Section 8. Study Product Considerations

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8.1 Overview of Section 8

This section provides instructions to the investigational pharmacist and the study staff for the proper management of study products used in HPTN 083-01 including storage, dispensing, administration, and record keeping of pharmacist-prepared, participant-specific study products. In addition to these specifications, the participating clinical research sites must adhere to the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trial Networks* and the site Pharmacy Establishment Plan approved by the DAIDS Pharmaceutical Affairs Branch (PAB). These specifications and the protocol take precedence over this document.

8.1.1 Chain of Custody

In addition to the requirements of the investigational pharmacist for maintaining the Study Product Accountability Record and participant-specific study product accountability record, if the investigational pharmacist is not dispensing study products directly to participants, the non-pharmacy study staff must help to ensure the chain of custody of study product by completing any applicable sections and/or the following documents in their entirety, as directed for each participant. Sites may choose to use the documents listed below for this purpose or develop their site-specific documents as long as these include all the required information.

- Record of Dispensation of Participant-Specific Study Product to Non-Pharmacy staff (Appendix Ia)
- Record of Return of Participant-Specific Study Product by Non-Pharmacy Staff (Appendix Ib)

In an instance when the participant returns their oral study products at any time during the study for reasons such as study product discontinuation, damage, spills, inappropriate storage, etc.; the return must be reconciled by documenting on the participant-specific study product accountability record when applicable and by following the instructions in the DAIDS pharmacy guidelines.

Each study site must designate its dispensing method(s) in HPTN 083-01 Standard Operating Procedures (SOPs) for participant-specific study product supply during clinic visits. These SOPs should be developed with input from both pharmacy and clinic staff. They must be provided to the DAIDS Protocol Pharmacist for review prior to study activation and may only be modified after consultation with the DAIDS Protocol Pharmacist.

8.1.2 Step 1: Enrollment/Week 0

Oral cabotegravir:

The investigational pharmacist will prepare and dispense participant-specific labeled oral cabotegravir 30 mg to the participant directly or will dispense it to the clinical staff to give to the participant. If oral cabotegravir is given to the study participant by the clinical staff, the Record of Dispensation of Participant-Specific Study Product to Non-Pharmacy Staff (Appendix Ia) must be completed.

Each participant is to receive a 5-week supply of oral cabotegravir upon enrollment. Each bottle of oral cabotegravir contains 30 tablets per bottle. Therefore, two bottles of oral cabotegravir should be dispensed in Step 1. Dosing should begin on the day of Enrollment.

8.1.3 Step 1: Weeks 2 and 4

No additional dispensing procedures are noted for these visits unless a participant requires additional oral cabotegravir at the Week 2 visit (e.g., participant lost or damaged the previously dispensed study product). Participants are to return with their bottles at the Week 2 and Week 4 visits. Any returned study product still in the bottles will be counted and that number will be captured in the participant's study chart and on the electronic case report form (e-CRF). Returned product at the Week 5 visit will also be counted and recorded by the PoR on the product accountability logs.

8.1.4 Step 2: Weeks 5, 9, 17, 25, 33

Injectable CAB LA:

The investigational pharmacist will prepare and dispense participant-specific labeled injectable CAB LA as outlined in the protocol.

The investigational pharmacist will dispense the participant-specific labeled injectable CAB LA to the clinic where it will be administered to the participant **within two hours**

from the time the syringe was prepared. The Record of Dispensation of Participant-Specific Study Product to Non-Pharmacy Staff (Appendix Ia) must be completed.

Injectable CAB LA will be administered as one 3 mL (600 mg) injection IM in the gluteal muscle at 8-week intervals after a 4-week load (Time points: **Weeks 5, 9, 17, 25, 33)**

8.1.5 Step 3: Oral PrEP or CAB LA Injections

8.1.5.1 Step 3 - Oral PrEP (Last Injection +8 Weeks, +12 Weeks, +24 Weeks, +36 Weeks)

If oral PrEP is chosen by the participant for Step 3, the investigational pharmacist will prepare and dispense locally sourced participant-specific labeled oral Tenofovir/Emtricitabine 200mg/300mg (Truvada®) or FDA-approved generic TDF/FTC to eligible participants directly, or will dispense it to the clinical staff to give to the participant. If locally sourced participant-specific labeled oral Truvada® or generic TDF/FTC is given to the study participant by the clinical staff, the Record of Dispensation of Participant-Specific Study Product to Non-Pharmacy Staff (Appendix Ia) must be completed.

Dispense a 3-months' supply of oral TDF/FTC in the original bottles, according to ONE of the following schedules:

- If all five CAB LA injection visits were completed: dispense TDF/FTC at Week 34, then every 3 months thereafter

- If participant received at least one CAB LA injection but discontinued injections prior to receiving all five injections: dispense TDF/FTC at 12 weeks post last injection, at 24 weeks post last injection, and at 36 weeks post last injection

The investigational pharmacist and site study staff must maintain close communication to ensure that adequate supply of participant's oral TDF/FTC is prescribed and dispensed. The participant should have a buffer of oral TDF/FTC supply in case the participant's next scheduled clinic visit date is rescheduled within the allowable study visit window per protocol (buffer enough for 90 days should suffice).

Follow Appendix III of the HPTN 083-01 protocol.

8.1.5.2 Step 3 - Continued CAB LA Injections (Last Injection +8 Weeks, +16 Weeks, +24 Weeks, +32 Weeks, +40 Weeks, +48 Weeks)

Continue CAB LA Injections as in Step 2 (see 8.1.4 above) and follow Appendix IV of the HPTN 083-01 protocol.

8.1.6 Short-Term Storage of Participant-Specific Study Product in the Clinic

Oral cabotegravir and oral Tenofovir/Emtricitabine (Truvada®) or generic TDF/FTC:

If the investigational pharmacist is not dispensing directly to participants and participant-specific oral study product is stored in the clinic for a short period of time (e.g., while the participant is undergoing the study visit procedures for a particular visit), the study product must be stored at the conditions described per protocol or per the package insert, in an area that is always locked and is accessible only to investigational pharmacists and authorized study staff as specified in the site's SOP and Pharmacy Establishment Plan.

If the participant or site staff believes that the study product storage temperature has reached outside the specified storage temperatures range per protocol or per the package insert, the PoR at the site must be contacted immediately so that she/he can dispense the appropriate participant-specific study product again as needed. In addition, the HPTN 083-01 DAIDS Protocol Pharmacist must be notified by email that this occurred, the reason that it occurred, and the corrective mechanism in place to assure that it will not occur again. This email should come from the Investigator of Record or designee and should copy the PoR at the site. The PoR is responsible for ensuring that the temperature in the storage cabinet is reviewed and recorded daily. These records must be reviewed by the PoR on a monthly basis. The monthly temperature records must be provided to the PoR to be maintained in the pharmacy. These records must be available for review by site monitors.

Injectable CAB LA:

Injectable CAB LA will be prepared in the pharmacy and delivered to the study clinic. Prepared injectable CAB LA in a syringe must be administered to a participant as soon as possible and **within two hours of preparation by the investigational pharmacist. The prepared CAB-LA in a syringe must be stored at controlled room temperature between 20 to 25° C (68.0 to 77.0° F) from the time it is prepared to the time it is administered (within two hours).** If injectable CAB LA is unable to be administered within two hours from the time it was prepared, the PoR at the site must be contacted immediately so that she/he can prepare and dispense the participant-specific injectable CAB LA study product again as needed. In addition, the HPTN 083-01 DAIDS Protocol Pharmacist must be notified by email that this occurred, the reason that it occurred, and the corrective mechanism in place to assure that it will not occur again. This email should come from the Investigator of Record or designee and should copy the PoR at the site, as well as the HPTN 083-01 Clinical Management Committee (083-01cmc@hptn.org).

8.2 Labeling and Accountability

8.2.1 Study Product Labeling

The investigational pharmacist must place a participant-specific label on the prepared study products in accordance with the local regulations and by following instructions provided in the manual, *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks.*

8.2.2 Study Product Accountability

The investigational pharmacist must maintain complete records of the study products received and subsequently dispensed, whether they are received from the NIAID CRPMC (oral cabotegravir, CAB LA) or from other sources (locally sourced Truvada® or generic TDF/FTC).

At US CRSs, all unused study products must be returned to the NIAID CRPMC (or as otherwise directed by the sponsor) after the study is completed or terminated. The investigational pharmacists at non-US CRSs must follow the instructions provided in the manual *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks*, in the section Study Product Management Responsibilities, for the destruction of unused study-provided products.