Section 4. Continuation in Protocol Version 3.0 (OLE)

4.1 Overview of Section 4

This section provides an overview of requirements and procedures for rolling participants over into the Open Label Extension (OLE)/ Protocol Version 3.0 Additional procedure-specific details can be found in the visit checklists in SSP Section 6, and in Section 5/ Schedule of Evaluations Appendices of the Protocol.

4.2 Continuation in Protocol V3.0

Participants who remain in follow-up will be offered the opportunity for another 48 weeks in HPTN 084 under v3.0 protocol (OLE). Update the Product Choice CRF to indicate whether the participant enrolled in the OLE.

Participants who permanently discontinued study product under Step 2 or Step 3 of the protocol, but are otherwise eligible for injectable CAB, may be eligible to restart study product under Version 3.0.

Note: The CMC may be contacted for questions related to safety and study product AEs of concern for participants interested in continuing or initiating CAB LA.

The Statistics and Data Management Center (SDMC) will provide reports with the number of participants enrolled based on data received and entered into the study database.

4.2.1 Informed Consent Process

After receiving notification to implement Version 3.0 of the protocol, sites will administer the addendum to the main informed consent form as participants present to the site. This form will document the participant's continued participation in the study. As part of the consent discussion, sites should explain to participants the options for ongoing study participation as outlined in the Informed Consent Appendices of the Protocol.

Contact the CMC for guidance if there are other scenarios for a discussion about choice and obtaining informed consent. Deliver All Required Information in a Manner that is Understandable to Potential Participants

If the participant is literate, give her a copy of the ICF to read during the Screening/Enrollment visits. Also provide the participant with other (IRB/EC-approved) informational materials developed to complement the ICF, if any**.** If the participant is not literate, the materials may be read to her verbatim. After the participant has read the written material (or had it read to her), verbally review the information provided. A checklist or the ICF itself may serve as a useful guide for this. For example, you may note the main points described in each paragraph of the informed consent form and ask if the participant has questions or concerns about each point. Listen carefully to the questions or concerns expressed by the participant and discuss these thoroughly. Take as much time as needed to address each question and concern.

If the participant is illiterate, **an impartial witness must be present during the entire informed consent discussion**. The witness will be asked to sign and date the ICF to attest that the information in the consent form was accurately explained to, and apparently understood by, the participant, and that informed consent was freely given by the participant. The ICH GCP guideline identifies an "impartial" witness as a person who is independent of the study, who cannot be unfairly influenced by people involved with the study. Each site must specify its procedures for obtaining informed consent from illiterate persons in its SOP for obtaining informed consent. The SOP should define who may serve as an impartial witness to the informed consent process. It is recommended that each site seek IRB/EC review and approval of these procedures. Refer to the HPTN MOP for additional information on impartial witnesses.
https://www.hptn.org/resources/manual-of-operations.

4.2.1.1. Assure That Informed Consent Is Obtained in A Setting Free of Coercion and Undue Influence

During the informed consent discussion, take care to not overstate the possible benefits of the study, nor to understate the risks. Also emphasize to the participant that medical care and other services routinely available from the clinic or hospital associated with the site will not be affected by their decision whether or not to take part in the study. Encourage the participant to take as much time as she needs — and to talk about her potential participation with others, if she chooses — before making a decision.

4.2.1.2. Confirm That the Participant Comprehends the Information

The participant must not be asked to agree to continue in the OLE, or to sign the ICF, until she fully understands the study. Study staff are responsible for implementing procedures to ensure that each participant understands the risks, benefits and goals of the amendment (OLE) study prior to signing the amended ICF, respectively, and undertaking any study procedures.

One approach to assessing comprehension is to use a "quiz" (either oral or written) or other assessment tool that participants complete as part of the consent process. Another approach is to use open-ended questions to ascertain participant understanding during the informed consent discussion. It is possible to incorporate a scoring system into these assessment tools and to re-review the contents of the

informed consent until the potential participant can answer a certain percentage of the questions correctly. Table 4-1 includes a sample informed consent assessment tool that sites may choose to adapt for their local use. For sites that choose to adopt tools such as those included in this section, detailed instructions for their use must be specified in the site SOP for obtaining informed consent.

Regardless of the method used to assess comprehension, if the assessment results indicate misunderstanding of certain aspects of the study, review those aspects again until the participant fully understands them. If after all possible efforts are exhausted, the participant is not able to demonstrate adequate understanding of the study, do not ask her to sign the informed consent form or screen /enroll in the study. Similarly, if the participant has concerns about possible adverse impacts on her if he/she were to take part in the study or indicates that she may have difficulty adhering to the study requirements, do not ask her to sign the informed consent form to continue (for HPTN 084 participants) or enroll into (for participants who were in HPTN 084-01 and qualify) HPTN 084 OLE (version 3.0).

4.2.1.3. Document the Process

U.S. regulations require that informed consent be documented by "the use of a written ICF approved by the IRB/EC and signed and dated by the subject or the subject's legally authorized representative at the time of consent."

To fulfill this requirement, complete all signature and date blocks on the ICF per local IRB/EC requirements. Participants must sign the ICF using their complete last name (not just initials); the policy also recommends, but does not require, that the participant's complete first name (not just an initial or nickname) be used as well. It is essential that the date documented on the form either precedes or coincides with the (first) study Screening date. In addition, enter a note in the participant chart documenting that informed consent was obtained prior to the initiation of any study procedures. Some sites find it helpful to use a cover sheet attached to the ICFs to document all items in this process. See Table 4.2 for a sample coversheet that sites may wish to adapt and use. Finally, regulations require that participants be offered a signed copy of the informed consent forms. If a participant opts not to receive a copy, document this in the research record.

The *DAIDS Score Manual https://www.niaid.nih.gov/research/daids-score-manual* including the section on Informed Consent of Participants provides detailed requirements and suggestions for documenting the informed consent process. https://www.niaid.nih.gov/sites/default/files/score-informed-consent.pdf. All requirements listed must be met. In order to meet some of the suggestions listed, site staff may consider the use of an informed consent "coversheet" similar to the example included in this section.

4.2.1.4. Continue the Informed Consent Process throughout the Study

The previous sections describe aspects of obtaining informed consent from study participants prior to initiating their involvement in the OLE. Given the ongoing nature

of informed consent, key elements of informed consent should also be reviewed at study follow-up visits. At these visits, study staff should review key elements of informed consent with the participant, focusing on the remainder of their study participation. For example, participants should be encouraged to ask questions as they arise and recognize that poor adherence to their study drug regimen will not affect their continued participation in the trial.

4.2.1.5. ICF Requirements for Protocol Amendments (including LoAs)

According to DAIDS policy (Protocol Registration Policy and Procedure Manual), the site's IRB/EC is/are ultimately responsible for determining whether study participants need to be re-consented for a protocol amendment. The details of re-consent for a protocol amendment will be determined based on the extent and content of the amendment, and instructions will be provided to sites in this regard, after consultation with DAIDS.

Table 4-1: HPTN 084 OLE Version 3.0 Sample Informed Consent Assessment Tool*

	Date: Participant ID:			Staff name/initials
		Participant's Response	Correct Answer	Notes
1	Participation in this research study is voluntary	□ True □ False	☒ True □ False	
2	The purpose of this research study is to find out whether a new drug is safe and prevents HIV infection, as this information has not been researched.	□ True □ False	□ True ☒False	
3	This research study is part of the regular medical care offered here at [clinic name].	□ True □ False	□True ☒ False	
4	We will test your blood for HIV throughout the study.	□ True □ False	☒ True □ False	
5	You can choose whether you are in the group of women who receive TDF/FTC (Truvada) or the group of women who receive cabotegravir.	□ True □ False	☒True □False	
6	If you join this research study, you must stay in the study for as long as the study staff says.	□ True □ False	□True ☒ False	
7	If you choose to take Cabotegravir, you MUST take the oral products before you receive any injections. You will be given a five-week supply of an oral pill to take every day at the beginning of the study.	□ True □ False	□True ☒ False	Note: depends on the site's ethics committee(s)/ decision
8	No matter whether you choose Cabotegravir or TDF/FTC, you will continue to receive injections.	□ True □ False	□True ☒ False	
9	Your participation in the study will be 48 weeks (unless you opt for the pregnancy follow-up).	□ True □ False	☒ True □ False	
10	There are no risks in continuing to take part in this research study.	□ True □ False	□True ☒ False	
11	If I have questions between study visits, I need to write them down and bring them with me at my next appointment.	□ True □ False	□True ☒ False	*no, but it's a good idea.

(* May be adapted as needed for local use)

Table 4-2: Sample Informed Consent Coversheet for HPTN 084 OLE*

Participant name:	
Date of informed consent discussion:	
Start time of informed consent discussion	
Version number/date of informed consent form used during informed consent process/discussion:	
Name of study staff person completing informed consent discussion (and this coversheet):	
In what language was informed consent obtained?	[*insert local language*] (note whether this was written and/ or verbal)
Were all participant questions answered?	☐ Yes ☐ No ⇒ Explain in Notes/Comments. ☐ NA (participant had no questions)
Did the participant accept a copy of the informed consent form (circle one option)?	☐ Yes ☐ No
End time of informed consent process/discussion:	
Notes/Comments (not documented elsewhere):	

(* May be adapted as needed for local use)

Table 4-3: Sample HPTN 084 Screening and Enrollment Log

	Participant ID	Participant Name	Date Screened	Eligible	Date of Enrollment (if not enrolled, note N/A)	If not enrolled, specify reason (include all applicable codes).	Did Participant Enroll in OLE Y/N	Staff name/ Initials
1				Y N				
2				Y N				
3				Y N				
4				Y N				
5				Y N				
6				Y N				
7				Y N				
8				Y N				
9				Y N				
10				Y N				

(*May be adapted as needed for local use. Note: There is no standard screen failure code list.)