CRF Completion Guidelines

HPTN091

Version 3.0

CRF Completion Guidelines

Protocol Name:	Integrating HIV Prevention, Gender-Affirmative Medical Care, and Peer Health Navigation for Transgender Women in the Americas: A Vanguard Study
Protocol Number:	HPTN091
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CRF Completion Guidelines

The following instructions are study-specific data completion instructions intended to assist site staff when completing electronic case report forms (eCRFs) and paper case report forms (CRFs). Detailed guidance on general data collection, entry, navigation and general use of Medidata Rave is provided in the Medidata Rave Electronic Data Capture (EDC) Training Manual, which is found on the HPTN091 Protocol page: https://atlas.scharp.org/cpas/project/HPTN/091/begin.view?

General Guidelines

- The Participant ID is automatically assigned by Rave EDC as a 9-digit field, starting with the 3-digit site number followed by a randomly assigned 5-digit participant number, and 1-digit check number.
- All data entered in Rave must match the data on any source documents/paper CRFs.
- Complete all required data fields. Ensure that all entries are in English and are accurate, consistent, complete and medically logical.
- If “Other” is chosen as a response, further details must be provided by responding to the “If ‘Other’, specify” field.
- Text box fields have character limits. Text exceeding the limit will not be saved and a “Non-conformant” icon will appear.
- Visit dates must be complete and in chronological order according to the protocol.
- Most date fields must be entered as Day/Month/Year (dd/mmm/yyyy) (e.g., 01 NOV 2020). Exceptions are detailed in specific form sections where applicable.
- Drop-down menus are available for many fields. Use these menus, when available, to select the appropriate response.
- Avoid using abbreviations, symbols or special characters.
- Avoid hitting the return or enter key in text fields.
- If a scheduled visit is missed, do not enter data on the forms required for the visit, except for the Date of Visit form. Marking “no” on the Date of Visit form will add the Missed Visit form to the visit folder for completion.
- Log forms allow you to make multiple entries over the course of the study. View all entries at the same time in ‘Complete View’ and view individual entries in portrait view.
- The following log forms for this study are available in the Ongoing logs folder at the bottom of the sidebar on the Participant’s home page:

  - Adverse Event
  - Concomitant Medications
  - Gender Affirming Hormone Therapy
  - Medical History
  - Peer Health Navigation Tracking
  - Pre-exposure Prophylaxis
  - Protocol Deviations
  - Social Impact
- Correct/update data fields by clicking the pencil icon at the far right of the field, correct/update the value and give the reason for the change, if applicable. Save the form to apply the changes.
- If an incorrect data entry is made, a system query will fire. Correct the error and save the form.
  - System generated queries with no query response will automatically close with a form correction.
  - System generated queries with a query response will change into a manual query that will need to be closed by the data management team.
- All actions performed on a data field are tracked in the audit trail. If data is modified inadvertently, the change is also shown in the audit trail for that field.
- The Investigator of Record (IoR) will sign all forms after the participant's data has been reviewed. After the signature is applied, no further changes or additions to the forms are expected.
- Any modifications that are made to forms after the IoR has signed off will remove the signature. Once the data has been reviewed, the signature will need to be applied again.
- The SCHARP Clinical Data Manager will provide direction for when the Investigator should perform the final review and sign the eCRF pages.

Add Event

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

GAHT Safety Visit

- Add a GAHT Safety Visit folder to a participant's casebook by clicking on the **Add Event** button on the PTID (Subject)-level page and selecting "GAHT Safety Visit", then clicking "Add". A GAHT Safety Visit folder will appear in the participant's casebook.
- Open the GAHT Safety Visit folder to access the applicable forms for this visit.
- On the Date of Visit form, enter the visit date as the earliest date visit procedures were performed for the GAHT Safety visit.

Interim Visits

- Add an Interim Visit folder to a participant's casebook by clicking on the **Add Event** button on the PTID (Subject)-level page and selecting "Interim Visit", then clicking "Add". An Interim Visit folder will appear in the participant's casebook.

- Open the Interim Visit folder to access the Interim Visit form. On the Interim Visit form, select the forms that were completed at the interim visit. The selected forms will then load in the folder.
- On the Interim Visit form, enter the visit date as the earliest date visit procedures were performed for that interim visit.

Seroconversion Termination Visit

- Add a Seroconversion Termination Visit folder to a participant's casebook by clicking on the **Add Event** button on the PTID (Subject)-level page and selecting "Seroconversion Termination Visit", then clicking "Add". A Seroconversion Termination Visit folder will appear in the participant's casebook.
- Open the Seroconversion Termination Visit folder to access the applicable forms for this visit.
- On the Date of Visit – Seroconvertor Schedule form, enter the visit date as the earliest date visit procedures were performed for the Seroconversion Termination visit.

Loading of Forms in Visit Folder

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

Loading of Folders in Participant Casebook

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

Table 1. Folder Dynamics

Folder	Action Required to Add Folder
V1 – Screening V2 – Enrollment Ongoing Logs Discontinuations	Save Participant Identifier form.
V3 – Week 13 GAHT Initiation Visit	Select "Yes" for "Is the participant ready to be randomized?" on the Randomization form in V2 folder.
V4-V8	• Select "Yes" for "Did the participant complete this visit?" on the Date of Visit form in the visit folder. • Select "No" for "Did the participant exit/terminate the study at this visit?" on the Date of Visit form in the visit folder.

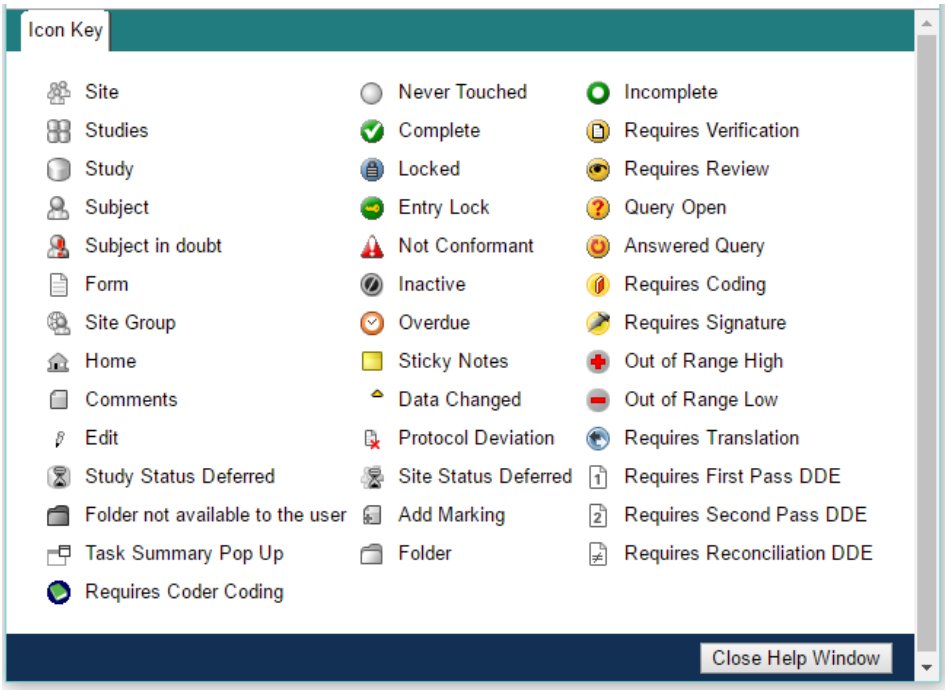
Dynamic Search Lists

- Some forms have data fields with 'dynamic' drop-down lists of available options. Options are populated by corresponding log form entries.
- Dynamic drop-down lists will be blank until entries are made and saved in the corresponding log form.
- Your selection in the dynamic search list can be deleted if entered in error.
- Changing the original log data or inactivating a log form entry that has been selected for a dynamic search list field, will make that field non-conformant and it will need to be updated.
- For Example:
    - An AE of '*FEVER*' started on 05DEC2020 and is reported on the Adverse Events log form
    - On the Concomitant Medications log form, if a listed medication was used for this AE, a dynamic search list can be used to select the applicable AE record from the dropdown list.
    - The start date for AE *'FEVER'* is corrected to 06DEC2020 on the Adverse Events log form.
    - The selection on the Concomitant Medication log form becomes non-conformant.
    - To resolve the non-conformant data, re-select the AE '*FEVER'* from the dynamic search list with the corrected start date.

Icon Key

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

Figure 1. Icon Key

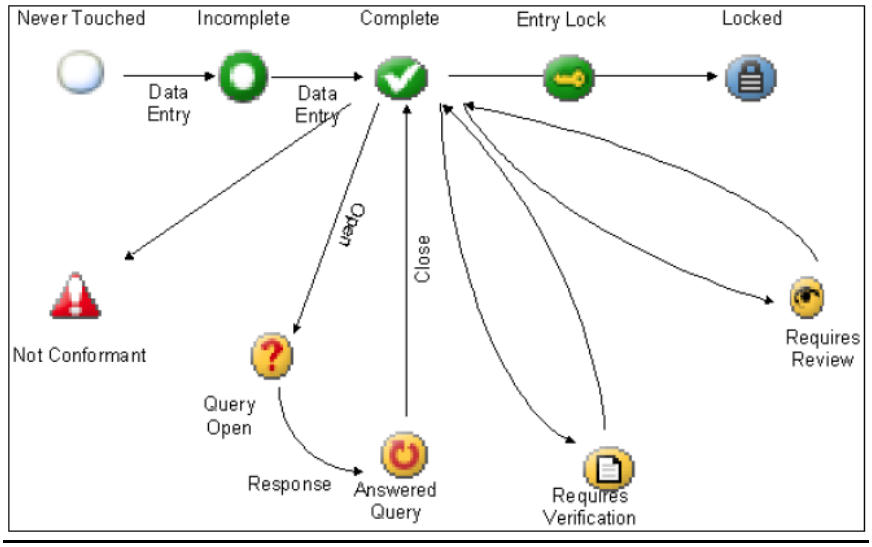


Icon Progression

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

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

Figure 2. Icon Progression



Task Summary

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

Figure 3. Site-Level Task Summary

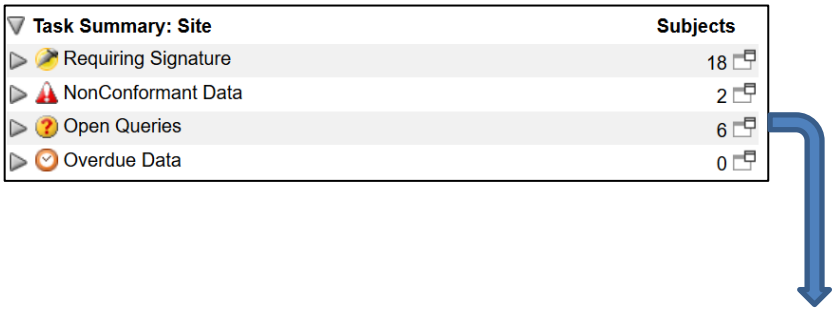
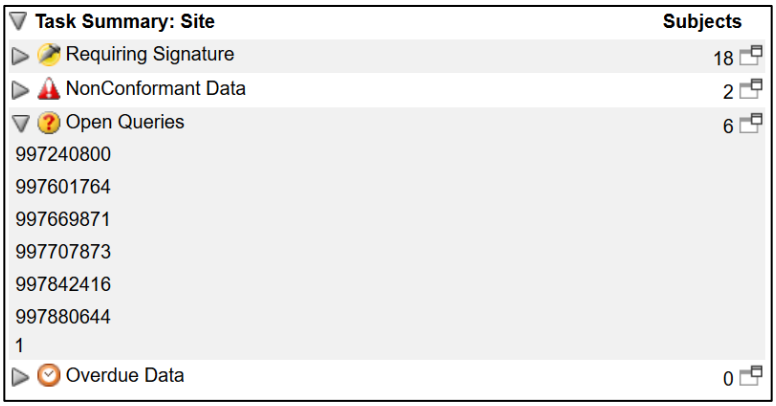
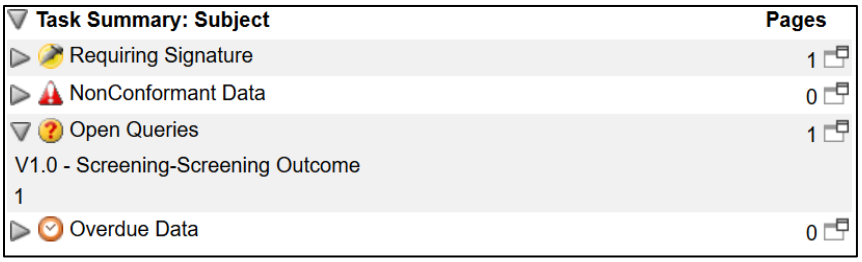


Figure 4. Site-Level Task Summary



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

Figure 5. Subject-Level Task Summary



General Guidelines – Paper CRF Completion

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

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

Recording Dates – Rave Form and/or Paper CRF

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

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

For example, record September 20, 2016 as: 

Recording Time - Rave Form and/or Paper CRF

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

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

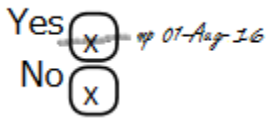
12-hour clock (a.m.)	24-hour clock	12-hour clock (p.m.)	24-hour clock
Midnight	00:00	Noon	12:00
1:00 a.m.	01:00	1:00 p.m.	13:00
2:00 a.m.	02:00	2:00 p.m.	14:00
3:00 a.m.	03:00	3:00 p.m.	15:00
4:00 a.m.	04:00	4:00 p.m.	16:00
5:00 a.m.	05:00	5:00 p.m.	17:00

6:00 a.m.	06:00	6:00 p.m.	18:00
7:00 a.m.	07:00	7:00 p.m.	19:00
8:00 a.m.	08:00	8:00 p.m.	20:00
9:00 a.m.	09:00	9:00 p.m.	21:00
10:00 a.m.	10:00	10:00 p.m.	22:00
11:00 a.m.	11:00	11:00 p.m.	23:00

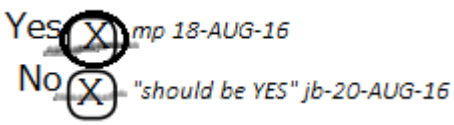
For example, record 2:25 p.m. as: 14 25 24-hour clock

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

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



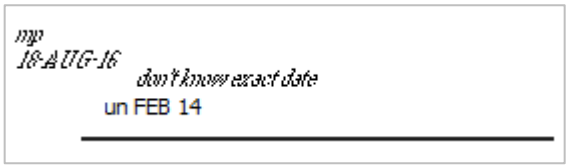
- If the correct answer has previously been crossed out, do the following:
  - circle the correct response,
  - write an explanation in the white space near the response, and
  - initial and date all corrections as shown below:



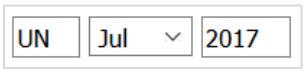
Missing and Unknown Data - Rave Form and/or Paper CRF

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

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



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



Form-Specific Instructions

ACASI Tracking

Purpose:
This form is used to document information about the Audio Computer-Assisted Self Interview (ACASI) at Enrollment and during follow-up.

General Instructions:
This form will be populated under the folders of all visits that require an ACASI survey (please refer to the protocol for the complete listing). It can be added to a folder as needed via ASP or Interim Visit forms.

Field-specific Instructions:

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

Additional Study Procedures

Purpose:
This form is used to record all additional procedures the participant received at his scheduled study visit (e.g., clinically indicated physical exam). Do *not* record any procedures required and performed per protocol on this form. Such procedures should be entered on the relevant CRF within the scheduled visit folder.

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

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

Adverse Event Y/N

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

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

Field-specific Instructions:

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

Adverse Event

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

General Instructions:

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

Field-specific Instructions:

Field	Instructions
Date Reported to Site	• Record the date the site first became aware of the AE. • For lab AEs, record the date the lab result was received. • A complete date is required

Field	Instructions
Adverse event (AE)	• Describe the AE using medical terminology. • Record a diagnosis/anatomical location if available. • Whenever possible, provide a diagnosis instead of listing a cluster of symptoms. If no diagnosis is identified, each symptom must be recorded on a separate AE log line. • If a cluster of symptoms reported on separate Adverse Experience Log lines are later attributed to a single diagnosis, change the earliest reported symptom to the final diagnosis. In addition, inactivate the AE Log lines for the other symptoms by selecting the 'Inactivate' option [Note: Before inactivating the log line, make sure all queries for that AE page have been resolved]. For lab abnormalities, format is (increased/decreased [test name]).
Onset date	At minimum, month and year are required. If day is unknown, enter "UN" for the day. Record one of the following, as appropriate: • The date on which the participant reports first experiencing the AE. • If the AE is discovered during a study visit, record the date of the study visit. • If the AE is an abnormal lab result, record the date on which the specimen was collected.
Visit AE was reported	• Select visit the site first became aware of the AE • If an interim visit, select "Interim Visit".
Is the AE still ongoing?	• Select "Yes" if the AE is continuing at the time it is first reported. • Select "No" if the condition is no longer present or returned to pre-enrollment severity/frequency. • If a participant is taking a medication to control an AE that arose during study participation, it is not considered resolved. • If "Yes", leave Outcome Date blank.
If "No", outcome date	If the AE is not ongoing, please enter an outcome date. At minimum, month and year are required. Record one of the following as appropriate: • The date on which the participant no longer experienced the AE. • The date of the study visit or specimen collection at which the change in status/outcome is first noted.

Field	Instructions
Severity grade	Record the severity grade using the most current version of the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events* (including relevant appendices/addendums) • Grade 1 (Mild) • Grade 2 (Moderate) • Grade 3 (Severe) • Grade 4 (Potentially life-threatening) • Grade 5 (Death)
Relationship to study product	Mark the assessment of the relationship between the AE and the study product. • "Related to PrEP" - reasonable possibility that the AE may be related to the PrEP product participant is on. • "Related to GAHT" - reasonable possibility that the AE may be related to the GAHT product participant is on. • "Related to both PrEP and GAHT" - reasonable possibility that the AE may be related to both PrEP and GAHT products participant is on. • "Not related" - not a reasonable possibility that the AE is related to either study product. Record pertinent details for relationship assessment in comments. For more information, refer to the *Manual for Expedited Reporting of Adverse Events to DAIDS,* most current version.

Field	Instructions

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

Other action(s) taken	• Select "None" or check all that apply. • Select "Medication" only if participant reports taking medication. Report medication(s) on the Concomitant Medications Log. • If "Other", specify relevant details in the "Other, specify" text field provided.

Field	Instructions
Status/Outcome	• ***Recovered/Resolved:*** AE is no longer present or returned to the pre-enrollment severity/frequency. If a participant is taking a medication to control an AE that arose during study participation, it is not considered resolved. • ***Recovering/resolving:*** AE is continuing and has not yet resolved or returned to baseline severity/frequency. • ***Recovered/resolved with sequelae:*** Participant has recovered from the AE, but with remaining effects or impairment. • ***Not recovered/not resolved***: Whenever an AE is continuing at the time of participant termination from the study • ***Fatal:*** Severity of this AE is grade 5. Update any other AEs continuing at the time of death to "Not Recovered/Not Resolved." • ***Severity/frequency increased:*** AE increases in severity or frequency after it has been reported on the AE Log: o On the original AE log line, update the "Status/outcome" field to "severity/frequency increased." Record the date of increase in the outcome field data. o Report the increase in severity or frequency of the AE on a new log line. For this new AE, the "onset date" will be the date that the severity or frequency increased. Update SAE form if applicable. o Note that decreases in severity should not be recorded as new AEs, .
Is this a serious adverse event according to ICH/GCP or protocol guidelines?	• If the AE is a Serious Adverse Event (SAE), complete the subsequent SAE criteria questions. Mark all the SAE criteria that apply. • If the AE is not an SAE, skip to "Has or will this AE be reported as an EAE?". For questions about ICH/GCP guidelines and SAEs, refer to current *Manual for Expedited Reporting of Adverse Events to DAIDS*
SAE/EAE onset date	• Provide the date the adverse event first meets ICH criteria for seriousness • A month and year are required
Has or will this AE be reported as an EAE? **If yes, EAE number**	• For questions about ICH/GCP guidelines and EAE reporting, refer to current *Manual for Expedited Reporting of Adverse Events to DAIDS* • If reported as an EAE (indicated as "Yes"), provide the EAE number and complete any subsequent updates to this form on the applicable EAE form. Refer to form instructions for EAE format. • Enter EAE number in the text field provided.
Comments	Comments are required for every AE. • Record pertinent details for relationship assessments. • When an AE is assessed as "not related," an alternative etiology, or explanation should be provided in the 'Comments' section of the CRF. • Record pertinent clinical information.

CD4 Test Results/Viral Load

To document CD4 and HIV viral load results for HIV infected participants.

General Instructions

Complete this form when collecting CD4 or viral load data or if a participant is HIV positive per Protocol Appendix IV. To add this form to a participant's visit folder, select "Yes" for "Was a viral load done?" on the HIV Test Results CRF. Once the HIV Test Results form is saved, the CD4/Viral Load Results form appears in the visit folder.

Item-specific Instructions

Field	Instructions
Was CD4+ specimen collected for testing?	• If "No" is selected, leave the rest of the CD4+ items blank and move on to the first question in the HIV RNA section.
Specimen collection date	• If CD4 was done enter the date the sample was collected. • A complete date is required.
Absolute CD4+	• Enter the absolute CD4 in units of "cells/mm3". • If sample was unable to be analyzed, mark "Unable to analyze".
Unable to analyze	• Mark this box if the sample was unable to be analyzed.
Was HIV RNA PCR testing completed?	• If "No" is selected, do not complete the remaining items on the form.
Specimen collection date:	• If viral load was done, enter the date sample was collected. • A complete date is required.
Operator	• If a number for the viral load is provided on the lab report, ">", "<", or "=" must be selected.
HIV RNA PCR	• Enter the HIV RNA PCR value in "viral copies/mL". • A maximum of nine digits is allowed.
HIV RNA PCR target not detected	If a lab result says, "HIV RNA target not detected", mark this box. Otherwise, leave blank.
Detected, less than LLQ or LLD	• If a lab result says "Detected, less than lower limit of quantification", mark this box. Otherwise, leave blank.

Field	Instructions
Detected, greater than the upper limit of quantification	• If a lab result says "Detected, greater than the upper limit of quantification", mark this box. Otherwise, leave blank.
Additional CD4 Test Results or Viral Load data collected	• If more CD4 or Viral Load data was collected mark this box. Otherwise, leave blank.

Chemistry Panel

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

General Instructions:

- The lab that collected the specimens used for these tests will automatically be selected from the Lab dropdown list at the top of the form. The units and lab ranges for each result will be populated at the bottom of the form.
  Note: The Demographics eCRF needs to be entered prior to entering data on the Chemistry Panel eCRF because the derived age from the Date of Birth on the Demographics eCRF is used to populate the reference ranges.
- For each lab test (e.g., Serum Chemistries), enter the specimen collection date at the top of the form for that specific test each time this form is completed unless it was not collected.
- For each individual lab result (e.g., AST, ALT, Creatinine), record the numeric results in the appropriate field at the bottom of the form.
- Enter the severity grade at the top of the form for that specific result (if applicable).

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

Lab Result Units and Rounding

- Results should be documented in the standard units of measurement used for this study. If the results from the local lab are not reported in the standard units of measurement, the units will need to be converted using the Lab Conversion Tool on Atlas before entry into the eCRF.

- Note that the following units are equivalent:

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

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

Reporting Severity Grade

- Record the severity grade at the top of the form by selecting from the drop-down menu for each corresponding lab analyte when applicable. If the analyte does not meet criteria for severity grade

1 or greater per the DAIDS Toxicity table (Corrected Version 2.1), select the 'Not gradable' option.

- Enter the severity grade for each specific result:
  - Alkaline Phosphatase
  - AST (SGOT)
  - ALT (SGPT)
  - Total Bilirubin
  - Creatinine
  - Creatinine Clearance
  - Albumin
  - Potassium

- 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 3 or higher lab values on the "Medical History" log or "Adverse Event" log as applicable.

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

Field-specific Instructions:

Field	Instructions
Was a sample collected for serum chemistries?	If "No" is selected, leave the rest of the items on the form blank.
Specimen collection date	Record the date that the specimen was *collected*, not the date results were reported or recorded on the form.

Field	Instructions
Severity grade	• Select laboratory value severity grade (1-4) according to the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events*, most current version. • Select 'Not gradable' for a value that does not meet grading criteria.
Adverse event	Select the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form to be visible in the drop-down list.
Not reportable as adverse event	Select this field if the participant has enrolled in the study but has an acceptable lab value that is outside the normal range and will continue with a sustained lab value that is out of normal range. In this case, an Adverse Event log entry is not expected. Note: This field is not expected to be selected if the severity grade is "Not gradable" because "Not gradable" values are not entered on the AE Log.

Concomitant Medications Y/N

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

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

Field-specific Instructions:

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

Concomitant Medications

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

General Instructions:
- Complete one log line for each reported concomitant medication.
- Add additional log lines by clicking "Add a new Log line".

Field-specific Instructions:

Field	Instructions
Medication name	Record the medication name as reported by the participant. For example, if the participant reports taking a trade name medication report the trade name. If a trade name is not available or not reportable per national guidelines, record the generic name of the medication. Any PrEP or GAHT medications the participant is on during the enrollment process should be noted on the PrEP and GAHT log forms, not the CM form.
Indication	• Record the underlying indication for which the medication was taken. • For health supplements, such as multivitamins, record "general health". • For preventive medications, record "prevention of [insert condition]" (e.g., for flu shot, record "prevention of influenza"). • For recreational drugs, record "recreation".
Check if this medication is a statin/an anti-hypertensive	• If the medication being reported is a statin or an anti-hypertensive type of drug, select the appropriate checkbox, otherwise leave blank.

Date started	• Enter the date the medication was initiated
	• If the participant is unable to recall the exact date, obtain participant's best estimate. At a minimum, the year is required.
	  ○ If the exact day is unknown, enter 'UN' for the day field.
	  ○ If the exact month is unknown, then select 'UNK' for the month field.
	  ○ For example, a partial date may be recorded as: UN-Jan-2010 or UN-UNK-2010
	• For injections
	  ○ If it is a one-time injection, record each injection as a separate entry, with the same date used for date started and stopped.
	  ○ If it is a series of injections, record the date of the first injection as date started and the date of the last injection as the date stopped.
	For contraceptive implants or devices, such as IUDs, record the date the implant or device was inserted.

Date stopped
Or
Ongoing
	• Enter the stop date of this medication if known.
	  ○ A month and year are required at minimum.
	  ○ If the medication is a vaccination, the "Date Started" and "Date Stopped" should be the same.
	  ○ For injectable contraception, record each injection the participant receives throughout the course of the study. The start and stop dates of the injection will be the same.
	  ○ For contraceptive implants or devices, such as IUDs, record the date the implant or device was removed.
	  ○ At the participant's Termination visit, the "Date Stopped" must be recorded for each medication OR the "Ongoing" must be checked. At a minimum, the month and year are required.
	• Select if medication is given on an ongoing basis.

Dose	Record the dose. If the participant does not know the exact dose units (e.g., “250 mg”), record an estimate (e.g., “1 tablet”). For multivitamin tablets or liquids, record the number of tablets or liquid measurement (e.g., “1” pill or “1” tablespoon”) if the exact dosage is unknown. If the dose is unknown, check “Unknown” and leave the dose field blank. When documenting medical devices with no active medication, such as an IUCD, enter the dose as “1”. For topical applications, if exact quantity is not known, record the number of applications instead (e.g., ‘one application’).
Dose Units	Select/record the applicable dose units provided in the drop-down list. If the participant does not know the exact dose units (e.g., “250 mg”), record an estimate (e.g., “1 tablet”). If no information on units is known, select the ‘Unknown’ option. When documenting medical devices with no active medication, such as an IUCD, mark the Dose Unit as ‘Other’ and specify “device” in the “If other dose units, specify” text field provided. For topical applications, if exact quantity is not known, record the number of applications instead (e.g., ‘one application’). If ‘Other’ is selected, specify in the corresponding “If other dose units, specify” text field provided.

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 QM: Every morning QH: Every hour ONCE: Single dose Other: alternative dosing schedule or unknown If 'Other' is selected, specify in the corresponding "If other frequency, specify" text field provided. For injections or single dose medications, frequency should be 'Once', with same date used for start and stop dates. If participant is currently using a contraceptive implant or IUD, select "Other" and indicate "Continuous" in "Specify other" text field.
Route	Select the route from options provided in the drop-down list. If 'Other' is selected, specify in the corresponding "If other route, specify" text field provided. If participant is using an intrauterine device, select "Other" as route and indicate "intrauterine" in the "Specify other" text field. If participant is using an implant, select "Other" as route and indicate "sub-dermal" in the "Specify other" text field.
Taken for Reported AE **If "Yes", select adverse event.**	If "Yes", choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.

Counseling

Purpose: This form documents any counseling that may have occurred at each of the participants' visits.

Field	Instructions
Were any of the following topics discussed at this visit?	• Select "Yes" or "No" • If "Yes", check each type of counseling that occurred. If "No", end form. • Select all topics covered during the counseling session
Indicate which topic areas were covered during this session. Mark all that apply.	Select all topics covered during the counseling session

Date of Visit

Purpose:
This form is used to document information about each follow-up visit.

General Instructions
Complete this form in order to generate the forms required at the current visit as well as to create the next visit folder with its respective Date of Visit CRF. See item level instructions for the data requirements to populate additional visits and forms.

Field-specific Instructions

Field	Instructions
Did the participant complete this visit?	• "Yes" must be answered if at least one assessment within the visit has been completed. This will also populate additional forms required within each visit. • "No" populates the Missed Visit CRF in the current folder.
Visit Date	• A complete date is required.
Did the participant exit/terminate the study at this visit?	• If "Yes" is selected, complete the Study Termination CRF located in the Discontinuations folder. • Even if it is a Missed Visit, this field is required to be answered.
Did participant have any changes or updates to their PrEP at this visit?	• Select "Yes" or "No". • If "Yes", complete the Pre-exposure Prophylaxis Log
Did participant have any changes or updates to their GAHT at this visit?	• Select "Yes" or "No". • If "Yes", complete the Gender Affirming Hormone Therapy Log
Were any new adverse events (AEs) reported at this visit?	• Select "Yes" or "No". • If "Yes", complete the Adverse Event Log

Field	Instructions
Is the participant taking any concomitant medications that have not been previously reported?	• Select "Yes" or "No". • If "Yes", complete the Concomitant Medications Log
Have any protocol deviations been reported at this visit?	• Select "Yes" or "No". • If "Yes", complete the Protocol Deviations Log
Did the participant have any additional procedures at this visit?	• If "Yes" is selected, the Additional Procedures CRF will be populated in the current folder.

Date of Visit – Seroconverter Schedule

Purpose:
This form is used to document information about the Seroconversion Termination Visit.

General Instructions
Complete this form in order to generate the forms required at the current visit. See item level instructions for the data requirements to populate additional visits and forms.

Field-specific Instructions

Field	Instructions
Did the participant complete this visit?	• "Yes" must be answered if at least one assessment within the visit has been completed. This will also populate additional forms required within the visit. • "No" populates the Missed Visit CRF in the current folder.
Visit Date	• A complete date is required.
Were any new adverse events (AEs) reported at this visit?	• Select "Yes" or "No". • If "Yes", complete the Adverse Event Log
Is the participant taking any concomitant medications that have not been previously reported?	• Select "Yes" or "No". • If "Yes", complete the Concomitant Medications Log

Field	Instructions
Have any protocol deviations been reported at this visit?	• Select “Yes” or “No”. • If “Yes”, complete the Protocol Deviations Log
Did the participant have any additional procedures at this visit?	• If “Yes” is selected, the Additional Procedures CRF will be populated in the current folder.

Demographics

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

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

Field-specific Instructions:

Field	Instructions
Date of birth	If the entire date of birth is unknown, record participant’s best estimate. At a minimum year is required.
Age	The age field is calculated automatically based on the “Date of birth” field. No data entry is required.
Sex assigned at birth	This is the sex that the participant was assigned at birth. The default value for this study is “Male”.
Ethnicity Race	Record the participant’s ethnicity and race based on self-definition.

Field	Instructions

Gender	• This response must be self-reported by the participant.
	• Site staff are encouraged to document in chart notes if the participant, during study participation, prefers to be referred to by a specific pronoun or gender.
	• Gender is the social part of being male or female and related to self-identity. Below are descriptions of each gender category:
	  ○ Female: Any person who identifies their gender as female.
	  ○ Transgender female/Transgender Woman (also known as trans female) refers to a person assigned male at birth, but whose gender identity is female or trans-female.
	  ○ Gender nonbinary/Genderfluid/Gender nonconforming: A person whose gender expression is different than gender norms and does not "fit" the male/female categories, regardless of their gender identity or sexual orientation.
	  ○ Another gender identity: Any other gender reported by the participant. Record what the participant reports in the "If 'Another gender identity', specify:" field.

How do you identify your sexual orientation?	Below are descriptions of each sexual orientation: • Bisexual: Attracted to both the same and different sex than yourself • Gay/Lesbian/Homosexual: Attracted to the same sex as yourself • Queer • Straight/Heterosexual: Attracted to a different sex than yourself • Two Spirit • Additional category: Any other sexual orientation reported by the participant. Record what the participant reports in the "If 'Additional category', specify:" field. • Not sure • Prefer not to answer
What is the participant's current employment status?	Select the most appropriate response from the dropdown menu.
What is the participant's highest level of education?	Select the most appropriate response from the dropdown menu.
In the last 6 months, did you have enough money to pay for rent, food, or utilities (gas, electric, phone, etc)?	Select the most appropriate response from the dropdown menu.

Enrollment

Purpose:
This form documents the assigned treatment arm of the participant and tracks if they will participate in the DHI Sub-Study. This CRF must be completed for every participant that has enrolled.

General Instructions:

Complete this form at the time of enrollment.

Field-specific Instructions:

Field	Instructions
Treatment Arm	This field auto-populates with assigned treatment arm once a participant has been randomized.
Will this participant participate in DHI Sub-Study?	Required for all participants to answer "Yes" or "No". If "Yes" selected, the appropriate forms and folders for the DHI Sub-Study will be populated.

Fasting Lipids Test Results

Purpose: This form is used to provide data on the participant's fasting lipid profile.

General Instructions:

- To generate this form at a follow-up visit where tests are not normally required, select 'Fasting Lipids Test Results' on the Additional Study Procedures form.
- The lab that collected the specimens used for these tests will automatically be selected from the Lab dropdown list at the top of the form. The units and lab ranges for each result will be populated at the bottom of the form.
  Note: The Demographics eCRF needs to be entered prior to entering data on the Fasting Lipid Test 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, 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., Total Cholesterol, HDL), record the numeric results in the appropriate field at the bottom of the form.
- Enter the severity grade at the top of the form for that specific result (if applicable).

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

Lab Result Units and Rounding

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

- Note that the following units are equivalent:

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

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

Reporting Severity Grade

- Record the severity grade at the top of the form by selecting from the drop-down menu for each corresponding lab analyte when applicable. If the analyte does not meet criteria for severity grade

1 or greater per the DAIDS Toxicity table (Corrected Version 2.1), select the 'Not gradable' option.

- Enter the severity grade for each specific result:
  - Total Cholesterol
  - Triglycerides
  - LDL Cholesterol

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

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

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

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

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

- Record any Grade 1 or higher lab values on the "Medical History" log or "Adverse Event" log as applicable.

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

Field-specific Instructions:

Field	Instructions
Date of collection	Record the date that the specimen was *collected*, not the date results were reported or recorded on the form.
Severity grade	• Select laboratory value severity grade (1-4) according to the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events*, most current version. • Select 'Not gradable' for a value that does not meet grading criteria.
Adverse event	Select the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form to be visible in the drop-down list.

Field	Instructions
Not reportable as adverse event	Select this field if the participant has enrolled in the study but has an acceptable lab value that is outside the normal range and will continue with a sustained lab value that is out of normal range. In this case, an Adverse Event log entry is not expected. Note: This field is not expected to be selected if the severity grade is "Not gradable" because "Not gradable" values are not entered on the AE Log.

Gender Affirming Hormone Therapy Y/N

Purpose:
This form is used to trigger the Gender Affirming Hormone Therapy log in Rave.

General Instructions:
This form is present in the "Ongoing Logs" folder in Rave and is completed whenever there is a status change in their gender affirming hormone therapy (i.e., the participant starts or stops a hormone therapy).

Field-specific Instructions:

Field	Instructions
Is the participant using GAHT?	• If "Yes" is selected, then the Gender Affirming Hormone Therapy log appears dynamically in the "Ongoing Logs" folder.

Gender Affirming Hormone Therapy Log

Purpose:
This form documents all gender affirming hormone therapies that are used by the participant during the study. This includes therapies that are sourced outside of the study.

General Instructions:
- Complete one log line for each reported gender affirming hormone therapy.
- Add additional log lines by clicking "Add a new Log line".

Field-specific Instructions:

Field	Instructions
Therapy name	Select the therapy type from the dropdown menu.
Dose	Record the dose number.

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. For topical applications, if exact quantity is not known, record the number of applications instead (e.g., ‘one application’). If ‘Other’ is selected, specify in the corresponding ‘If “Other”, specify’ text field provided.
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 QM: Every morning QH: Every hour ONCE: Single dose Other: alternative dosing schedule or unknown If ‘Other’ is selected, specify in the corresponding “If other frequency, specify” text field provided. For injections or single dose medications, frequency should be ‘Once’, with same date used for start and stop dates.
Route	Select the route from options provided in the drop-down list. If ‘Other’ is selected, specify in the corresponding “If other route, specify” text field provided. If participant is using an implant, select “Other” as route and indicate “sub-dermal” in the “Specify other” text field.
How was GAHT obtained?	Select the source from options provided in the drop-down list. If ‘Other’ is selected, specify in the corresponding “If “Other”, specify” text field provided.

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

Ongoing	• Select "Ongoing" if medication is given on an ongoing basis. • Update this field once a product stoppage has been reported.
What kind of product stoppage is being reported?	Select the category of the product stoppage. Product Hold – Clinic or Management (Safety included) decision to hold treatment. Permanent Discontinuation – This prescription is ending for an indicated reason, not necessarily ending product use in the study. Participant Reported – A stoppage of treatment that is not initiated by the study team, such as misplacing pills or a drug holiday.
Date of product stoppage as reported by participant	• Enter the stop date of this medication if known. ○ Day, month, and year are required.
Why was product stopped?	• Select the reason for stopping from the dropdown list. All stopped therapies must have a reason provided.
Date participant resumed study product:	• Enter the date the participant reported resuming study product. • Day, month, and year are required
Product Hold **Date when this study product hold was initiated:**	• Enter the date the product hold started. • Day, month, and year are required
Why is the study product being held?	• Select the reason for product hold from the dropdown list. All stopped therapies must have a reason provided.
If product hold was associated with an adverse event, select the applicable AE1:	• Choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.

If product hold was associated with an adverse event, select the applicable AE2:	• Choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.
If product hold was associated with a new or updated concomitant medication, select applicable medication(s):	• Choose the applicable CM log entry from the drop-down list. Note: The applicable CM must first be entered on the CM form in order to be visible in the drop-down list.
Date participant resumed study product:	• Enter the date the participant resumed study product. • Day, month, and year are required
Is this a permanent discontinuation? **Date stopped**	• Enter the date this prescription was discontinued. • A month and year are required
Primary reason for ending study product use	When ending this specific therapy type, select the reason for stopping from the dropdown list. All stopped therapies must have a reason provided.
If "Other", specify:	If primary reason for ending study product use was “Other” specify in this field.
If "Investigator decision", specify:	If primary reason for ending study product use was “Investigator decision” specify in this field.
If "Adverse event", select applicable adverse event #1	Choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.
If "Adverse event", select applicable adverse event #2	If more than one AE is related choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.
Is this a permanent discontinuation from study product?	Select “Yes” if the stoppage of product is a permanent discontinuation of study product for the duration of the study. Select ‘No’ if it is only a change to the prescription and the participant is still on a form of GAHT for the study.

Hematology

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

General Instructions:

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

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

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

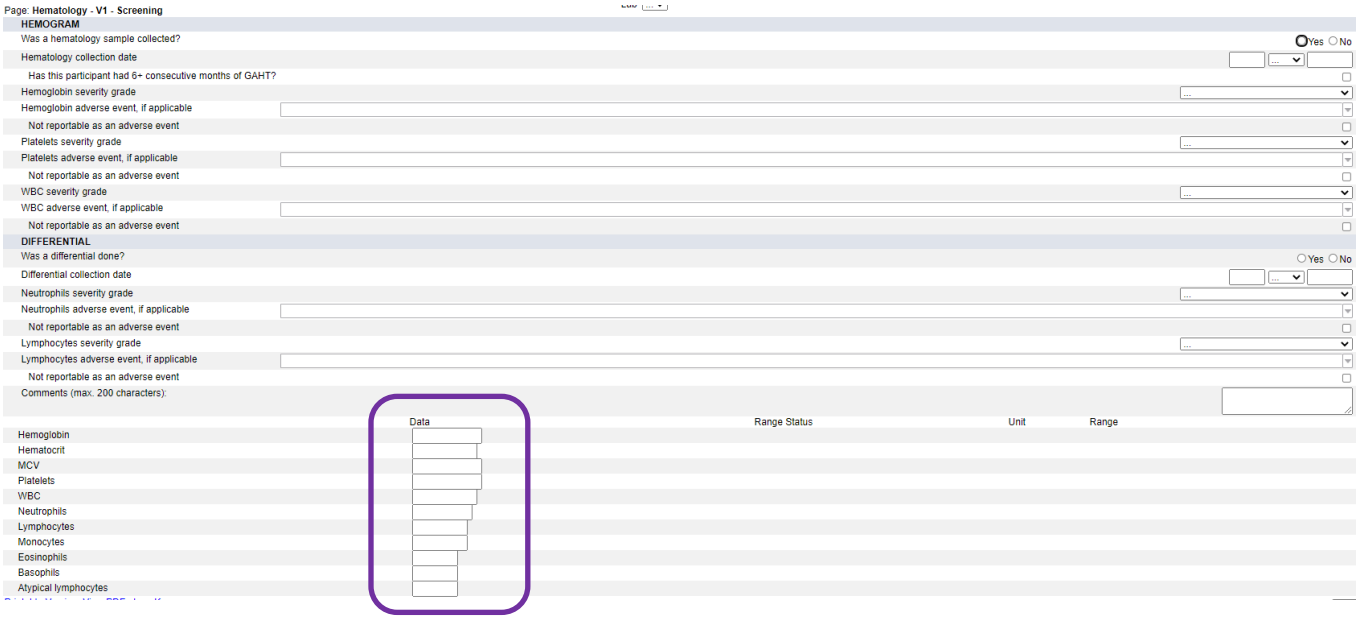
During follow-up, if a test result(s) recorded on this form indicates that the participant has a new (or increased severity) laboratory-confirmed infection or diagnosis, this infection/diagnosis must be recorded as an adverse event on an Adverse Event (AE) Log form if it meets AE reporting criteria.

Entering Laboratory Results

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

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

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



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

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

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

Lab Result Units and Rounding

- Results should be documented in the standard units of measurement used for this study. If the results from the local lab are not reported in the standard units of measurement, the units will need to be converted using the Lab Conversion Tool on Atlas before entry into the eCRF.

- Note that the following units are equivalent:

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

Reporting Severity Grade

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

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

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

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

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

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

- Record any Grade 3 or higher lab values on the "Medical History Log" or "Adverse Event Log" eCRF(s) as applicable.

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

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

Field-specific Instructions:

Field	Instructions
Hematology collection date	Record the date that the specimen was *collected*, not the date results were reported or recorded on the form.
Has this participant had 6+ consecutive months of GAHT?	Select this checkbox if the participant has been on GAHT for 6 or more months consecutively at the time of sample collection.
Severity grade	• Select laboratory value severity grade (1-4) according to the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events*, most current version. • Select 'Not gradable' for a value that does not meet grading criteria.
Adverse event	Select the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form to be visible in the drop-down list.
Not reportable as adverse event	Select this field if the participant has enrolled in the study but has an acceptable lab value that is outside the normal range and will continue with a sustained lab value that is out of normal range. In this case, an Adverse Event log entry is not expected. Note: This field is not expected to be selected if the severity grade is "Not gradable" because "Not gradable" values are not entered on the AE Log.

Hepatitis B Vaccination Tracking

Purpose:
This form is used to document Hepatitis B vaccination status at enrollment.

General Instructions:
Complete this form at the Enrollment Visit. Record if the participant is vaccinated for Hepatitis B and at what date the vaccination occurred. 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 Hepatitis Test Results form. If the participant enrolls, the updated results should be submitted into the study database.

Field-specific Instructions:

Field	Instructions
Is participant vaccinated for Hepatitis B?	Select 'Yes' or 'No'. If 'No', the date of vaccination does not need to be filled out.

Hepatitis Test Results

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

General Instructions:
Complete this form at the Screening and Enrollment Visits 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 Hepatitis Test Results form. If the participant enrolls, the updated results should be submitted into the study database.

Field-specific Instructions:

Field	Instructions
Was a sample collected for Hepatitis B Surface Antigen (HBsAG) testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for HBsAG testing do not need to be completed.
Date of collection	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
Hepatitis B Surface Antigen (HBsAG)	Select "Positive" or "Negative" or "Indeterminate".
Was a sample collected for Hepatitis B Surface Antibody (HBsAb) testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for HBsAb testing do not need to be completed.
Date of collection	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
Hepatitis B Surface Antibody (HBsAb)	Select "Positive" or "Negative" or "Indeterminate".
Was a sample collected for Hepatitis B Core Antibody (HBcAb) testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for HBcAb testing do not need to be completed.
Date of collection	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
Hepatitis B Core Antibody (HBcAb)	Select "Positive" or "Negative" or "Indeterminate".
Was a sample collected for Hepatitis C Antibody (HCAb) testing?	Select 'Yes' or 'No'. If 'No', then the remaining items for HCAb testing do not need to be completed.
Date of Collection	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
Hepatitis C Antibody (HCAb)	Select "Positive" or "Negative" or "Indeterminate".

HIV Test Results

Purpose

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

General Instructions

- Complete this form at protocol-specified visits and if clinically indicated at any other visit.
- Only one specimen collection date can be recorded on the HIV test results CRF, any re-testing with a new sample requires an additional new log line. Please do not remove previous test results.
- Every HIV Test result should have a corresponding plasma entry on the Specimen Collection form with matching dates.
- Record HIV specimen test results on this form as they become available from the local lab.
- If test results are discordant or discrepant at a time point, refer to the HIV algorithm for next steps regarding additional HIV testing.
- **If a sample is positive, all confirmatory testing for that sample will be put on the same HIV Test Results Log form in the same visit folder (new log lines will be added for each specimen collected).**

Item-specific Instructions

Field	Instructions
Specimen Collection Date	• Enter the date the specimen was collected. • A complete date is required.
Was this sample collected for additional testing?	• Select “Yes”, if this is a re-draw for confirmation of a previous reactive or positive result. • Select “No” if this blood draw is not to confirm prior test results.
HIV Rapid test result	• Select “Reactive/Positive”, “Non-reactive/Negative”, “Invalid”, or “Not Done”, as appropriate. [Note: Per the HIV Testing Algorithm, this is always required at Screening]
HIV Laboratory based immunoassay test result	• Record the results of the laboratory-based HIV immunoassay here. • Select “Reactive/Positive”, “Non-reactive/Negative”, “Invalid”, or “Not Done”. [Note: Per the HIV Testing Algorithm, this is always required at Screening]

Field	Instructions
HIV RNA Qualitative test result	• If an HIV RNA Qualitative test is done, record the results here. • Select “Reactive/Positive”, “Non-reactive/Negative”, “Invalid”, or “Not Done”. • If an HIV RNA Qualitative test is not done, select “Not Done”.
Was a viral load done?	• If “Yes” is selected, complete the HIV RNA section on the CD4 Test Results/Viral Load CRF
Final HIV Status	• This is a required field. • Select final HIV Status based on local testing. • If final HIV status is “Reactive/Positive”, refer to the protocol and SSP for next steps. • If final HIV status is “Non-reactive/Negative”, proceed with the visit. • If final status is “Additional testing required”, add a new log line to the current HIV Test Results form and record additional test results.

Hormone Tests

Purpose:
This form is used to document the participant’s hormone test results.

General Instructions:
Record specimen test results on this form as they become available from the local lab. This form is required at V2 – Enrollment and all follow-up visits through V3 – V8. Record if a specific test was done by entering ‘Yes’ or ‘No’ for item “Was a [hormone] sample collected?”. If ‘No’ is selected, leave the applicable sub-items blank.

Field-specific Instructions:

Field	Instructions
Date of Collection	Record the date that the hormone test was collected and NOT the date the results were reported or recorded within the form for this visit. A complete date is required.
Test Result	Record the result of the applicable test as recorded on the lab results form.
Testosterone	Select "<" or "=" as reported by the lab results form. For example, if a participant's Testosterone value is reported as < 0.25, then select the "<" symbol. If there is no lower limit of detection (i.e., absence of the "<" symbol, then select the "=" symbol.
Estradiol	Select "<" or "=" as reported by the lab results form. For example, if a participant's estradiol value is reported as < 15 pg/mL, then select the "<" symbol. If there is no lower limit of detection (i.e., absence of the "<" symbol, then select the "=" symbol.

Inclusion Exclusion Criteria

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

General Instructions:
Complete this form for each participant screened in HPTN091. Complete this form when it is determined whether the participant will enroll in the study. If the participant has a second screening attempt, update this form with data from the second screening attempt (do not complete a new form).

Field-specific Instructions:

Field	Instructions
Has the participant screened before?	Select “Yes” if this is a rescreening attempt.
If Yes, enter the first RAVE PTID assigned	Enter the PTID previously assigned to the participant in their previous screening.
Did the participant meet all eligibility criteria?	Select ‘Yes’ or “No’ to indicate if the participant met all eligibility criteria.
Eligibility Status	Record the applicable eligibility status by selecting from the drop-down menu. If participant met all eligibility criteria, and Eligibility Status is ‘Eligible and enrolled’, then end of form.
Date "Eligible and Enrolled" or "Incomplete screening"	Record the date of the eligibility decision.
Date "Eligible/Not Enrolled" or "Ineligible"	Record the date of the eligibility decision.
Select reason(s) why participant is ineligible	If participant is deemed ineligible per inclusion or exclusion criteria, use the drop-down menu to select a reason and save. Note that it may be necessary to scroll to the right to access drop down menu. Alternatively, the first few characters of each criterion can be keyed in to bring up a more selective list. If there is more than one reason for ineligibility per inclusion or exclusion criteria, click on the “Add a new Log line” and select another reason. Add all applicable reasons as appropriate.
If investigator decision, specify	If E7 was selected, record reason in the specify text box. If any other response was selected, leave this field blank.
If eligible but participant declined enrollment, specify reason.	Record the reason an eligible participant did not enroll. This text field should only be completed if “Eligibility status” is ‘Eligible, but participant did not enroll’.

Informed Consent

Purpose: This form is used to document the administrative details of the participant’s informed consent.

General Information/Instructions
Complete this form when the participants complete a consent form (or re-consent form). Add additional log lines as appropriate. This form is in the Screening folder.

Field-specific instructions:

Field	**Instructions**
Date initial informed consent sign	Record the date that the participant signed the informed consent form. A complete date is required.

Field	Instructions
Consent type	Select which consent is applicable. For the first consent of the study choose Screening and Enrollment. For additional consents or reconsents select the most applicable option.
Consent version	Enter the version number of the consent the participant signed. For example: 1.0.
Did the participant consent to long-term specimen storage and future testing?	Select “Yes” or “No” or “Not applicable”
Did the participant consent to IDI Sub-study?	Select “Yes” or “No” or “Not applicable”
Did the participant consent to DHI Sub-study?	Select “Yes” or “No” or “Not applicable” if DHI Sub-study not being done at that site

Interim Visit

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

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

Field-specific Instructions:

Field	Instructions
Interim 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 Discontinuation of Study Product eCRF within the Discontinuations folder.
Did the participant exit/terminate the study at this visit?	Select 'Yes' or 'No'. If 'Yes', then complete a Study Termination eCRF within the Discontinuations folder.
Did participant have any changes or updates to their PrEP at this visit?	Select "Yes" or "No". If "Yes", complete the Pre-exposure Prophylaxis Log
Did participant have any changes or updates to their GAHT at this visit?	Select "Yes" or "No". If "Yes", complete the Gender Affirming Hormone Therapy Log
Were any new adverse events (AEs) reported at this visit? If yes, complete the AE Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one Adverse Event (AE) was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable AE(s).
Is the participant taking any concomitant medications that have not been previously reported? If yes, complete the Concomitant Medications Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one concomitant medication was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable CM(s).
Have any protocol deviations been reported at this visit? If yes, complete the Protocol Deviations Log.	Select 'Yes' or 'No'. Select 'Yes' if at least one protocol deviation was newly completed for this visit. Navigate to the Ongoing Logs folder to complete an entry for the applicable PD(s).

Reason for interim visit	Select all that apply.
If other, specify	If "Other" is selected for reason for interim visit, then specify the reason in the text field provided.
Were vital signs (such as weight) taken at this visit?	Select "Yes" or "No". If "Yes", add Vital Signs form.
Mark all forms completed at this visit.	Select the applicable procedures that were completed at the study visit. The applicable eCRF(s) will then be added to the participant's visit folder. For example, if a physical exam was performed, select the checkbox corresponding to **Physical Exam**.

Medical History Y/N

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

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

Field-specific Instructions:

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

Medical History

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

General Instructions:

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

Field-specific Instructions:

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

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

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

Missed Visit

General Instructions:

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

Field-specific Instructions:

Field	Instructions
Target visit date	Record the target date of the visit that was missed.
Reason visit was missed	Select the reason for the missed visit from the dropdown menu. If "Other" is selected, please specify the reason.

Participant Identifier

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

Field-specific Instructions:

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

Participant Receipt

Purpose:
Complete this form when a participant is transferring to another clinic/site within this study.

General Instructions
This form is completed by the receiving site only when the participant being transferred has provided informed consent at the receiving study clinic/site. Marking "Participant Receipt" under the Additional Forms section on any Date of Visit or Interim Visit form will add the Participant Receipt form to the current visit folder.

Item-specific Instructions

Field	Instructions
Name of receiving study site:	• Select the applicable site from the dropdown list. • Site should match the name of receiving site on the Participant Transfer form.

Name of transferring study site:	• Select the applicable site from the dropdown list. • Site should match the name of transferring site on the Participant Transfer form.
Date informed consent signed at receiving site	• A complete date is required.
Date participant received at receiving site	• A complete date is required.

Participant Transfer

Purpose:
Complete this form when a participant is transferring to another study clinic/site.

General Instructions
This form is completed by the transferring site (the site the participant is leaving). Marking "Participant Transfer" under the Additional Forms section on the Date of Visit or Interim Visit form will add the Transfer form to the visit folder.

To complete a participant transfer, contact the SCHARP Clinical Data Manager (CDM) to confirm all outstanding queries are resolved before the participant is transferred to a new site.

Item-specific Instructions

Field	Instructions
Name of transferring study site	• Select the applicable site from the dropdown list.
Name of receiving study site	• Select the applicable site from the dropdown list.
Visit of last completed contact with participant	• Select the applicable visit from the dropdown list. • If "Interim Visit" is selected, record interim visit code in the text box provided.
Date participant records were sent to receiving study site	• A complete date is required.

Patient Health Questionnaire

Purpose:
This form documents the baseline mental health of the participant. The score is auto calculated from the participant's answers to the questionnaire. The following chart will be used as a guide to interpret the depression scale.

Score	Severity
0-4	None-minimal
5-9	Mild
10-14	Moderate
15-19	Moderately Severe
20-27	Severe

General Instructions
Complete all fields at enrollment and based on their experiences over the last 2 weeks.

Field-specific Instructions

Field	Instructions
For the first 9 questions	• Select “Not at all”, “Several days”, “More than half the days”, or “Nearly every day”

PHQ Calculated Total	• Auto calculated after the form is saved
	• If the score is indicative of depressive symptoms according to the table above, enter it into the Medical History Log
	  ○ In the description of medical event, enter “Depressive symptoms” and include the PHQ score
	  ○ For the question “Is the condition/event gradable”, select “No” since this is a self-reported value and do not enter a grading.

If you mentioned any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	• Select “Not difficult at all”, “Somewhat difficult”, “Very difficult”, or “Extremely difficult”

Peer Health Navigation Tracking Y/N

Purpose:
This form is used to trigger the Peer Health Navigation Tracking log in Rave.

General Instructions:
This form is present in the “Ongoing Logs” folder in Rave and is completed whenever there is a Peer Health Navigation interaction to report.

Field-specific Instructions:

Field	Instructions
Is the participant engaging with Peer Health Navigation?	• If “Yes” is selected, then the Peer Health Navigation Tracking log appears dynamically in the “Ongoing Logs” folder.

Peer Health Navigation Tracking

Purpose:
This form documents all Peer Health Navigation encounters between participant and Peer Health Navigator.

General Instructions:
- Complete one log line for each reported Peer Health Navigation encounter.
- Add additional log lines by clicking “Add a new Log line”.

Field-specific Instructions:

Field	Instructions
Date of completion	Date log line was completed
Visit Log completed at	Select the applicable visit from the dropdown list. If completing the form between study visits select the upcoming scheduled visit. Revise if a different visit occurs first (e.g. an Interim Visit occurs prior to scheduled study visit). If “Interim Visit” is selected, record interim visit code in the text box provided.
Was this encounter a PHN Session?	Select ‘Yes’ if the encounter being reported is one of the scheduled PHN sessions as defined in protocol section 6.9.1 (see LOA 1)
Type of Encounter	Select the applicable type of encounter being reported from the drop-down list.
Duration of Encounter	Select the applicable time duration of encounter being reported from the drop-down list.
Number of Encounters (number of contacts on a given day)	Enter in the number of this type of encounter that occurred on that day (i.e., the number of messages that day)
Encounter initiated by	Select who initiated the encounter, the participant or the Peer Health Navigator
Content of Encounter Mark all that apply	Select all applicable topics covered during encounter. Complete “If "Other", specify:” if “Other” is selected.

Physical Exam

Purpose:
This form documents physical exam findings.

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

Field-specific Instructions

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

PK Dose Time

General Instructions:
The PK Dose Time CRF will auto-populate at each required visit. Use this CRF to record the Daily Observed Treatment (DOT) times and dates leading up to the DHI Sub-Study sample collection days. The DOT days are auto populated.

Field-specific Instructions:

Field	Instructions
DOT Day	• The days leading up to PK Collection Day at populated on the form
Was dose observed? **If “No”, record why dose was not observed**	• Select “Yes” or “No” • If a dose was not observed, record the reason.
Observed Dose date	• A complete date is required
Observed Dose time	• Use a 24-hour clock (00:00-23:59)

PK Specimen Collection

General Instructions:
The PK Specimen Collection CRF will auto-populate at each required visit. The specimen type fields are auto populated.

Field-specific Instructions:

Field	Instructions
PK Specimen type	• Specimen types are auto populated
Was specimen collected?	• Select "Yes" or "No" • If "Yes" record collection date and time • If "No" record reason why not collected
Specimen collection date	• A complete date is required
Specimen collection time	• Use a 24-hour clock (00:00-23:59)
Was sample stored? **If "No", record why sample was not stored**	• Select "Yes" or "No" • If a sample was not stored, record the reason.

Pre-exposure Prophylaxis Y/N

Purpose:
This form is used to trigger the Pre-exposure Prophylaxis log in Rave.

General Instructions:
This form is present in the "Ongoing Logs" folder in Rave and is completed whenever there is a status change in their Pre-exposure Prophylaxis treatment (i.e., the participant starts or stops a Pre-exposure Prophylaxis treatment).

Field-specific Instructions:

Field	Instructions
Is the participant taking PrEP?	• If "Yes" is selected, then the Pre-exposure Prophylaxis log appears dynamically in the "Ongoing Logs" folder.

Pre-exposure Prophylaxis Log

Purpose:
This form documents all Pre-exposure Prophylaxis treatments that are used by the participant during the study. This includes treatments that are sourced outside of the study.

General Instructions:
- Complete one log line for each reported Pre-exposure Prophylaxis treatment.
- Add additional log lines by clicking "Add a new Log line".

Field-specific Instructions:

Field	Instructions
Medication name	Select the PrEP type from the dropdown menu.
How was PrEP obtained?	Select the source from options provided in the drop-down list. If 'Other' is selected, specify in the corresponding "If "Other", specify" text field provided.

Date started	• Enter the date the medication was initiated
	• If the participant is unable to recall the exact date, obtain participant's best estimate. At a minimum, the year is required.
	  ○ If the exact day is unknown, enter 'UN' for the day field.
	  ○ If the exact month is unknown, then select 'UNK' for the month field.
	  ○ For example, a partial date may be recorded as: UN-Jan-2010 or UN-UNK-2010

Ongoing	Select "Ongoing" if medication is given on an ongoing basis. Update this field once a product stoppage has been reported.
What kind of product stoppage is being reported?	Select the category of the product stoppage. Product Hold – Clinic or Management (Safety included) decision to hold treatment. Permanent Discontinuation – This prescription is ending for an indicated reason, not necessarily ending product use in the study. Participant Reported – A stoppage of treatment that is not initiated by the study team, such as misplacing pills or a drug holiday.
Date of product stoppage as reported by participant	• Enter the stop date of this medication if known. ○ Day, month, and year are required.
Why was product stopped?	• Select the reason for stopping from the dropdown list. All stopped therapies must have a reason provided.
Date participant resumed study product:	• Enter the date the participant reported resuming study product. • Day, month, and year are required
Product Hold **Date when this study product hold was initiated:**	• Enter the date the product hold started. • Day, month, and year are required

Why is the study product being held?	• Select the reason for product hold from the dropdown list. All stopped therapies must have a reason provided.
If product hold was associated with an adverse event, select the applicable AE1:	• Choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.
If product hold was associated with an adverse event, select the applicable AE2:	• Choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.
If product hold was associated with a new or updated concomitant medication, select applicable medication(s):	• Choose the applicable CM log entry from the drop-down list. Note: The applicable CM must first be entered on the CM form in order to be visible in the drop-down list.
Date participant resumed study product:	• Enter the date the participant resumed study product. • Day, month, and year are required
Is this a permanent discontinuation? **Date stopped**	• Enter the date this prescription was discontinued. • A month and year are required
Primary reason for ending study product use	When ending this specific therapy type, select the reason for stopping from the dropdown list. All stopped therapies must have a reason provided.
If "Other", specify:	If primary reason for ending study product use was “Other” specify in this field.
If "Investigator decision", specify:	If primary reason for ending study product use was “Investigator decision” specify in this field.
If "Adverse event", select applicable adverse event #1	Choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.

If "Adverse event", select applicable adverse event #2	If more than one AE is related choose the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form in order to be visible in the drop-down list.
Is this a permanent discontinuation from study product?	Select “Yes” if the stoppage of product is a permanent discontinuation of study product for the duration of the study. Select ‘No’ if it is only a change to the prescription and the participant is still on a form of PrEP for the study.

Protocol Deviation Y/N

Purpose:
This form is used to document if a protocol deviation has occurred.

Generation Instructions
This form is present within the “Ongoing Logs” folder and needs to be marked only once.

Item-specific Instructions

Field	Instructions
Have any protocol deviations occurred?	If “Yes” is selected, the Protocol Deviation Log will appear in the Ongoing Logs folder and can then be completed.

Protocol Deviation Log

Purpose
This form documents reportable protocol deviations identified for study participants during the implementation of HPTN091.

General Information/Instructions
Complete this form each time a reportable protocol deviation is identified. Complete one page per protocol deviation when entering in the study database. If a deviation applies to more than one PTID complete a Protocol Deviation Log for each PTID that is affected; each PTID needs to have a record of the Protocol Deviation on their own Deviation Log. To add an additional deviation within Medidata Rave, click “Add a new Log line” to add an additional log line.

Reportable protocol deviations are defined by the HPTN (HPTN MOP Section 12) as individual incidents, trends or omissions that result in:

- Significant added risk to the participant
- Non-adherence to significant protocol requirements
- Significant non-adherence to GCP

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.
Has or will this deviation be reported to local IRB/EC?	• Select "Yes" or "No".
Has or will this deviation be reported to DAIDS as a critical event?	• Select "Yes" or "No".
Type of deviation	• Select the applicable deviation from the search list. *See drop-down menu for the types of deviations.*
Description of deviation	• Use text field to briefly describe specific details of deviation.
Plans and/or action taken to address the deviation	• Use text field to provide a brief description of plans to address deviation.
Plans and/or action taken to prevent future occurrences of the deviation	• Use text field to provide a brief description of plans to prevent similar deviations in the future.
Deviation reported by (staff name):	• Enter name of staff member that reported the deviation.

Randomization

Purpose:
This form completes the randomization process for enrolling a participant.

General Instructions:
Complete this form when a participant is ready to be randomized and enrolled in the study.

Field-specific Instructions:

Field	Instructions

Is the participant ready to be randomized?	Select "Yes" or "No", saving the form will complete Randomization. A statement saying Randomization was successful will appear.

Screening Date of Visit

Purpose:
This form is used to document the date of the first screening procedure(s).

Generation Instructions
This form is present within the screening folder and needs to be entered once.

Item-specific Instructions

Field	Instructions
Screening visit date	Enter date of the first screening procedure(s)

Social Impact Y/N

Purpose:
This form is used to document if a social impact has occurred.

Generation Instructions
This form is present within the "Ongoing Logs" folder and needs to be marked only once.

Item-specific Instructions

Field	Instructions
Has the participant experienced any social impacts related to study participation?	• If "Yes" is selected, the Social Impact Log will appear in the Ongoing Logs folder and can then be completed.

Social Impact Log

Purpose:
This form is used to document information about reported social impacts.

General Instructions
Complete this form when a participant reports a social impact. A social impact is defined as a participant reported non-medical adverse consequence or benefit as a result of participation in the study. Refer to the SSP, section 10, for more information on reporting Social Impacts.

Item-specific Instructions

Field	Instructions
Date reported to site	• A complete date is required.

Field	Instructions
Concisely describe social impact	• A maximum of 200 characters is allowed in this text field.
Onset date	• Enter the date on which the impact began/occurred. • A complete date is required.
Reported at visit code	• Select the visit from the dropdown menu • If "Interim visit", enter the interim visit code.
Social impact	• Select appropriate social impact type from the dropdown list. • If "Other – Had other problems not covered in the codes above" is selected, specify social impact type in the "If other, specify" text field provided.

Specimen Collection and Storage

General Instructions:
Refer to the SSP Section 8 for the number and type of specimens or aliquots required at each visit.

The Specimen Collection and Storage CRF will auto-populate at each required visit, but it can also be added through the Additional Study Procedures CRF. On each form, the specimen type fields are auto populated.

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

Field-specific Instructions:

Field	Instructions
Specimen type	• Specimen types are auto populated
Was specimen collected?	• Select "Yes" or "No" • If "Yes" record collection date and time. • If "No" record reason why not
Specimen collection date	• A complete date is required
Specimen collection time	• Use a 24-hour clock (00:00-23:59)

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

STI Tests

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

General Instructions:
Complete this form at required protocol visits and as clinically 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 Test Results form. If the participant enrolls, the updated results should be submitted into the study database.

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

Field-specific Instructions:

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

Field	Instructions
Collection Date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
N. gonorrhea – urine test result	Select “Detected”, “Non-detected”, “Equivocal”, or “Invalid”
C. trachomatis – urine test result	Select “Detected”, “Non-detected”, “Equivocal”, or “Invalid”
Was a rectal swab sample collected for N. gonorrhea or C. trachomatis testing?	Select ‘Yes’ or ‘No’. If ‘No’, then the remaining items for rectal swab N. gonorrhea and C trachomatis testing do not need to be completed. Proceed to “Was a sample collected for Syphilis testing?”
Collection Date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
N. gonorrhea – rectal swab test result	Select “Detected”, “Non-detected”, “Equivocal”, or “Invalid”
C. trachomatis – rectal swab test result	Select “Detected”, “Non-detected”, “Equivocal”, or “Invalid”
Was a sample collected for Syphilis testing?	Select ‘Yes’ or ‘No’. If ‘No’, then the remaining items for Syphilis testing do not need to be completed.
Collection date	Record the date that the specimen was collected, NOT the date the result was reported or recorded on the form for this visit. A complete date is required.
Algorithm used	Select either Traditional or Reverse to reflect algorithm used for syphilis testing
Treponemal	Select if Treponemal test was Not Done or the appropriate result option for the test.
Non-Treponemal	Select if Non-Treponemal test was Not Done or the appropriate result option for the test.
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. If titer not done, select the “N/A” checkbox.
Second Treponemal test	Select if Second Treponemal test was Not Done or the appropriate result option for the test.
Second Non-Treponemal test	Select if Second Non-Treponemal test was Not Done or the appropriate result option for the test.
Syphilis titer	Record the titer for Second Non-Treponemal test in the format 1: XXXX. When completing this form in Medidata Rave, please include the “1:” in the same field for the syphilis titer.

Field	Instructions
Third Treponemal test	Select if Third Treponemal test was Not Done or the appropriate result option for the test.

Study Termination

Purpose:
This form documents participant's termination from the study.

General Instructions:
Complete this form for each enrolled participant at either the scheduled exit/end of study visit or when the participant is confirmed to no longer be participating in the study. This form is in the Discontinuations folder.

Field-specific Instructions:

Field	Instructions
Date of Study Exit	A complete date is required.
Primary reason for completion/ discontinuation	Select one reason for study termination from the drop-down menu.
If "Other", specify	If the primary reason is Other', then provide additional details in the text field provided.
If death, enter date of death	If the primary reason for study non-completion is 'death', provide the date of death. A complete date is required.
If "Adverse Event", select applicable adverse event	Select the applicable Adverse Event from the list of AEs 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.
Does participant have a desire for future co-located Gender Affirming Hormone Therapy?	Select appropriate response for participant's desire for future co-located Gender Affirming Hormone Therapy.

Supplemental HIV Results

Purpose
This form is used to document additional HIV testing used to evaluate seroconversion.

General Instructions
Use this form as needed following HIV algorithm per the SSP.

Item-specific Instructions

Field	Instructions
HIV 1/2 Discriminatory Assay	
Not Done	• Mark if HIV 1/2 Discriminatory Assay was not done. • Skip to "Laboratory Reported HIV Interpretation" Section.

Field	Instructions
Specimen Collection Date	• If HIV 1/2 Discriminatory Assay was done, enter the date the specimen was collected. • A complete date is required.
Assay Result	• Select assay result from dropdown list.
Other assay result:	• If "Other" is selected from the drop-down list, provide other assay results here.
Comments	• Maximum allowed characters: 200.
Laboratory Reported HIV Interpretation	
Not reported	• Mark if Laboratory Reported HIV Interpretation was not performed or not reported by lab.
Interpretation	• Select interpretation result from dropdown list.
Other interpretation	• If "Other" is selected from the drop-down list, provide other interpretation(s) here.
Comments	• Maximum allowed characters: 200.
HIV DNA	
Not performed/Not reported by Lab	• Mark if HIV DNA test was not performed or not reported by lab. • Provide comments at the end of the form.
Specimen Collection Date	• If HIV DNA test was done, enter the date the specimen was collected. • A complete date is required.
DNA Result	• Select HIV DNA result from dropdown list.
Detectable DNA result:	• If DNA Result is "Detectable DNA result" record the value in copies per million cells. • Value format expected XXX.XX

Field	Instructions
Comments	• Maximum allowed characters: 200.

Urinalysis

Purpose:
This form is used to document the participant's urinalysis test results.

General Information/Instructions

Complete this form at required protocol visits and as clinically indicated during the study.

Item Specific Instructions

Field	Instructions
Was a sample collected for urine tests?	• If "No" is selected, leave the remaining items on the form blank.
Date of collection	• Enter the date the specimen was collected. • A complete date is required.
Protein (Urine)	• Select the applicable result from the dropdown menu.
Protein (Urine) Severity Grade	• Select a severity grade (1-4) or "not gradable" from the dropdown list. • If a severity grade is selected, the test result field must not be blank. • Enter any grade 3 or higher events into the AE log or Medical History log as appropriate
Protein (Urine) Adverse Event	• If test is linked to a reported AE, select the AE in the dropdown list provided. • An AE form must be completed before it can be selected on the Urinalysis form.

Field	Instructions
Glucose (Urine)	• Select the applicable result from the dropdown menu.
Glucose (Urine) Severity Grade	• Select a severity grade (1-4) or "not gradable" from the dropdown list. • If a severity grade is selected, the test result field must not be blank.
Glucose (Urine) Adverse Event	• If test is linked to a reported AE, select the AE in the dropdown list provided. • An AE form must be completed before it can be selected on the Urinalysis form.

Vital Signs

Purpose:
These forms document vital signs.

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

Field-specific Instructions:

Field	Instructions
Were vital signs done?	Select 'Yes' or 'No'.
Date of Assessment	Enter the date the participant's vital signs were measured. A complete date is required.
Height	Enter the participant's height in centimeters. The value must be reported in whole numbers (e.g., 180 cm).
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 blood pressure	Enter the participant's systolic blood pressure in mmHg (e.g., 120 mmHg).
Diastolic blood pressure	Enter the participant's diastolic blood pressure in mmHg (e.g., 60 mmHg).
Blood pressure severity grade	• Select laboratory value severity grade (1-4) according to the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events*, most current version. Select 'Not gradable' for a value that does not meet grading criteria.
Blood Pressure adverse event, if applicable	Select the applicable AE log entry from the drop-down list. Note: The applicable AE must first be entered on the AE form to be visible in the drop-down list.
Pulse	Enter the participant's pulse in beats per minute (e.g., 60 beats/min).
Rate of respiration	Enter the participant's respiratory rate in breaths per minute (e.g., 14 breaths/min).

Change History

Summary of Changes to Study CRF Completion Guidelines

Version		Affected Section(s) or Form(s)	Summary of Revisions
Number	Date		
1.0	14Dec2020	All sections	Original Document
1.1	25May2021	Demographics, GAHT Log, Hematology, Hormone Tests, Informed Consent, PrEP Log, Vital Signs;	Updated per Migration #1
2.0	01Jun2021	Final Version	Finalized updates for Migration #1
2.1	20Oct2022	Draft updates per Migration #3	
3.0	24Feb2023	Final Version	Finalized updates per Migration #3