

## **HIV Prevention Trials Network**

### **Full Protocol Amendment of:**

**HPTN 083-01:**

**Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Males – A sub-study of HPTN 083**

**DAIDS Study ID: 38654**

### **The Amended Protocol is identified as:**

**Version 3.0 – 2 July 2021**

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The modifications included in this protocol amendment and the associated rationale is briefly summarized below. HPTN 083-01 study investigators will submit this Summary of Changes and the corresponding protocol Version 3.0 and informed consents to all relevant regulatory authorities and Institutional Review Boards/Ethics Committees (IRBs/ECs) for approval. Upon receipt of all IRB/EC approvals, the site should begin implementation of the amended protocol immediately. The site will submit all required documents to DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center.

This Amendment and all related IRB/EC correspondence must be retained in the site regulatory file and in other pertinent files.

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### **RATIONALE**

During implementation of Version 2.0, the Protocol Team identified several changes and clarifications to the protocol. These are considered numerous and substantial enough to be compiled in a Full Protocol Amendment, including (but not limited to) providing an option to remain on CAB LA in Step 3, adding self-consent, bringing on a fourth site, and extending the enrollment period.

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## Summary of Revisions and Rationale

1. [Revision 1](#): Title and Protocol Signature Pages  
The title and protocol signature pages are updated for this protocol amendment.  
Updated to reflect current date and version.
2. [Revision 2](#): Changes to the Schema
  - a. Recruitment period is lengthened from 12 to 18 months.
  - b. An alternative Step 3 is offered. Participants can opt to stay on CAB LA during Step 3, instead of switching to oral PrEP (Truvada®).
  - c. A fourth study site is added: Children's Hospital Colorado CRS, Aurora, CO
3. [Revision 3](#): Section 2.3 – Study Design and Overview
  - a. The option to stay on injections is presented.
  - b. Other clarifying language around begin of qualitative interviews.
  - c. Section 2.3.2: study recruitment period lengthened to 18 months.
4. [Revision 4](#): Section 3.1 – Inclusion Criteria
  - a. 3.1.4: Clarification that participant self-consent is determined by local law.
  - b. 3.1.6: Note added to neutrophil and hemoglobin count requirements, indicating that site PI, in consultation with the CMC, can allow enrollment despite this, if it can be demonstrated that the potential participant is healthy otherwise.
5. [Revision 5](#): Section 3.3 – Recruitment Process
  - a. Recruitment period lengthened to 18 months.
6. [Revision 6](#): Sections 4.1 and 4.2 – Study Product
  - a. The option for participants to continue with CAB LA injections during Step 3 is added and the option to enroll in a local open-label CAB study is removed.
  - b. Clarification that ViiV will provide study product (CAB LA) during Step 3 is included.
7. [Revision 7](#): Section 5.7, Step 3, Follow-up Phase
  - a. The option to continue on CAB LA during Step 3 is added.
  - b. Clarifying language regarding timing of completion of PK monitoring of drug levels of CAB is added.
  - c. Clarification is provided in that a participant can switch from TDF/FTC to CAB LA in Step 3, but this situation will not extend Step 3 any longer.
8. [Revision 8](#): Section 5.13 provides clarification on HBV and HCV testing.
9. [Revision 9](#): Section 6.6, Critical Events Reporting, is removed, given that DAIDS is retiring this policy.
10. [Revision 10](#): Section 8.1, Ethical Review, lists Investigator responsibilities in lieu of the retired Critical Events Policy.
11. [Revision 11](#): Section 8.2, Informed Consent, contains edits to organize the consent/assent forms and clarifying language regarding adolescent ability to consent for themselves (self-consent) in this protocol.

12. [Revision 12](#): Sections 9.4 and 9.5 remove reference to any specific laboratory assessment.
13. [Revision 13](#): Section 12.2, Appendix II:
  - a. Step 3 product choice discussion and assessment is added to the Schedule of Evaluations for Step 2.
  - b. Clarifying language around provision of TDF/FTC only if choosing to move to Step 3-Oral is added.
14. [Revision 14](#): Section 12.3, Appendix III, introduces the first of the two options for Step 3:
  - a. Title clarifies “Step 3-Oral PrEP”.
  - b. CBC with differential, GC/CT testing (urine, rectal, and oral pharyngeal swabs), and Urinalysis are reduced. (Thus, urine and rectal swab collection are reduced.)
  - c. Syphilis testing is moved, to be in line with the parent protocol (HPTN 083).
  - d. HIV testing is added to the safety visits, to correspond with changes made in the parent protocol (to quickly and accurately diagnose any new HIV infections).
  - e. HBsAb and HBcAb will be tested in participants who received the HBV vaccine at Week +48 and Early Discontinuation. HCVAb will be tested at Week +48 and Early Discontinuation.
15. [Revision 15](#): Section 12.4, Appendix IV, is a new schedule of evaluations (SOE) for Step 3-Injection.
  - a. Six injection visits, starting with Weeks +8 and to take place every 8 weeks, are listed.
  - b. This SOE is modelled after the original Step 3 SOE and the revised Appendix III, which is aligned with the parent protocol (HPTN 083) open-label extension.
  - c. The Week +8 visit is still primarily a blood draw visit (now, plus injection).
  - d. Urinalysis is removed, as clinically relevant and to be in-line with the parent protocol (HPTN 083) open-label extension.
  - e. HBsAb and HBcAb will be tested in participants who received the HBV vaccine at Week +48 and Early Discontinuation. HCVAb will be tested at Week +48 and Early Discontinuation.
16. [Revision 16](#): Section 12.6, Appendix VI, Toxicity Management:
  - a. In the Guidance on Toxicity Management for Specified Toxicities section, the table is re-organized to clarify management between the oral (Step 1) and injection phases (Step 2).
17. [Revision 17](#): Section 12.7, Appendix VII, the main informed consent for parents/guardian and assent for adolescent participants 14 to age of majority (AOM):
  - a. Participants who reach the AOM are excluded, as that sub-demographic is now included in the new adolescent self-consent informed consent form (Appendix VIII).
  - b. Under the Study Visit Procedures section, clarifying language about the requirement by law to report any positive of STI testing is included.
  - c. The Tables of Study Procedures are edited for Step 2, Step 3-Oral PrEP, and Step 3-Injection, per changes made to those SOEs. Step 3-Injection is an altogether new table.
  - d. Other minor clarifying edits made to the section, “Risk of HIV Resistance to CAB”.
18. [Revision 18](#): Section 12.8, Appendix VIII, is a new main informed consent for adolescents who can consent for themselves (self-consent) and those reaching the AOM.

- a. This informed consent is based off the newly revised Appendix VII (see Revision 16).
19. [Revision 19](#): Section 12.10, Appendix X, is an informed consent for adolescent interviews for parents/guardians and assent for adolescent interviews for adolescents aged 14 to majority.
- a. The sub-demographic of participants who reach the age of majority is removed and placed in the next ICF (Appendix XI).
  - b. Other minor changes include specifying last injection in Step 2 versus “last injection”, since now participants can choose to continue injections in Step 3 and specifying oral PrEP when mentioning TDF/FTC, since CAB LA is also considered PrEP.
20. [Revision 20](#): Section 12.11, Appendix XI, is a new informed consent for the interviews for adolescents who can consent for themselves (self-consent) and those reaching the AOM.
- a. This informed consent is based off the newly revised Appendix X (see Revision 18).
21. [Revision 21](#): Section 12.14, Appendix XIV, is the main storage consent/assent, the revised informed consent for specimen storage and future use for parents/legal guardians and assent for participants aged 14 to AOM.
- a. The sub-demographic of participants who reach the age of majority is removed and placed in the next ICF (Appendix XV).
22. [Revision 22](#): Section 12.15, Appendix XV, is a new informed consent for specimen storage and future use for adolescents who self-consent and those who reach the AOM.
- a. This informed consent is based off the newly revised Appendix XIV (see Revision 20).

**Other minor changes have been made (not included in the Implementation Section, beginning on the next page):**

1. The Table of Contents is revised accordingly.
2. The Protocol Team Roster information is updated for Lynda Stranix-Chibanda. Katherine Shin, Amber Babinec, Jontraye Davis, Molly Dyer, and Aundria Charles are added as protocol team members. Irene Rwakazina, Tanette Headen, Marcus Bryan, and Kathryn Myers are removed from the roster. Any external links to email addresses were removed.
3. Minor editorial and eCTD compliance comments have been made, per Regulatory review by DAIDS.
4. CAB LA has been included as an option in places where Step 3 is discussed. “Quarterly” (visits) has been replaced with “per Appendix III and IV” or simply deleted, to allow for potential continuation of CAB LA injections in Step 3, which are every 2 months.
5. “Last injection visit” has been changed to edited to read “in Step 2”, to allow for potential continuation of CAB LA injections in Step 3.
6. Section 2.3.2: Addition of clarifying language that states visits for 48 weeks after the final *Step 2* injection. Step 2 is 29 weeks, not 34 weeks (34 weeks included the 5 weeks for Step 1.)
7. Mention of an open label CAB study (or OLE, open label extension) has been removed, since the study will now be offering CAB LA injections to participants in Step 3 within this study.  
Study product choice discussion was added as an option for Week 34, to allow sites flexibility for this discussion.

8. “TRADE NAME: TDF/FTC, TRUVADA®” has been changed to “Trade name: TDF/FTC, Truvada®” in appropriate places.
9. Section 7.1, Statistical Considerations: a strikethrough typo is now removed.
10. Section 10 now includes the option for remote monitoring.
11. Appendices have been re-numbered accordingly and internal links to have been added to appropriate appendices.
12. Informed consent and assent forms are written to be more inclusive of transgender and gender non-conforming people by using “adolescents” instead of “adolescent men” and “young people” instead of “young men”.
13. Appendix XIV, the informed consent for parents and legal guardians and assent for participants aged 14 to majority, clarifies a few pronouns and possessives, given the signer’s point of view.
14. Clarifications have been made in the ICFs to inform the participant that they may now get benefit from receiving CAB LA injections, but that it has still not been approved by the FDA and is, therefore, considered experimental.
15. Clarifications have been made in the ICFs to inform the participant that if they acquire HIV in Step 1, they will exit the study, but if they acquire in Steps 2 or 3, they will remain on study without CAB LA or TDF/FTC.
16. Mention of qualitative interviews now includes the fact that recordings will be destroyed once all analyses are completed.
17. In the ICFs, any mention of study “medication” has now been replaced with study “drug”. Study “product” is still used within the protocol itself, per DAIDS’ preference.
18. Descovy as an option for PrEP has been included as an alternative in the ICFs.
19. Disclosure of STI results has explicitly been added to Appendices VII and VIII. Appendix XVI now explains that genetic testing may be performed (but not Whole Genome Sequencing).
20. An explanation to Appendix VIII has been added to state that, if the participant has reached the age of majority, they will not be in the study for an additional 1.5 years.
21. The fact that the team will use a code number for participants’ interviews has now been added to the interview consents.

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Deletions to the protocol text are indicated by ~~strikethrough~~; additions are indicated in **bold**.

<b>Revision 1: Title and Protocol Signature Pages</b>
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Title Page

HPTN 083-01:  
Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention  
of HIV among Adolescent Males – A sub-study of HPTN 083

DAIDS Document ID: 38654

A Study by the HIV Prevention Trials Network (HPTN)

Sponsored by:  
Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious  
Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human  
Development (NICHD),  
US National Institutes of Health (NIH)

Support Provided by:  
ViiV Healthcare

IND Holder:  
DAIDS, NIAID, NIH

IND #: 122,744

Protocol Chair:  
Sybil Hosek, PhD

Protocol Co-Chair:  
Lynda Stranix-Chibanda, MBChB, MMED

**FINAL** Version **3.0**

**2 July 2021**~~23 August 2020~~

Protocol Signature Page

Protocol Signature Page

Version **3.02.0**

**2 July 2021**~~23 August 2020~~

DAIDS Document ID: 38654

## A Study of the HIV Prevention Trials Network (HPTN)

Sponsored by:

Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD),

US National Institutes of Health (NIH)

Support Provided by:

ViiV Healthcare

### Revision 2: Schema

Study Duration:

Participant recruitment will take approximately ~~12-18~~ months. Oral study product will be administered for 5 weeks, followed by 29 weeks on injectable product, then ~~quarterly~~ visits for 48 weeks per Appendix III or IV ~~after final injection~~. All participants who have received at least one injection will be followed for 48 weeks after their last injection. Waning levels of cabotegravir (the PK tail) will be covered with **continued CAB LA** or locally sourced oral TDF/FTC for daily use for 48 weeks. Total study duration per participant will be approximately 21 months.

Study Sites:

Adolescent and Young Adult Research at The CORE Center (AYAR at CORE), Chicago, IL; St. Jude Children's Research Hospital CRS, Memphis, TN; Fenway Health CRS, Boston, MA; **Children's Hospital Colorado CRS, Aurora, CO**

Study Regimen:

Step 1 – oral cabotegravir (30mg tablet); Step 2 – 3 mL (600 mg) intramuscular (IM) CAB LA injection; Step 3 – **continued 3 mL (600 mg) intramuscular (IM) CAB LA injection** or Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) (300mg/200mg tablet)

### Revision 3: Section 2.3 - Study Design and Overview

#### 2.3 Study Design and Overview

Study participation includes, Step 1: a 5-week oral CAB 30mg QD safety lead-in followed by a series of 5 intramuscular (IM) injections of 3 mL (600 mg), administered at 8-week intervals after a 4-week loading dose (injections at weeks 5, 9, 17, 25 & 33) in Step 2. Adherence support strategies (e.g., counseling, reminders, pill cases) will be included to support pill-taking during the first five weeks and to support retention during the injectable phase. A safety visit will follow each injection to ascertain pharmacokinetic-peak safety data, including injection site reactions. Step 3: a blood draw visit, the +8 Week Visit, will follow the last **Step 2** injection to monitor CAB drug levels. All participants who have received at least one injection will be followed for 48 weeks after their last **Step 2** injection. Waning levels of cabotegravir (the PK tail) will be covered with locally sourced oral Tenofovir/Emtricitabine

(Trade name: TDF/FTC, Truvada®) for daily use for 48 weeks **or the participant can opt to continue CAB LA injections for the duration of Step 3.** ~~Participants may be offered the opportunity to join an open label CAB study instead, if such a study is being implemented in their area at the time.~~ Behavioral and acceptability data will be collected via computer-assisted self-interview (CASI).

Finally, in-depth qualitative interviews will be conducted **after the end of Step 2** ~~at the end of the product exposure period~~ (Week 34) with 10 participants (total, across all sites) to explore issues of acceptability and preference for oral tablets and/or injections. Additionally, up to 10 parents/guardians of participants (total, across all sites) will be asked to participate in in-depth interviews to explore facilitators and barriers to adolescent enrollment in biomedical clinical trials as well as parental acceptability of injectable prevention products for youth.

### 2.3.2 Study Duration

The initial phase, Step 1, will be an oral lead-in phase of 5 weeks. After that, follow up on study product will be for ~~29~~**34** weeks, followed by ~~quarterly~~ visits for 48 weeks after the final **Step 2** injection **per Appendix III or IV**. Total participant commitment for the entire study is approximately 82 weeks, or approximately 1.5 years. We anticipate recruitment for the study will take approximately ~~42~~**18** months.

## Revision 4: Section 3.1 – Inclusion Criteria

### 3.1.4

- *If not of legal age or otherwise not able to provide independent informed consent as determined by ~~site SOPs~~**local law** and consistent with site IRB/EC policies and procedures: Parent or legal guardian is willing and able to provide written informed consent for study participation and potential participant is willing and able to provide written assent for study participation.*

- *If of legal age or otherwise able to provide independent informed consent as determined by **local law** ~~site SOPs~~ and consistent with site IRB/EC policies and procedures: Willing and able to provide written informed consent for study participation.*

### 3.1.6

- Absolute neutrophil count > 799 cells/mm<sup>3</sup>, ±
- Hemoglobin > 11g/dL, ±

**± Participants below the cutoff may be considered for enrollment at the discretion of the PI and in consultation with the CMC if the PI can demonstrate that participant is in general good health despite being below the cutoff.**

## Revision 5: Section 3.3 – Recruitment Process

The study will be targeted towards at-risk, sexually active adolescent populations of MSM in the US. Enrollment will occur over approximately ~~42~~**18** months.

## Revision 6: Sections 4.1 and 4.2 – Study Product

#### 4.1 Study Product Regimens/Administration/Formulation Content

##### Step 3 – Follow-up Phase

All participants who have received at least one injection will be followed for 48 weeks after their last injection, beginning with a blood draw visit, +8 Week Visit, that will follow eight weeks after the last injection to monitor CAB drug levels. Waning levels of cabotegravir (the PK tail) will be covered with locally sourced oral Tenofovir/Emtricitabine (**Trade name: TDF/FTC, Truvada®**)~~TRADE NAME: TDF/FTC, TRUVADA®~~ for daily use for 48 weeks. Participants **will also have the option to remain on CAB LA injections, as one 3 mL (600 mg) IM every 8 weeks for 48 weeks, should they choose.**~~may also be provided the opportunity to enroll in a local open label study of CAB, if available.~~

#### 4.2 Study Product Acquisition and Accountability

The CAB study products (oral and LA injectable) for Steps 1, ~~and 2~~ **and 3** are being provided by ViiV Healthcare. For Step 3, the sites will provide locally sourced Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) for 48 weeks after the participants' last CAB LA injection.

#### **Revision 7: Section 5.7, Step 3 – Follow-up Phase**

##### Follow-up Phase

All participants will be followed quarterly for 48 weeks following their last injection and **will have the choice of continuing on CAB LA or being** provided with Tenofovir/Emtricitabine (**Trade Name: TDF/FTC, Truvada®**)~~TRADE NAME: TDF/FTC, TRUVADA®~~). ~~Participants may also join a local open label CAB study, if available.~~ **If participants would like to switch from TDF/FTC to CAB LA in Step 3, that is allowable, but it will not lengthen Step 3.**

Step 3 will begin with the +8 Week Visit, in which participants who received the Week 33 injection will return for a blood draw eight weeks afterwards, in order **to complete PK monitoring of** drug levels of CAB. ~~(if moving to Truvada®).~~ Participants who do not receive the week 33 injection will have a +8 Week Visit after their last injection visit and continue to be followed per the Step 3 Follow-up Phase ~~(see Appendix III).~~

Both clinical and laboratory evaluations will occur during follow-up phase visits as well as CASI administration for either behavioral or acceptability assessments (see ~~Appendices~~ **III. and IV.:** Schedule of Evaluations for Follow-up Phase – Step 3-**Oral PrEP and Step 3-Injection**).

#### **Revision 8: Section 5.13 provides clarification on HBV and HCV testing**

##### 5.13 HBV and HCV

Testing for HBV and HCV will be performed at Screening (HBsAg ~~and HCAb~~). Persons positive for **HBsAg** ~~these tests~~ will not be enrolled in the study and will be referred to their primary provider for management. Participants will be tested for Hepatitis B surface antibody (HBsAb), and Hepatitis B core antibody (HBcAb, total) at Screening or Enrollment. Participants who do not have evidence of immunity to HBV (e.g., negative HBsAb) will be provided HBV vaccination, starting ideally at week 2. For participants who do not have evidence of HBV immunity at Enrollment, HBV testing should be repeated at the discretion of the IoR or designee during the study if clinically indicated, if the participant has elevated AST/ALT results (elevated level at discretion of IoR or designee), or if the participant expresses a concern about having acquired HBV infection after enrollment. Refer to the SSP Manual for persons who have a positive result

for HBcAb (total) only. **For participants who are negative for HBsAb at enrollment, HBsAb and HBcAb (total) will be checked at the end of the study.**

For enrolled individuals, HCV antibody testing will be performed at Screening (see [Appendix I](#)). **Those who are HCV antibody positive will be referred to their primary provider for management. For participants who do not have HCV antibody at Enrollment, HCV antibody testing should be repeated at the discretion of the IoR or designee during the study if clinically indicated, if the participant has elevated AST/ALT results (elevated level at discretion of IoR or designee), or if the participant expresses a concern about having acquired HCV infection after enrollment. HCV antibody testing will be repeated in all participants at the end of the study.** Incident HCV infection during follow-up will not mandate discontinuation of study product absent other requirements per [Appendix VI - Toxicity Management](#).

**Revision 9: Section 6.6, Critical Events Reporting, is removed, given that DAIDS is retiring this policy.**

#### 6.6 — Critical Events Reporting

~~Per the DAIDS policy on Identification and Classification of Critical Events, a critical event is defined as an unanticipated study-related incident that is likely to cause harm or increase the risk of harm to participants or others or has a significant adverse impact on study outcomes or integrity. All such events must be reported following procedures specified in the DAIDS Critical Events Manual, available at:~~

~~<https://www.niaid.nih.gov/sites/default/files/criticaleventsmanual.pdf>.~~

**Revision 10: Section 8.1, Ethical Review, lists Investigator responsibilities in lieu of the retired Critical Events Policy.**

#### 8.1 Ethical Review

This protocol and the template informed consent/**assent** forms contained in **the appendices Appendix V** will be reviewed and approved by the HPTN Scientific Review Committee (SRC) and DAIDS Prevention Science Review Committee (PSRC) with respect to scientific content and compliance with applicable research and human subjects regulations.

Subsequent to initial review and approval, the responsible IRBs/ECs will review the protocol at least annually. The Investigator will make safety and progress reports to the IRBs/ECs at least annually, and within three months of study termination or completion. These reports will include the total number of participants enrolled in the study, the number of participants who completed the study, all changes in the research activity, and **must comply with the requirements of 45 CFR 46.108(a)(4) and 21 CFR 56.108b for promptly reporting the following:** all unanticipated problems involving risks to human subjects or others; **serious or continuing noncompliance with applicable regulations or the requirements or determinations of their IRBs/ECs; and any suspension of termination of IRB approval.** Study sites are responsible for the submission of continuing review to the DAIDS Protocol Registration Office (PRO), in accordance with the current DAIDS Protocol Registration Policy and Procedure Manual.

**Revision 11: Section 8.2, Informed Consent, contains edits to organize the consent/assent forms and clarifying language regarding adolescent ability to consent for themselves (self-consent) in this protocol.**

Appendices ~~VII-IX~~ provides sample informed consent/assent forms for obtaining parent or legal guardian permission and adolescent assent for study participation. **Appendices X-XIII provide sample informed consent/assent forms for adolescent qualitative interviews and parent/legal guardian interviews.** Appendices ~~XIV-XVI~~, ~~VII~~, ~~VIII~~ and ~~IX~~ provide sample informed consent/~~permission~~ and assent forms for specimen storage and future use., ~~adolescent qualitative interviews and parent/legal guardian interviews.~~ All sample informed consent and assent forms may be modified by sites to meet IRB/EC requirements. If the participant, parent, or guardian (as applicable) is unable to read, the process for consenting illiterate participants, as defined or approved by the local IRB/EC, should be followed.

As indicated above, parental consenting requirements at each site will depend on the IRB/EC risk determination and all IRB/EC requirements will be followed. ~~Participants enrolling in the study as minors will generally require permission from a parent or guardian.~~

In general, each participant is expected to take part in the informed consent process **and** with his or her parent or legal guardian, **if appropriate**, and both the assent of the participant and the permission of the parent or legal guardian will be required for all consent decisions, **if the participant does not self-consent.** ~~For example, if the participant does not provide assent, or the parent or legal guardian does not provide permission, the participant will not be enrolled in the study.~~

**Revision 12: Sections 9.4 and 9.5 remove reference to any specific laboratory assessment.**

#### 9.4 Pharmacology

Blood samples will be collected throughout the study from all participants and assayed for plasma CAB concentrations. PK sample times include predose trough samples at W5, W9, W17, W25, and W33, (final concentration in injection phase) and 1-week post injection samples at W6, W10, W18, W26, W34. In addition, follow-up samples will be collected **for 48 weeks at +8, +24, +36 and +48 weeks following the final injection** (Appendix II and Appendix III **or IV**) and at HIV confirmatory visit (Appendix IV).

Plasma samples will be processed and frozen locally for subsequent shipment to the HPTN LC following procedures outlined in the SSP Manual. Pharmacology testing will be performed at the HPTN LC or at an outside laboratory designated by the HPTN LC. The primary pharmacologic assessments will be performed using assays that have been validated ~~and approved by the~~ **in accordance with regulatory requirements** Clinical Pharmacology Quality Assurance (CPQA) Committee (reference assay validation report). Results will not be returned to the study participants or study sites.

#### 9.5 Quality Control and Quality Assurance Procedures

Study sites will document that their laboratories are certified under the Clinical Laboratory Improvement Amendments Act of 1988 (CLIA-certified) and/or participate in **an DAIDS-sponsored** External Quality Assurance (EQA) programs. HPTN LC staff will conduct periodic visits to each site to assess the implementation of on-site laboratory quality control (QC) procedures, including proper maintenance of laboratory testing equipment and use of appropriate reagents. HPTN LC staff will follow up directly with site staff to resolve any QC or QA problems identified through proficiency testing and/or on-site assessments.

**Revision 13: Section 12.2, Appendix II**

APPENDIX II. SCHEDULE OF EVALUATIONS – INJECTION PHASE (STEP 2)

WEEKS in Study (shaded column = injection visit)	Wk 5	Wk 6	Wk 9	Wk 10	Wk 17	Wk 18	Wk 25	Wk 26	Wk 33	Wk 34
<b>ADMINISTRATIVE, BEHAVIORAL, REGULATORY</b>										
Locator information	X	X	X	X	X	X	X	X	X	X
HIV prevention counseling	X	X	X	X	X	X	X	X	X	X
Condoms per local SOC	X	X	X	X	X	X	X	X	X	X
Behavioral/Acceptability assessment (CASI)	X		X		X		X		X	
Qualitative interviews begin (approximately)										X
<b>CLINICAL EVALUATIONS &amp; PROCEDURES</b>										
Adherence, risk reduction counseling	X	X	X	X	X	X	X	X	X	X
Medical history <sup>1</sup> , concomitant medications, targeted physical exam	X	X	X	X	X	X	X	X	X	X
Hep B vaccination (if needed) <sup>2</sup>		X							X	
Blood collection	X	X	X	X	X	X	X	X	X	X
Urine collection	X	X	X	X	X	X	X	X	X	X
Rectal swab collection					X				X	
Injections for all participants	X		X		X		X		X	
ISR evaluation		X		X		X		X		X
<b>Step 3 product choice discussion</b>									<b>X</b>	<b>X</b>
<b>Interviewer administered product choice assessment</b>										<b>X</b>
<b>If product chosen is oral PrEP:</b> Provision of Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) (3 months' worth)										X
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>										
HIV testing <sup>3</sup>	X	X	X	X	X	X	X	X	X	X
CBC with differential	X	X	X	X	X	X	X	X	X	X
Chemistry testing <sup>4</sup>	X	X	X	X	X	X	X	X	X	X
Liver function testing <sup>5</sup>	X	X	X	X	X	X	X	X	X	X
Fasting lipid profile <sup>6</sup>										X
Syphilis testing									X	
GC/CT testing (urine, rectal, and oral pharyngeal swabs)					X				X	
Urinalysis (protein, glucose; at the clinic or local lab)	X	X	X	X	X	X	X	X	X	X
Plasma storage <sup>7</sup>	X	X	X	X	X	X	X	X	X	X

**Revision 14: Section 12.3, Appendix III, introduces the first of the two options for Step 3.**

APPENDIX III. SCHEDULE OF EVALUATIONS –FOLLOW-UP PHASE (STEP 3-ORAL PrEP)

WEEKS SINCE LAST INJECTION	Wk +8	Wk +12	Wk +24	Wk +36	Wk +48	Early Discontinuation
<b>ADMINISTRATIVE, BEHAVIORAL, REGULATORY</b>						
Locator information	X	X	X	X	X	X
HIV prevention & risk reduction counseling	X	X	X	X	X	X
Condoms per local SOC	X	X	X	X	X	X
Behavioral/Acceptability assessment (CASI)		X	X	X	X	X
<b>CLINICAL EVALUATIONS &amp; PROCEDURES</b>						
Qualitative interviews continue (approximately)		X	X			
Medical history <sup>1</sup> , concomitant medications, targeted physical exam		X	X	X	X	
Hep B vaccination (if needed) <sup>2</sup>						X
Blood collection	X	X	X	X	X	
Urine collection		X	X	X	X	X
Rectal swab collection		X	X	X	X	
Provision of Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) (3 months' worth)		X	X	X		X
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>						
HIV testing <sup>3</sup>		X	X	X	X	
CBC with differential		X	X	X	X	X
Chemistry testing <sup>4</sup>		X	X	X	X	X
Liver function testing <sup>5</sup>		X	X	X	X	X
Syphilis testing			X	X		X
GC/CT testing (urine, rectal, and oral pharyngeal swabs)		X	X	X	X	
Urinalysis (protein, glucose; at the clinic or local lab)		X	X	X	X	X
Plasma storage <sup>6</sup>	X	X	X	X	X	
DBS storage		X	X		X	
<b>HBsAb and HBcAb<sup>7</sup></b>					X	X
<b>HCVAb</b>					X	X

FOOTNOTES FOR APPENDIX III:

<sup>1</sup> Medical history must include pulse, blood pressure, weight and Body Mass Index (BMI) calculated at each visit

<sup>2</sup> The initial dose of the HBV vaccination is ideally given at Week 2, though there is flexibility around the timing of the vaccination. Subsequent doses may be given at different visits than indicated in this SOE, as long as sites follow manufacturer guideline timing.

<sup>3</sup> The HIV testing algorithm is provided in the SSP Manual. If HIV rapid testing is indicated, this testing may be performed in the clinic or the laboratory. At least one HIV assay result must be available and reviewed the same day as sample collection and before product is administered.

<sup>4</sup> ~~BUN, urea, c~~ Creatinine **only (for Step 3-Oral PrEP)**, ~~CPK, calcium, phosphorous, glucose, amylase, and lipase.~~

<sup>5</sup> AST, ALT, TBili, and alkaline phosphatase.

<sup>6</sup> Stored plasma will be used for Quality Assurance testing and other assessments at the HPTN LC (see Section 9) including potential assay for plasma CAB concentrations. Assessments will be performed retrospectively; results will not be returned to study sites or participants, except as noted in SSP. Samples cannot be used by site or other lab for local purposes without specific instructions from the LC w/ CMC consult.

<sup>7</sup> HBsAb and HBcAb will be tested in participants who received the HBV vaccine.

Revision 15: Section 12.4, Appendix IV, is a new schedule of evaluations (SOE) for Step 3-Injection.

**APPENDIX IV. SCHEDULE OF EVALUATIONS – FOLLOW-UP PHASE (STEP 3-INJECTION)**

WEEKS SINCE LAST INJECTION	Wk +8	Wk +16	Wk +24	Wk +32	Wk +40	Wk +48	Early Discontinuation
<b>ADMINISTRATIVE, BEHAVIORAL, REGULATORY</b>							
Locator information	X	X	X	X	X	X	X
HIV prevention & risk reduction counseling	X	X	X	X	X	X	X
Condoms per local SOC	X	X	X	X	X	X	X
Behavioral/Acceptability assessment (CASI)		X	X	X	X	X	X
<b>CLINICAL EVALUATIONS &amp; PROCEDURES</b>							
Qualitative interviews continue (approximately)		X	X				
Medical history <sup>1</sup> , concomitant medications, targeted physical exam		X	X	X	X	X	
Hep B vaccination (if needed) <sup>2</sup>							X
Blood collection	X	X	X	X	X	X	
Urine collection			X			X	X
Rectal swab collection			X			X	
Injections (CAB LA)	X	X	X	X	X	X	X
ISR evaluation	X	X	X	X	X	X	X
Adherence counselling	X	X	X	X	X	X	X
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>							
HIV testing <sup>3</sup>	X	X	X	X	X	X	X
CBC with differential			X			X	
Chemistry testing <sup>4</sup>	X		X			X	X
Liver function testing <sup>5</sup>	X		X			X	X
Syphilis testing			X				X
GC/CT testing (urine, rectal, and oral pharyngeal swabs)			X			X	X
Plasma storage <sup>6</sup>	X	X	X	X	X	X	
DBS storage		X	X		X	X	
HBsAb and HBcAb <sup>7</sup>						X	X
HCVAb						X	X

**FOOTNOTES FOR APPENDIX IV:**

<sup>1</sup> Medical history must include pulse, blood pressure, weight and Body Mass Index (BMI) calculated at each visit.

<sup>2</sup> The initial dose of the HBV vaccination is ideally given at Week 2, though there is flexibility around the timing of the vaccination. Subsequent doses may be given at different visits than indicated in this SOE, as long as sites follow manufacturer guideline timing.

<sup>3</sup> The HIV testing algorithm is provided in the SSP Manual. If HIV rapid testing is indicated, this testing may be performed in the clinic or the laboratory. At least one HIV assay result must be available and reviewed the same day as sample collection and before product is administered.

<sup>4</sup> BUN/urea, creatinine, CPK, calcium, phosphorous, glucose, amylase, and lipase.

<sup>5</sup> AST, ALT, TBili, and alkaline phosphatase.

<sup>6</sup> Stored plasma will be used for Quality Assurance testing and other assessments at the HPTN LC (see Section 9) including potential assay for plasma CAB concentrations. Assessments will be performed retrospectively; results will not be returned to study sites or participants, except as noted in SSP. Samples cannot be used by site or other lab for local purposes without specific instructions from the LC w/ CMC consult. Blood collected for plasma storage purposes must be collected prior to injection.

<sup>7</sup> HBsAb and HBcAb will be tested in participants who received the HBV vaccine.

**Revision 16: Section 12.6, Appendix VI, Toxicity Management**

GUIDANCE ON TOXICITY MANAGEMENT FOR SPECIFIED TOXICITIES:

CONDITION AND SEVERITY	FOLLOW-UP AND MANAGEMENT
<b>ELEVATIONS in ALT</b>	
<p><b>Grade 2 and higher – Oral Phase</b></p>	<p><u>Oral phase:</u> A Grade 2 ALT abnormality reported at Week 2 or Week 4, regardless of relatedness to the study product, should be confirmed within one week. Oral study drug may continue until the confirmatory results are available; no injections should be administered until confirmatory results are available during consideration of the Week 4 ALT value. If the repeat value is <math>\leq</math> Grade 2 at Week 3, study drug may continue to Week 4. If the repeat value is <math>&lt;</math> Grade 2 at Week 4, the participant may proceed to the injection phase. If the repeat value is Grade 2 or higher at Week 4, study product should be stopped, and the participant will be discontinued from the study. All such cases must be reported to the CMC. In addition, participants will be followed with weekly ALT assessments until they return to <math>\leq</math> Grade 1.</p> <ul style="list-style-type: none"> <li><del>A Grade 3 or higher ALT abnormality, regardless of relatedness to the study product, will result in permanent study product discontinuation and will prohibit a participant from entering the injection phase of the study. All such cases must be reported to the CMC. In addition, participants will be followed with weekly ALT assessments until they return to <math>\leq</math> Grade 1.</del></li> </ul>
<p><b>Grade 3 and higher – Oral Phase</b></p>	<p><b>Oral Phase: A Grade 3 or higher ALT abnormality, regardless of relatedness to the study product, will result in permanent study product discontinuation and will prohibit a participant from entering the injection phase of the study. All such cases must be reported to the CMC. In addition, participants will be followed with weekly ALT assessments until they return to <math>\leq</math> Grade 1.</b></p>

CONDITION AND SEVERITY	FOLLOW-UP AND MANAGEMENT
<b>ELEVATIONS in ALT</b>	
Grade 2 and higher – <b>Injection Phase</b>	<p><u>Injection phase:</u> The CMC should be notified as soon as possible.</p> <p>For a Grade 2 ALT, the CMC will determine whether further injections may be given in cases where levels are <math>\leq</math> Grade 2 prior to the next scheduled injection. Unless otherwise specified by the CMC, for Grade 2 ALT, repeat testing should be performed weekly until levels are <math>\leq</math> Grade 1.</p> <ul style="list-style-type: none"> <li>For Grade 3 and higher ALT, study product will be permanently discontinued. For Grade 3 and 4 ALT, repeat testing should be performed as soon as possible, and participants should be followed weekly until levels are <math>\leq</math> Grade 1. Participants who are permanently discontinued from study product should continue to be followed 48 weeks post-last injection.</li> </ul>
Grade 3 and higher – <b>Injection Phase</b>	<p><b>Injection Phase: For Grade 3 and higher ALT, study product will be permanently discontinued. For Grade 3 and 4 ALT, repeat testing should be performed as soon as possible, and participants should be followed weekly until levels are <math>\leq</math> Grade 1. Participants who are permanently discontinued from study product should continue to be followed 48 weeks post-last injection.</b></p>

**Revision 17: Section 12.7, Appendix VII, the main informed consent for parents/guardian and assent for adolescent participants 14 to age of majority (AOM), is revised.**

**12.7 APPENDIX VII: INFORMED CONSENT FOR PARENTS/LEGAL GUARDIANS AND PARTICIPANTS WHO REACH THE AGE OF MAJORITY AND ASSENT FOR ADOLESCENT PARTICIPANTS AGES 14 – AGE OF MAJORITY**

**Study Visit Schedule**

- Step 3 (5 or 6 visits) – After a blood draw 8 weeks after your last injection, you will come to the clinic quarterly (every 3 months) for 1 year to check how you are doing and to see how long CAB remains in your body after your last injection (+8, +12, +24, +36, +48 weeks). In most people, CAB disappears from the body slowly over 6 months, but it may last for a year or so. During this Step, you will be provided with Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) to take daily or be offered the opportunity to join an open label CAB study if available, so we will be following you to see how well things are going on oral PrEP, doing bloodwork, as well as HIV and other STI testing.

**Study Visit Procedures**

*Laboratory tests –*

- Blood – To check for infections (HIV, hepatitis B and C, Syphilis), your general health, the health of the liver and kidneys, the amount of cholesterol (a fatty substance in your blood) and the amount of the study drug that is in your blood. How much blood is taken depends on

which tests are due at each visit and is between 1 and 4 teaspoons each time (5-20mL). Study staff will tell you more about fasting before the cholesterol test. The study staff may be required by law to report **any positive** the result of the HIV, and Hepatitis, **and syphilis** tests to the local health authority.

Tables of Study Visit Procedures

Step 2 – to give you the CAB injections and check your health (grey columns mean injection weeks)

	Week 5	Week 6	Week 9	Week 10	Week 17	Week 18	Week 25	Week 26	Week 33	Week 34
Questions/CASI	√		√		√		√		√	
Counselling	√	√	√	√	√	√	√	√	√	√
Brief physical exam	√	√	√	√	√	√	√	√	√	√
Blood	√	√	√	√	√	√	√	√	√	√
Urine	√	√	√	√	√	√	√	√	√	√
Rectal and oral pharyngeal swabs					√				√	
CAB injection	√		√		√		√		√	
PrEP pills offered										√
<b>Step 3 product choice discussions</b>									√	√

**Step 3: your choice of moving to oral PrEP or remaining on CAB LA injections.**

Step 3-Oral PrEP Follow-Up Visits – to see how long the CAB remains in your body

	+8 Weeks	+12 Weeks	+24 Weeks	+36 Weeks	+48 Weeks
Questions/CASI		√	√	√	√
Counselling	√	√	√	√	√
Brief physical exam		√	√	√	√
Blood	√	√	√	√	√
Urine		√	√	√	√
Rectal and oral pharyngeal swabs		√	√	√	√
PrEP pills offered		√	√	√	

**OR:**

**Step 3-Injection Follow-Up Visits – remain on CAB LA, instead of switching to oral PrEP**

	+8 Weeks	+16 Weeks	+24 Weeks	+32 Weeks	+40 Weeks	+48 Weeks
Questions/CASI		√	√	√	√	√
Counselling	√	√	√	√	√	√
Brief physical exam		√	√	√	√	√
Blood	√	√	√	√	√	√
Urine			√			√

<b>Rectal and oral pharyngeal swabs</b>			√			√
<b>CAB LA injections</b>	√	√	√	√	√	√

**WHAT ARE THE RISKS OF TAKING PART IN THIS STUDY?**

Risk of HIV Resistance to CAB – We do not know if using CAB for PrEP will mean that CAB will not work to treat the HIV if you get infected with HIV during the study or in the future (this is called drug resistance). Drug resistance usually occurs when the amount of a drug in the body is too low to kill the virus. You will have low levels of CAB in the body for about one year after the last injection, or if you don't get the injections when they are due. This is why it is very important that you use other methods to protect against HIV infection whenever you are at risk, like using condoms and-, **if you are no longer receiving CAB, using** Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) PrEP pills.

**CONSENT TO TAKE PART IN THIS STUDY FOR ADOLESCENT PARTICIPANTS WHO HAVE REACHED THE AGE OF MAJORITY**

~~I have read this form. I know that this is a research study. I have been told about the risks and potential benefits of taking part in the study. I have asked all the questions I have about the study and have gotten answers to my questions. I know that I am free to quit the study at any time without any penalties or loss of benefits. I will tell the study doctor or the study staff if I choose to stop the study so that I can stop in the best way to not harm my health. I will be given a signed and dated copy of this form to keep.~~

~~I agree to take part in this research study.~~

\_\_\_\_\_  
Participant's Name (print)

\_\_\_\_\_  
Signature and Date

**Revision 18: Section 12.8, Appendix VIII, is a new main informed consent for adolescents who can consent for themselves (self-consent) and those reaching the AOM.**

**12.8 APPENDIX VIII: INFORMED CONSENT FOR ADOLESCENT PARTICIPANTS ABLE TO CONSENT FOR THEMSELVES (SELF-CONSENT) AND PARTICIPANTS WHO REACH THE AGE OF MAJORITY**

**Sponsor / Study Title:** Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “HPTN 083-01: Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Males – A sub-study of HPTN 083”

**Protocol Number:** HPTN 083-01

**Principal Investigator:** «PiFullName»  
(Study Doctor)

**Telephone:** «lcfPhoneNumber»

Address: «PiLocations»

**Key Information:**

The first two pages of this document include summary information about this study that will help you decide whether or not you should participate. More detailed information is provided after this summary section.

**About this research**

You are being asked to join a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future. This form explains the research study and your part in the study. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand. You may take this description home and discuss it with your family or friends to help you decide.

**Taking part in this research study is voluntary**

You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled and will not affect your relationship with the study site.

**Important Information**

This information gives you an overview of the research. More information about these topics may be found in the pages that follow.

**1. Why is this research being done?**

There is a new drug called cabotegravir (CAB) that can treat people who have human immunodeficiency virus (HIV) infection. CAB is also being tested to see if it can protect people from getting HIV and has been found to be effective at preventing HIV among adult men and transgender women. In this study, we want to know if it is safe and acceptable for adolescents who do not have HIV to take CAB. For more information, please see the *What is this Study About* section below.

**1. What will happen to me during the study?**

You will move through the study in 3 steps:

- Step 1: You will take one CAB pill every day for five weeks
- Step 2: You will receive a total of 5 CAB injections over 6 months
- Step 3: You will come to the clinic for study visits for up to one year.

Different procedures are done at different study visits. The procedures include:

- *Physical examinations* – We will examine you to check on your health by measuring height, weight, temperature and blood pressure.

- **Questions** – We will ask general questions about your age, living situation, medical health, and as well as beliefs about HIV, opinions about taking pills and getting injections, sexual behavior, and any alcohol or drug use.
- **Counseling** – We will discuss ways to protect you from getting HIV and offer condoms. We will discuss any challenges you have taking the CAB pill or attending study visits.
- **CAB pills or injection** – During Step 1, we will explain how to take the study pills, watch you take a study pill, and explain any side effects the pills may cause. In Steps 2 and 3, if you decide to stay on CAB LA, the CAB injection will be given into your buttock.
- **Laboratory tests** – We will collect blood, urine, rectal swabs, and oral pharyngeal swabs to test for HIV, Hepatitis, liver and kidney health, cholesterol, and sexually transmitted infections (STIs). If you have an STI, you will be told so, and referred for appropriate treatment.
- **HIV Prevention** – We will offer you Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) tablets as pre-exposure prophylaxis (PrEP) after you stop the CAB injections. You may, instead, choose to remain on CAB LA injections.

For more information on each procedure and when it happens, please see the *What Will I have to Do in the Study* section below.

2. How long will I participate in the study?

If you decide to join the study, participation will last about 1.5 years and include a maximum of 18 study visits at this clinic. If you reach the age of majority while already on study, you will continue participation along your original schedule (and not a new 1.5 years).

3. Will I benefit from the study?

It is possible that you may benefit from taking part in this study. The study drug being used has been shown to prevent HIV infections among some adults. You will get information about your health and the results of the tests, as well as treatment for sexually transmitted infections. The counseling you get during this study may help you avoid HIV and other sexually transmitted infections. For more information, please see the *What are the Potential Benefits of Taking Part in the Study* section below.

4. Will taking part in the study expose me to risks?

Taking part in this research may expose you to risks. We may not know or understand all the risks at this time. Some people may experience side effects or discomfort, some of which may be serious. It is very important that you understand the risks in this research study before you decide whether you will participate. For details and a list of risks you should know about, please see the *What Are the Risks of Taking Part in the Study* section below.

5. Will I be paid to participate?

Payment for your time or travel is available if you decide that you will take part in this study. For more information, please see the *What Will I Get for Taking Part in this Study* section below.

**6. Will it cost me anything to participate?**

There is no cost to you for taking part in this study.

Please review the rest of this document for details about these topics and additional things you should know before making a decision about whether you will participate in this research.

## **INTRODUCTION**

We invite you to take part in a research study about PrEP for Human Immunodeficiency Virus (HIV). PrEP is short for Pre-Exposure Prophylaxis. Pre-exposure means before being exposed to HIV. Prophylaxis is the way people prevent a disease from infecting them. With PrEP for HIV, medications are being developed to prevent people from getting infected if they are exposed to HIV.

This form gives information about what it means to join the study. Please read it and ask any questions that you may have. You can take as much time as you need to fully understand the study. We will ask questions to see if we have explained the study clearly. After you understand the study, if you decide that you will take part, we will ask you to sign and date this form. You will be offered a copy to keep. This process is called “informed consent.”

## **WHAT IS THIS STUDY ABOUT?**

In this study, we want to know if it is safe and acceptable for adolescents who do not have HIV to take an anti-HIV drug called cabotegravir (CAB). We would also like to look at the tolerability, or side effects, of CAB. CAB is a new drug that is still being studied and is not yet approved by the FDA, or U.S. Food and Drug Administration. Other studies showed that CAB can treat people who have HIV infection, and it has recently been shown as a way to protect people from getting HIV. First, we must study if CAB is safe for people who do not have HIV. CAB comes in the form of a pill and also as an injection. CAB pills and injections are not yet approved for the treatment or prevention of HIV infection by the United States Food and Drug Administration (FDA) and are therefore considered experimental. Recently, the FDA asked for more information about how the CAB pills and injections are manufactured and agreed that studies that investigate CAB should continue while they complete their review.

You are being invited to join this study because you live in the United States, where 21% of new HIV infections occur among young people ages 13 to 24. Most of these infections occur due to sexual activity and about half of the youth who have HIV don't know it. This study will be offered to about 50 young men under 18 years old across several study sites in the US. The person in charge of the study at the study site is listed on the first page of this form. The United States National Institutes of Health is paying for the study.

Some of the questions that we want to answer with this study are:

Is it safe for adolescents to take CAB pills and CAB injections?  
Is it acceptable and tolerable for adolescents to use CAB for HIV prevention?  
Are adolescents able to make it to the clinic for injection appointments?  
What do parents/guardians think about their sons using CAB for HIV prevention? (if applicable)

This study will *not* show us if CAB prevents new infections with HIV. There are other studies being done that will answer that question, but those studies only involve adults. Currently, the only known way to prevent HIV infection from sex is to use condoms and/or take one of the two PrEP pills available called Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) or Tenofovir Alafenamide/Emtricitabine (Trade name: TAF/FTC, Descovy®) every day. But some people have a hard time remembering to take a pill every day, so it is a good idea to have other HIV prevention options. With CAB, people would get injections every 8 weeks and would not have to remember to take a pill every day. It is important that we learn what happens when adolescents use CAB for HIV prevention and whether it is safe and acceptable.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

#### **DO I HAVE TO JOIN THIS STUDY?**

You do not have to be in this study. The study staff can tell you about other places where you can get the care you need even if you do not join the study. If you join the study today, you can still change your mind later and leave the study at any time for any reason without penalty. If you decide not to take part in this study, you can join another study at a later time if one is available and you qualify for it.

You can't join this study if you are taking part in another study of drugs, HIV vaccines, or medical devices. You must tell the study staff about any other studies you are taking part in or thinking of taking part in. *This is very important for your safety. [Some sites may have biometric fingerprint screening and, if so, sites should add information regarding that here.]*

#### **HOW LONG WILL THE STUDY LAST?**

If you decide to join the study, participation will last about 1.5 years and include about 18 study visits at this clinic. You will move through the study in 3 steps:

Step 1: You will take one CAB pill every day for five weeks

Step 2: You will receive a total of 5 CAB injections over approximately 6 months

Step 3: You will come to the clinic for study visits for up to one year

#### **WHAT WILL I HAVE TO DO IN THE STUDY?**

If you want to be in this study, you will sign and date this form before you begin the study.

## Study Visit Schedule

**Screening (1 visit)** – First, we will find out if you qualify to be in the study.

**Step 1 (3 visits)** – If you qualify and decide to join the study, you will swallow 1 CAB tablet every day for 5 weeks starting at the Entry, or Enrollment, Visit.

Step 1 is done to make sure your body is tolerating the CAB well, so you should take the tablets every day. You will come back for a medical check-up at weeks 2 and 4. If Step 1 goes well for you, then you will move to Step 2.

**Step 2 (10 visits)** – If you qualify, you will get the first CAB injection at week 5, then again at weeks 9, 17, 25 and 33 (5 injection visits). You will come back to the study clinic for a brief check-up 1 week after each injection at weeks 6, 10, 18, 26 and 34 (5 safety visits).

**Step 3 (5 or 6 visits)** – After a blood draw 8 weeks after your last injection, you will come to the clinic (every 2 or 3 months) for 1 year to check how you are doing and to see how long CAB remains in your body after your last injection (+8, +12, +24, +36, +48 weeks). In most people, CAB disappears from the body slowly over 6 months, but it may last for a year or so. During this Step, you will be provided with Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) to take daily or have the opportunity to continue on CAB LA injections, so we will be following you to see how well things are going, doing bloodwork, as well as HIV and other STI testing.

You will be in the study for the about 1.5 years. The study visits will take from 1 to 4 hours each **[sites to modify accordingly]**. It is important that you attend all of these study visits. If you do not come for a scheduled visit or if a test result comes back abnormal, study staff will contact you or visit you. We will ask for your address and contact information so that we will be able to get in touch with you. You should not join the study if it's not okay for study staff to contact you and visit you where you stay. If at any time you feel sick, you should let the study staff know right away and we may ask you to come back for a check-up.

## Study Visit Procedures

Different procedures are done at different study visits. We will now explain each of the procedures and then show you which ones are done at which visits.

**Physical examinations** – We will examine you to check on your health by measuring height, weight, temperature and blood pressure. At each study visit, we will check on whether CAB may be causing side effects. We will also tell you what to do if you have side effects.

**Questions** – We will ask general questions about your age, living situation, medical health, and any medications or vitamins that you take. At some visits, you will also answer questions on a computer about your beliefs about HIV, opinions about taking pills and getting injections, sexual behavior, and any alcohol or drug use (we call these questions “CASI” for computer-assisted self-interview).

**Counselling** – We will discuss ways to protect you from getting HIV and offer condoms. We will discuss any challenges you have about taking the CAB pill or attending study visits.

**CAB pills or injection** – During Step 1, we will explain how to take the study pills, watch you take a study pill, and explain any side effects the pills may

cause. In Steps 2 and 3, if you decide to stay on CAB LA, the CAB injection will be given into your buttock.

**Laboratory tests** – We will collect blood and urine. Some of these tests are done right away and we will tell you the results when they are available. The HIV results will be available before you are given CAB each time. Other tests are stored and then done later in a batch. More details are shown in the table below this section. Some tests are done in laboratories in other states, so your samples may be shipped there for testing. The laboratory tests are done for the following reasons:

**Blood** – To check for infections (HIV, hepatitis B and C, Syphilis), your general health, the health of the liver and kidneys, the amount of cholesterol (a fatty substance in your blood) and the amount of the study drug that is in your blood. How much blood is taken depends on which tests are due at each visit and is between 1 and 4 teaspoons each time (5-20mL). Study staff will tell you more about fasting before the cholesterol test. The study staff may be required by law to report any positive results of the HIV, Hepatitis, and syphilis tests to the local health authority.

**Urine** – To test if there is sugar or protein in your urine and for sexually transmitted infections.

**Hepatitis B vaccination** – At Week 2 or soon thereafter, you will be given the hepatitis B vaccination if testing shows you are not already immune. Additional vaccination (boosters) will be given at approximately Weeks 6 and 33).

**HIV Prevention** – We do not know for sure if CAB will protect you from getting HIV. Also, the amount of CAB remaining in the body disappears slowly after you stops the CAB injections – it can last in the body for about one year, so you must use other ways of preventing HIV if you are at risk of infection. For this reason, we will offer you Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) tablets as PrEP after you stop the CAB injections or allow you to stay on CAB LA injections, if chosen. Before you leave the study, we will help you find a place where you can continue getting HIV prevention care [*sites to add information here or elsewhere in the consent form*].

## Tables of Study Visit Procedures

Step 1 – to see if your body is tolerating the CAB well

	screening	entry	Week 2	Week 4
Receive CAB pills (5 weeks' worth)		√		
Pill count			√	√
Questions/CASI	√	√	√	√
Counselling	√	√	√	√
Physical exam	√	√	√	√
Blood	√	√	√	√
Urine	√	√		
Rectal and oral pharyngeal swabs	√			

**Step 2 – to give you the CAB injections and check your health (grey columns mean injection weeks)**

	Week 5	Week 6	Week 9	Week 10	Week 17	Week 18	Week 25	Week 26	Week 33	Week 34
Questions/CASI	√		√		√		√		√	
Counselling	√	√	√	√	√	√	√	√	√	√
Brief physical exam	√	√	√	√	√	√	√	√	√	√
Blood	√	√	√	√	√	√	√	√	√	√
Urine	√	√	√	√	√	√	√	√	√	√
Rectal and oral pharyngeal swabs					√				√	
CAB injection	√		√		√		√		√	
Step 3 drug choice discussions									√	√

**Step 3: your choice of moving to oral PrEP or remaining on CAB LA injections.**

**Step 3- Oral PrEP Follow-Up Visits – to see how long the CAB remains in your body**

	+8 Weeks	+12 Weeks	+24 Weeks	+36 Weeks	+48 Weeks
Questions/CASI		√	√	√	√
Counselling	√	√	√	√	√
Brief physical exam		√	√	√	√
Blood	√	√	√	√	√
Urine		√	√	√	√
Rectal and oral pharyngeal swabs			√		√
PrEP pills offered		√	√	√	

**OR:**

**Step 3-Injection Follow-Up Visits – remain on CAB LA, instead of switching to oral PrEP**

	<b>+8 Weeks</b>	<b>+16 Weeks</b>	<b>+24 Weeks</b>	<b>+32 Weeks</b>	<b>+40 Weeks</b>	<b>+48 Weeks</b>
<b>Questions/CASI</b>		√	√	√	√	√
<b>Counselling</b>	√	√	√	√	√	√
<b>Brief physical exam</b>		√	√	√	√	√
<b>Blood</b>	√	√	√	√	√	√
<b>Urine</b>			√			√
<b>Rectal and oral pharyngeal swabs</b>			√			√
<b>CAB LA injections</b>	√	√	√	√	√	√

**Permanently Stopping Study Drug**

**CAB pills are only given in Step 1, and then stopped permanently. If you need to leave the study before you receive any CAB injections, we'd still like to do a final study visit, which will include the same activities as the Step 3 Follow-Up Visits. If you permanently stop taking CAB after you had at least 1 CAB injection, then you will move straight to Step 3 follow-up visits, if you agree to stay in the study. If you choose oral PrEP for Step 3, then 3 months' supply of Truvada will be provided at Week 34.**

**WHAT IF I BECOME INFECTED WITH HIV?**

**Being in this study will not cause HIV infection, but you could become infected with HIV through sex or other activities while in this study. If you get HIV infection in Step 1, you will stop using oral CAB and exit the study, but if you get HIV infection in Steps 2 or 3, you will continue on study with no injections, to make sure that you are doing okay. The study staff will counsel you and refer you for HIV treatment and other available services, but the study will not pay for this treatment. We will share any test results that will help you get the treatment you need. Testing, which will take an additional 1-3 mL of blood, will be done to see if your HIV is resistant to any drugs that are used to treat HIV infection. This testing will help select the best drugs to treat your HIV infection.**

**Tables of Study Visit Procedures if you become infected with HIV during Step 2 or Step 3**

**If you become infected with HIV infection before your first injection, you will have the oral CAB stopped permanently and will be referred to local HIV-related care and exit from the study.**

	<b>HIV Confirmation Visit</b>	<b>+12 weeks</b>	<b>+24 weeks</b>	<b>+36 weeks</b>	<b>+48 weeks</b>
<b>Questions/CASI</b>	√	√	√	√	√

Counselling	√				
Brief physical exam	√	√	√	√	√
Blood	√	√	√	√	√

**WHAT OTHER TESTS WILL BE DONE?**

After all the laboratory tests mentioned above for this study have been done, there may be some of your samples left over. We want to keep these in storage for future tests related to HIV and other infections, including testing for the drugs used in this study and other anti-HIV medications, or tests about your genes. There is a separate form with more information about this. We will not use DNA from your stored samples to study your whole genetic sequence (also called your "genome"). If you agree to this future research, identifiers might be removed from your identifiable private information or identifiable biospecimens collected during this study. That information could then be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

**WHAT ARE THE RISKS OF TAKING PART IN THIS STUDY?**

Taking part in this study may involve some risks and discomfort.

**Risk from Blood Draws** – The needle can cause pain, swelling, bruising, or bleeding from the needle site. Drawing blood can cause fainting or infection, but this is very rare.

**Risk from Receiving CAB Injections** – People who got CAB injections in other studies had pain, skin irritation, skin redness, bumps, swelling, itching, or bruising at the spot where they got the shot. Most reactions go away in a week or less but sometimes they can last a long time. The injection could be given too deeply or not deeply enough, missing the muscle and entering your skin, blood, or a nerve. Everything possible will be done to decrease this risk, including watching you for problems during the study. If we think that the injection was not given the right way, you might be asked to stay in the clinic up to 2 hours after the injection to watch how you are doing. Receiving injections can cause some people to feel lightheaded or feel like they might pass out, or 'faint'. This is called a 'vasovagal reaction' and it can occur with many medical procedures but usually resolves quickly.

**Risk of CAB Side Effects** – All drugs can cause side effects. Some side effects are minor; others can be severe. Some side effects are common; others are rare. Some people who take the study drug have some of the side effects. Other people have different side effects, or no side effects. The most common side effects for CAB are listed below. It is not known if CAB, other drugs or the participant's other health problems caused these side effects. There may be other side effects that we do not know about now. This may be especially true for adolescents, because this is the first study of CAB in adolescents.

<b>Very Common Side Effects of CAB</b>	<b>Common Side Effects of CAB</b>
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<ul style="list-style-type: none"> <li>• Nausea (feeling sick to the stomach)</li> <li>• Diarrhea or loose stools</li> <li>• Runny nose, sore throat/Upper respiratory tract infection</li> <li>• Headache</li> <li>• Fever</li> <li>• Lack of energy</li> </ul>	<ul style="list-style-type: none"> <li>• Rash</li> <li>• Itching</li> <li>• Vomiting (being sick)</li> <li>• Stomach pain and discomfort</li> <li>• Problems sleeping</li> <li>• Abnormal dreams/nightmares</li> <li>• Feeling light headed</li> <li>• Depression</li> <li>• Passing gas or wind</li> <li>• Joint or muscle pain</li> <li>• Increase in the level of enzymes made in the muscles (creatine phosphokinase)</li> </ul>
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Some of the people who received CAB in other studies also had abnormal liver tests. In most people, this was explained by other things such as a new virus infection with Hepatitis. Very few people did not have another possible reason, so it is possible that a mild form of liver damage happened from taking CAB. In those people, the liver tests got better after stopping CAB, showing that any damage was temporary. Seizures have been seen (rarely) in people who had CAB. They are not thought to be caused by CAB, but the study staff will ask you about them. We have an information sheet about CAB and its side effects for you to keep.

**Allergic Reaction Risks** – As with taking any drug, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash
- Wheezing and difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the study doctor and study staff if you have any of these symptoms.

**Risk of HIV Resistance to CAB** – We do not know if using CAB for PrEP will mean that CAB will not work to treat the HIV if you get infected with HIV during the study or in the future (this is called drug resistance). Drug resistance usually occurs when the amount of a drug in the body is too low to kill the virus. You will have low levels of CAB in the body for about one year after the last injection, or if you don't get the injections when they are due. This is why it is very important that you use other methods to protect against HIV infection whenever you are at risk, like using condoms and, if you are no longer receiving CAB, using Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) PrEP pills.

**Risks potentially related to Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) for PrEP** - Like all other drugs, you may have symptoms or side effects while taking PrEP. These symptoms or side effects may be due to participation in

the study or due to illnesses that have no relation to the study, like a cold or flu. You should tell the study staff at the study clinic about any symptoms that you feel while you are participating in the study. In past PrEP research studies, nausea and diarrhea were the most common side effects, and happened in about 10% or 1 in 10 people. Nausea and diarrhea mainly happened in the first month and then went away. A small number (less than 1% or 1 out of 100 people) in PrEP studies showed a small decrease in how their kidneys work, but this stopped when the people stopped taking the study drug. Other side effects were very rare and usually resolved when the study drug was stopped.

**Risks of Asking Sensitive Questions** – You may feel uncomfortable when we ask personal questions. You do not have to answer any question that you do not want to and you can stop answering the questions at any time.

**Risk of Disclosure of Private Information** – We will make every effort to keep your information private and confidential. It is possible that others may learn that you are part of this study and they may think that you are infected with HIV or are at high risk for HIV. Because of this you may feel stigma, stress or embarrassment. We will not share any information about you or your health with anyone, even your parent/guardian, without talking to you first, except when *[sites to insert relevant information about any legal obligations for disclosure, for example...your life is thought to be in danger]*.

**Risks of Rectal Swabs** – You may have mild discomfort when the swab is performed, particularly if you have hemorrhoids. In some cases, a very small amount of bleeding may occur. If you are already having pain in the rectal area, be sure to let the study staff know.

**Risks of Oral Pharyngeal Swabs** – There are no risks or complications associated with this collection procedure. The procedure may cause momentary gagging because the back of the throat is a sensitive area, but it shouldn't be painful.

**Other Risks** – There may be uncommon or previously unknown risks that might occur. You should report any problems to the study staff immediately.

#### **WHAT ARE THE BENEFITS OF TAKING PART IN THIS STUDY?**

You may get direct benefit from being in this study. CAB LA has been shown to prevent HIV infections among adult men and transgender women. You will get information about your health and the results of the tests, as well as treatment for sexually transmitted infections. The counseling you get during this study may help you avoid HIV and other sexually transmitted infections. You or others in your community may benefit from this study later. The information gathered during this study may help to prevent the spread of HIV. This may be beneficial to you and your community.

#### **ARE THERE ANY COSTS TO ME FOR TAKING PART IN THIS STUDY?**

You will pay no money to be in the study. The study drug CAB will be provided and study procedures will be performed at no additional cost to you and/or your insurance company.

#### **WHAT OTHER CHOICES DO I HAVE?**

It is possible that Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) or Tenofovir Alafenamide/Emtricitabine (Trade name: TAF/FTC, Descovy®) for PrEP are available in your local area for HIV prevention. If you prefer to take PrEP instead of joining the study, ask the study staff to refer you for HIV prevention medical services.

*[Sites to include/amend the following if applicable: There may be other studies going on here or in the community that you may be eligible for. If you wish, we will tell you about other studies that we know about. There also may be other places where you can go for HIV counseling and testing. We will tell you about those places if you wish.]*

#### **WILL I BE TOLD IF THERE IS NEW INFORMATION?**

You will be told about any new information learned during the course of the study that might cause you to change your mind about being in the study. At the end of the study, you will be told when study results may be available and how we will let you know about the results.

#### **COMMERCIAL PROFIT**

Your biospecimens collected during this study will not be used for commercial profit.

#### **CLINICALLY RELEVANT RESULTS**

Research results that are clinically relevant, including individual research results, will be disclosed to you under these conditions:

- HIV diagnostic testing results
- Any results that affect the treatment of HIV

#### **ARE THERE ANY REASONS WHY I MAY BE ASKED TO STOP TAKING PART IN THIS STUDY?**

You may be withdrawn from the study if any of the following occur:

You are unable or unwilling to attend clinic visits and/or follow all of the study procedures or instructions.

You could be harmed by continuing to take the pills or getting an injection.

The study is stopped or canceled.

The study doctor feels that staying in the study would be harmful to you.

Other reasons, as decided by the study staff.

#### **WHAT WILL I GET FOR TAKING PART IN THIS STUDY?**

You will be paid up to a total of **\$xx.xx** if you complete this study. You will be paid for the visits you complete according to the following schedule:

- **\$xx.xx for Visits xxx.**
- **\$xx.xx for Visits xxx.**
- **\$xx.xx for Visits xxx.**

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid \_\_\_\_\_ [*“after each visit,” “annually,” “bi-weekly,” etc.*]

If you have any questions regarding your compensation for participation, please contact the study staff.

#### **HOW WILL MY PRIVACY BE PROTECTED?**

To keep your information private, your samples will be labeled with a code that can only be traced back to the study clinic. Your name, where you live, and other personal information will be protected by the study clinic. The results of any tests done will not be included in your health records without your permission. Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. Your records may be reviewed, under guidelines of the United States Federal Privacy Act, by the United States Food and Drug Administration (FDA); the sponsor of the study (United States National Institutes of Health [NIH]), other US, local and international regulatory entities may also review your study records, as well as the Advarra Institutional Review Board (IRB), Ethics Committees (EC), study staff, study monitors, the company that makes CAB, and other local authorities. Groups that oversee the study include:

- Advarra IRB
- [*insert name of other site regulatory entities*]
- Representatives of the HPTN
- The United States National Institutes of Health and its study monitors (including NICHD and its monitor, Westat)
- The United States Food and Drug Administration
- The United States Office for Human Research Protections
- Other U.S., local, and international regulatory entities
- ViiV Healthcare (the company that makes CAB)

The study staff and these groups are required to keep study records private and confidential. The results of the study may be presented publicly or published. However, no presentation or publication will use your name or identify you personally. Your study information may be given to other authorities if required by law, including diagnoses of sexually transmitted infections. For example, we are required to follow state laws and report any risk of harm to you or others. This would include sexual activity with an adult while you are a minor.

In addition to the efforts made by the study staff to help keep your personal information confidential, we have obtained a Certificate of Confidentiality from the U.S. Federal Government. This Certificate protects researchers from being forced to tell people who are not connected with this study about your participation. The Certificate of Confidentiality does not prevent you from

releasing information about yourself and your participation in the study. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, we will tell the proper authorities.

#### **WHAT HAPPENS IF I AM INJURED DURING THE STUDY?**

Your health is important to us. We will make every effort to protect your well-being and minimize risks. It is possible, however, that you could have an illness or injury that is study-related. This means that the illness or injury occurred as a direct result of the study procedures or the study drug.

If a study-related illness or injury occurs, we will treat you or tell you where you can get treatment. The cost for this treatment may be charged to you or your insurance company. There is no program for compensation either through the study site or the U.S. National Institutes of Health.

By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

#### **WHOM TO CONTACT ABOUT THIS STUDY**

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:  
Study Subject Adviser  
Advarra IRB  
6940 Columbia Gateway Drive, Suite 110  
Columbia, MD 21046
- or call toll free: 877-992-4724
- or by email: [adviser@advarra.com](mailto:adviser@advarra.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00040790.

#### **SCREENING AND ENROLLMENT CONSENT**

Your signature and date on this form means that:

- You understand the information given to you in this form,
- You accept the provisions in the form, and
- You agree to join the study

You will not give up any of your legal rights by signing and dating this consent form.

I have read this form. I know that this is a research study. I have been told about the risks and potential benefits of taking part in the study. I have asked all the questions I have about the study and have gotten answers to my questions. I know that I am free to quit the study at any time without any penalties or loss of benefits. I will tell the study doctor or the study staff if I choose to stop the study so that I can stop in the best way to not harm my health. I will be given a signed and dated copy of this form to keep.

I agree to take part in this research study.

\_\_\_\_\_  
Participant's Name (print)

\_\_\_\_\_  
Signature and Date

**CONSENT TO TAKE PART IN THIS STUDY FOR ADOLESCENT PARTICIPANTS WHO HAVE REACHED THE AGE OF MAJORITY**

I have read this form. I know that this is a research study. I have been told about the risks and potential benefits of taking part in the study. I have asked all the questions I have about the study and have gotten answers to my questions. I know that I am free to quit the study at any time without any penalties or loss of benefits. I will tell the study doctor or the study staff if I choose to stop the study so that I can stop in the best way to not harm my health. I will be given a signed and dated copy of this form to keep.

I agree to take part in this research study.

\_\_\_\_\_  
Participant's Name (print)

\_\_\_\_\_  
Signature and Date

\_\_\_\_\_  
Study Staff Conducting  
Consent Discussion (print)

\_\_\_\_\_  
Study Staff Signature and Date

**Revision 19: Section 12.10, Appendix X, is an informed consent for adolescent interviews for parents/guardians and assent for adolescent interviews for adolescents aged 14 to majority.**

12.8 **12.10 APPENDIX XVIII: INFORMED CONSENT FOR ADOLESCENT INTERVIEW FOR PARENTS/LEGAL GUARDIANS AND PARTICIPANTS WHO REACH THE AGE OF MAJORITY AND ASSENT FOR ADOLESCENT PARTICIPANTS AGES 14 – AGE OF MAJORITY**

*Entering the interview*

In order to understand better what makes it easier or harder for young ~~men~~ **people** in this study to get CAB injections as directed, we will be doing interviews with up to 10 young ~~men~~ **people** at participating sites. You have been selected to take part in one interview sometime after your last **Step 2** CAB injection.

During the interview we will ask you questions about:

- If you are taking daily Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) pills, how you feel about being on **oral** PrEP

~~CONSENT FOR PARTICIPANTS WHO REACH THE AGE OF MAJORITY~~

~~Write your initials and sign and date below.~~

~~\_\_\_\_\_ I agree to be interviewed for the study and to have the interview audiotaped.~~

\_\_\_\_\_  
Name of Participant (print)

\_\_\_\_\_  
Signature and Date

**Revision 20: Section 12.11, Appendix XI, is a new informed consent for the interviews for adolescents who can consent for themselves (self-consent) and those reaching the AOM.**

**12.11 APPENDIX XI: INFORMED CONSENT FOR ADOLESCENT INTERVIEW FOR ADOLESCENT PARTICIPANTS ABLE TO CONSENT FOR THEMSELVES (SELF-CONSENT) AND PARTICIPANTS WHO REACH THE AGE OF MAJORITY**

**Sponsor / Study Title:** Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “HPTN 083-01: Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Males – A sub-study of HPTN 083”

**Protocol Number:** HPTN 083-01

**Principal Investigator:** «PiFullName»  
(Study Doctor)

**Telephone:** «IcfPhoneNumber»

Address:

«PiLocations»

## **INTRODUCTION**

You are being asked to take part in an interview as part of the research study listed above. Participating in this interview is voluntary. You may refuse to join, or you may withdraw your consent to be interviewed for any reason. Before you decide whether to take part in the interview, we would like to explain the purpose of the interview, the risks and benefits to you and what is expected of you.

This consent form gives information about taking part in the interview. We will help you to understand the form and answer your questions before you sign and date this form. Once you understand the details about taking part in the interview, and if you agree to take part, you will be asked to sign your name and date this form. You will be offered a copy of this form to keep.

### ***Participation is voluntary***

Before you learn about the interview, it is important that you know the following:

Your participation is voluntary. You do not have to take part in this interview if you do not want to. You may decide not to take part in the interview, or you may decide to leave the interview at any time without losing your regular medical care.

You are not required to participate in this interview in order to remain in the rest of the main study.

### ***About the interview***

The main study is being done to find out if it is safe and acceptable for adolescents who do not have HIV to take an experimental HIV drug called cabotegravir (CAB) as PrEP to prevent HIV. The interview portion will ask adolescents what they like and do not like about getting CAB injections. We will also ask questions to find out what makes some adolescents more or less interested in starting PrEP. Finally, we will ask about difficulties you had getting CAB injections and things that made that easier.

### ***Entering the interview***

In order to understand better what makes it easier or harder for young people in this study to get CAB injections as directed, we will be doing interviews with up to 10 young people at participating sites. You have been selected to take part in one interview sometime after your last Step 2 CAB injection.

### ***What will happen during the interview***

The interview will be led by a member of the research team that you do not work with during the study. It should take about 1 hour. *[To be modified to reflect site practices: The interview will take place in a location that the study staff have determined will provide you with privacy and confidentiality such as the clinic, or another appropriate place. The study team will talk with you about this so you know where to go for the interview].*

During the interview we will ask you questions about:

- How and when you decided to join the study
- Whether you feel that you personally are at risk of HIV
- How you made daily pill-taking part of your routine in Step 1
- Where you kept your CAB pills
- Whether you talked to your family members, peers, or partner(s) about being in this study or getting CAB injections in Step 2
- If you had any bad effects from the CAB injections, and if this influenced your decision to keep getting the injections
- If you are taking daily Tenofovir/Emtricitabine (Trade name: TDF/FTC, Truvada®) pills, how you feel about being on oral PrEP
- Other related topics

If any of the questions make you upset, either you or the interviewer may stop the interview at any time. You will also be provided with contact and referral information if any of the questions raise issues that you would like to talk about later.

#### ***Benefits of taking part in the interview***

There may be no benefit from being interviewed. You may not receive any other direct benefit from being in this part of the study; however, you or others in your community may benefit from this study later.

#### ***Risk of taking part in the interview***

There is little risk from the interview. To minimize any discomfort and to protect your privacy, the interview will be conducted in a private area that will allow you to speak comfortably without being overheard. Although we hope that you will be comfortable answering all of the questions openly and honestly, please keep in mind that you may refuse to answer any of the questions, or stop the interview completely, at any time. The greatest risk may involve your privacy and confidentiality. The steps that the study team have taken to protect your privacy are described below.

#### ***Other information about the interview***

**Privacy** – Every effort will be made to keep your personal information confidential. Your personal information (name, address, phone number) will be protected by the research clinic. Your name, or anything else that might identify you personally, will not be used in any publication of information about this study.

To help assure that we get the best understanding possible from your answers during the interview, the entire interview **will be audio-recorded**. After the interview is finished, the recording will be typed (called a transcript) by people who know how to do this. All identifying information will be removed from the transcript. Your name will not be included on the transcript. These recordings will be destroyed after all analysis is completed.

Your records may be reviewed by the following groups, involved with the study:

- Advarra Institutional Review Board

- **[insert name of other site regulatory entities]**
- Representatives of the HPTN
- The United States National Institutes of Health and its study monitors (including NICHD and its monitor, Westat)
- The United States Food and Drug Administration
- The United States Office for Human Research Protections
- Other U.S., local, and international regulatory entities
- ViiV Healthcare (the company that makes CAB)

If the study staff learns that you are at risk of harm, we will tell the proper authorities as we are required to do by the law. We are also required to follow state laws regarding reporting of sexual activity of minors with adults.

**New Information** – You will be told any new information learned during this study that might affect your willingness to stay in the study. You will also be told when the results of the study may be available, and how to learn about them.

#### Alternatives to participating

You can talk to the study staff at any time about your experiences in the study, without taking part in the interview.

There are no costs to you for being interviewed

There will be no cost to you for participating in the in-depth interview.

#### «Compensation»

You will receive \$XX for being interviewed. You will be paid \_\_\_\_\_ **[“after each visit,” “annually,” “bi-weekly,” etc.]**

If you have any questions regarding your compensation for participation, please contact the study staff.

#### Whom to contact

If you have questions about the interview, please contact the study staff listed on page 1 of this document.

If you have a research-related injury, please contact: **[insert name of site contact]**

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- **By mail:**  
 Study Subject Adviser  
 Advarra IRB  
 6940 Columbia Gateway Drive, Suite 110  
 Columbia, MD 21046
- **or call toll free: 877-992-4724**

- or by email: [adviser@advarra.com](mailto:adviser@advarra.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00040790.

## SIGNATURE PAGE

### ADOLESCENT SELF-CONSENT FOR IN-DEPTH INTERVIEW

If you decide to join this interview portion of the main study, sign and date below. Before deciding whether to be interviewed, make sure you have read this form, or had it read to you, and that all of your questions have been answered. You should feel that you understand the study, its risks and benefits, and what is expected of you if you decide to join. You can ask questions or request more information at any time. You do not give up any rights by signing and dating this form.

Write your initials and sign and date below.

\_\_\_\_\_ I agree to be interviewed for the study and to have the interview audiotaped.

\_\_\_\_\_  
Name of Participant (print)

\_\_\_\_\_  
Signature and Date

### CONSENT FOR PARTICIPANTS WHO REACH THE AGE OF MAJORITY

Write your initials and sign and date below.

\_\_\_\_\_ I agree to be interviewed for the study and to have the interview audiotaped.

\_\_\_\_\_  
Name of Participant (print)

\_\_\_\_\_  
Signature and Date

\_\_\_\_\_  
Study Staff Conducting  
Consent Discussion (print)

\_\_\_\_\_  
Study Staff Signature and Date

Revision 21: Section 12.14, Appendix XIV, is the main storage consent/assent, the revised informed consent for specimen storage and future use for parents/legal guardians and assent for participants aged 14 to AOM.

~~12.14~~ **12.14** APPENDIX XI: ~~APPENDIX XIV~~: INFORMED CONSENT FOR SPECIMEN STORAGE AND FUTURE USE FOR PARENTS/LEGAL GUARDIANS AND PARTICIPANTS WHO REACH THE AGE OF MAJORITY AND ASSENT FOR ADOLESCENT PARTICIPANTS AGES 14 – AGE OF MAJORITY

~~CONSENT FOR ADOLESCENT PARTICIPANTS WHO REACH THE AGE OF MAJORITY~~  
I have read this form. I have asked all the questions I have about the study and have gotten answers to my questions. I will be given a signed and dated copy of this form to keep.

For your leftover samples, write your initials next to your choice (choose only one).

~~\_\_\_\_\_ I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I also allow my samples to be used for tests of my genes.~~

~~\_\_\_\_\_ I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I do not allow my samples to be used for tests of my genes.~~

~~\_\_\_\_\_ I do not allow my leftover samples to be used for any research.~~

\_\_\_\_\_  
Participant's Name (print)

\_\_\_\_\_  
Signature and Date

\_\_\_\_\_  
Study Staff Conducting  
Consent Discussion (print)

\_\_\_\_\_  
Study Staff Signature and Date

**Revision 22: Section 12.15, Appendix XV, is a new informed consent for specimen storage and future use for adolescents who self-consent and those who reach the AOM.**

**Sponsor / Study Title:** Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), US National Institutes of Health (NIH) / “HPTN 083-01: Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Males – A sub-study of HPTN 083”

**Protocol Number:** HPTN 083-01

**Principal Investigator:** «PiFullName»  
(Study Doctor)

**Telephone:** «lcfPhoneNumber»

**Address:** «PiLocations»

## **INTRODUCTION**

**You have decided to join the study named above. As part of the study, you will have blood, urine, rectal swab, and oral pharyngeal swabs collected. After all the tests for this study have been done, there may be some samples left over. We call these left over samples. The study doctor would like to keep these left over samples and use them for other research in the future. This form gives information about use of left over samples. Please read it and ask any questions you may have. After we discuss the information with you, you will record your decisions on use of extra samples at the end of the form.**

**It is your decision whether or not to allow the left over samples to be used.**

**You are free to say yes or no, and to change your mind at any time. Your decision will not affect your participation in the study. If you say no, all left over samples will be destroyed.**

**If you agree, your left over samples will be kept in a repository.**

**A repository is a secure facility that is used to store samples. The HPTN repository is in the United States. If you agree to have left over samples stored, the samples will be kept in this repository. There is no limit on how long the samples will be kept.**

**Left over samples could be used for different types of research.**

**Left over samples may be used for research on HIV and other infections, including testing for the medicines used in this study and other anti-HIV medicines, the immune system, and other diseases. The research may be done in the United States or in other locations. If you agree, the leftover samples could also be used for research that looks at your genes. Genes are passed to children from their birth parents. They affect how people look and how their bodies work. Differences in people's genes can help explain why some people get a disease while others do not. Your samples would only be used to look at genes related to how the body responds to the study drugs and the immune system. These tests would not include whole genome sequencing (WGS).**

**Any research done with the leftover samples must be reviewed and approved by the HPTN. The research must also be approved by an ethics committee. The role of an ethics committee is to review the research plan and protect the rights and well-being of the people whose samples will be used.**

**The research done with left over samples is not expected to give any information relevant to your health. Therefore, the results will not be given to the study staff or to you. The results also will not be placed in your study records.**

**There is little risk to you.**

**When left over samples are used for research, they are labeled with a code number only. To protect your privacy, no names are used. However, information such as age, gender, HIV status, and other health information may be linked to the samples. There may be some risks from tests of your genes. If others found**

out the results of these tests, they could treat you badly or unfairly. However, this is almost impossible because the results will not be given to the study staff or to you and will not be in your study records.

Any identifiers will be removed from the identifiable private information or biospecimens and, after removal, the information or biospecimens can be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

There may be no benefit to you.

You will not get direct benefit from storage of the samples. You or others in your community may benefit from this study later. The information gathered during this study may help to prevent the spread of HIV. This may be beneficial to you and your community.

You will not be paid for use of your samples.

There is no cost to you for use of your leftover samples. The samples will not be sold, and you will not be paid for use of the samples. It is possible that research done with the samples could lead to a new discovery or a new product. If this happens, there is no plan to share any money with you.

Information from research using extra samples may be reviewed by groups that oversee the research.

These groups include:

- Advarra Institutional Review Board
- [insert name of other site regulatory entities]
- Representatives of the HPTN
- The United States National Institutes of Health and its study monitors (including NICHD and its monitor, Westat)
- The United States Food and Drug Administration
- The United States Office for Human Research Protections
- Other U.S., local, and international regulatory entities
- ViiV Healthcare (the company that makes CAB)

The people who do research with the leftover samples and the groups listed above are required to make efforts to keep information private and confidential.

The results of research done with the leftover samples may be presented publicly or published. However, no presentation or publication will use your name or identify you personally.

**Whom to contact about this sub-study**

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this

consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:

Study Subject Adviser  
Advarra IRB  
6940 Columbia Gateway Drive, Suite 110  
Columbia, MD 21046

- or call toll free: 877-992-4724
- or by email: [adviser@advarra.com](mailto:adviser@advarra.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00040790.

#### **SPECIMEN STORAGE AND FUTURE USE INFORMED CONSENT (SELF-CONSENT)**

Before deciding about storage of laboratory specimens, make sure you have read this form and that all of your questions have been answered. You should feel that you understand your options and the possible risks and benefits before making your decision. You do not give up any rights by signing and dating this form.

For your leftover samples, write your initials next to your choice (*choose only one*).

\_\_\_\_\_ I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I also allow my samples to be used for tests of my genes.

\_\_\_\_\_ I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I do not allow my samples to be used for tests of my genes.

\_\_\_\_\_ I do not allow my leftover samples to be used for any research.

\_\_\_\_\_  
**Participant's Name (print)**

\_\_\_\_\_  
**Signature and Date**

**Study Staff Conducting  
Consent Discussion (print)**

**Study Staff Signature and Date**

**CONSENT FOR ADOLESCENT PARTICIPANTS WHO REACH THE AGE OF  
MAJORITY**

**I have read this form. I have asked all the questions I have about the study and have gotten answers to my questions. I will be given a signed and dated copy of this form to keep.**

**For your leftover samples, write your initials next to your choice (*choose only one*).**

\_\_\_\_\_ **I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I also allow my samples to be used for tests of my genes.**

\_\_\_\_\_ **I allow my leftover samples to be used for research on HIV and other infections, including testing for the study drugs and other anti-HIV medicines, the immune system, and other diseases. I do not allow my samples to be used for tests of my genes.**

\_\_\_\_\_ **I do not allow my leftover samples to be used for any research.**

\_\_\_\_\_  
**Participant's Name (print)**

\_\_\_\_\_  
**Signature and Date**

\_\_\_\_\_  
**Study Staff Conducting  
Consent Discussion (print)**

\_\_\_\_\_  
**Study Staff Signature and Date**