Appendix VII: SSP Manual Updates Per LoA #1 to Version 3.0 of the Protocol

1.1 Overview of Appendix VII

This appendix includes specifics updates, guidance, and considerations for implementation of LoA #1 to Version 3.0 of the HPTN 083 protocol. As per LoA #1, the updates outlined in this Appendix are applicable to all SSP Manual sections immediately following approval of the LoA#1 by the site's IRBs/ECs/other regulatory entities overseeing the research. **That is, updates to the individual SSP sections impacted by LoA # 1 are not being made; rather, this Appendix serves as the document that outlines the updates, as follows:**

- Provide participants with the Participant Letter. Please follow the guidance provided on the *Updated Instructions for Submission and Approval of HPTN 083 LoA # 1, dated May 21, 2020, and Sample Participant Letter, dated May 19, 2020, to Protocol Version 3.0, dated October 31, 2019, and LoA # 1 Protocol Signature Page, dated May 19, 2020.*
- No further screening or enrollment will occur under Version 3.0 of the protocol, dated October 31, 2019.
- Provide participants their randomization assignment.
- Once a participant is informed of their randomization assignment, participants will no longer receive placebo study product. For participants randomized to CAB, sites should collect all remaining oral placebo study products as quickly as possible.
- Step 2 Safety Visits will no longer be conducted. All safety procedures and evaluations will be done at the Injection Visits only. Please note that although the visits are called injection visits, participants randomized to TDF/FTC will not be receiving a placebo injection; these participants will be provided active oral TDF/FTC at these visits.
- Participants still receiving study drug will be offered to continue the active study drug to which they were originally assigned until further notice as follows:
    - Participants in Step 1: If any participants remain in Step 1, contact the HPTN 083 CMC for guidance.
    - Participants in Step 2 assigned to active CAB LA: These participants will be offered to continue active CAB LA on the current Step 2 study visit schedule for injection visits only.
    - Participants in Step 2 assigned to active oral TDF/FTC: These participants will be offered to continue active TDF/FTC on the current Step 2 study visit schedule for injection visits only. These participants will be offered CAB when it becomes available.
    - Participants in Step 2 who reach the Week 153 visit during the time the LoA #1, dated May 19, 2020, is in effect will transition to Step 3 and be followed on the current Step 3 visit schedule. That is, participants receiving active CAB LA will receive open-label TDF/FTC per the current Step 3 visit schedule, and participants on active TDF/FTC will remain on it and be followed on the current Step 3 visit schedule. These participants will be offered CAB when it becomes available.
    - Participants in Step 3 will continue visits per the current Step 3 visit schedule. Participants who reach the final visit of Step 3 prior to obtaining additional CAB drug supply will be referred to local HIV prevention services and transition to annual follow-up. When CAB supply is obtained, these participants will be contacted and offered CAB.

Additional information or clarifications beyond the updates per the LoA #1 listed above have impacted the SSP manual sections listed below. If a section is not mentioned below, it means that no additional updates related to LoA #1 are indicated.

The purpose of this appendix is to provide additional guidance to the LoA #1 to Version 3.0 of the protocol; as always, all study procedures must be conducted in accordance with the study protocol. Unless instructed by the HPTN Leadership and Operations Center (LOC), if there is inconsistency between this appendix and the protocol, the specifications of the protocol take precedence. Please alert the HPTN Leadership and Operations Center (LOC) of any such inconsistencies.

1.2 Updates to SSP Manual Sections

1.2.1 Section 2: Protocol

The following protocol documents to Version 3.0 of the Protocol were added to the table in Section 2 of the SSP:

Document	Date
• Clarification Memo # 2 (COVID-19)	2 April 2020
• Clarification Memo # 3	4 May 2020
• HPTN 083 Letter of Amendment #1	19 May 2020
• HPTN 083 Letter of Amendment #2	1 July 2020
• HPTN 083 Letter of Amendment #3	23 July 2020
• Clarification Memo #4 (Updated COVID-19)	5 February 2021

1.2.2 Section 3.0: Document Requirements

- Section 3.2: Essential Documents – Sites are required to file as part of their essential documents all documentation related to the DSMB review outcome as well as the participants' unblinding list. Also, all communication with the IRB/EC/other regulatory entities overseeing the research and approvals related to the DSMB outcome and the implementation of the LoA #1 must be filed as part of the study essential documents.
- Section 3.3.2: Source Documentation – File the signed Participant Letter. For participants who receive the content of the Participant Letter in another form other than in-person, the method of communication and acknowledgement of receipt of the information should be documented in the participant's study record.
- Section 3.4: Reportable Protocol Deviations – Sites will need to report as a reportable deviation if a participant was unblinded and/or any aspects of LoA #1 were implemented before IRB approval.

1.2.3 Section 5: Study Procedures Overview

See Table A: *Schedule of Procedures and Evaluations - Step 2 – Blinded Injections + Blinded Daily Oral Pills Open-Label CAB Injections OR Open-Label Daily Oral TDF/FTC* and Table B*: Schedule of Procedures and Evaluations - Step 3 – Open Label Daily Oral TDF/FTC Post-Last Injection* found at the end of this section for an updated listing of procedures and evaluations per LoA#1.

- Section 5.3: Study Visits:
  - There are no changes to the guidance for missed or late injection visits.
  - Information regarding merged study visits is no longer applicable.

- Section 5.3.1: Follow-up Visit Procedures:
  - Behavioral assessments – interviewer questionnaires and CASI surveys, will be done for the last time at the next scheduled visit at which these assessments are scheduled to occur. Following that visit, these assessments will no longer be administered. For example, if the participant's next visit is Week 49, when a behavioral assessment is scheduled to occur, site staff will administer the assessment at this time. When participant presents to the clinic for Week 57 study visit, that behavioral assessment will not be completed at that visit or any subsequent visits. Please refer to Data Communique #7 for additional information.
  - For participants randomized to TDF/FTC, there is no changes to the number of bottles to dispense at each visit. Sites should ensure participants have an extra month supply between visits.

1.2.4 Section 6: Visit Checklists

Relevant visit checklists have been updated and found at the end of this section. Please note, new information is highlighted yellow.

1.2.5 Section 8: Study Product Considerations

- Documentation to be Provided to the Site Pharmacy Record:
  - When the site has LoA # 1 to HPTN 083, Version 3.0 approved by their IRB/EC/other regulatory entities and the participant is informed of their randomized assignment, the site investigator or designated study staff must provide a written notification to the pharmacy that the participant has been informed of their randomized assignment for pharmacy record. This documentation can be in an email to the site Pharmacist of Record (PoR) from the site investigator or designee or on a prescription for un-blinded study product that is signed by an authorized prescriber. If the written notification was not provided prior to the implementation of Appendix VII of the HPTN 083 SSP, then the site investigator or designee should provide retroactive written notification to the PoR of participant(s) who have been informed of their randomized assignment for pharmacy records.

- Section 8.3 and 8.9.2 - Participants Assigned to the TDF/FTC Arm in Steps 1 and 2:

- When the participant has been informed of their randomized assignment to the TDF/FTC arm, a new prescription for un-blinded oral active TDF/FTC signed by an authorized prescriber must be provided to the site pharmacist.
- The pharmacist will take the following steps to prepare and dispense un-blinded active oral TDF/FTC to the participant:
  1) Retrieve oral active TDF/FTC bottle with two part-label from Step 2 supply.
  2) Retain both the un-blinded part and the blinded part of the two-part label on the TDF/FTC bottle. Do not tear off the un-blinded part of the two-part label from the bottle.
  3) Place pharmacist prepared participant-specific un-blinded label in such a way that the blinded part of the two-part label on the bottle is covered.
- The pharmacist-prepared, participant-specific, un-blinded oral active TDF/FTC bottle will have the manufacturer's unblinded part of the two-part label and site pharmacist generated participant-specific un-blinded label visible on the prepared bottle before dispensation.
- Alternatively, retrieve open-label oral active TDF/FTC supply from Step 3 supply if the site no longer has oral active TDF/FTC bottles with a two-part label from Step 2 supply. Place pharmacist prepared participant-specific un-blinded label on the bottle and dispense.
- If a participant assigned to the TDF/FTC arm in Step 2 wishes to switch to CAB, then the authorized prescriber will write a prescription for CAB in Step 4 per HPTN 083 protocol version 4.0.

- Section 8.3 and 8.9.2 - Participants Assigned to the CAB Arm in Step 1:
  - When the participant has been informed of their randomized assignment to the CAB arm, a new prescription for unblinded oral active CAB signed by an authorized prescriber must be provided to the site pharmacist.
  - The pharmacist will take the following steps to prepare and dispense unblinded active oral CAB to the participant:
    1) Retrieve oral active CAB bottle with two part-label from Step 1 supply.
    2) Retain both the un-blinded part and the blinded part of the two-part label on the CAB bottle. Do not tear off the un-blinded part of the two-part label from the bottle.
    3) Place pharmacist-prepared participant- specific un-blinded label in such a way that the blinded part of the two-part label on the bottle is covered.
  - The pharmacist prepared, participant-specific, un-blinded oral active CAB bottle will have the manufacturer's unblinded part of the two-part label and site pharmacist generated participant specific un-blinded label visible on the prepared bottle before dispensation.

- Section 8.7 and 8.9.2 - Participants Assigned to the CAB Arm in Step 2:
  - When the participant's treatment assignment has been unblinded and the participant is assigned to the CAB arm, a new prescription for unblinded injectable CAB-LA signed by an authorized prescriber must be provided to the site pharmacist.

- The pharmacist will take the following steps to prepare and dispense unblinded active injectable CAB-LA to the participant:
  1) Retrieve injectable CAB-LA vial(s) from storage.
  2) Prepare the injectable CAB dose in a syringe per protocol. The overlay tape that covers the syringe barrel of the prepared unblinded, injectable CAB-LAB in a syringe is not required.
  3) Place pharmacist-prepared participant-specific un-blinded label on the prepared syringe.

- Section 8.8 - Participants in Step 3:
  Participants in Step 3 will continue to take open-label TDF/FTC from Step 3 supply per protocol.

1.2.6 Section 9: Clinical Considerations

- As per LoA#1, participants will not be receiving placebo study product; therefore, any reference to blinded study product is updated to assigned study product.
- As per LoA#1, all safety procedures and evaluations will be performed at injection visits only.
- Section 9.3.5.4: Injection site reaction (ISR) assessment - As part of the required safety evaluations, the injection site reaction evaluation should be done at all injection visits with participants randomized to the CAB arm **only**.
- Section 9.3.5.5: Exercise assessment - As part of the required safety evaluations, the Post-injection Exercise Assessment should be done at all injection visits when an injection was given at the previous injection visit.
- Section 9.7: Clinical Management Committee: When communicating with the CMC, please include participant's randomization assignment.
- Section 9.9: Suspected or Confirmed HIV infection - Although participants are no longer using blinded study product, sites should continue to contact the 083HIV team for any HIV-related questions.

1.2.7 Section 10: Adverse Event Reporting and Safety Monitoring

- Section 10.5: Adverse Event Relationship to Study Product - When assessing an AE's relationship to study product, the site clinician should consider the unblinded study product assigned to the participant – either injectable CAB or oral TDF/FTC.
- Section 10.9: Expedited Reporting of Adverse Events to DAIDS - The study agents for the purposes of expedited adverse event (EAE) reporting are: CAB LA injectable suspension (600 mg/mL) **or** TDF/FTC fixed dose combination tablet containing 200 mg of FTC and 300 mg of TDF.

1.2.8 Section 11: Laboratory and Specimen Management Procedures

All required laboratory procedures are included in Table A and Table B found at the end of this section.

1.2.9 Section 12: Counseling Considerations

- Section 12.3: Product Use Instructions and Adherence Counseling:
  - Product use and adherence counseling should be tailored to participant's assigned study product.
  - Let participants know that all participants will be offered active CAB when it becomes available unless they permanently discontinued CAB due to an adverse event assessed as related to study product. The timeframe for when adequate supply of CAB becomes available is currently unknown. Clinic staff will inform all participants when this occurs.
  - For participants receiving Truvada, let them know that the label will say active/placebo, but they are receiving active product. Alternately, site could use their own label.

1.2.10 Section 13: Data Management

- Section 13.5: Visit Scheduling: Target Days and Visit Windows
  - The note at the end of the section as well as the last paragraph was updated as follow (updated text in italic):

    Note: If the participant moves to Step 3, remaining target dates will be based on the combined final Step 2/Step 3 Day 0 visit date. *If the Day 0 visit is missed, the target for the remaining Step 3 visits is based on the target date for the Day 0 visit, which is 8 weeks after the final injection.*

    The following table lists the HPTN 083 visit codes, target days and visit windows for each study visit for scheduling guidance *after LOA #1 to v3.0 approval*. All windows are listed in days.
  - Table 13-1: HPTN 083 Visit Codes, Target Days, and Visit Windows

Week	**Visit Code**	**Target day**	**Target visit window (±varies days)**	**Allowable visit window (± varies days)**	**Allowable visit window**
Step 2					
Week 5	5.0	35	(32 , 38)	-3 / +17	(32 , 52)
Week 9	7.0	63	(60 , 66)	-10 / +34	(53 , 94)

Week	Visit Code	Target day	Target visit window (±varies days)	Allowable visit window (± varies days)	Allowable visit window
Week 17	9.0	119	(112 , 126)	-24 / +34	(95 , 153)
Week 25	11.0	175	(168 , 182)	-21 / +34	(154 ,209)
Week 33	13.0	231	(224 , 238)	-21 / +34	(210 , 265)
Week 41	15.0	287	(280 , 294)	-21 / +34	(266 , 321)
Week 49	17.0	343	(336 , 350)	-21 / +34	(322 , 377)
Week 57	19.0	399	(392 , 406)	-21 / +34	(378 , 433)
Week 65	21.0	455	(448 , 462)	-21 / +34	(434 , 489)
Week 73	23.0	511	(504 , 518)	-21 / +34	(490 , 545)
Week 81	25.0	567	(560 , 574)	-21 / +34	(546 , 601)
Week 89	27.0	623	(616 , 630)	-21 / +34	(602 , 657)
Week 97	29.0	679	(672 , 686)	-21 / +34	(658 , 713)
Week 105	31.0	735	(728 , 742)	-21 / +34	(714 , 769)
Week 113	33.0	791	(784 , 798)	-21 / +34	(770 , 839)
Week 121	35.0	847	(840 , 854)	-21 / +34	(826 , 881)
Week 129	37.0	903	(896 , 910)	-21 / +34	(882 , 937)
Week 137	39.0	959	(952 , 966)	-21 / +34	(938 , 993)
Week 145	41.0	1015	(1008, 1022)	-21 / +34	(994 , 1049)
Week 153*	43.0	1071	(1064, 1078)	-21 / +34	(1050 , 1078)

[+] Per LOA #1 to Version 3.0 of the protocol safety visits are no longer required and have been removed from the list of visit windows.

* For sites with all local and national approvals in place for protocol V3.0, participants who reach Step 2 Week 153 will transition to Step 3 at that visit.

Step 3					
Day 0 (combined with final Step 2 visit)	Step 2 Visit Code	<8 weeks from last injection	(0 , 14)	+42	(0 , 42)
Week 12	54.0	84	70, 98	-41 / +42	(43 , 126)
Week 24	55.0	168	154, 182	-41 / +42	(127 , 210)
Week 36	56.0	252	238, 266	-41 / +42	(211 , 294)
Week 48	57.0	336	322, 350	-41 / +42	(295 , 378)
Annual Visits					
Yearly 1	80.0	~52 weeks or 365 days after last Step 2 visit	NA	- 182 / +182	(183, 547)
Yearly 2	81.0	Day 730	NA	- 182 / +182	(548, 912)
Yearly 3	82.0	Day 1095	NA	- 182 / +182	(913, 1277)

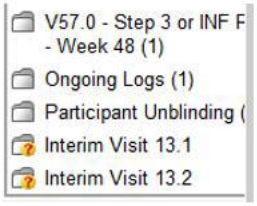
Yearly 4	83.0	Day 1460	NA	- 182 / +182	(1278, 1642)

- Section 13.6: HPTN 083 Injection Schedule – Late/Missed Injections
  - Item #3 under Coding the injection visits has been updated: Safety visits are no longer required and have been removed from the Schedule of Forms. Any procedures previously required at safety visits are now performed at the next injection visit as appropriate, e.g. Post-Injection Exercise Assessment is expected if an injection was administered at the previous visit.
  - The information related to Late/Missed Safety Visits has been deleted

- Section 13.7.4: Interim Visits
  - The following text has been added: After approval for LOA #1 to v3.0, Safety visits will no longer be done. This means that interim visit codes should be based on the previous injection visit. For example, an interim visit done after v29.0 but before the window opens for v31.0 should be coded v29.1.
  - Note added at the end of the section: NOTE: One exception to this is a phone call made to terminated participants for unblinding purposes. In this case complete the Participant Unblinding form but do not create an interim visit folder.

- New Section – 13.7.5: Participant Unblinding Visits

  Each enrolled participant has a Participant Unblinding folder that falls below the Ongoing Logs folder:



  The Participant Unblinding form found in this folder documents the date a participant is informed of their study arm assignment and should be completed for all enrolled participants, including those who have terminated. Complete when unblinding occurs or, if a participant is lost to follow up, do not complete until the end of study participation or termination form is submitted. If a terminated participant is unblinded, do not complete an Interim Visit form for this event.

- Section 13.8: Step 3 Transition (new text in italics, deleted text is strikethrough)
  - Second paragraph updated as follow:
    At the final Step 2 visit where open label Truvada is first administered, mark "Yes" to moving to Step 3 on the Date of Visit or Interim Summary form. Complete all expected Step 2 procedures for the visit and add other eCRFs to the visit folder *as necessary to complete Step 3 Day 0 requirements*. ~~For example, the STI form and SMSQs are required for the Step 3 Day 0 visit; if those are not~~

~~already required at the visit where Step 3 transition is occurring, add the forms to the folder.~~ The next required visit is then Step 3 Week 12.

- Third paragraph updated as follow:
  Transition to Step 3 after completion of Step 2 (Protocol V3.0)
  For sites with all local and national approvals in place for protocol V3.0, participants who reach Step 2 Week 153 will transition to Step 3 at that visit; indicate on the form as described above that the participant is moving to Step 3 and add ~~the SMSQs survey into the visit folder~~ *other Day 0 forms as appropriate*.

1.2.11 Section 16: Data Communiqués

Data Communique #7 provides data-related guidance per LoA#1.

Data Communique #8 provides information about new reports available on Rave and clarifications regarding documentation of early transition to Step 3.

Data Communiqué #9 provides guidelines based on the recent LOA as well as other common data issues.

1.2.12 Appendix III: Schedule of Forms

The updated schedule of forms is found at the end of this section.

1.2.13 Appendix VI: Emergency Unblinding by CRS IoR for Medical Reasons

Appendix VI is no longer applicable to the study.

Table A: Schedule of Procedures and Evaluations - Step 2 Open-Label CAB Injections OR Open-Label Daily Oral TDF/FTC

WEEKS (injection/ dispense pills visit)	5	9	17	25	33	41	49	57	65	73	81	89	97	105	113	121	129	137	145	Week 153/ Day 0*
Locator Information	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HIV Counseling	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Condoms and lubricant	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Acceptability Assessment*			X			X			X			X						X		
Behavioral Assessment **	X	X	X	X	X	X	X	X		X		X		X		X		X		X
Adherence Counseling	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
History, concomitant medications, physical exam±	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight, blood pressure, pulse data entry to Medidata Rave	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG								X						X						X*
DXA (subset only, 175 per arm)[1]								X						X						
Blood Collection	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine collection for urinalysis testing								X						X						X*
Urine collection for GC/CT testing					X			X			X			X			X			X*
Rectal swab for GC/CT testing[2]					X			X			X			X			X			X*
Injection/Dispense pills	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X[8]
HIV testing[3]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
HCV testing[4]								X						X						X*
CBC with differential		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Chemistry testing[5]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Liver function tests[6]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Fasting glucose and fasting lipid profile[7]								X						X						

WEEKS (injection/ dispense pills visit)	5	9	17	25	33	41	49	57	65	73	81	89	97	105	113	121	129	137	145	Week 153/ Day 0*
Syphilis serologic testing					X			X			X			X			X			X*
Urine GC/CT testing					X			X			X			X			X			X*
Rectal swab GC/CT					X			X			X			X			X			X*
Urinalysis								X						X						X*
Plasma storage	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
DBS storage		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

FOOTNOTES FOR Table A

*For participants who transition to Step 3 at Week 153, the first day of Step 3 begins at Week 153 and is also considered Day 0 of Step 3. The timeline for Step 3 continues whether or not a participant attends the Week 153/Day 0 visit or any subsequent visits.

For participants who are already beyond Week 153 of Step 2 in their follow-up schedule, the timeline for Step 3 begins 8 weeks following their last injection and continues whether or not a participant attends the Day 0 visit or subsequent visits.

For participants who transition to Step 3 prematurely, the timeline for Day 0 begins 8 weeks after that participant's last injection, even if the participant does not report to the Day 0 visit (or the Week 12 visit, etc.). Sites may contact the CMC for questions regarding participants who transition to Step 3 prematurely who are then subsequently missing, though it is not required to do so.

Per Section 5.8 of the protocol, note the following:

- Do not perform the following tests/procedures if they occurred within the last three months prior to either prematurely transitioning to Step 3, or the Week 153/Day 0 visit was missed for any reason, or if the Week 153 visit already occurred under Version 2.0 of the protocol and the participant now needs to move to Step 3 under Version 3.0 of the protocol: ECG; urine collection for urinalysis and GC/CT testing; rectal swab for GC/CT testing; HCV testing; and syphilis testing, and perform these requirements only at Weeks 24 and 48 (except for HCV testing, which is not required at Weeks 24 and 48). Refer to Appendix IC.
- For participants who either prematurely transition to Step 3, or the Week 153/Day 0 visit was missed for any reason, or if the Week 153 visit already occurred under Version 2.0 of the protocol and the participant now needs to move to Step 3 under Version 3.0 of the protocol, administer the acceptability assessment at the Week 153/Day 0 visit (whenever it occurs) as the final assessment if not done in the previous 6 months prior to transitioning, to include a brief preference assessment.
- Regarding the behavioral assessment, for participants who either prematurely transition to Step 3, or the Week 153/Day 0 visit was missed for any reason, or if the Week 153 visit already occurred under Version 2.0 of the protocol and the participant now needs to move to Step 3 under Version 3.0 of the protocol, (see Table B).

** The interviewer-administered questionnaires and computer-assisted self-interviewing surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. Following that visit, these assessments will no longer be administered. Refer to Data Communique # 7, dated June 5, 2020.

± Safety procedures and evaluations will be performed at injection visits only. As part of the required safety evaluations, the Post-injection Exercise Assessment and injection site reaction evaluation should be done at all injection visits only with participants receiving injections.

[1] To include dietary calcium and Vitamin D assessment

[2] If testing cannot be performed at the local laboratory, testing at another laboratory will be considered (see SSP Manual).

[3] The HIV testing algorithm is provided in Appendices IE-G and the SSP Manual. If HIV rapid testing is indicated, this testing may be performed in the clinic or the laboratory.

[4] Testing does not need to be repeated if infection was documented at a prior visit. HCV Ab testing is required.

[5] Required chemistry testing: BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

[6] Required LFTs: AST, ALT, total bilirubin, and alkaline phosphatase.

[7] Required for lipid profile: Total cholesterol, HDL, triglycerides, and LDL (either calculated or measured). Participants should have fasted for at least 8 hours, preferably 12 hours, prior to sample collection

[8] Per Section 5.8 of Protocol V3.0 and Table A of this SSP section, the last injection in Step 2 will occur at the Week 145 visit. An injection will not be administered at the Step 2 Week 153/Step 3 Day 0 visit.

Table B: Schedule of Procedures and Evaluations - Step 3 – Open Label Daily Oral TDF/FTC Post-Last Injection

Procedures*	Week 12	Week 24	Week 36	Week 48
ADMINISTRATIVE, BEHAVIORAL, REGULATORY				
Locator Information	X	X	X	X
HIV Counseling	X	X	X	X
Offer Condoms and lubricant	X	X	X	X
Behavioral Assessment**		X		X
Adherence Counseling	X	X	X	
CLINICAL EVALUATIONS & PROCEDURES				
History, concomitant medications, physical exam	X	X	X	X
Weight, blood pressure, pulse data entry to Medidata Rave	X	X	X	X
Blood Collection	X	X	X	X
Urine collection for GC/CT testing		X		X
Rectal swab for GC/CT testing[1]		X		X
Dispense pills	X	X	X	
HIV testing[2]	X	X	X	X
Chemistry testing[3]		X		X
Liver function tests[4]		X		X
Syphilis serologic testing		X		X
Urine GC/CT testing		X		X
Rectal swab GC/CT testing		X		X
Plasma storage	X	X	X	X

FOOTNOTES FOR Table B

*See Week 153/Day 0 of Table A for Step 3 Day 0 procedures.

**The interviewer-administered questionnaires and computer-assisted self-interviewing surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. Following that visit, these assessments will no longer be administered. Refer to Data Communique # 7, dated June 5, 2020. If the behavioral assessment was not done at Day 0, administer at Week 12 ONLY if last visit at which these assessments are scheduled to occur.

[1] If testing cannot be performed at the local laboratory, testing at another laboratory will be considered (see SSP Manual).

[2] The HIV testing algorithm is provided in Appendices IE-G of the protocol and the Section 11 of the SSP Manual. If HIV rapid testing is indicated, this testing may be performed in the clinic or the laboratory.

[3] Required chemistry testing: BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

[4] Required LFTs: AST, ALT, total bilirubin, and alkaline phosphatase.

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Step 2: (Injection/ dispense pills Visits) Weeks 9, 17, 25, 33, 41, 49, 57, 65, 73, 81, 89, 97, 105, 113, 121, 129, 137, and 145 *Circle applicable visit week*			
Initial/date	**Completed**	**Procedures**	**Comments**
_____	☐	Confirm participant identity and PTID	
_____	☐	Review/update locator information	
_____	☐	At the first participant study visit following IRB/EC approval of the LoA #1: • Provide DSMB review outcome information and provide the Dear Participant Letter. Ensure participants' understanding of the information and obtain signature to acknowledge they received and understood the information. • Inform participants of their randomization assignment • Collect any remaining placebo pills as applicable	
_____	☐	Confirm last time participant ate. (**Weeks 57, 105 only**) *Reminder: Participants should have fasted for at least 8 hours (preferably 12 hours) prior to blood collection*	
_____	☐	Collect targeted medical history (including concomitant medications)	
_____	☐	Perform targeted physical exam *(Note: As part of the safety evaluations, please complete the **Post-injection Exercise Assessment (see Data Communique #7) and ISR evaluations at injection visits. ISR evaluations will be done only with participants receiving injections.**)*	
_____	☐	Perform ECG (**Weeks 57 and 105 only**)	
_____	☐	Administer Step 2 CASI* (Weeks 9, 17, 25, 33, 41, 49, 57, 65, 73, 81, 89, 97, 105, 121, and 137)	

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Step 2: (Injection/ dispense pills Visits) Weeks 9, 17, 25, 33, 41, 49, 57, 65, 73, 81, 89, 97, 105, 113, 121, 129, 137, and 145 *Circle applicable visit week*			
Initial/date	**Completed**	**Procedures**	**Comments**
_____	☐	Interviewer-Administered*: Follow-up 1 (Weeks 17, 33, 49, 65, 81, 97, 105, 121 and 137)	
_____	☐	Interview-Administered*: Follow-up 2 (Weeks 9, 25, 41, 57, 73, 89)	
_____	☐	Collect rectal swab for GC/CT testing (**Weeks 33, 57, 81, 105, 129**)	
_____	☐	Collect urine for: ☐ Urinalysis (**Weeks 57, 105**) ☐ GC/CT testing (**Weeks 33, 57, 81, 105, 129**)	
_____	☐	DXA Scan **subset only; Weeks 57, 105 only**)	
_____	☐	Provide HIV pre-test counseling	
_____	☐	Collect blood for ☐ HIV testing ☐ FDA-cleared HIV rapid test ☐ 4th or 5th generation HIV immunoassay ☐ HCV testing (**Weeks 57, 105)** ☐ CBC with differential ☐ Chemistry panel (BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, lipase) ☐ LFTs (AST, ALT, total bilirubin, alkaline phosphatase) ☐ Fasting lipid profile (**Weeks 57, 105**) ☐ Syphilis serology (**Weeks 33, 57, 81, 105, 129**) ☐ Plasma storage ☐ DBS storage ☐ Plasma storage for pharmacology testing (must be drawn PRIOR to injection)	
_____	☐	Provide HIV post-test counseling	

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Step 2: (Injection/ dispense pills Visits) Weeks 9, 17, 25, 33, 41, 49, 57, 65, 73, 81, 89, 97, 105, 113, 121, 129, 137, and 145 *Circle applicable visit week*			
Initial/date	**Completed**	**Procedures**	**Comments**
NOTE BEFORE INJECTION: *All HIV test results from previous visits and at least one HIV test result from the current visit must be available and confirmed to be negative/non-reactive PRIOR to injection of study product. The injection must not be given if any HIV test is reactive/positive.* *Results from the other laboratory evaluations (e.g., chemistry, LFTs, hematology) from the current visit are NOT required prior to injection.* *Results from all the previous safety visit clinical and laboratory evaluations (e.g., chemistry, LFTs, hematology) must be available and be reviewed by the IoR or their designee prior to injection.*			
_____	☐	Based on participant's randomization assignment: • Administer CAB injection (with counseling about possible side effects and reminder that the use of anticoagulant and/or antiplatelet medications are prohibited within 7 days before and after injections) • Provide oral TDF/FTC study drug (with adherence counseling)	
_____	☐	Offer condoms and lubricant	
_____	☐	Provide site contact information and instructions to report symptoms and/or clarify any questions	
_____	☐	Schedule next study visit	
_____	☐	Provide participant reimbursement, if applicable	

Notes for injection visits:
Please refer to Section 5.6 of the HPTN 083 Protocol
****The interviewer-administered questionnaires and CASI surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. Following that visit, these assessments will no longer be administered (see Data Communique #7 for further information).***

Comments: _____
_____
_____

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Week 153, Last Visit of Step 2/Day 0, First Visit of Step 3

NOTE: Participants who transition to Step 3 prematurely, the timeline for Day 0 begins 8 weeks after participant's last injection, even if the participant does not report to the Day 0 visit. See Protocol Section 5.8 and Appendix IB for detailed informaiton.

Initial/date	Completed	Procedures	Comments
_____	☐	Confirm participant identity and PTID	
_____	☐	Review/update locator information	
_____	☐	At the first participant study visit following IRB/EC approval of the LoA #1: • Provide DSMB review outcome information and provide the Dear Participant Letter. Ensure participants' understanding of the information and obtain signature to acknowledge they received and understood the information. • Inform participants of their randomization assignment • Collect any remining placebo pills as applicable	
_____	☐	Collect targeted medical history (including concomitant medications)	
_____	☐	Perform targeted physical exam *(Note: As part of the safety evaluations, please complete the **Post-injection Exercise Assessment (see Data Communique #7) and ISR evaluations at injection visits. ISR evaluations will be done only with participants receiving injections.**)*	
_____	☐	Dispense open-label TDF/FTC	
_____	☐	Administer Step 3 Day 0 CASI*	
_____	☐	Interviewer-Administered: Follow-up 1*	
_____	☐	SMSQs*	

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Week 153, Last Visit of Step 2/Day 0, First Visit of Step 3

NOTE: Participants who transition to Step 3 prematurely, the timeline for Day 0 begins 8 weeks after participant's last injection, even if the participant does not report to the Day 0 visit. See Protocol Section 5.8 and Appendix IB for detailed informaiton.

Initial/date	Completed	Procedures	Comments
_____	☐	Collect urine for urinalysis and GC/CT testing (do not collect/do not perform test if testing occurred within 3 months prior to entering Step 3)	
_____	☐	Collect rectal swab for GC/CT testing (do not collect/do not perform test if testing occurred within 3 months prior to entering Step 3)	
_____	☐	Perform ECG (do not perform procedure if done within 3 months prior to entering Step 3)	
_____	☐	Provide HIV pre-test counseling	
_____	☐	Collect blood for: ☐ HIV testing ☐ FDA-cleared HIV rapid test ☐ 4th or 5th generation HIV immunoassay ☐ CBC with differential ☐ HCV testing (do not perform test if testing occurred within 3 months prior to entering Step 3) ☐ Chemistry panel (BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, lipase) ☐ LFTs (AST, ALT, total bilirubin, alkaline phosphatase) ☐ Syphilis serology (do not perform test if testing occurred within 3 months prior to entering Step 3) ☐ Plasma storage ☐ DBS storage	
_____	☐	Provide HIV post-test counseling	

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Week 153, Last Visit of Step 2/Day 0, First Visit of Step 3

NOTE: Participants who transition to Step 3 prematurely, the timeline for Day 0 begins 8 weeks after participant's last injection, even if the participant does not report to the Day 0 visit. See Protocol Section 5.8 and Appendix IB for detailed informaiton.

Initial/date	Completed	Procedures	Comments
_____	☐	Provide adherence counseling	
_____	☐	Offer condoms and lubricant	
_____	☐	Provide site contact information and instructions to report symptoms and/or clarify any questions	
_____	☐	Schedule next study visit, if applicable	
_____	☐	Provide participant reimbursement, if applicable	

Notes for Week 153:
Please refer to Section 5.8 of the HPTN 083 Protocol
****The interviewer-administered questionnaires and CASI surveys will be completed if this is the next scheduled visit at which these assessments are scheduled to occur. Following that visit, these assessments will no longer be administered.***

Comments: _____
_____
_____
_____

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Step 3: (Open-label daily oral TDF/FTC) Weeks 12, 24, 36, 48 *Circle applicable visit week* *(See Protocol Section 5.9 and Appendix IC for detailed information)*			
Initial/date	**Completed**	**Procedures**	**Comments**
_____	☐	Confirm participant identity and PTID	
_____	☐	Review/update locator information	
_____	☐	At the first participant study visit following IRB/EC approval of the LoA #1: • Provide DSMB review outcome information and provide the Dear Participant Letter. Ensure participants' understanding of the information and obtain signature to acknowledge they received and understood the information. • Inform participants of their randomization assignment • Collect any remining placebo pills as applicable	
_____	☐	Collect targeted medical history (including concomitant medications)	
_____	☐	Perform targeted physical exam	
_____	☐	Administer Step 3 CASI (**Week 24, and 48**)*	
_____	☐	Interviewer-Administered: Follow-up 1 (**Weeks 24, 48 only**)*	
_____	☐	Collect urine for GC/CT testing (**Weeks 24, 48 only**)	
_____	☐	Collect rectal swab for GC/CT testing (**Weeks 24, 48 only**)	
_____	☐	Provide HIV pre-test counseling	

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Step 3: (Open-label daily oral TDF/FTC) Weeks 12, 24, 36, 48
Circle applicable visit week
(See Protocol Section 5.9 and Appendix IC for detailed information)

Initial/date	Completed	Procedures	Comments
_____	☐	Collect blood for: ☐ HIV testing ☐ FDA-cleared HIV rapid test ☐ 4th or 5th generation HIV immunoassay ☐ Chemistry panel (BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, lipase; **Weeks 24 and 48**) ☐ LFTs (AST, ALT, total bilirubin, alkaline phosphatase; **Weeks 24 and 48**) ☐ Syphilis serology (**Weeks 24, 48**) ☐ Plasma storage	
_____	☐	Provide HIV post-test counseling	
_____	☐	Provide oral study drug (**Weeks 12, 24, 36**)	
_____	☐	Provide adherence counseling (**Weeks 12, 24, 36**)	
_____	☐	Offer condoms and lubricant	
_____	☐	Provide site contact information and instructions to report symptoms and/or clarify any questions	
_____	☐	Schedule next study visit, if applicable	
_____	☐	Provide participant reimbursement, if applicable	

Notes for Step 3:
Please refer to Section 5.9 of the HPTN 083 Protocol
**** The interviewer-administered questionnaires and CASI surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. Following that visit, these assessments will no longer be administered.***

Comments: _____
_____
_____
_____

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Procedures for Enrolled Participants who Seroconvert (HIV confirmation visit, Week 12, 24, 36, 48) *Circle applicable visit week*			
Initial/date	**Completed**	**Procedures**	**Comments**
_____	☐	Confirm participant identity and PTID	
_____	☐	Review/update locator information	
_____	☐	At the first participant study visit following IRB/EC approval of the LoA #1: • Provide DSMB review outcome information and provide the Dear Participant Letter. Ensure participants' understanding of the information and obtain signature to acknowledge they received and understood the information. • Inform participants of their randomization assignment • Collect any remining placebo pills as applicable	
_____	☐	Collect targeted medical history (including concomitant medications)	
_____	☐	Perform targeted physical exam	
_____	☐	Provide HIV pre-test counseling (**HIV confirmation visit only**)	

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Procedures for Enrolled Participants who Seroconvert (HIV confirmation visit, Week 12, 24, 36, 48) *Circle applicable visit week*			
Initial/date	**Completed**	**Procedures**	**Comments**
_____	☐	Collect blood for: ☐ HIV testing (**HIV confirmation visit only**) ☐ HIV resistance (**HIV confirmation visit only**) ☐ DBS storage (**HIV confirmation visit only**) ☐ CD4 cell count (**HIV confirmation visit, Weeks 24, 48 only)** ☐ HIV viral load (**HIV confirmation visit, Weeks 24, 48 only**) ☐ Chemistry (BUN/Urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, lipase; **Weeks 12, 24, 36, 48 only**) ☐ LFTs (AST, ALT, total bilirubin, alkaline phosphatase; **Weeks 12, 24, 36, 48 only**) ☐ Plasma storage	
_____	☐	Provide HIV post-test counseling (**HIV confirmation visit only)**	
_____	☐	Offer condoms and lubricant	
_____	☐	Provide site contact information and instructions to report symptoms and/or clarify any questions	
_____	☐	Schedule next study visit, if applicable	
_____	☐	Provide participant reimbursement, if applicable	

Notes for Procedures for Enrolled Participants who Seroconvert: Please refer to Appendix II of the HPTN 083 Protocol. For any questions related to the requirements for suspected or confirmed HIV infection or clinical management questions, email 083HIV@hptn.org.

Comments: _____

_____

_____

_____

Visit Checklists

Participant ID **Visit Date**

INSTRUCTIONS: Enter staff initials next to each procedure completed. Do not initial procedures another staff member completed. If other staff members are not available to initial next to the procedure they completed, add a note on the checklist documenting who completed the procedure. If all procedures listed on a checklist are performed on the date entered in the top section of the checklist, it is not necessary to enter the date beside each item. If procedures listed on a checklist are performed on multiple dates, enter the date upon which each procedure is performed beside each item. Bracketing procedures which are consecutive and all done on the same date is also acceptable. If a procedure listed on the checklist is not performed, enter "ND" for "not done" or "NA" for "not applicable" beside the item and record the reason why (if not self-explanatory); initial and date this entry.

NOTE: For a listing of forms required at each visit, please refer to SSP Appendix III, HPTN 083 Schedule of Forms

Procedures for Annual HIV Testing Visits			
Initial/date	**Completed**	**Procedures**	**Comments**
_____	☐	Confirm participant identity and PTID	
_____	☐	Review/update locator information	
_____	☐	At the first participant study visit following IRB/EC approval of the LoA #1: • Provide DSMB review outcome information and provide the Dear Participant Letter. Ensure participants' understanding of the information and obtain signature to acknowledge they received and understood the information. • Inform participants of their randomization assignment • Collect any remining placebo pills as applicable	
_____	☐	Collect targeted medical history (including concomitant medications)	
_____	☐	Perform targeted physical exam	
_____	☐	Provide HIV pre-test counseling	
_____	☐	Collect blood for ☐ HIV testing ☐ FDA-cleared HIV rapid test ☐ 4th or 5th generation HIV immunoassay ☐ Plasma storage ☐ DBS storage	
_____	☐	Provide HIV post-test counseling	
_____	☐	Offer condoms and lubricant	
_____	☐	Provide site contact information and instructions to report symptoms and/or clarify any questions	
_____	☐	Schedule next study visit, if applicable	
_____	☐	Provide participant reimbursement, if applicable	

HPTN 083 Schedule of Forms and CASI Surveys – per LOA #1 to Protocol v3.0

Step 2 Injections/Dispense Pill Visits weeks 5 – 41

	Week 5 V5.0	**Week 9 V7.0**	**Week 17 V9.0**	**Week 25 V 11.0**	**Week 33 V 13.0**	**Week 41 V 15.0**
Date of Visit	x	x	x	x	x	x
DXA Scan						
Hematology		x	x	x	x	x
Hepatitis Test Results						
HIV Test Results	x	x	x	x	x	x
Injection Administration	x	x	x	x	x	x
Interviewer Administered: Follow-up 1	x		x		x	
Interviewer Administered: Follow-up 2		x		x		x
Local Laboratory Results		x	x	x	x	x
Post-Injection Exercise Assessment		x	x	x	x	x
Sexually Transmitted Infections					x	
Specimen Storage	x	x	x	x	x	x
Vital Signs	x	x	x	x	x	x
CASI Survey	x	x	x	x	x	x

Per LOA #1 to Version 3.0 of the protocol:

- ***Safety visits are no longer required and have been removed from the Schedule of Forms.***
- ***The interviewer-administered questionnaires and CASI surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. The SMSQs was previously required at safety visits and should now be completed one last time at the next scheduled visit.***

Step 2 Injections/Dispense Pill Visits weeks 49 - 89

	Week 49 V 17.0	**Week 57 V 19.0**	**Week 65 V 21.0**	**Week 73 V 23.0**	**Week 81 V 25.0**	**Week 89 V 27.0**
Date of Visit	x	x	x	x	x	x
DXA Scan		x				
Hematology	x	x	x	x	x	x
Hepatitis Test Results		x				
HIV Test Results	x	x	x	x	x	x
Injection Administration	x	x	x	x	x	x
Interviewer Administered: Follow-up 1	x		x		x	
Interviewer Administered: Follow-up 2		x		x		x
Lead Electrocardiogram		x				
Local Laboratory Results	x	x	x	x	x	x
Post-Injection Exercise Assessment	x	x	x	x	x	x
Sexually Transmitted Infections		x			x	
Specimen Storage	x	x	x	x	x	x
Vital Signs	x	x	x	x	x	x
CASI Survey	x	x	x	x	x	x

Per LOA #1 to Version 3.0 of the protocol:

- ***Safety visits are no longer required and have been removed from the Schedule of Forms.***
- ***The interviewer-administered questionnaires and CASI surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. The SMSQs was previously required at safety visits and should now be completed one last time at the next scheduled visit.***

Step 2 Injections/Dispense Pill Visits weeks 97 - 137

	Week 97 V 29.0	**Week 105 V 31.0**	**Week 113 V 33.0**	**Week 121 V 35.0**	**Week 129 V 37.0**	**Week 137 V 39.0**
Date of Visit	x	x	x	x	x	x
DXA Scan		x				
Hepatitis Test Results		x				
HIV Test Results	x	x	x	x	x	x
Injection Administration	x	x	x	x	x	x
Interviewer Administered: Follow-up 1	x	x		x		x
Lead Electrocardiogram		x				
Local Laboratory Results	x	x	x	x	x	x
Post-Injection Exercise Assessment	x	x	x	x	x	x
Sexually Transmitted Infections		x			x	
Specimen Storage	x	x	x	x	x	x
Vital Signs	x	x	x	x	x	x
CASI Survey	x	x		x		x

Per LOA #1 to Version 3.0 of the protocol:

- ***Safety visits are no longer required and have been removed from the Schedule of Forms.***
- ***The interviewer-administered questionnaires and CASI surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. The SMSQs was previously required at safety visits and should now be completed one last time at the next scheduled visit.***

Step 2 Injections/Dispense Pill Visits weeks 145 and 153

	Week 145 V41.0	**Week 153 /Day 0 V 43.0***
Date of Visit	x	x
DXA Scan		x
Hepatitis Test Results		x
HIV Test Results	x	x
Injection Administration	x	
Interviewer Administered: Follow-up 1		x
Lead Electrocardiogram		x
Local Laboratory Results	x	x
Post-Injection Exercise Assessment	x	x
Sexually Transmitted Infections		x
Specimen Storage	x	x
Vital Signs	x	x
CASI Survey		x

**** Visit 43.0 now functions as the Step 3 Day 0 visit for participants who complete Step 2. If the transition to Step 3 occurs at an earlier visit, it is combined with a final step 2 visit and will receive that Step 2 visit code. Complete all procedures required at that Step 2 visit and add STI testing and any behavioral surveys as needed to fulfill Day 0 requirements:***

- ***If Interviewer Administered Follow-up 2 is already required at the final Step 2 visit, complete only Follow-Up 1.***
- ***The Day 0 CASI is not required if behavioral assessment was done in the last 4 weeks AND acceptability assessment was done in the previous 24 weeks.***
- ***- SMSQs is not required if completed within the last 24 weeks.***

Per LOA #1 to Version 3.0 of the protocol:

- ***Safety visits are no longer required and have been removed from the Schedule of Forms.***
- ***The interviewer-administered questionnaires and CASI surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. The SMSQs was previously required at safety visits and should now be completed one last time at the next scheduled visit.***

Step 3 Open label Oral

Step 3 Day 0 should occur within 8 weeks after last injection and is combined with a Step 2 visit per above. If Step 3 Day 0 is missed, all procedures required for the Day 0 visit should be added to the next visit where the participant is seen, e.g., Step 3 Week 12, etc.

	Week 12 V 54.0	**Week 24 V 55.0**	**Week 36 V 56.0**	**Week 48 V 57.0**
Date of Visit	x	x	x	x
HIV Test Results	x	x	x	x
Interviewer Administered: Follow-up 1		x		x
Local Laboratory Results		x		x
Sexually Transmitted Infections		x		x
Specimen Storage	x	x	x	x
Vital Signs	x	x	x	x
CASI Survey	x	x		x

Step 2 participants with confirmed HIV Infection

Note that the confirmation visit in Step 2 serves as "Day 0" in this scenario; visit 54.0 should occur approximately 12 weeks after HIV infection is confirmed.

	Week 12 V 54.0	**Week 24 V 55.0**	**Week 36 V 56.0**	**Week 48 V 57.0**
Date of Visit	x	x	x	x
CD4/Viral Load		x		x
Local Laboratory Results		x	x	x
Specimen Storage	x	x	x	x
Vital Signs	x	x	x	x

Additional / As Needed CRFs:

Concomitant Medications Y/N
Adverse Event Y/N
ART Medication Y/N
Protocol Deviation Y/N
Social Impact Y/N
Product Hold Y/N
Injection Site Reaction Y/N

Found in Participant Unblinding Folder

Participant Unblinding

Found in "Add Event" function

Interim Visit
Yearly Visit

Additional Forms

Participant Transfer
Participant Receipt
Supplemental HIV Results
Termination

HPTN 083 Survey Information according to the protocol appendix labels

Per LOA#1 to Version 3.0 of the protocol, the interviewer-administered questionnaires, SMSQs, and CASI surveys will be completed one last time at the next scheduled visit at which these assessments are scheduled to occur. Following that visit these assessments will no longer be administered. Refer to Data Communiqué #7, dated June 5, 2020.

Baseline Acceptability Assessment
CASI pages 16 (starting with "Attitudes toward PrEP methods") - 18

Baseline Behavioral Assessment
CASI pages 5-6
Interviewer Administered: Baseline

Follow Up Acceptability Assessment
CASI Pages 16 (starting with Overall satisfaction with study product") - 18
Interviewer Administered: Follow Up 1 – Bottom of Page 65 of the PDF ("I would like to ask you about your preferences…") – 66; Study Medication Satisfaction
Questionnaire (SMSQ), SMSQ (Change).

Follow Up Behavioral Assessment
CASI pages 5-6, 8-15
Interviewer Administered: Follow Up 1 (all but bottom of page 65 -66) Interviewer Administered: Follow Up 2

HPTN 083 Adherence Counseling Updates

Overview:

The existing counseling tool can still be used effectively, even in the context of recent study results, which demonstrated the superiority of cabotegravir. This memo details important information about how to use the adherence counseling tool as participants begin the unblinding process and ultimately choose a study product. **It is important to note that daily oral TDF/FTC works extremely well when taken as prescribed, and if a participant prefers taking pills over injections, and is able to maintain high levels of adherence, switching is not required.** Depending on which arm the participant has been randomized to, and when cabotegravir becomes available to offer to participants who want it, the adherence counseling will either center on (1) helping individuals take their Truvada daily, OR (2) report to the clinic on time for their injections. Of note, when additional cabotegravir becomes available, participants who wish to initiate active cabotegravir for the first time will be asked to take a daily oral cabotegravir pill for 5 weeks before starting injections (like in Step 1 of the trial). Thus, some adherence counseling on how to take pills daily most effectively for a short period of time may be useful for those participants before focusing on injection visit adherence.

Timing:

An adherence counseling session should occur (1) as close as possible to the time of unblinding to which arm they have been assigned to, and (2) when participants makes their choice about what study product to use, and/or at the time a new study drug is dispensed (this will be possible when additional cabotegravir becomes available).

Counseling messages:*

1. Review of adherence definitions. Participants should be reminded about what level of adherence is needed for their particular product to work optimally. For participants who are randomized to or who choose to remain on Truvada when a choice can be offered (when additional cabotegravir becomes available), this is daily pill taking. For those who are randomized to or who choose to use cabotegravir when a choice can be offered (when additional cabotegravir becomes available), this is daily pill adherence for 5 weeks, followed by injection visits every two months. It is important to stress that we don't yet know how "forgiving" cabotegravir is (either formulation), so it is important to be as close as possible to on time for injection visits.
2. Review of Lifesteps.
    a. Participants randomized to Truvada, or participants who choose Truvada (when additional cabotegravir becomes available): Participants will have received Lifesteps counseling at the beginning of their time in the trial. However, a brief review of Lifesteps (see slides 12 and 24 for a list of steps) may be helpful as people are unblinded, and when they start their

study product of choice. If participants have done well with oral pill adherence during the trial, a brief review or check in of their plans for each of the steps is sufficient. For participants who have struggled with pill adherence during the trial, review the Lifesteps content in greater detail as outlined in slides 23-35.

b. Participants randomized to active cabotegravir or participants who choose cabotegravir (when additional cabotegravir becomes available): Adherence counseling should center around getting to the clinic for on time injections. For participants who were not randomized to cabotegravir but who wish to switch to cabotegravir (when this is possible), participants can be reminded that good pill adherence for 5 weeks/the lead in period is important to make sure that their body will not react poorly to the medication before moving to injections (material from slide 16 may be useful), at which time they will only need to worry about getting to their injection visits. Once participants begin injections, adherence counseling should focus on problem-solving barriers to injection visits. It may be helpful to know that while the majority of people (80%) receiving active CAB injections had some pain-tenderness after injection, it was almost always mild to moderate and only 2% of people decided it was so uncomfortable that they didn't want to continue injections.

c. Of note, COVID-19 has the potential to disrupt attendance at visits (including injection visits) and/or ability to secure refills. It is suggested that you discuss this (and plan for such interruptions) with study participants, regardless of product choice.

3. Subsequent adherence counseling. At each subsequent adherence counseling visit, the adherence counseling tool may generally be used as written based on whatever product participants are using. For example, an open discussion of adherence to pills and/or injection visits should occur (see slide 39). Reviewing plans for ongoing adherence (specific to product), including a discussion of anticipated barriers to adherence and/or injection visits before the next counseling session (e.g., see slide 34) is all that is required for those who are doing well with respect to adherence. For those who have missed doses of oral medication and/or an injection visit(s), additional counseling messages may be utilized (for some, this will be adjusting one of the steps in Lifesteps, for others, this may involve utilizing additional problem solving skills as described in slides 46-52 and 55-58).

**Please note that because the counseling tool has not been modified, there is content in the tool that is no longer needed or is outdated, such as references to blindedness and certain timelines of study procedures. Please reference the most up to date protocol for any questions about timing of visits.*