

Letter of Amendment # 1 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**

Final Version of LoA # 1: 9 March 2017

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 impacts 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.

Summary of Revisions and Rationale

1. Several modifications were made to the Protocol Team Roster to add new members of the study team and remove those who were no longer involved. Also, two minor corrections within the roster were made.
2. Clarified the use of dried blood spots for feedback about drug levels in the intervention arm and ensured that analysis of drug levels could be based on drug levels in either plasma or dried blood spots.
3. Brought Section 4.3 into alignment with the Sample Informed Consent Forms (SIC) regarding the use of one-way messaging.
4. Revised the SIC to simplify language and bring drug risks in line with side effects of Truvada when used alone as PrEP based on Phase 3 trials rather than Truvada in combination with other categories of ARVs as part of HIV treatment.
5. Made a few minor corrections throughout several sections of the protocol.

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

**Denni Lennon, DrPHc, MA, MB(ASCP)CM
HPTN LC International QA/QC Laboratory Coordinator
Johns Hopkins University
Department of Pathology
600 North Wolfe Street, Pathology 304
Baltimore, MD 21287, USA
Phone: 410 502 5721
Fax: 410 614 0430
Email: dcatala1@jhu.edu**

**Heather Noble, MPH
HPTN Clinical Data Manager
SCHARP-FHCRC
1100 Fairview Avenue North E3-129
Seattle, WA 98109, USA
Phone: 206 667 3329
Email: hnable@scharp.org**

**Marcus Bolton, M.Ed.
Senior Community Programs Manager
FHI 360
359 Blackwell Street, Suite 200
Durham, NC 27701, USA
Phone: 919 544 7040, Ext. 11678
Fax: 919 544 7261
Email: mbolton@fhi360.org**

~~Estelle Piwovar Manning, BS, MT (ASCP) SI
HPTN LC Deputy Director
1600 North Wolfe Street, Pathology 306
Baltimore, MD 21287, USA
Phone: 410 614 6736
Fax: 410 614 0430
Email: epiwowa@jhmi.edu~~

~~Rhonda White, BS
Community Programs Manager
FHI 360
359 Blackwell Street, Suite 200
Durham, NC 27701, USA
Phone: 919 544 7040, Ext. 11515
Fax: 919 405 1402
Email: rwhite@fhi360.org~~

Yaw O. Agyei **MPH**, BS, MT (ASCP)
Johns Hopkins University
600 North Wolf Street
Baltimore, MD 21287, USA
Phone: 410 614 6736
Email: yagyeil@jhmi.edu

Adeola Adeyeye MD, MPA (e)
Medical Officer, Prevention Science Program,
DAIDS, NIAID, NIH
Room 8B36 MSC 9831, 5601 Fishers Lane
Rockville, MD 20852, USA
Phone: 240 669 5005
Email: adeyeyeao@niaid.nih.gov

Revision 2

1.2.2. Adherence to open-label PrEP (last paragraph)

In summary, for the HPTN 082 intervention, we will support the formation of effective PrEP adherence habits among all women who accept PrEP through: 1) brief adherence counseling based on CBT for women who accept PrEP at enrollment with monthly visits in the first three months to support adherence habit formation; 2) two-way weekly SMS text messaging to provide cognitive reminders about visits and support for PrEP adherence, using an existing platform for SMS reminders, and 3) peer support through HPTN 082 adherence support clubs;. All of these will be described in more detail in Section 4.3. In addition, we will randomize women in a 1:1 ratio to have counseling about their early ~~TFV~~ or TFV-DP levels to assess whether this intervention affects adherence.

4.3. Adherence Support for PrEP Acceptors

Counseling based on drug levels

Women who are randomized to enhanced counselling will have adherence monitoring based on ~~plasma or DBS TFV~~/TFV-DP levels obtained 4 and 8 weeks after PrEP acceptance as described in Section 4.6.4. Adherence counseling based on drug levels will be provided at the next visit (i.e., for participants who accept PrEP at enrollment Week 4 levels will be provided at the Week 8 visit, Week 8 levels will be provided at the Week 13 visit). Pictorial tools will be developed in conjunction with the youth CABs in order to provide youth-relevant representations of drug levels (e.g., cell phone bars or wireless signal strength symbols).

4.6.4. Counseling based on feedback from drug level data

Participants who are randomized to enhanced counseling will have measurements of ~~plasma TFV or DBS~~ **Intracellular** TFV-DP levels ~~enfrom~~ **DBS** samples taken 4 and 8 weeks after PrEP acceptance. These will be “convenience” or “untimed” samples with respect to the previous dose. Thresholds will be developed and included in the SSP and counseling manuals. These will be used for counseling women about their adherence. The adherence counseling based on ~~TFV~~ or TFV-DP levels will be provided at the next visit (i.e., Week 4 level will be provided at the Week 8 visit, and Week 8 drug levels will be provided at the Week 13 visit). A semi structured feedback guide will be included for site adaption in the SSP. Women will receive the following counseling during their cognitive behavioral counseling sessions:

- For those with ~~TFV~~ or TFV-DP levels consistent with a dose within 24 hours or consistent dosing (for example, at least 6 doses per week) in the preceding month: Positive re-enforcement with continued encouragement to maintain adherence.
- For those with ~~TFV~~ or TFV-DP levels that are quantifiable but consistent with less frequent dosing: Discuss details about their dosing patterns in the past month and encourage greater adherence in order to get optimal protection from PrEP.
- For those with ~~TFV~~ or TFV-DP **levels** which are undetectable: Discuss willingness and/or need to continue PrEP use and if willing and in need of PrEP, emphasize the need for greater adherence and explore barriers to taking PrEP, avoiding punitive language.

4.6.5. Primary Adherence Assessment

For the primary adherence outcome measurement (adherence in the cohort by randomization arm) drug levels will be measured retrospectively. The main adherence assessment will be performed using plasma and/or DBS samples. The testing plan will be determined at a later date, based on evaluations of plasma TFV levels and DBS TFV-DP levels in women that are currently underway.

We will utilize plasma TFV levels to assess recent dosing within the last 5 days and DBS TFV-DP levels to assess cumulative dosing in the prior month. DBS has been used to detect intracellular levels of TFV-DP in red blood cells, providing a measure of cumulative adherence behavior over the prior one-two months. A threshold of 700 fmol/punch predicted 100% efficacy among MSM in iPrEX OLE. 24 Given the long half-life for TFV-DP, gradients of cumulative adherence can also be estimated, such as those described in iPrEX OLE as follows: Below limit of quantitation (BLQ, no doses), BLQ to 349 fmol/punch (fewer than two tablets per week), 350–699 fmol/punch (two or three tablets per week), 700–1249 fmol/punch (four to six tablets per week), and ≥ 1250 fmol/punch (daily dosing). Women may respond to TDF/FTC differently compared with men due to differences in mucosal drug distribution, and ongoing analyses of HPTN 066 and DOT-DBS will be used to compare plasma ~~tenofovir~~ TFV and intracellular TFV-DP in DBS to identify the appropriate thresholds indicating high, intermediate, and ~~low~~ recent adherence based on plasma TFV and cumulative dosing based on intracellular TFV-DP in women.

7.2.1. Primary Endpoints

Consistent with the primary study objective to assess the difference in PrEP adherence using drug levels in young women randomized to the enhanced versus standard arms, the following endpoint(s) will be assessed:

- TFV levels in plasma **and/or TFV-DP in DBS** at Weeks 13, 26 and 52 after PrEP acceptance among those who accept PrEP and are randomized. This will include young women who accept PrEP after enrollment.

7.2.2. Secondary Endpoints

Covariates assessed at baseline and follow-up visits will include:

- TFV/~~TFV-DP~~ levels in plasma **and/or TFV-DP in DBS**
- Sexual risk
- Alcohol use
- Number of partners
- Age of partner
- Transactional sex
- Intimate partner violence

Consistent with the secondary study objective to assess the specificity and predictive value of a PrEP readiness tool (based on the HPRM and PBM) to predict uptake and adherence to oral PrEP, the following endpoint(s) will be assessed:

- Acceptance of PrEP at Enrollment or during follow up
- TFV levels in plasma **and/or TFV-DP in DBS** at Week 13, 26 and 52 amongst those women who accept (based on CRFs) and remain on PrEP (based on drug dispensed)

Consistent with the secondary study objective to assess HIV incidence in those who accept PrEP compared to those who do not, and to assess the association with detectable TFV in PrEP users who acquire HIV infection during the study, the following endpoint(s) will be assessed:

- HIV seroconversion, assessed at Weeks 4, 8, 13, 26, 39 and 52.

Covariates assessed will be:

- Detectable and quantitative concentrations of TFV in plasma **and/or TFV-DP in DBS** at Weeks 4, 13, 26 and 52.

7.4.1. Primary Analyses

The proportion of women who accept PrEP at study enrollment, if the cap of 200 is not reached, will be assessed as the proportion of women who choose to accept PrEP at enrollment among the total number of women enrolled, including those who declined PrEP at enrollment. If the limit of 200 declining PrEP is reached, we would assess the proportion who accepted PrEP at enrollment up to the time these 200 enrollments are achieved. Confidence limits will be computed using the binomial distribution. Logistic regression will be used to assess the association of baseline characteristics of young HIV uninfected women between those who accept versus decline PrEP at enrollment.

Amongst those who accepted PrEP and were randomized, we will report average adherence to daily PrEP as described previously based on ongoing analysis from relevant studies at Weeks 13, 26 and 52 after accepting PrEP. The difference in proportion adherent at weeks 13, 26 and 52 will be compared between arms using a t-test (assuming the normal approximation to the binomial) at each visit. Women who are missing drug level assessment but did not have drug dispensed at their most recent visit will be defined as non-adherent. Among all women who accept PrEP, the primary assessment will compare the proportion with **plasma** TFV levels **and/or DBS** TFV-DP levels consistent with a dose within 24 hours or consistent dosing (for example, at least 6 doses per week) in the preceding month across all visits between arms using logistic regression accounting for repeated measures. If DBS is used, a TFV-DP threshold consistent with high adherence as determined from ongoing studies will be used when available.

Revision 3

4.3. Adherence Support for PrEP Acceptors

Weekly SMS reminders

PrEP accepters will receive weekly SMS text messaging until Week 13, with the option to continue throughout follow up if desired. **Participants may also receive one-way messages celebrating participation milestones, general health messaging, etc.**

Revision 4

Appendix IIA: Sample Screening/Enrollment Informed Consent Form INTRODUCTION

You are/your child is being asked to take part in a research study. **The purpose of this consent form is to give you/your child the information you will need to help you/your child decide if you/she want to be in the study. We will tell you/your child the purpose of the study, what you/she will be asked to do in this study, the possible risks and benefits, and your/her rights as a volunteer.** Joining this study is voluntary. You/your child may refuse to join (or you may refuse to allow your child to join), or you may withdraw your consent (or consent for your child) to be in the study, for any reason. This research study is for young women who may be at risk for getting Human Immunodeficiency Virus, or HIV. HIV is the virus that causes Acquired Immunodeficiency Syndrome, or AIDS.

~~Before you decide whether you/your child will join the study, we would like to explain the purpose of the study, the risks and benefits to you/your child, and what is expected of you/your child.~~ **We want you/her to ask any questions you/she may have about this study. When all of your/her questions are answered, you/she can decide if you want/agree for your child to be in the study then you will be asked to sign this consent form. You will be given a signed copy of this form to keep. This process is called “informed consent.”**

If you are under X years, we will also need to obtain the consent of your parent or legal guardian in order for you to participate.

If your child is under X years, you are being asked to allow your child to participate in this research study.

PARTICIPATION IS VOLUNTARY

~~This consent form gives information about the study that will be discussed with you/your child. We will help you/and your child understand the form and answer your questions before you sign this form. Once you understand the study, and if you agree/agree for your child to take part, you will be asked to sign your name or make your mark on this form. You will be offered a copy of this form to keep.~~

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

- ~~• Your participation/your child’s participation is voluntary. You do not/your child does have to take part in any of the tests or procedures in the study.~~
- ~~• You/your child may decide not to take part in the study, or you/your child may decide to leave the study at any time without losing your/her regular medical care.~~
- ~~• If you/and your child decide not to take part in the study, you/she can still join another study at a later time if there is one available and you/she qualify.~~
- ~~• You/your child cannot join this study if you are/she is taking part in another study of drugs or medical devices. You are/she is asked to tell the study staff about any other studies you are/she is taking part in or thinking of taking part in. This is very important for your/her safety.~~

DO I/MY CHILD HAVE TO JOIN THIS STUDY?

Your participation/your child’s participation in this study is completely voluntary. You decide if you want/want your child to be in this study. You/your child may decide not to take part in this study. You/She may also stop taking part in the study at any time without penalty or losing your/her medical benefits. You/she will still be eligible for future studies even if you decide/she decides not to join this study.

PURPOSE OF THEWHAT IS THIS STUDY ABOUT?

~~Young women in southern Africa have a high risk of becoming HIV infected. Recent studies make us believe that either between 1 in every 10 or 1 in every 20 young southern African women will become HIV infected every year. Taking medication to prevent becoming HIV-infected is called “pre-exposure prophylaxis” or “PrEP.” Four studies that compared PrEP to placebo (a pill which looks like the regular pill but does not have the real drug)~~ **Many studies** have shown that PrEP works very well in preventing

HIV infection, and that the main thing which impacts how much protection PrEP provides is whether someone takes PrEP every day. **However, some studies have shown that PrEP does not work if you do not take it.** ~~However two other studies that compared PrEP to placebo in young African women did not show protection against HIV with PrEP because too few women took their pills. Very few women (fewer than 1 out of 3 women) had PrEP drug that could be found in their blood. Now that we know that PrEP works from multiple studies, it is important to understand whether young women in southern Africa are interested in and able to take PrEP.~~ **PrEP has been approved for HIV prevention after reviewing data about how well it has worked and whether it is safe by regulatory bodies in the US, South Africa, Zimbabwe and other countries. PrEP is recommended to be taken daily, because PrEP studies showed that the degree of protection from HIV with Truvada® was dependent on how often people actually take their pills and how much PrEP drug was in their blood.**

Now that we know that PrEP works from multiple studies **and it is approved for use for HIV prevention in populations at risk of HIV infection**, it is important to understand whether young women in southern Africa are interested in and able to take PrEP. The purpose of the HPTN 082 study is to find out whether young women in southern Africa at risk of HIV **and between the ages of 16-25** are willing to start and continue to take PrEP every day for up to one year. This study will ask young women what they like and do not like about taking PrEP. We will also ask questions to find out what makes some young women more or less interested in starting PrEP. We also hope to find out if young women find it helpful to hear about how much PrEP drug is in their blood during their first two follow-up visits with counselors.

~~HPTN 082 is enrolling young women ages 16-25, only women ages 18 and above were included in the PrEP trials we have discussed. Other studies are currently underway of oral PrEP in 16 and 17 year olds.~~

The name of the pills being used for PrEP in this study is Truvada®. Truvada® is a tablet that contains two medications called “emtricitabine” and “tenofovir” that are commonly used to treat HIV infection. It is not a cure for HIV or AIDS but is generally safe when used as treatment for HIV. ~~Several studies have also shown that Truvada® is safe and effective in preventing HIV when taken by people who are HIV-negative.~~ There are some side effects of Truvada® that sometimes occur. These are described later in this consent form.

~~The US FDA recommends taking Truvada® daily. This is because PrEP studies show that the ability of Truvada® to prevent HIV depends a lot on how often people actually take their pills. In PrEP studies among people in Africa, those who took PrEP and PrEP drug was found in their blood were more likely to not get HIV.~~ Remember that PrEP will not protect you/your child from pregnancy or other sexually transmitted infections you/she can get while having sex so it is important to keep using condoms or other means of pregnancy prevention. Condoms will be given to you/your child at every visit.

To help young women who decide to take PrEP remember to take their pills, we will ask you/your child to sign up with a special confidential system that will send you/your child a text message every week for the first 13 weeks. We ~~will~~**may** send you/your child messages ~~that provide information about HIV and pregnancy prevention~~, to remind you/your child to attend study visits, and ask you/your child about your/her health. We will not refer specifically to your/her health status or your/her use of PrEP. If you have/your child has a problem, we will provide you/her with a 24 hour number to contact study staff messages. We can always call back. We can help you/your child to understand how to delete these message from your/her phone if you are/she is concerned about others seeing them. At 13 weeks you/she

can decide to continue to receive the text messages or stop. We will not be able to see any information on your/her mobile phone and any texts you/she send us will not be shared with anyone outside of our research team.

We will also provide counseling about taking PrEP regularly at each visit ~~to learn if you/your child are having difficulty with taking the pill every day and~~ to help find ways to make it easier for you/your child to take PrEP daily. You/your child will be able to come to a monthly peer group club to talk about taking PrEP with other participants on this study as well as have fun.

STUDY PROCEDURES

WHAT WILL I/MY CHILD HAVE TO DO IN THE STUDY?

WHAT ARE THE RISKS AND/OR DISCOMFORTS OF TAKING PART IN THIS STUDY?

Risks potentially related to the Truvada® medication

~~You/Your~~ **Like all other medicines, you/your** child may have symptoms or side effects while ~~participating in the study.~~ **taking PrEP.** These symptoms or sides 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/Your child should tell the staff at the study clinic about any symptoms that you/she feel while you are/she is participating in the study. You/she will be given a telephone number so you/she can contact the clinic. You/your child should call them if you/she experience any symptoms.

~~The side effects that might happen in a few people taking Truvada® are well known because the medication has been used by many people. Some mild side effects are expected to occur in up to 1 in 10 persons who take Truvada®. Other side effects are more serious, but are expected to occur in less than 1 in 100 persons who take Truvada® and resolve when Truvada® is stopped. Occasional side effects include: mild problems of kidney function that are only detected by laboratory tests; lack of energy/fatigue; upset stomach, vomiting, soft or liquid stools; dizziness. Many of these side effects only last for the first month of taking the pills and then go away completely or get better with time.~~

~~Rare side effects include: rash; problems with how your/your child's liver works; serious kidney damage; allergic reaction. In some people, there was a slight difference in the thickness of their bones which doctors could see in special x-rays. But people who had these changes did not have broken bones more often than people who did not take Truvada®. Lactic acidosis has occurred in HIV infected persons taking Truvada®, in combination with other drugs. Lactic acidosis is a rare condition that can cause shortness of breath, nausea, and liver failure. This is a serious side effect of some medications used for HIV infection but is infrequently observed with Truvada. You/your child should call or come to the study clinic if you have/she has unexplained increased or decreased urination, weight loss, cramps, muscle pain, dizziness, excessive fatigue, nausea, vomiting, or shortness of breath. If you have/your child has these symptoms, or any other symptoms that concern you/her, the study staff will evaluate your/your child's symptoms and determine whether you/she should stop Truvada® pills. Depression, headache, inability to sleep, and unusual dreams have also been reported in HIV infected persons taking Truvada.®~~

~~The use of potent antiretroviral drug combinations may rarely be associated with an abnormal placement of body fat and wasting. Some of the body changes include:~~

- ~~• Increase in fat around the waist and stomach area~~
- ~~• Increase in fat on the back of the neck~~

- ~~Thinning of the face, legs and arms~~
- ~~Breast enlargement~~

In PrEP research studies, nausea and diarrhea were the most common side effects, but happened in only about 10% or one in ten people. Nausea and diarrhea mainly happened in the first month and then went away. A small number (<1% or one in one hundred people) in PrEP studies showed a small decrease in how their kidneys work, but this stopped when the people stopped taking the drug.

Other side effects, such as changes in bone mineral density (how much calcium and other minerals are in your bone which keeps them strong) were very rare in people taking the drug who did not have HIV and have always gotten better when the drug was stopped.

- **You could have these side effects or other side effects that we do not know about. Please tell the staff here if you have any side effect that bothers you or does not go away.**

Risk of acquiring HIV infection and drug resistance

You/your child may become infected with HIV during this study. It is very important to talk to your/her counselor about all the different ways you/your child might be able to keep yourself/herself from getting HIV, like using condoms every time you have/she has sex and keeping your/her number of sexual partners low. If you/your child becomes infected with HIV while you are/she is taking PrEP, **it is possible that the medications in Truvada (tenofovir and emtricitabine) would not work against the HIV in your/her body. If this happened, it could limit your/her options for HIV treatment. It is for this reason that we ask you/your child to return for regular HIV testing and why you/your child must stop using Truvada if you/she become infected with HIV.** ~~you/she could become infected with a strain of the HIV virus that might be harder to treat with Truvada® or other medications used for HIV treatment. We call this “resistance” which is very rare in people who take PrEP. Resistance to any medications used to treat HIV may make effective HIV treatment more difficult and may limit your/your child’s treatment options. If you/your child become infected with HIV, we will offer testing for HIV drug resistance to you/your child as part of your/her care. You/your child will be able to discuss treatment and the generation of resistance to medications with the study doctor. If you have/your child has any questions about the risks of symptoms or side effects, including anything we have said here please talk to your/your child’s study doctor.~~

Pregnancy

During this study, you/your child will receive counseling at each visit about the potential that you/she may become pregnant. You/your child will also receive counseling about your/her options for preventing pregnancy. You/your child can receive some forms of contraception from the study clinic or be referred to an appropriate clinic for contraception. You/your child may choose whether or not you/she want to receive contraception.

~~Although infants~~**Infants** born to HIV-infected **or HIV-uninfected** women taking Truvada® during pregnancy have not been found to have a greater chance of being born early, weighing less or having birth defects than babies from women who were not taking PrEP, ~~we~~. **We** do not know for sure if these drugs are safe to the fetus in women who become pregnant. One study of women who were infected with HIV found that women who were taking one of the drugs in Truvada while they were pregnant did have babies that were born early or lower weight more often. For this reason, if you/your child become pregnant, you/she will need to stop taking PrEP while you/she continue to be followed in this study until your/her last visit. If you are/she is still pregnant after your/her last visit, we will ask you/your child or your/her

doctor to provide updates on the progress of your/your child's pregnancy and its outcome. The study doctor will make this information available to the study sponsor for safety monitoring follow-up.

Among family planning methods, only condoms reduce both the chances of becoming pregnant and getting HIV. Some studies found a small increase in HIV risk when using injectable contraceptives, and using PrEP can reduce that risk. ~~Not all ways to prevent becoming pregnant can prevent HIV transmission, and some may actually increase the risk of getting HIV.~~ We will talk with you/your child throughout the study about ways to protect yourself/herself from getting HIV. You/your child should also discuss with your/her health care provider and the study clinic staff ways to continue using **pregnancy prevention methods** ~~contraception~~ that works during your/her participation in the study.

WHAT ARE THE BENEFITS OF TAKING PART IN THIS STUDY?

We will test you/your child for HIV and other sexually transmitted infections throughout this study. If you/your child ~~take~~**takes** your/her Truvada® every day, it **most likely** will help you/her to avoid HIV. The counseling you/she can get during this study may help you/your child to avoid HIV and other sexually transmitted infections. If you have/your child has or become infected with HIV, this counseling may help you/her to learn how to better care for yourself/herself and avoid passing HIV to your/her sexual partners. If you/she become HIV infected, or have another sexually transmitted infection, we will either treat you/your child here or refer you/her for care and treatment. At the screening visit, we will also check if you have/she has hepatitis B infection. If you have/your child has never had hepatitis B infection, we will offer you/her hepatitis B vaccination. During the study, you will have tests to check on the health of your/her kidneys. If any health problems are found, you/she will be referred for care. At every visit, you/she will receive condoms free of charge.

WILL I/MY CHILD BE TOLD IF THERE IS ANY NEW INFORMATION?

You/your child will be told any new information learned during this study that might affect your/her willingness to stay in the study. For example, if information becomes available that shows that the medication may be causing bad effects, you will be told about this. You/your child will also be told when the results of the study may be available, and how to learn about them.

ARE THERE ANY REASONS WHY YOU/MY CHILD MAY BE WITHDRAWN FROMASKED TO STOP TAKING PART IN THE STUDY WITHOUT YOUR CONSENT?

You/your child may be withdrawn from the study without your/her consent if any of the following occur:

- You/She could be harmed by continuing to take tablets.
- The study is stopped or canceled.
- The study staff feels that staying in the study would be harmful to you/your child.
- You/your child are not able to attend clinic visits or complete all of the study procedures.
- Other reasons, as decided by the study staff.
- If you are under X years, you may be withdrawn because your parent or guardian withdraws consent for you to participate.

You/your child will NOT be withdrawn from this study only because you tell/she tells us that you do not/she does not want to or did not take the PrEP pills.

If you/your child withdraw early from the study, we will ask you/your child to come in for a final visit with all the exams and tests listed above.

WHAT ARE THE ALTERNATIVES TO ~~PARTICIPATION~~ TAKING PART IN THIS STUDY (WHAT OTHER CHOICES DO I/MY CHILD HAVE)?

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

ARE THERE ANY COSTS TO YOU/ME/MY CHILD IF I JOIN THIS STUDY? There will be no cost to you/your child for study related visits, study products, physical examinations, laboratory tests, or other procedures. [Sites to amend if applicable: Phone cards will be provided to help pay for SMS costs on your/her mobile phones.]

REIMBURSEMENT

WHAT WILL I/MY CHILD GET FOR TAKING PART IN THIS STUDY?

You/your child will receive [\$xx] for your/her time, effort, and travel to and from the clinic at each scheduled visit. [Sites to insert information about local reimbursement for the study.]

CONFIDENTIALITY

HOW WILL MY/MY CHILD'S PRIVACY BE PROTECTED?

To keep your/your child's information private, your/her samples will be labeled with a code that can only be traced back to your/her study clinic. Your/your child's name, where you live/she lives, and other personal information will be protected by the study clinic. The results of any tests done on these samples will not be included in your/your child's health records. Every effort will be made to keep your/her study records, test results, and personal information confidential to the extent permitted by law, but we cannot guarantee absolute confidentiality. Your/your child's personal information may be disclosed if required by law.

The study staff will also use your/your child's personal information, if needed, to verify that you are not/she is not taking part in any other research studies. This includes other studies conducted by [site name] and studies conducted by other researchers that study staff ~~know~~ knows about. Any publication of this study will not use your/your or your child's name or identify you/ you or her personally.

A description of this study will be available on www.ClinicalTrials.gov. This ~~web site~~ website will not include information that can identify you. At most, the ~~web site~~ website will include a summary of the results. You can search this ~~web site~~ website at any time.

You/your child will be invited to participate in monthly adherence clubs which are events where participants will come together to talk about any problems or successes they have taking the PrEP pills. We will ask everyone at these events not to tell friends, family or others about who attends. Participants should be aware that in a group setting it is not possible to maintain confidentiality. They should consider carefully **the** information that they wish to disclose in a group setting as it is not possible to guarantee confidentiality. You/your child can also use a nickname, so others do not know your/her real name. But it is possible that someone may recognize you/your child and tell others.

If you are under X years, we will also need to obtain the consent of your parent or legal guardian in order for you to participate. We will explain to your parent/legal guardian that we will not share the results of your HIV, pregnancy, or other tests with them, but if you become HIV infected, pregnant or have any

serious medical conditions, we will strongly encourage you to tell your parent/legal guardian yourself. We will also not share with them the results of any questions you answer including when or if you are having sex, your use of contraception, if you are using drugs or alcohol and/or if you are taking your PrEP pills.

To protect you from harm, we will encourage you to tell a trusted adult (this does not have to be your parents/legal guardian) about certain situations, but we will not inform your parents without your permission. We will help and support you when you tell others about these hard situations:

- If you become pregnant or end a pregnancy.
- If you have a positive HIV or STI test result.

RESEARCH RELATED INJURY

WHAT HAPPENS IF I/MY CHILD GET INJURED?

[Sites to specify institutional policy:] It is unlikely that you/your child will be injured as a result of study participation. If you are/she is injured, the [institution] will give you/her immediate necessary treatment for your/her injuries. You/She [will/will not] have to pay for this treatment. You/your child will be told where you/she can get additional treatment for your/her injuries. There is no program to pay money or give other forms of compensation for such injuries either through this institution or the US NIH. You do not/your child does not give up any legal rights by signing this consent form.

WHO SHOULD I CONTACT IF I HAVE PROBLEMS OR QUESTIONS ABOUT THE STUDY?

If you/you and your child ever have any questions about the study, or if you have/she has a research-related injury, you/you and your child should contact [insert name of the investigator or other study staff] at [insert telephone number and/or physical address].

Appendix IIB: Sample Storage Informed Consent Form

WHAT ARE THE POSSIBLE TESTS YOU WOULD CONDUCT ON MY/MY CHILD'S BLOOD IN THE FUTURE TESTS?

As we said in the consent form for the study, blood samples collected at the enrollment and follow-up visits will be stored for all participants for testing that is part of this study. Some of your/your child's blood drawn for this study may be ~~left over~~**left over** after all of the study tests are completed.

Revision 5

1.1. Background and Prior Research

Efficacy of daily oral tenofovir disoproxil fumarate (TDF) or TDF co-formulated with emtricitabine (FTC) (FTC/TDF) ranged from 44% to 75%, and was strongly related to adherence, which ranged from 52% to 82% based on plasma ~~tenofovir~~**tenofovir** (TFV) testing in a subset of participants.³⁻⁶

LIST OF ABBREVIATIONS AND ACRONYMS

SMS	short Short message service
SOC	standard Standard -of-care

Appendix IIA: Sample Screening/Enrollment Informed Consent Form

Follow up visits:

After enrollment, you/she will be asked to come back for visits at one month (Week 4), two months (Week 8) →, three months (Week 13), six months (Week 26), nine months (Week 39) and one final visit a year later (week 52). During these visits, the study staff will:

Stored Samples

Some of the blood samples collected at the enrollment and follow-up visits will be stored for other testing that is part of this study. Samples may be tested for drugs used to prevent and treat HIV infection, including Truvada®. If you/your child have/has HIV or hepatitis infection, the stored blood may also be used to study the HIV and hepatitis virus, and the body's response to ~~these~~ **this** infection.