated or would have been initiated in instances where the participant has chosen not to use the ring. A complete date is required.
Why is study product being held?	Record the reason that study product is being held. If study product is held for any reason not specified, mark “Other, specify” and specify the reason in the space provided. Note that participant decline or refusal of study product is not documented as a product hold. Do not record this as a reason in ‘other, specify”.
Adverse Event	If study product is being held due to “Adverse Event”, select the applicable AE from the drop-down field provided. **<u>Note</u>**: If study product is being held due to an AE, the AE log page must be entered into Rave prior to completion of the Clinical Product Hold log form in order for the AE to be available to select with the drop down field.
Concomitant Medication	If study product is being held due to “Reported use of PEP for HIV exposure”, “Reported use of PrEP for HIV prevention”, or “Use of heparin, Lovenox, warfarin, Plavix, or other anticoagulant”, specify the corresponding concomitant medications log form on which the medication was reported in from the drop down field provided with Rave. At least one medication must be specified and up to four medications can be recorded. **<u>Note</u>**: If the product hold is due to report of medication use, the corresponding concomitant medications log page must be entered into Rave prior to completion of the Product Hold log form in order the medication be to be available within the drop down field.
Date of last study product use	Record the last date the study product was present in the vagina. Use a best estimate if the actual date cannot be determined.
Was the participant instructed to resume study product use?	Mark, “No – hold continuing for another reason” if the participant would have been instructed to resume study product based on the resolution of the reason indicated on this form. If ‘No – hold continuing for another reason’, enter below the ‘date study product hold continuing for another reason’. Mark, “No – early termination” if the product hold was ongoing at the visit at which the participant terminated early from the study. Mark, “No – hold continuing at Visit 10” if the product hold was ongoing at time of the participant’s scheduled Product Use End Visit. Mark, “No – permanently discontinued” if the participant was permanently discontinued from study product due the reason indicated on this form. If ‘yes’, enter below the date that the participant was instructed to resume study product. <u>If 'no - permanently discontinued', 'no - early termination' or 'no - hold continuing at Visit 10)', complete the Product Discontinuation form.</u>

Product 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:

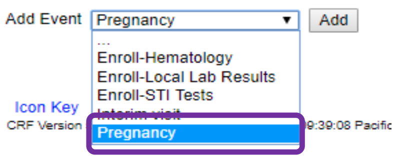
Field	Instructions
Date study product use was permanently discontinued	A complete date is required. Record the date when the participant completed or was permanently discontinued from study product.
Primary reason for ending study product use	Record the primary reason from the drop-down menu. If 'Scheduled study product use period completed', then end the form. If 'Adverse Event' is selected, specify the AE entry from the AE dynamic drop-down list. <u>Note</u>: If study product is permanently discontinued due to an AE or allergic reaction to the vaginal ring, the AE log page must be entered into Rave prior to linking the AE on the Product Discontinuation eCRF in order for the AE to be available to select with the drop down field. If the primary reason is "Other", provide additional details in the "If other, specify" text field provided.

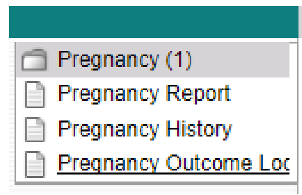
Pregnancy Report

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

General Instructions:
A Pregnancy Report 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, use the Add Event dropdown menu on the participant's home page to add a Pregnancy folder. This will generate add a Pregnancy

folder to the participant's case book. The Pregnancy folder will contain the Pregnancy Report, Pregnancy History, and Pregnancy Outcome Log eCRFs.





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 fields blank.
Estimated date of delivery	A complete date is required.
What primary information was used to estimate the date of delivery?	Choose the primary method that was used to estimate the date of delivery. If another method was used which are not covered by the currently listed methods, please select 'Yes' for "Other" and describe them in the 'If other, specify' text field provided.

Pregnancy History

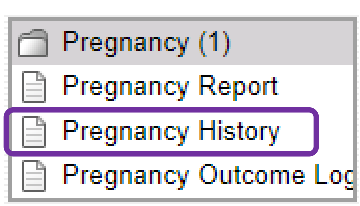
Purpose:

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

General Instructions:

A Pregnancy History form is required once for a participant who becomes pregnant during the study.

To complete a Pregnancy History form within Medidata Rave, navigate to the Pregnancy folder and complete the **Pregnancy History** eCRF.



Item-specific Instructions:

Field	Instructions
Has the participant ever been pregnant before?	If the participant has never been pregnant before, select "No" and end the form. If 'yes', an entry is required for each of the following: Number of full term live births (>=37 weeks), Number of premature live births (less than 37 weeks), Number of spontaneous fetal deaths and/or still births (>=20 weeks), Number of spontaneous abortions (less than 20 weeks), Number of therapeutic/elective abortions, Number of ectopic pregnancies. Enter '0' for any that do not apply.
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 Log

Purpose:

This form is used to report pregnancy outcome information for a pregnancy reported post-enrollment. A Pregnancy Outcome Log line must be completed for each pregnancy reported during the study.

General Instructions:

This form will be in the Pregnancy folder of a participant's casebook. To add another outcome, click "Add a new Log line".

Item-specific Instructions:

Field	Instructions
Is the pregnancy outcome data obtainable?	If site staff were able to ascertain an outcome for this pregnancy from the participant, select "Yes". If site staff were not able to ascertain an outcome for this pregnancy from the participant (i.e. the participant refuses further contact), select "No" and end the form.
How many pregnancy outcomes resulted from this reported pregnancy?	If the pregnancy results in two or more outcomes, complete a Pregnancy Outcome Log eCRF (new log line) for each outcome. If the item is completed as greater than "1", add additional Pregnancy Outcome Log lines to the Pregnancy Outcome Log eCRF, as needed.
Outcome Date	A complete date is required.
Place of delivery/outcome	Enter the place of delivery/outcome from the drop-down menu. If 'Other' is selected, specify in the corresponding "Other, specify" text field.

Field	Instructions
Specify Outcome	Specify the outcome from the drop-down menu. If the outcome is spontaneous fetal death, still birth, spontaneous abortion, therapeutic/elective abortion, or ectopic pregnancy, the outcome itself is not an adverse event (AE). If a therapeutic/elective abortion is performed due to a pregnancy complication, the pregnancy complication should be reported on an Adverse Event (AE) Log, if prior to termination, with 'therapeutic procedure/surgery' checked for item "Other action(s) taken". If there are any maternal complications as a result of the pregnancy outcome, refer to the protocol, Study-specific Procedures (SSP) manual, and *Manual for Expedited Reporting of Adverse Events to DAIDS, Version 2* for guidance on AE and expedited AE reporting requirements. If 'other' is selected, specify in the corresponding "If Other, specify" text field.
Method	Select the method from the drop-down menu only if the outcome is 'full term live birth (≥37 weeks)' or 'premature term live birth (< 37 weeks)'. "Operative Vaginal" delivery includes delivery with forceps and/or vacuum. If the outcome is 'full term live birth', skip to "Were there any complications related to the pregnancy outcome?"
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".

Field	Instructions
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.

HIV Test Results

Purpose:

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

General Instructions:

Complete this form at V1.0 – Screening, V2.0 – Enrollment, V10.0 – Day 91, and as indicated during follow-up.

Item-specific Instructions:

Field	Instructions
Was Sample 1 collected for HIV Testing?	Select 'Yes' or 'No'. If 'No', end of form
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.
Sample 1 HIV test result	If the Rapid test is positive or indeterminate, complete the HIV Confirmatory Test Result form and alert the MTN Laboratory Core.

HIV Confirmatory Tests

Purpose:
This form is used to document HIV confirmatory results from local lab confirmatory HIV testing.

General Instructions:
This form will be dynamically added if 'positive' or 'indeterminate' is selected on the HIV Test Results eCRF.

Item-specific Instructions:

Field	Instructions
Was Sample 1 collected for HIV Confirmatory testing?	Select 'Yes' or 'No'.
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.
Sample 1 HIV Confirmatory test result	If the Sample 1 HIV Confirmatory test result is negative, indeterminate, or invalid, contact the MTN Virology Core. If positive at a follow-up visit, collect sample 2 and plasma for testing by the MTN Virology Core.
Was sample 2 collected for HIV Confirmatory testing?	Select 'Yes' or 'No'. If Sample 2 was collected, complete the remaining items.
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.
Sample 2 HIV Confirmatory test result	Select 'Positive', 'Negative', or 'Indeterminate'.
Was a sample for testing by the MTN Virology Core stored?	Select 'Yes' or 'No'.

Field	Instructions
Final HIV Status	Once a participant's HIV status has been determined, record the final HIV status from the drop-down menu. If the participant's final HIV status is determined to be positive (according to the protocol testing algorithm), update the Product Discontinuation 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.

STI Test Results

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.
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 in Baseline Medical Conditions Log form when applicable.

Item-specific Instructions:

Field	Instructions
Was a sample collected for Syphilis testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for Syphilis testing do not need to be completed. Proceed to "Was a urine sample collected for N. gonorrhea 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.
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. If the result is "non-reactive" or "not reported", skip to "Was a vaginal wet prep sample collected?".
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').

Field	Instructions
Was a vaginal wet prep sample collected?	If “Vaginal wet prep” was not done or not collected, select the ‘No’ option for “Was a vaginal wet prep sample collected?”, and do not complete the “Date of collection” or corresponding test results. If a vaginal wet prep was performed but not all assays were completed, select “Not done” for each uncompleted wet prep assay.
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.
Vaginal pH	Record the vaginal pH (e.g., 4.1).
Homogenous vaginal discharge	Select ‘Positive’ if homogeneous vaginal discharge was observed.
Whiff test	Select ‘Positive’ if a fishy, amine odor is detected.
Clue Cells ≥20%	Select ‘Positive’ if 20% or more of the cells were clue cells.
Trichomonas vaginalis	Select ‘Positive’ if trichomonas were observed.
Buds and/or hyphae (yeast)	Select ‘Positive’ if yeast buds and/or hyphae were observed
Was a sample collected for NAAT for GC/GT and trichomonas?	If “NAAT” was not done or not collected, select the ‘No’ option for “Was a sample collected for NAAT for GC/CT?” and do not complete the “Date of collection” or corresponding test result.
N. gonorrhoeae	If “N. gonorrhoeae” was not done or not collected, select the ‘Not done’ option. If the specimen was collected, complete the test result (either ‘Positive’ or ‘Negative’).
C. trachomatis	If “C. trachamotis” was not done or not collected, select the ‘Not done’ option. If the specimen was collected, complete the test result (either ‘Positive’ or ‘Negative’).
Trichomonas	If “Trichomonas” was not done or not collected, select the ‘Not done’ option. If the specimen was collected, complete the test result (either ‘Positive’ or ‘Negative’).

Local Laboratory Results

Purpose:

This form is used to provide data on the participant’s baseline and follow-up laboratory test results.

General Instructions:

Use this form to report the serum chemistries and urinalysis from specimens collected at Visit 1.0 – Screening and Visit 10.0 – Day 91, and as indicated during the study. Record results on this form as they become available.

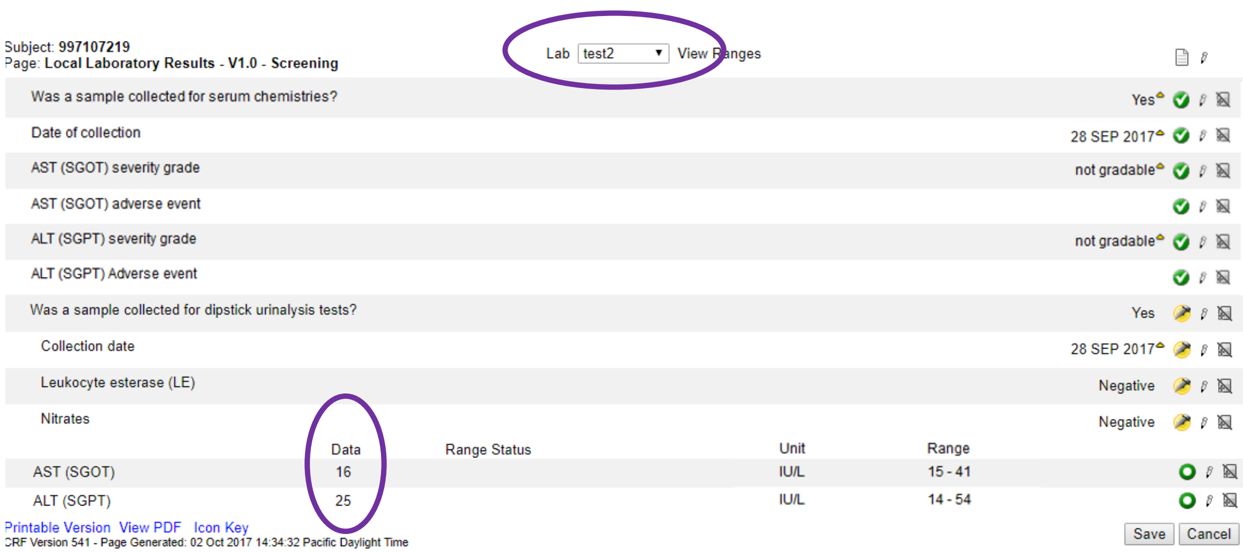
If any or all of the lab tests listed on this form are repeated (re-drawn) between the Screening and Enrollment Visit, document the repeated results on the same Local Laboratory Results form. If the participant enrolls, the updated results should be submitted into the study database.

At Screening, record any applicable diagnoses within 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), record the numeric results in the appropriate field at the bottom of the form.


Subject: 997107219
Page: Local Laboratory Results - V1.0 - Screening
Lab test2 View Ranges

Was a sample collected for serum chemistries?	Yes
Date of collection	28 SEP 2017
AST (SGOT) severity grade	not gradable
AST (SGOT) adverse event	
ALT (SGPT) severity grade	not gradable
ALT (SGPT) Adverse event	
Was a sample collected for dipstick urinalysis tests?	Yes
Collection date	28 SEP 2017
Leukocyte esterase (LE)	Negative
Nitrates	Negative

	Data	Range Status	Unit	Range
AST (SGOT)	16		IU/L	15 - 41
ALT (SGPT)	25		IU/L	14 - 54

Printable Version View PDF Icon Key
CRF Version 541 - Page Generated: 02 Oct 2017 14:34:32 Pacific Daylight Time
Save Cancel

- 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)

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

Lab Result Units and Rounding

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

- Note that the following units are equivalent:

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

  The following analytes should be recorded in the following format:

  - **AST/SGOT** (U/L for all sites): Up to a two digit integer is allowable for the AST/SGOT analyte.
  - **ALT/SGPT** (U/L for all sites): Up to a two digit integer is allowable for the AST/SGOT analyte.

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 current version of the DAIDS Toxicity table, 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.

Hematology

Purpose:
This form is used to provide data on the participant's laboratory test results.

General Information/Instructions:
Use this form to report the hematology and differential test results obtained from specimens collected at Visit 1.0 – Screening and Visit 10 – Day 91, and as indicated during the study as they become available. If the Hematology form is needed at Enrollment, use the "Add Event" drop down menu on the participant's home page.

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 within the Baseline Medical History Log eCRF, when applicable.

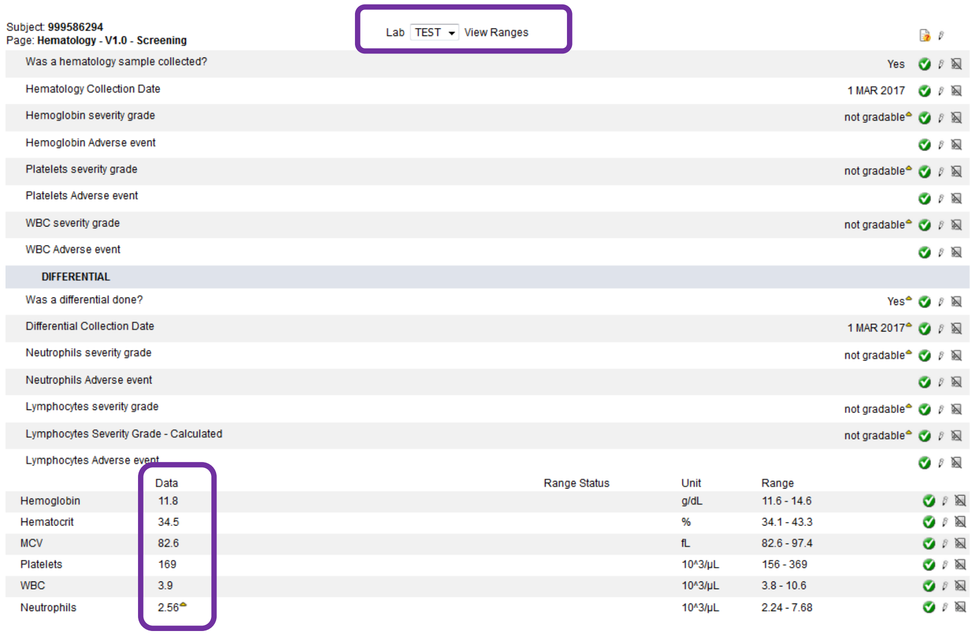
During follow-up, if a test result(s) recorded on this form indicates that the participant has a new (or increased severity) laboratory-confirmed infection or diagnosis, this infection/diagnosis must be recorded as an adverse event on an Adverse Event (AE) Log form.

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 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 Hematology eCRF because the derived age from the Date of Birth on the Demographics eCRF is used to populate the reference ranges.

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



Subject: 999586294
Page: Hematology - V1.0 - Screening

Lab TEST View Ranges

Was a hematology sample collected?	Yes
Hematology Collection Date	1 MAR 2017
Hemoglobin severity grade	not gradable
Hemoglobin Adverse event	
Platelets severity grade	not gradable
Platelets Adverse event	
WBC severity grade	not gradable
WBC Adverse event	
DIFFERENTIAL	
Was a differential done?	Yes
Differential Collection Date	1 MAR 2017
Neutrophils severity grade	not gradable
Neutrophils Adverse event	
Lymphocytes severity grade	not gradable
Lymphocytes Severity Grade - Calculated	not gradable
Lymphocytes Adverse event	

	Data	Range Status	Unit	Range
Hemoglobin	11.8		g/dL	11.6 - 14.6
Hematocrit	34.5		%	34.1 - 43.3
MCV	82.6		fL	82.6 - 97.4
Platelets	169		10^3/µL	156 - 369
WBC	3.9		10^3/µL	3.8 - 10.6
Neutrophils	2.56		10^3/µL	2.24 - 7.68

- Enter the severity grade at the top of the form for that specific result. The following results require entry of the severity grade (if applicable):
  - **HEMATOLOGY:** Hemoglobin, Platelets, WBC
  - **DIFFERENTIAL:** Neutrophils, Lymphocytes

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

Lab Result Units and Rounding

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

- Note that the following units are equivalent:

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

  The following analytes should be recorded in the following format:

  - **Hemoglobin** (g/dL for all sites): Round Hemoglobin values up or down to the nearest tenth place. For example, a lab-reported Hemoglobin value of 11.06 g/dL would be recorded as 11.1 g/dL.

  - **MCV** (fl for all sites) – Enter value up to 1 decimal for MCV analyte.

- **Platelets** (10^3/uL for all sites): Up to a three-digit whole integer is allowable for Platelets.

- **WBC** (10^3/uL), **Neutrophils** (cells/mm^3), **Lymphocytes** (cells/mm^3), **Monocytes** (cells/mm^3), **Eosinophils** (cells/mm^3), **Basophils** (cells/mm^3): Enter value using the same level of precision according to 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 (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.

Pregnancy Test Results

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 8.0 – Day 28, Visit 9.0 – Day 56 and Visit 10.0 – Day 91, and at other visits if indicated.

Item-specific Instructions:

Field	Instructions
Was a pregnancy test done?	Record if a pregnancy test was done by entering 'Yes' or 'No'. If 'No' is selected, then end of form and leave remaining items blank. • If a pregnancy test was not done, please do NOT complete the "Date of Pregnancy Test", "time" or "Test result". • 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 that 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 Product Discontinuation eCRF, Study Discontinuation eCRF, and Pregnancy Report 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-036.

Specimen Storage

Purpose:

This form is used to document collection and storage of plasma and rectal swabs by the local site laboratory for storage and DPV level testing.

General Instructions:

Complete this form at Visit 2.0 - Enrollment, Visit 3.0 – Day 1, Visit 4.0 – Day 2, Visit 5.0 – Day 3, Visit 6.0 – Day 7, Visit 7.0 – Day 14, Visit 8.0 – Day 28, Visit 9.0 – Day 56, Visit 10.0 – day 91, and Visit 11.0 – Final contact.

Item-specific Instructions:

Field	Instructions
Was plasma for archive/storage collected?	Select 'Yes' or 'No'. If 'No', then skip to 'Was plasma for PK collected?'
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 the specimen was collected using 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.

Field	Instructions
Was plasma for PK collected?	Select ‘Yes’ or ‘No’. If ‘No’, then skip to ‘Was a rectal swab for PK collected?’
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.
Time relative to ring insertion or removal	Select the time point that corresponds to the applicable sample collection time. If a visit has multiple time points, click “Add a new Log line” to add an entry for each time point. At Visit 2.0 – Enrollment, complete three log line entries with the following time points: 1 hour following ring insertion, 2 hours following ring insertion, and 4 hours following ring insertion. At Visit 10.0 – Day 91, complete four log line entries with the following time points: prior to ring removal, 1 hour following ring removal, 2 hours following ring removal, and 4 hours following ring removal. At visits when only one sample is collected (Visit 3.0 – Visit 9.0, and Visit 11.0) select ‘Not applicable’.
Collection time	Record the time each specimen was collected using 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.
Was a rectal swab for PK collected?	Select ‘Yes’ or ‘No’. If ‘No’, then end of form.
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 the specimen was collected using 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 timing of cervical and vaginal laboratory specimens.

General Instructions:

Complete this form at Visit 2.0 - Enrollment, Visit 3.0 – Day 1, Visit 4.0 – Day 2, Visit 5.0 – Day 3, Visit 6.0 – Day 7, Visit 7.0 – Day 14, Visit 8.0 – Day 28, Visit 9.0 – Day 56, Visit 10.0 – day 91, and Visit 11.0 – Final contact.

Item-specific Instructions:

Field	Instructions
Did the participant experience any vaginal spotting or bleeding in the past seven days?	Select 'Yes' or 'No'. If 'No', then skip to 'Was CVL collected?'
On how many of these days did the participant experience heavy bleeding?	Heavy bleeding is defined as soaking a tampon/pad every two hours or less.
Was CVL collected?	Select 'Yes' or 'No'. If 'No', then skip to 'Was CVF for PK collected?'
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 the specimen was collected using the 24-hour clock.
Cervicovaginal lavage (CVL) - cell pellet	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.
Cervicovaginal lavage (CVL) - supernatant	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.
Was CVF for PK collected?	Select 'Yes' or 'No'. If 'No', then skip to 'Were cervical biopsies for PK collected?'
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.
Time point of CVF collection	Select the time point that corresponds to the applicable sample collection time. If a visit has multiple time points, click "Add a new Log line" to add an entry for each time point. At Visit 2.0 – Enrollment, there should be 3 log line entries with the following time points: 1 hour following ring insertion, 2 hours following ring insertion, and 4 hours following ring insertion. At Visit 10.0 – Day 91, there should be 4 log line entries with the following time points: prior to ring removal, 1 hour following ring removal, 2 hours following ring removal, and 4 hours following ring removal. At visits when only one sample is collected (Visit 3.0 – Visit 9.0, and Visit 11.0) select 'Not applicable'.
Collection time	Record the time each specimen was collected using the 24-hour clock.

Cervicovaginal fluid (CVF) for PK	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.
Were cervical biopsies for PK collected?	Select 'Yes' or 'No'. If 'No', then skip to 'Were vaginal swabs for microbiota culture collected?'
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 each specimen was collected using the 24-hour clock.
Cervical tissue for PK	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.
Were vaginal swabs for microbiota culture collected?	Select 'Yes' or 'No'. If 'No', then skip to 'Were vaginal swabs for qPCR collected?'
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.
Vaginal swabs for microbiota culture	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.
Were vaginal swabs for microbiota qPCR collected?	Select 'Yes' or 'No'. If 'No', then skip to 'Was a vaginal gram stain collected?'
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.
Vaginal swabs for microbiota qPCR	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.
Was a vaginal gram stain collected?	Select 'Yes' or 'No'. If 'No', then end of form.
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.
Vaginal gram stain	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

Behavioral Summary

Purpose:

This form is used to document whether a Computer-assisted Self Interview (CASI) questionnaire or In-Depth Interview (IDI) was completed.

General Instructions:

This form is completed at Visit 2.0 – Enrollment, Visit 8.0 – Day 28, Visit 9.0 – Day 56, and Visit 10.0 – Day 91.

Item-specific Instructions:

Field	Instructions
Was a CASI questionnaire completed at this visit?	Select 'Yes' or 'No'. If 'Yes' is selected, then the CASI Tracking form appears dynamically. Complete the "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.
Was an in-depth interview completed at this visit?	Select 'Yes' or 'No'. If 'No' is selected at Visit 10.0, then record the reason why it was not done in the text field below.
If no, please explain:	At Visit 10.0, record the reason why an IDI 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. This form is completed at Visit 2.0 – Enrollment, Visit 8.0 – Day 28, Visit 9.0 – Day 56, and Visit 10.0 – Day 91.

Item-specific Instructions:

Field	Instructions
CASI collection date	A complete date is required.

Field	Instructions
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.