Section 5. Study Procedures Overview

5.1 Overview of Section 5

This section provides a brief overview of requirements and procedures to be conducted during study implementation of Protocol Version 3.0 (OLE). Additional procedure-specific details can be found in the HPTN 084 Protocol version 3.0 and relevant SSP manual sections (e.g. clinical, laboratory, data management procedures, etc. for Protocol version 3,0).

5.2 Study Overview

All participants who agree to remain on either open label TDF/FTC or CAB LA for the OLE will be offered an additional 48 weeks of study participation.

1) Step 4a- Procedures for Participants Initially Randomized to TDF/FTC Who Elect to Move to OL CAB LA with Optional Oral Lead-in first
2) Step 4b- Procedures for Participants Initiating or Re-starting CAB LA without the Optional Oral Lead-in; the Initial Dose Visit
3) Step 4c- Procedures for Participants on Maintenance Doses of CAB LA or TDF/FTC
4) Step 4d- Procedures for Pregnant/Breastfeeding Participants
5) Step 5- Procedures for Participants Taking OL TDF/FTC for 48 Weeks after Premature CAB LA discontinuation

Refer to the protocol for further details.

5.3 Study Visits

Protocol-required visits: Steps 4 and 5 have protocol-required study visits, which are described in Appendix VIII of the Protocol: Procedures for Offering Open Label (OL) Cabotegravir- The Next Part of HPTN 084

For each required study visit, there is an allowable visit window specifying on which study days (Day 0) the visit is "allowed" to be completed. The allowable visit windows are contiguous from visit to visit, and do not overlap. Within each allowable visit window, there is a target visit window. These windows are outlined in Section 13 of the OLE SSP. Efforts should be made to conduct study visits within the target visit window and may be conducted over multiple days within the target visit window if necessary (see

below regarding Split visits); however, if it is not possible to complete the required visit within the target visit window, the visit may be completed within the allowable visit window.

Interim visits:

Interim contacts and visits may take place between regularly-scheduled visits. These contacts/visits may be done at participant request (e.g., to receive further counseling or clarify any questions) or as deemed necessary by the IoR or designee at any time during the study (e.g., to follow-up on an adverse event). Procedures to be performed during these contacts/visits will be specific to the reason for the additional PPT interaction.

Split visits:

A Split visit is defined as visits conducted over multiple days. Ideally, all procedures specified by the protocol to be performed at a visit will be completed at a single visit on a single day. In the event that all required procedures cannot be completed on a single day (e.g., because the participant must leave the study site before all required procedures are performed), the remaining procedures may be completed on subsequent day(s) within the **allowable target visit window**. When this occurs, the visit is considered a split visit. All case report forms completed for a split visit are assigned the same visit code (even though the dates recorded on the case report forms may be different).

Considerations for Split Visits:

- HIV testing is required on the second day of a split visit only if it was not already performed on the first day of that split visit OR if study product will be dispensed/administered on that day – even if the required HIV testing was performed at the first part of the split visit. Please remember, the required HIV testing must be performed and resulted prior to the administration of study product.

Missed visits:

Efforts should be made to contact any participant who does not attend a protocol-required visit prior to the end of the target window period. A Missed Visit e-CRF should be completed to document the missed visit at the end of the allowable window period.

In general, when a visit is missed altogether and a participant reports to the site in the interim or for the next scheduled visit, the procedures from the missed visit that are not also required for the current visit should be performed. In the case of a missed injection visit, the CMC should be contacted for guidance regarding whether the injection should be given at another visit (and before the next scheduled injection).

Because of the nature of study procedures, all visits must be completed at the study clinic only. Sites should contact the CMC regarding any questions about procedures performed outside of the study clinic if the situation arises (e.g., participant is incapacitated and

cannot report to the clinic). Details regarding the CMC are described in SSP manual Section 9.

5.3.1 Study Visit Procedures

- Refer to Protocol Appendix VIII for the Schedule of Evaluations.

- Participants may withdraw from the study for any reason at any time. IoRs may, in consultation with the HPTN 084 CMC, withdraw participants before their scheduled termination visit to protect their safety, and/or if participants are unable or unwilling to comply with study procedures. The CMC also should be consulted regarding procedures to be performed in the case of early termination (e.g., final HIV testing, etc.), if a participant is willing to undergo such procedures.

- In general, participants should not be withdrawn from the study except in the case of a) explicit withdrawal of consent by the participant; b) death; or c) extreme/unusual circumstances to protect participant safety. Any such safety-related participant terminations should only be implemented after consultation with the Protocol Chair, Division of AIDS (DAIDS) Medical Officer, Statistical and Data Management Center (SDMC) Protocol Statistician, representatives from the Laboratory Center (LC), the Leadership and Operations Center (LOC) Clinical Research Manager (CRM), and others. Consultation is conducted through the CMC alias.

5.4 Participant Transfers

During the course of the study, participants may leave the area where they enrolled. If they move to the vicinity of another HPTN 084 study site, they should be encouraged to transfer to that study site and continue study participation. To accomplish this, study staff at both sites will complete the participant transfer process. The same process should be followed for temporary or permanent transfers.

Upon identifying the need for a participant transfer to another site, the transferring site is responsible for notifying the HPTN LOC, HPTN SDMC, the HPTN (LC) and the DAIDS Protocol Pharmacist (see Section 1.2 of the SSP manual for contact information). The transferring site is responsible for notifying the site to which the participant wishes to transfer (the "receiving site"). After the logistical details of the transfer have been agreed upon, the following steps will be completed:

- The transferring site will explain the transfer arrangements to the participant and obtain written permission for the release of information that will authorize the transfer of his study records to the receiving site.

- Both the transferring and receiving sites should follow the instructions for participant transfers within Medidata Rave in Appendix IV of the SSP manual.

- The transferring site will ship **certified copies*** of all of the participant's study

records to the receiving site via courier or overnight mail service. The transferring site will track the shipment and the receiving site will confirm receipt of the shipment with the HPTN LOC, SDMC, and the transferring site. The receiving site will verify receipt of said materials with the transferring site. At this point in time, follow-up of the participant becomes the receiving site's responsibility.

- The transferring site will complete the Participant Transfer e-CRF.
- The transferring site will email the HPTN LC representative confirming transfer to the new site. The transferring site will retain archived samples for the participant unless otherwise instructed by the HPTN LC.
- Study drug supply should be discussed with the DAIDS Protocol Pharmacist in cases of participant transfer.
- The receiving site will establish contact with the participant, obtain a copy of the original screening and enrollment consent (and any others), along with his/her informed consent to continue in the study (have the participant sign a consent at the receiving site).
- Upon receipt of the Participant Transfer form and confirmation that the transferring IoR has signed off on the participant's eCRF casebook, the SDMC will re-map the participant's ID number (PTID) and any e-CRFs in the study database to reflect the change in study site follow-up responsibility. This will ensure that future questions and/or QCs will be sent to the appropriate site. The participant's original ID number, treatment-arm assignment, and follow-up visit schedule will remain unchanged.
- The receiving site will complete a Participant Receipt eCRF to complete the transfer process.
- If the participant returns to the clinic where she/he enrolled, the same process should be followed to complete the transfer process. However, the certified copies to be sent to the enrolling site will only include those applicable to the visits conducted at the non-enrolling site. This is because the original records are at the enrolling site and the only records needed would be those for visits conducted at the non-enrolling site.

Note: If it is unlikely that the participant can return to the clinic where she enrolled and she is not close to another HPTN 084 clinic to transfer, the site should complete Missed Visit Forms for each visit the participant does not complete in case the participant is later able to rejoin the study. In cases where the site strongly suspects that the participant will never return to the study, the CMC should be contacted to discuss possible termination.

* See the DAIDS Site Clinical Operations and Research Essentials (SCORE) Manual https://www.niaid.nih.gov/research/daids-score-manual for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (listed under

Certified Copies) for requirement for certification. https://www.niaid.nih.gov/sites/default/files/score-source-documentation-requirements.pdf

5.5 Protocol-Required and Interim Visits at Sites Other Than Where Participants Enrolled

During the course of the study, while it is likely rare, it may happen that a participant is temporarily (for a few days, or a week or more) in another location where there is an HPTN 084 clinic other than the one in which they originally enrolled (their "home clinic"). If the participant is in this temporary location during a protocol-required visit or when she requires medical attention, these protocol-required or interim visits may be conducted at the alternative clinic ("temporary clinic") if both sites have an SOP in place to cover this situation. In addition, the local IRB/EC must have agreed to the procedures outlined in the site-specific SOP, which must cover the following areas:

- Informed consent will need to be re-administered at the temporary clinic.
- A method to transfer study information from the temporary to the home clinic.
- A standard method of communication between the two sites prior to the initiation of any procedure, for clinical information, final decision-making about primary care, and determination of the duration of time during which care and visits will be conducted at the temporary clinic.
- Procedures for the management of drug dispensation and accountability should be developed with the HPTN 084 Protocol Pharmacist.