Section Number	Section Title	Current Version Number	Current Version Date	Updates and Comments
1	Introduction	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Updated contact information in Table 1-1 • Updated list of participating sites in Table 1-2 • Updated links in Section 1.5.6
2	Protocol	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Added HPTN 083-01 Protocol, Version 3.0
3	Document Requirements	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Section 3.2: Added references to the DAIDS Score Manual • Section 3.3: Added reference to the Investigators Responsibilities document within the DAIDS Score Manual • Section 3.3.1: Added reference to the Source Document sections of the DAIDS Score Manual. • Table 3-1a: Added "CAB" to row for Dispense CAB Pills (enough for 5 weeks). Added "if chosen for Step 3" to row for Provision of TDF/FTC, if chosen for Step 3. • Table 3-2: Added clarifying language to the Informed Consent Form section. Added clarifying language to the Lab Results section for Hemoglobin. Added clarifying language to the Lab Results section for the Absolute Neutrophil count. • Section 3.4: Updated Westat Project Coordinator contact information. • Section 3.4: The DAIDS Critical Event (CE) policy is no longer applicable; therefore, sites will not need to report critical events. • Section 3.5: Updated Record Retention Requirements to include EMA requirements for sites to retain files for more than 15 years from the end of data collection, or longer.
4	Recruitment Screening and Enrollment	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Section 4.2: Changed accrual period to up to 18 months. • Section 4.5.1: Added clarifying language surrounding the ability for a participant to now self-consent. • Table 4-1: Changed question on ICF Assessment Tool to reflect recent approval of CAB in HIV treatment (turned focus to HIV prevention). • Table 4-2: Updated the type of consent section to update names of

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				consent and add consents for Parent/guardian consent for qualitative interview, participant self-consent and consent for those reaching age of majority for storage/future use of samples, minor participant assent for storage/future use of samples, parent/guardian consent and age 14 to age of majority assent for storage/future use of samples. The study now has a total of 10 ICFs and these ICF changes were reflective of the sIRB's instructions.
5	Study Procedures	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Section 5.2: Removed option to join an OLE CAB in Step 3 and added option for participant to continue CAB LA injections for the duration of Step 3. • Section 5.3: Added Appendix IV of the Protocol as a new Appendix describing the schedule of evaluations for participants who choose injections for Step 3.. • Section 5.3.1: Added Appendix V of the protocol as a resource for follow-up procedures. • Section 5.4: Updates Appendices numbers for accuracy. Updated Appendix IV to V in the diagram on Guidance for participants with confirmed HIV-infection during the study. • Section 5.5: Updated link for additional information on certified copies (now links to DAIDS Score Manual).
6	Visit Checklists	3.1	16Nov2021	Updates for Version 3.1 (16Nov2021) • Throughout updated terminology for HIV assays. • In the Step 3 checklists, clarified that HIV testing is done at all visits. • In the Step 3- Injection Checklist, corrected the weeks for DBS storage Updates for Version 3.0 (13Sep2021) • Section 6.4: Eligibility Checklist updated to add several clarifications to the inclusion and exclusion criteria. • Step 2 (Safety Visits) Weeks 6, 10, 18, 26, 34 – Added HIV pre-test counseling, checklist items for blood collection, and HIV post-test counseling, given that the study will test for HIV at every visit now. • Step 2 (Remaining Injection Visits) Weeks 9, 17, 25, 33 – Added Step 3 product choice discussion at Week 34 (and only if discussion not held at or finished at Week 33 injection visit). • Step 3 – Changed title to be in line with title of Appendix III (for ease of

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				reference). Added specificity about weeks, given those instructions in Appendix III. All participants will now have repeat testing for HCV antibodies at the end of the study, as well as hepatitis B virus surface antibody and hepatitis B virus core antibody testing. A new checklist was added for the protocol's new Appendix (Appendix IV), describing Step 3 injection visits at Weeks +8, +16, +24, +32, +40, and +48.
7	Participant Retention	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Only the footer was updated as per updated version of the SSP manual. No other edits were made.
8	Study Product Considerations	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Section 8.1.6: Added clarifying language about the short-term storage of prepared CAB-LA in a syringe
9	Clinical Considerations	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Throughout added generic TDF/FTC as an option for sites (vs. using brand-name Truvada®) • Section 9.1: Added differentiating language about frequency of visits for Step 3-Oral vs. Step 3-Injection (Oral has 5 quarterly visits and Injection has 6 visits every two months). • Section 9.3.2: The PHQ score should be added to the Medical History Log (not the AE Log). • Section 9.4.6: Actively assessing neurologic symptoms (vs. passive) is no longer required, per changes in the parent protocol SSP (HPTN 083). • Section 9.4.8.1: Precautionary and Prohibited Medications o Systemically administered immunomodulators are removed as a prohibited medication; that is, they can be administered to a participant on CAB. • Section 9.11: Updated references to appendices to be used for confirmed seroconversion to include Appendices III or IV (for Step 3) and Appendix V (Seroconversion); updated Appendix from IV to V in confirmed seroconversions diagram. • Section 9.12.1: Added language about new testing in Appendices III and IV: all participants will now being repeat testing for HCV antibodies at the end of the study, as well as hepatitis B virus surface antibodies and hepatitis B virus core

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				antibodies. • Section 9.14: Enrollment Violations – changed header number from 9.17 • Toxicity Diagrams: o General Toxicity Management Considerations: The toxicity management guidance is now in the Appendix VI of the protocol, where previously it was Appendix V (Step 3 – Injection Appendix was added).
10	Adverse Event Reporting and Safety Monitoring	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Section 10.1: Updated protocol versioning information to Version 3.0, dated 02 July 2021
11	Laboratory and Specimen Management Procedures	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Section 11.1: Added new links • Section 11.3.2: Added note about hepatitis testing • Table 11-1: Moved HC antibody testing to its own line and added a footer (#8) • Table 11-2: Added HIV testing at Weeks 6, 10, 18, 26, 34 • Table 11-3: Removed CBC with differential from two visits; Removed BUN/urea, CPK, calcium, phosphorous, glucose, amylase and lipase from chemistry testing; moved syphilis testing to Post-Injection Week +36; removed two visits- Urine GC/CT testing, rectal swab testing and oral pharyngeal swab GC/CT testing and Urinalysis (protein, glucose); Added line for HCV antibody testing and HBsAb and HBcAb (total); added footnotes #5 and #6. • Table 11-4: Added table and footnotes • Figure 11.2: HIV Testing Algorithm at the Enrollment Visit o Added new figure • Figure 11.3: HIV Testing Algorithm at all Other Visits with HIV Testing o Added new figure • Table 11-5: This was previously Table 11-4 (Additional Procedures for Participants who have a Reactive or Positive HIV test at any time after Enrollment). o Added bolded text below table “The CMC must be notified immediately if one or more reactive, **positive, or detectable** HIV test results are obtained at any follow-up visit **after**

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				enrollment. • Section 11.4: Clarification about LDMS entry • Section 11.6: Added clarification that aliquots can be shipped along with shipments from HPTN 083.
12	Counseling Considerations	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • HIV testing is now done at all visits including safety visits and the +8 week visit in Step 3. • In several sections: o Removed text in parentheses in several places. HIV Pre-/ Post-Test counseling is required at all study visits when an HIV test is done ~~(not done at the injection safety visits in Step 2 and the +8 Week visit in Step 3).~~ • Section 12.2: Added clarifying language reflecting the efficacy results from parent protocol (HPTN 083). • Section 12.6: Added paragraph about product choice at Weeks 33 and 34. • Section 12.7: Added a note that if the participant chooses to remain on CAB LA injections for Step 3, counseling in Step 3 will mimic that of Step 2.
13	Data Management	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Table 13-1: HPTN 083-01 Visit Codes, Target Days, and Visit Windows o Step 3 split out into Oral TDF/FTC and Injection CAB LA • Section 13.13 Schedule of Forms o (Oral) W+8, W+12, W+24, W+36, W+48 – Added a few clarifications o (Injection) W+8, W+16, W+24, W+32, W+40, W+48 – Added forms
14	CASI	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Only the footer was updated as per updated version of the SSP manual. No other edits were made.

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15	Reporting Plan	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Only the footer was updated as per updated version of the SSP manual. No other edits were made.
16	Data Communiques	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Only the footer was updated as per updated version of the SSP manual. No other edits were made.
Appendix Ia	Record of Dispensation of Participant-Specific Study Product to Non-Pharmacy Staff	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Only the footer was updated as per updated version of the SSP manual. No other edits were made.
Appendix Ib	Record of Return of Participant-Specific Study Product by Non-Pharmacy Staff	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Only the footer was updated as per updated version of the SSP manual. No other edits were made.
Appendix II	Participant Transfer and Receipt	3.0	13Sep2021	Updates for Version 3.0 (13Sep2021) • Only the footer was updated as per updated version of the SSP manual. No other edits were made.
Appendix III	Guidance for Management of "discordant/discrepant " HIV testing results.	1.2	06Mar2019	No edits were made were made to this version
Appendix IV	Study Schema Graphic	2.0	14May2021	This is an updated study schema graphic, now including the option for CAB LA injections in Step 3.