

**Letter of Amendment # 2 to:**

**HPTN 082: Uptake and adherence to daily oral PrEP as a primary prevention strategy for young African women: A Vanguard Study  
Version 1.0, 8 December 2015  
DAIDS Document ID: 12068**

**LoA #2: 19 July 2017**

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**The following information impacts the HPTN 082 study and must be forwarded to all responsible Institutional Review Boards (IRBs) as soon as possible for their information and review. This Letter of Amendment must be approved by all responsible IRBs before implementation.**

**The following information does not impact the sample informed consents. Your IRB will be responsible for determining the process of informing subjects of the contents of this letter of amendment (LoA).**

**Upon receiving final IRB and any other applicable Regulatory Entity (RE) approval(s) for this LoA, sites should implement the LoA immediately. Sites are still required to submit an LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). Sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. An LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with this letter and any IRB correspondence should be retained in the site's regulatory files.**

**If the HPTN 082 protocol is amended in the future, this Letter of Amendment will be incorporated into the next version.**

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**Summary of Revisions and Rationale**

1. Revisions were made to sections 4.6.6, 6.7.2 and 6.7.4 to clarify that product will be held for participants if the CrCl decreases below 60 ml/min.
2. Per recent DAIDS requirement, the protocol signature language was revised.

### Implementation of the Protocol Modification

The modifications detailed below will be formally incorporated into the body of the protocol with the next full amendment. Deletions to the protocol text are indicated by ~~strike through~~; additions are indicated in **bold**.

#### Revision 1

#### 4.6.6. Toxicity Management

The site investigator has the discretion to interrupt FTC/TDF at any time if s/he feels that continued medication use would be harmful to the participant or would interfere with treatment deemed clinically necessary according to the judgment of the investigator. Clinical or laboratory abnormalities that require follow-up will be documented, and the research associate or clinician will contact the participant to schedule an interim visit for follow-up and/or repeat laboratory testing if indicated. All participants reporting an adverse event (AE) Grade 3 or higher ~~or any grade for creatinine~~ will be followed clinically until the occurrence resolves (returns to baseline grade, defined as grade at Screening/Enrollment) or stabilizes. ~~Participants enrolled with a Grade 2 creatinine clearance (CrCl between 60 and 90 ml/min) will be followed if CrCl increases in severity from baseline levels.~~ PrEP will be discontinued if the CrCl decreases below 60 ml/min and serum creatinine will be monitored. All participants who discontinue PrEP (either for toxicity reasons or personal choice) will be followed under the procedures identified in Appendix IB for PrEP decliners.

#### 6.7.2. AE Grade 3

FTC/TDF may be continued at the discretion of the site investigator if a Grade 3 toxicity is considered to be unrelated to the study medication **except in the case of CrCl where PrEP will be temporarily withheld if the CrCl decreases below 60 ml/min.** Study medication will be temporarily withheld if Grade 3 toxicity is considered to be related to the study medication. After a Grade 3 toxicity returns to Grade 1, the participant can be reintroduced to medication after consultation with the site investigator, DAIDS Medical Officer, and other members of the CMC. If a Grade 3 toxicity recurs and is considered to be related to study medication, FTC/TDF will be permanently discontinued.

#### 6.7.4. Creatinine Clearance

Eligibility for enrollment in HPTN 082 mirrors CDC guidelines for starting PrEP.<sup>97,98</sup> Participants who enroll with a Grade 2 CrCl will discontinue PrEP only if there is an increase in severity (to Grade 3 or 4). ~~Participants who enroll with CrCl >90ml/min who develop a Grade 2 CrCl should discontinue study drug temporarily and be followed clinically until level returns to baseline (screening value).~~ **PrEP will be temporarily withheld if the CrCl decreases below 60 ml/min and serum creatinine will be monitored.**

Revision 2

HPTN 082

Uptake and adherence to daily oral PrEP as a primary prevention strategy for young African women: A Vanguard Study

Final Version 1.0/ 8 December 2015

INVESTIGATOR SIGNATURE PAGE Non-IND

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)

US National Institute of Mental Health (NIMH)

US National Institutes of Health (NIH)

I, the Investigator of Record (IoR), agree to conduct this study in full accordance with the provisions of this protocol **as well as in compliance with all applicable United States (US) Code of Federal Regulations (CFR); International Conference on Harmonisation (ICH) Good Clinical Practices (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., US National Institutes of Health, Division of AIDS) and institutional policies.**

I agree to maintain all study documentation for a minimum of three years after submission of the site's final Financial Status Report to the Division of AIDS (DAIDS), unless otherwise specified by DAIDS or the HIV Prevention Trials Network (HPTN) Leadership and Operations Center (**LOC**). Publication of the results of this study will be governed by HPTN policies. Any presentation, abstract, or manuscript will be made ~~available~~ **submitted by the investigator** to the HPTN Manuscript Review Committee (**MRC**) and DAIDS for review prior to submission.

I have read and understand the information in this protocol and will ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about the obligations incurred by their contribution to the study.

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Name of Site Investigator of Record

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Signature of Site Investigator of Record

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Date