Section 8. Medication Considerations

8.1 Overview of Section 8

This section provides instructions to the Pharmacist of Record (PoR) and the clinic staff for the proper management of study-supplied medications used in HPTN 094 including ordering, storage, dispensing, transport, administration, and record keeping. For study-supplied medications, the participating clinical research sites must adhere to the HPTN 094 protocol, HPTN 094 SSP, the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trial Networks* as well as the procedures outlined in the site's Pharmacy Establishment Plan approved by the DAIDS Pharmaceutical Affairs Branch (PAB). If a site pharmacy will also dispense non-study-supplied medications used in HPTN 094, it is recommended that the pharmacy develop equivalent procedures for management of the non-study-supplied medication.

Note that all the medication that will be provided as part of this study will be US Food and Drug Administration (FDA)-approved medications used for their FDA-approved indication; this study does not involve any investigational study products or evaluation of a new indication. As well, there is no blinding of treatment assignment in this study, so all drugs will be provided open label to participants.

8.2 Study-Supplied Medication

Throughout this section, the term "study-supplied medication" refers to medications that will be centrally supplied by the study to sites, which will be the following:

- emtricitabine/tenofovir disoproxil fumarate 200 mg/300 mg (FTC/TDF, Truvada®)
- emtricitabine/tenofovir alafenamide 200 mg/25 mg (FTC/TAF, Descovy®)
- bictegravir/emtricitabine/tenofovir alafenamide 50 mg/200 mg/25 mg (BIC/FTC/TAF, Biktarvy®)

Any additional medication to be utilized for study conduct will not be supplied through the study and must be locally procured by the site. Study staff should refer to *Table 2- Overview of Medical Care Provided in the Mobile Unit for Intervention Arm Participants* in the protocol for detail

about the expected scope of medications that may be prescribed, administered or dispensed by clinicians in the mobile unit. Some examples of such medications include:

- prescriptions for alternative antiretroviral therapy (ART) or pre-exposure prophylaxis (PrEP) regimens
- prescriptions, administration, or dispensation of medications for opioid use disorder (MOUDs)
- prescriptions, administration, or dispensation of treatment for sexually transmitted infections (STI)
- prescriptions for minor acute illnesses or infections
- prescriptions for oral contraception

8.3 Ordering and Receiving Study-Supplied Medication

Study medications may be obtained by the site via multiple sources, including locally obtained/sourced by the site.

The following study-supplied medications will be available from CRPMC for the site PoR to order after a site successfully completes initial DAIDS protocol registration to the study protocol:

- Emtricitabine/tenofovir disoproxil fumarate 200 mg/300 mg (FTC/TDF, Truvada®)
- Emtricitabine/tenofovir alafenamide 200 mg/25 mg (FTC/TAF, Descovy®)
- Bictegravir/emtricitabine/tenofovir alafenamide 50 mg/200 mg/25 mg (BIC/FTC/TAF, Biktarvy®)

Upon receipt of a shipment, the PoR will verify the content of the shipment against the Study Product Request Packing Slip from the CRPMC. Once verified, the PoR will log into COSMOS and complete the Shipment Receipt Confirmation. If the study-supplied medications listed above are missing, damaged, inconsistent with the information on the packing list, or the storage conditions have not been maintained, the PoR should contact the HPTN 094 DAIDS Protocol Pharmacist and the CRPMC immediately by email (preferred), facsimile, or telephone.

If the study-supplied medication appears damaged, the PoR should not dispense it until she/he has been notified in writing by the HPTN 094 DAIDS Protocol Pharmacist or the CRPMC that the study-supplied medication is safe for use. A hard copy of such notification and the signed verification of receipt should be retained in the site pharmacy records.

8.4 Accountability of Study-Supplied Medication

In accordance with the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks*, the PoR is responsible for maintaining detailed records regarding all study-supplied medications used in HPTN 094. Accountability Record forms are provided in the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trial Networks*. The PoR is responsible for documenting all information related to study-supplied medication receipt, storage, dispensing, and

final disposition. The PoR is responsible for maintaining all study-supplied medication-related documents including original prescriptions, shipping invoices, and return log in the pharmacy file.

8.4.1 Chain of Custody: Study-Supplied Medication

Chain of custody procedures must be implemented to document dispensing of all study-supplied medication. Pharmacy and clinical staff must work together to ensure the chain of custody log is maintained by completing any applicable sections of the following document in its entirety, as directed, for each participant.

The sites may choose to use the document listed below for this purpose or develop their own site-specific documents, incorporating the required elements.

- HPTN 094 Record of Dispensation of Study-Supplied Medication from Pharmacy Staff to Mobile Unit or to Participants (and, as Applicable, Returns to Pharmacy) (Appendix A)

The site pharmacy must maintain chain of custody documentation for all study-supplied medications dispensed to clinic staff to be stored on the mobile unit, all study-supplied medications dispensed directly from pharmacy-designated staff directly to participants, and any medication that is returned to the pharmacy.

At any time during HPTN 094 study conduct, a participant may return medications that were dispensed to them for reasons such as therapy discontinuation, damage, spills, inappropriate storage, etc. to the site. If a participant returns a study-supplied medication, the return must be reconciled by documenting on the participant specific accountability record when applicable and returned to the CRPMC by following the instructions in the DAIDS pharmacy guidelines.

The clinic staff working on the mobile units must maintain chain of custody documentation for medication provided to participants. This can be documented by clinic staff documenting the provision in a continuation line of the pharmacy chain of custody log or on a separate document.

8.4.2 Chain of Custody: Non-Study-Supplied Medication

Sites must maintain chain of custody documentation for all locally sourced (non-study-supplied) medications that include where a prescription is sent, receipt of the prepared prescription from the pharmacy and documentation of provision of the medication to the participant. Documentation should include details such as name of medication prescribed, quantity, and dates and times when a prescription was sent to a pharmacy, received from the pharmacy, and provided to the participant.

Sites may choose to use the document listed below for this purpose or develop their own site-specific documents, incorporating the required elements.

- HPTN 094 Record of Prescription and Provision of Non-Study-Supplied Medication from Mobile Unit Staff to Participants (Appendix B)

8.5 Transportation of Study-Supplied Medications to and from Clinic Mobile Units

All study supplied medication that will be transported to and from the clinic mobile unit must be done so in a secure manner. Staff should monitor temperatures during transport of study supplied medication to ensure compliance with manufacturer's temperature recommendations and document whether medications were received in good condition and within temperature range. Pharmacy and clinic staff must maintain chain of custody documentation for all study supplied medication (refer to section 8.4 for more information).

8.6 Storage of Study-Supplied Medications

All study-supplied medications must be stored in the original bottles and in accordance with the manufacturer's recommendations. Study provided medications must be stored in a limited-access area in the pharmacy, which is accessible only to authorized pharmacy staff as specified in the site SOP and Pharmacy Establishment Plan. Storage temperatures must be monitored and documented per the site study specific SOP and the PAB approved Pharmacy Establishment Plan.

If study-supplied medication is dispensed to clinic staff to be transported to and stored on the mobile unit, all study-supplied medications must be stored in a limited-access area on the mobile unit which is accessible only to authorized pharmacy and clinic staff as specified in the site SOP. Study-supplied medication must be transported and stored in accordance with the manufacturer's temperature recommendations. Temperatures in all storage areas must be monitored with, at minimum, a min/max thermometer. Temperatures must be monitored and documented per the site study specific SOP.

If a temperature excursion occurs in these storage areas, it must be documented appropriately and the PoR at the site must be notified immediately to determine whether medication needs to be replaced. All temperature logs from the storage areas in the mobile unit must be provided to the PoR at least monthly to be reviewed by the PoR and maintained in the pharmacy. The PoR must document that they have reviewed the temperature storage logs from the mobile unit at least monthly. These records must be available for review by site monitors.

8.7 Dispensing and Provision of Study Medication

Study-supplied medication will be dispensed by the PoR only upon the written/signed order of the Investigator of Record or other clinician listed on the current investigator's agreement who is authorized to prescribe in the site's jurisdiction. Designated clinic staff members may assist in the preparation of prescriptions by adding the participant ID number and verifying and initialing that informed consent has been provided prior to signing by the prescriber. The authorized prescriber must sign and date the prescription only after all required information has been completed for the pharmacist to dispense study products. Study supplied FTC/TDF, FTC/TAF and BIC/FTC/TAF must be prepared and dispensed by the site pharmacist in original whole bottles. The oral tablets should not be transferred from the original bottle to a prescription vial for dispensation by the site pharmacist. All pharmacist-prepared participant-specific medication must be labeled in accordance with the local regulations and the manual, *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks.*

Non-study-supplied medication that needs to either be dispensed or provided to the mobile unit will be done so per local institutional SOPs and pharmacy laws and regulations. It the responsibility of the Site Investigator and Site Pharmacist of Record to ensure that all procedures related to dispensing of non-participant-specific medication adhere to all local, state, and regulatory rules and regulations and that all staff that perform activities perform them according to their licensure and training.

It is expected that the clinic staff and site pharmacy will work together to allow the site pharmacy adequate time to prepare study medication in advance of expected need and/or participant expected visits with the site clinic staff on the mobile unit. The site pharmacist and site clinic staff should maintain close communication to ensure that adequate supply of participant-specific and non-participant-specific study medication is prescribed, dispensed and/or provided to the clinic staff. The site pharmacy must record all dispensations to a participant or clinic staff on the Pharmacy Accountability Logs and Participant-specific Study Log.

8.7.1 Pharmacist-Prepared, Participant-Specific Labeled Medication:

Depending on the specific medications to be dispensed and local institutional and pharmacy requirements, it is expected that pharmacist-prepared, participant-specific study medication will be provided to participants through one or more of the following general procedures that may be adapted locally:

- Dispensed to appropriate clinic staff by the pharmacy staff at the beginning or during workday and stored on the mobile unit in anticipation of a visit scheduled with the participant. If the medication is not provided to the participant by the end of the day for any reason, it will be returned to the pharmacy by the end of the day.
- Provided directly to the participant at the mobile unit in the field by pharmacy-designated staff for immediate and direct dispensation to the participant, with no storage on the mobile unit.
- Delivered to the prescribing clinician at the mobile unit in the field for immediate injection by the clinician, with no storage on the mobile unit.

8.7.2 Non-Participant-Specific Medication:

Non-participant-specific medications may need to be stored on the mobile unit for point-of-care provision to participants by clinic staff. These medications may be dispensed from the site pharmacy to the appropriate clinic staff or obtained through other means per local institutional procedures and regulations. All non-participant-specific medication not provided to a participant by the end of the day must be removed from the mobile unit and either returned to the site pharmacy (if originally provided by the pharmacy) or stored appropriately within clinic per manufacturer's guidelines.

- If allowable per local institutional policies and pharmacy laws and regulations, the site pharmacy may dispense non-participant-specific medication, or partially labeled medication to the appropriate clinic staff for provision to a participant.

- If a site pharmacy is permitted to, and will, dispense partially labeled medication to clinic staff, the following documentation procedures must occur:

1. Clinic staff must complete the label with participant-specific information before providing medication to the participant.
2. Clinic staff must document which specific participant received which partially labeled medication and provide documentation to support that the participant has been prescribed the dispensed medication (e.g., prescription, medication order, etc.) to the site pharmacy by the end of the day.
3. Site pharmacy must then complete applicable participant-specific accountability log(s) along with a comment that the medication was dispensed to the participant by clinic staff on the mobile unit.
4. Site pharmacy must file all clinic-provided documentation of dispensed study medication in the pharmacy files.

8.7.3 Dispensing and Providing Controlled Substances (Buprenorphine)

Buprenorphine - oral sublingual tablets or film - will be used in HPTN 094 study conduct to treat opioid use disorder (OUD) for participants randomized to the Intervention Arm.

Buprenorphine is a schedule III controlled substance and sites, and site pharmacies must comply with all local regulations and pharmacy laws, including Drug Enforcement Administration (DEA) rules and regulations, regarding prescribing, prescription requirements, storage requirements, provision to participants, etcetera, required for management of a schedule III controlled substance.

DEA guidance and/or local regulations may dictate that pharmacy-designated staff must dispense buprenorphine-containing tablets or films directly to participants, in which case these products may never be in the possession or the clinical staff or stored on the mobile unit. If, however, the clinic (mobile unit) staff are allowed to dispense tablets or films to participants, the following guidance applies:

- Buprenorphine must be dispensed with a participant-specific label attached. It is strongly recommended that the clinic staff have a 2-person verification procedure to verify that buprenorphine is being provided or administered to the correct participant as a quality control measure and this process should be documented.

- Clinic staff must maintain a daily inventory log of the number of units (i.e. tablets, films, syringes) that are stored on the mobile unit and document updates to the inventory quantity in real time when buprenorphine is provided to a participant. Clinic staff should reconcile the buprenorphine inventory log at the end of the day by performing a physical count of the inventory to ensure that all units are accounted for, verifying the count by signing the log and documenting date and time of the reconciliation. A second member of the clinic staff should double check the inventory count for quality control and document date and time of QC check along with signing the log.

- All unused buprenorphine must be removed from the mobile unit at the end of each day and either returned to the pharmacy or stored securely in the clinic according to the site's SOPs, local institutional policies and procedures and pharmacy laws and regulations.

8.8 Study Medication Management and Required Standard Operation Procedures

Each site must develop and follow protocol-specific SOPs that specify how the management of medications for HPTN 094 will be accomplished locally. The SOPs should be approximately 3-5 pages and developed with input from both the site pharmacist and clinic staff and all procedures must be in accordance with local and Federal regulation and the DAIDS *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks*. The SOP 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.

The site SOPs should include, but is not limited to, the following elements:

- Communication between clinic and pharmacy staff:
    - How will the clinic staff communicate anticipated needs for participant-specific study medication and non-participant-specific medication to be stored on the mobile unit, and how far in advance will anticipated needs be communicated by the clinic staff to the site pharmacy.

    - Site procedure for when a participant misses a scheduled visit, how this is communicated with the pharmacy and how participant-specific labeled medication previously dispensed to clinic staff will be handled in this situation.

- Chain of custody documentation:
    - How Chain of Custody for study medication will be documented throughout the course of the study. Chain of custody must document all transfer of study medication (e.g. pharmacy to clinic, clinic to participant, clinic to pharmacy, etc.).

- Dispensation of study-supplied medication:
    - For study-supplied medication, will the site pharmacy only dispense labeled participant-specific medications or will the site pharmacy also dispense partially labeled or non-labeled study-supplied medication also.

    - Whether the site pharmacy will only dispense study-supplied medications to the mobile unit, only dispense study-supplied medications to participant, or a mixture of both procedures.

- Dispensation of non-study-supplied medication:
    - How will the site procure/obtain non-study-supplied medication and will non-study-supplied medication be dispensed/provided by the site pharmacy, by another institutional pharmacy, or by other means. The SOP must contain detailed information on the site's plan for procurement, dispensation and/provision of non-study-specific medication.

- Transportation/storage of medications to and on Mobile units:
    - How pharmacy and clinic staff will maintain storage and temperature requirements for all study-supplied medications. The SOP must include procedures for security and temperature requirements during transport to/from mobile unit and while medication is stored on the mobile units.

- Provision of Controlled Substances:
    - The site must include in the SOP how MOUDs will be provided to the mobile unit and how inventory and use will be documented. The SOP should include details on how the site will comply with local and federal pharmacy laws and regulations for controlled substances and any documentation or processes required for dispensation of controlled substances to a mobile clinic.

8.9 Study-Specific Timelines

In HPTN 094, the medications that the study aims to provide participants from the mobile unit are medication for opioid use disorder (MOUD) and either HIV treatment (ART) or HIV prophylaxis (PrEP). These medications will only be dispensed to participants in the intervention arm. Clinic staff will endeavor to initiate all intervention arm participants onto MOUD and ART or PrEP as soon after enrollment as possible. These participants may continue to receive MOUD, ART and/or PrEP through the study until the Week 26 visit, but not longer. By this time point, participants must have transitioned to receive future care from brick-and-mortar facilities in their community, with the support of referrals from site staff and assistance from peer navigators. Note that participants are not required to receive study supplied medications to remain in the study.

Study clinicians will also provide medications for empiric treatment of symptomatic sexually transmitted infections (STI) to participants in both arms at enrollment and at the Week 26 and Week 52 visits. Participants in the intervention arm will also receive treatment for suspected or confirmed STIs between the enrollment and Week 26 visits.

HPTN 094 Record of Dispensation of Study-Supplied Medication from Pharmacy Staff to Mobile Unit Staff or to Participants (and, as Applicable, Returns to Pharmacy)

CRS Number:	Investigator's Name:
CRS Name:	
Date and time dispensed medication is collected from pharmacy: Date (DD-MMM-YY)	Time (HH:MM)

Table 1: Dispensation Information

Line #	**Medication Dispensed**	**PTID (if applicable)**	**# of Units Dispensed and Unit Description** (Bottles, tablets, syringes, etc.)	**Pharmacy Staff Initials**	**Clinic Staff Initials (enter N/A if not applicable)**	**Courier Initials (if applicable)**	**Medication experience a Temp Excursion During Transit? (Y/N)**	**Provided to Participant (Y/N)**	**Comments:** Check box & add comments on Page 2 of Record
1									☐
2									☐
3									☐
4									☐
5									☐
6									☐
7									☐
8									☐

Table 2: Returns Information

Medication Returned to Pharmacy (List line number from above table)	**Date** (DD-MMM-YY) **Collected from Mobile Unit**	**Time** (HH:MM) **Collected from Pharmacy**	**# of Units Returned to Pharmacy and Unit Description** (Bottles, tablets, syringes, etc.)	**Clinic Staff Initials**	**Pharmacy Staff Initials**	**Courier Initials (if applicable)**	**Medication experience a Temp Excursion During Transit? (Y/N)**	**Comments:** Check box & add comments on Page 2 of Record
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HPTN 094 Record of Dispensation of Study-Supplied Medication from Pharmacy Staff
to Mobile Unit Staff or to Participants (and, as Applicable, Returns to Pharmacy)

List all medications returned to the site pharmacy that are not listed in table 1 above and reason for return (e.g. participant return):

Table 3: Miscellaneous Return Information			
Medication Returned	**PTID**	**# of Units Returned to Pharmacy and Unit Description** (Bottles, tablets, syringes, etc.)	**Reason for Return**

COMMENTS (list line number from above table 1 or 2 to provide additional comments):

Instructions:

- Complete one row for each study supplied medication dispensed by the pharmacy and given to clinic staff to be provided to participant or dispensed directly from pharmacy staff to participant

- Complete all applicable sections of log every day study supplied medication is dispensed and given to clinic staff. Completed log should be return to site pharmacy by the end of the same day.

Appendix B Page: ____ of ____

HPTN 094 Record of Prescription and Provision of Non-Study-Supplied Medication from Mobile Unit Staff to Participants

CRS Number:	Investigator's Name:
CRS Name:	

Table 1: Dispensation Information										
Line #	**PTID**	**Medication Prescribed**	**# of Units Prescribed and Unit Description** (tablets, capsules, syringes, etc.)	**Pharmacy Prescription (Rx) sent to** (Check "*Handed to ppt*" as applicable)	**Date/Time Rx was sent to pharmacy** (Check appropriate method)	**Initials of clinic staff**	**Date/Time Rx was received from pharmacy** (Check "N/A - *Direct Delivery*" as applicable)	**Initials of clinic staff**	**Date/Time Rx was provided to ppt** (Check "*F/U*" as applicable)	**Initials of clinic staff**
1				Pharmacy: _____ _____ _____ ☐ *Handed to ppt*	Date: _____ Time: _____ ☐ *Faxed* ☐ *Emailed* ☐ *Other:* _____		Date: _____ Time: _____ ☐ *N/A – Direct Delivery*		Date: _____ Time: _____ ☐ *F/U Call as ppt received direct delivery*	
1				Pharmacy: _____ _____ _____ ☐ *Handed to ppt*	Date: _____ Time: _____ ☐ *Faxed* ☐ *Emailed* ☐ *Other:* _____		Date: _____ Time: _____ ☐ *N/A – Direct Delivery*		Date: _____ Time: _____ ☐ *F/U Call as ppt received direct delivery*	

1				Pharmacy: _____ _____ _____ ☐ *Handed to ppt*	Date: _____ Time: _____ ☐ *Faxed* ☐ *Emailed* ☐ *Other:* _____		Date: _____ Time: _____ ☐ *N/A – Direct Delivery*		Date: _____ Time: _____ ☐ *F/U Call as ppt received direct delivery*	

Instructions:

- Complete page number sequencing for as additional pages are needed; making sure to fill in total number of pages when log is complete
- Complete one row for each Non-Study-Supplied medication prescribed by the clinic staff to be provided to participant by clinic staff or directly delivered to a participant from designated pharmacy
- Clinic Staff is responsible for ensuring that all columns for each row are completed
- Any additional comments may be recorded on the back of each page by referencing the appropriate line number

Abbreviations:

CRS: Clinical Research Site
F/U: Follow-up
N/A: Not applicable
PTID: Participant Identification Number
Rx: Prescription