HPTN 083-01 Study-Specific Procedures Manual Overview and Version Control

Section Number	Section Title	Current Version Number	Current Version Date	Updates and Comments
1	Introduction	3.1	24Feb2022	Updates for Version 3.1 (24Feb2022) • Updated contact information in Table 1-1 • Removed asterisked note referencing Children's Hospital Colorado CRS's site activation status • Section 1.4: Added references to the DAIDS Score Manual and removed references to archived DAIDs policy. • Section 1.5.4: Added clarifying note about local IRB submissions. • Section 1.6: Added a clarifying note about protocol-level IRB submission.
2	Protocol	3.2	08Dec2022	Updates for Version 3.2 (08Dec2022) • Added HPTN 083-01 LoA #2 to Protocol Version 3.0 • Added HPTN 083-01 LoA #3 to Protocol Version 3.0
3	Document Requirements	3.1	24Feb2022	Updates for Version 3.1 (24Feb2022) • Section 3.2: Added reference to generic (FDA-approved) TDF/FTC, now allowable for site procurement in V3.0 of the protocol. • Section 3.3.3.1: Added references to Source Documentation Requirements within the DAIDS Score Manual. • Tables 3-1a: Added "and in Step 3, if ppt chooses to continue on Step 3 – Injection SOE" to row for Injections • Table 3.2 – Removed exclusion criteria regarding alcohol or substance use
4	Recruitment Screening and Enrollment	3.1	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 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

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				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	3.2	08Dec2022	Updates for Version 3.2 (08Dec2022) • Section 5.4 – Corrected a typo in the Table number specifying where to find procedures for participants with discordant or discrepant HIV test results. Updates for Version 3.1 (24Feb2022) • Section 5.3: Updated the number of Appendices to include V. • Made edits to further clarify transition from Step 2 to choice of TDF/FTC or continued injections in Step 3.
6	Visit Checklists	3.4	08Dec2022	Updates for Version 3.4 (08Dec2022) • Step 2 (Safety Visits) Week 34 - Removed specific length of time (3 month supply) for prescription of TDF/FTC for Step 3, if oral PrEP is chosen. Updates for Version 3.3 (24Feb2022) • Step 3 (Oral PrEP) Weeks +8, +12, +24, +36 and +48 (post-last injection) – Corrected the weeks where medical history is collected, and physical exam was performed. Added HIV testing to Week +8 and removed Week +12 and +36 for the chemistry panel and LFTs. Corrected weeks for adherence counseling. Removed the asterisks referencing footnote that noted the error in the SOE of protocol v3.0. • Step 3 (Injection) Weeks +8, +16, +24, +32, +40, and +48 (post-last injection) - Corrected the weeks where medical history is collected, and physical exam was performed. Removed the chemistry panel and LFT from week +8. Added urinalysis to Week +24 and +48 and ISR evaluation to all weeks except +8; Removed the asterisks referencing footnote that noted the error in the SOE of protocol v3.0. • Procedures for Enrolled Participants who Seroconvert – Removed blood collection for Chemistry and LFTs from Week +12 and +36. Updates for Version 3.2 (05Jan2022) • Throughout added back the HIV rapid test (that was erroneously removed from V3.1) • Screening and Enrollment Checklists- added clarifying language around Hepatitis testing.

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				• Step 1 Enrollment – Removed collection of rectal and oral pharyngeal swabs for GC/CT testing and GC/CT testing • Step 1 Weeks 2 and 4 – Updated terminology for HIV assays. • Step 2 Week 5 – Listed out individual chemistry and liver function tests • Step 2 (Safety Visits) Weeks 6, 10, 18, 26, 34 – Added lipid profile to Week 34 • Step 2 (Remaining Injection Visits)- Clarified that GC/CT testing is by urine, rectal, *and* pharyngeal (not *or*). • Step 3 (Oral Prep) Weeks +8, +12, +36 and +48 – Corrected the weeks where labs are collected, added footnote noting the error in the SOE of protocol v3.0 and that an LOA 1 is forthcoming. The protocol v3.0 should be followed while waiting for the protocol change. • Step 3 (Injection) Weeks +8, +16, +24, +32, +40, and +48 – Corrected weeks and removed the Urinalysis, added footnote.
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	3.2	08Dec2022	Updates for Version 3.2 (08Dec2022) • Section 8.5.1 Step 3 – Removed specific length of time (3 month supply) for prescription of oral TDF/FTC, if oral PrEP is chosen in Step 3. Updates for Version 3.1 (24Feb2022) • Section 8.1.5 – Added FDA-approved generic TDF/FTC as an option for participants who choose oral PrEP in Step 3. Appendix III should be followed for this option. • Section 8.1.5.2 – Added section for participants who choose continued CAB LA injections. Appendix IV should be followed for this option. • Section 8.2.2 - Added generic TDF/FTC as an option for sites (vs. using brand-name Truvada®).
9	Clinical Considerations	3.1	24Feb2022	Updates for Version 3.1 (24Feb2022) • Section 9.1 – Added data communiqués as a resource for instructions on the EDC systems. • Section 9.4 – Corrected weeks for targeted physical examination, which now includes week +8.

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				• Section 9.4.4 – Weight will be recorded at every visit, including week +8. • Section 9.4.7 – Added clarifying language about the frequency of ISR evaluations in Step 3 – Injection. • Section 9.4.8.1 – Added clarifying language about IBs when prescribing generic TDF/FTC. • Section 9.4.8.2 – CMC consultation is required when prescribing precautionary or prohibited medications. • Section 9.7.3 – Added a note about reload injections in the case of missed or late injections. • Section 9.11: – Added clarifying language to HIV considerations during study conduct.
10	Adverse Event Reporting and Safety Monitoring	3.1	24Feb2022	<u>Updates for Version 3.1 (24Feb2022)</u> • Section 10.3 – Added clarifying language about the occurrence of ISR evaluations. • Section 10.9 – Updated links. • Section 10.11 – Added clarifying language about IRB submission of product safety information. •
11	Laboratory and Specimen Management Procedures	3.1	04Mar2022	<u>Updates for Version 3.1 (04Mar2022)</u> • Table 11-3: Added HIV testing to Post Injection Week +8 and Early Discontinuation visit. Added footnote #1 to provide further clarification. Removed Chemistry testing and LFT from Weeks +12 and Week +36. • Table 11-4: Removed chemistry testing and LFT from Week +8; Added Urinalysis to Weeks +24, +48, and Early Discontinuation; Added footnote #2. • Section 11.3.1: Provided clarifying language to include HIV RNA. • Section 11.3.4: Added clarifying language on creatinine clearance.

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12	Counseling Considerations	3.1	24Feb2022	Updates for Version 3.1 (24Feb2022) • Section 1.2.1: Added clarifying language on the rationale of HIV testing at all study visits. • Section 12.3: Made edits to further clarify transition from Step 2 to choice of TDF/FTC or continued injections in Step 3 • Section 12.4: Added a note explaining that TDF/FTC is not considered a "study product" per the protocol.
13	Data Management	3.1	04Mar2022	Updates for Version 3.1 (04Mar2022) • Section 13.13: Added CD4/Viral load testing to all visits and updated the required forms for Step 3 (oral and injection) to match what's in the protocol.
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.
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.
17	Qualitative	1.0	24Feb2022	Updates for Version 1.0 (24Feb2022) • New section
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.

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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.	2.1	16Nov2021	This is an updated Guidance for HIV testing results, to reflect parent study milestones.
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.