HIV Prevention Trials Network

Letter of Amendment # 1 to:

HPTN 083-02

Factors Influencing Adherence To Injectable Prep And Retention In An Injectable Prep Research Study

DAIDS Study ID: 38645

Version 1.0, dated 01 July 2019

Date of Letter of Amendment: 16 September 2020

LETTER OF AMENDMENT SIGNATURE PAGE

I will conduct the study in accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable U.S. Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (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 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."

Signature of Investigator of Record

Date

Name of Investigator of Record
(printed)

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The following information impacts the HPTN 083-02 study and must be forwarded to all responsible Institutional Review Boards/Ethics Committees (IRBs/ECs) as soon as possible for their information and review. This Letter of Amendment (LoA) must be approved by all responsible IRBs/ECs before implementation.

The information contained in this LoA does not impact the informed consent forms (ICFs).

Upon receiving final IRB/EC approval for this LoA, sites should implement the LoA immediately. Sites are required to submit an LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). As part of the registration package, sites must submit the Letter of Amendment Investigator Signature Page, signed and dated by the Investigator of Record. 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 the LoA and any IRB correspondence should be retained in the site's regulatory files.

If the full HPTN 083-02 protocol is amended in the future, the changes in this LoA will be incorporated into the next version.

Summary of Revisions and Rationale

1. Prior to the interruption of conduct of this qualitative sub-study due to COVID-19, 40 interviews out of a planned 200-300 had been conducted. While the sub-study was paused, the blinded component of the main 083 study was stopped and the results of the analysis were made public. As soon as sufficient medication is available, all participants enrolled on the main study will be given the option to continue open label PrEP with either oral Truvada or injectable Cabotegravir. The discontinuation of the main study as originally designed rendered obsolete the categories of participants that were being targeted for interviews in this substudy, as described in version 1.0 of this study's protocol. The revisions to that protocol contained in this Letter of Amendment have been made to redefine the groups that will be interviewed for this qualitative study. Each site will now be asked to enroll approximately 60 participants overall, divided evenly between arms among those who wish to continue open-label PrEP with either the regimen they received during the blinded study or the other regimen. Sites that had enrolled participants prior to the pause of this sub-study will enroll new participants to the maximum of 60 participants in total (old and new) for their site. The enrollment criteria for the study have been adjusted to reflect the revised group definitions. The objectives of this qualitative study and the total target enrollment remain unchanged.

2. The timeline in Figure 1 and references to where, during conduct of the main study, participants would be recruited for this sub-study have been deleted from the protocol since the original design of the main protocol no longer applies. A new section has been added…Section 2.3.4…to describe the revised anticipated study timeline.

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

Revision 1: Schema

Study Population: Participants in Step 2 **or 3** of the Main HPTN 083 Trial who **have been unblinded to their study regimen and have indicated a wish to continue on open label medication** ~~are:~~

~~1. Adherent to injectable PrEP/placebo~~
~~2. Imperfectly or nonadherent to injectable PrEP/placebo~~
~~Or~~
~~3. Discontinue their injectable PrEP/placebo after getting at least one injection~~

~~And participants from Step 3 of the parent study~~

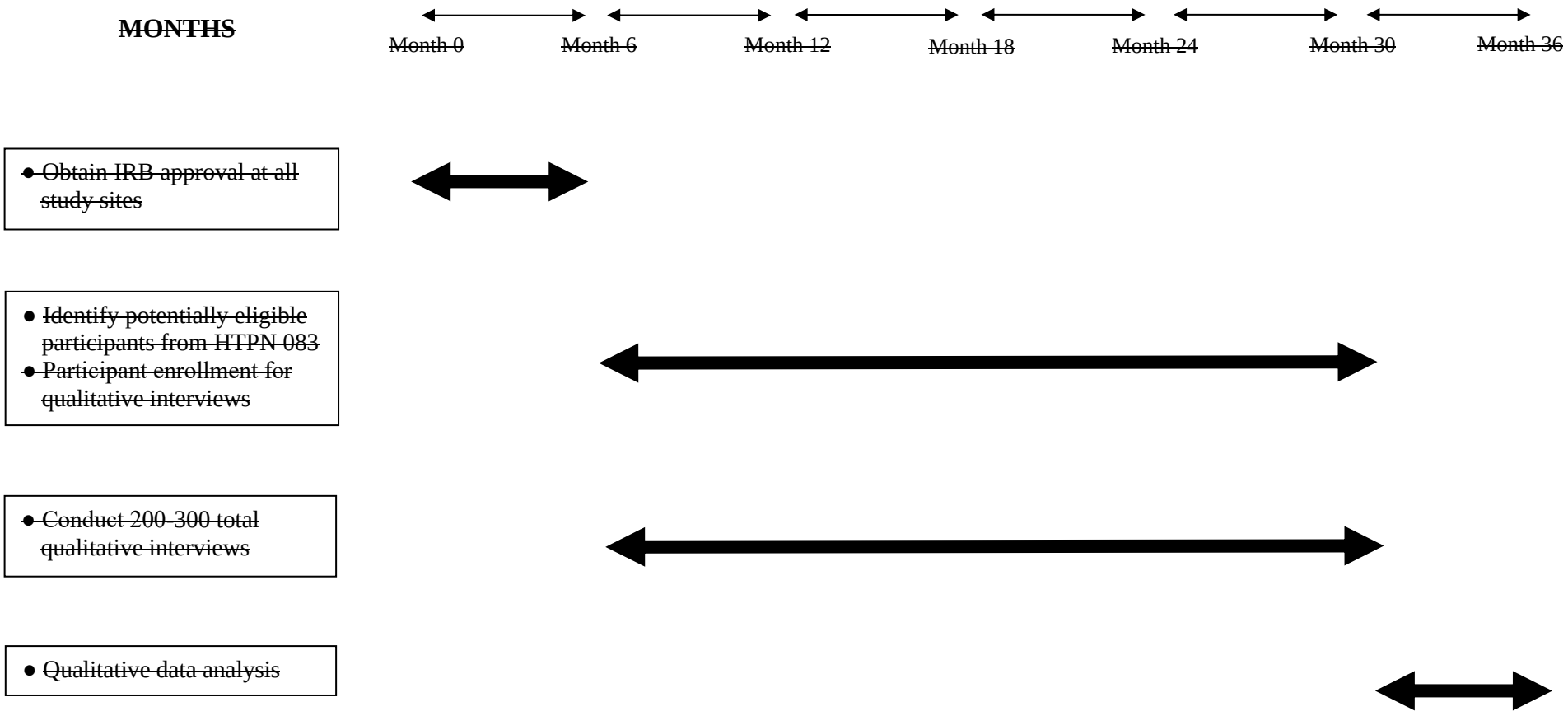
We will recruit from 2 U.S. sites (Chicago, IL; Decatur, GA) and 3 international sites (Rio de Janeiro, Brazil; Cape Town, South Africa; and Bangkok, Thailand).

Study Size: We expect a total N of ~~150-225~~ **200-300** ~~for~~ participants interviewed in Step**s** 2 and ~~a total N of 50-75 participants for participants interviewed in Step~~ 3.

HPTN 083-02

Factors Influencing Adherence to Injectable PrEP and Retention in an Injectable PrEP Research Study

Figure 1. Study Timeline



Revision 2: Section 2.3.1- Study Type

This will be a three-year qualitative study of individuals who have enrolled in HPTN 083 (and therefore met HTPN 083 study inclusion and exclusion criteria) across both domestic and international study sites. We will collect qualitative data from ~~three groups of~~ HTPN 083 participants in Step 2 ~~(blinded, randomized, after oral lead-in)~~ and ~~from participants in~~ Step 3 ~~(open label phase)~~ of the parent study. The main study participants who will be enrolled for this sub-study are described in Section 3.0.

Participants will complete one individual semi-structured qualitative interview, lasting 30-60 minutes. ~~Participants who complete a qualitative interview in Step 2 will not be excluded from completing an interview in Step 3.~~ Qualitative data will be collected around factors influencing HPTN 083 participants' adherence to injectable PrEP and retention in the study.

The total anticipated N is ~~150-225~~**200-300** ~~for~~ participants ~~interviewed in Step 2, and 50-75 for participants interviewed in Step 3~~. The study will begin when IRB approval is received and continue until the end of the trial. We expect that data analysis will occur for up to 6 months after the conclusion of data collection.

Revision 3: Section 2.3.4- Study Timeline

2.3.4 Study Timeline

It is anticipated that conduct of interviews will be complete approximately six to nine months after sites begin to offer participants a choice of open-label PrEP medication. Analysis is expected to require six additional months, for a total timeline of 12-15 months.

Revision 4: Section 3.0- Study Population

~~Three~~ **Four** groups of HTPN 083 participants from Step 2 ~~(blinded, randomized, after oral lead-in; see group descriptions below)~~ and ~~participants from~~ Step 3 ~~(open label phase)~~ of the parent study, will participate in this qualitative sub-study. ~~In Step 2 of the trial, we will collect qualitative data from three groups of participants across 2 U.S. sites and 3 international sites: (1) those who are adherent, (2) those who are imperfectly or non-adherent, and (3) those who discontinue their randomized blinded study product after getting at least 1 injection. Definitions for t~~**T**he ~~three~~**four** groups are as follows:

1) **Participants who received injectable PrEP during the blinded phase of the main study (oral placebo) and wish to continue to receive open-label injectable PrEP after unblinding** ~~The "adherent "group will be comprised of individuals who receive at least two consecutive injections within 10 weeks of their prior injection (the timeline of which will begin once injections are scheduled every eight weeks), at any point in Step 2~~.

2) **Participants who received oral PrEP during the blinded phase of the main study (placebo injection) and wish to continue to receive open-label oral PrEP after unblinding** ~~The "imperfectly adherent" or "non-adherent" group will consist of individuals who receive any injection outside of the aforementioned window of 10 weeks for the adherent group at any point in Step 2, but have not been lost to follow-up or prematurely left the trial.~~

3) **Participants who received injectable PrEP during the blinded phase of the main study (oral placebo) and wish to receive open-label oral PrEP after unblinding.** ~~Those who may not be actively engaged in the study or are engaged in a way other than described above i.e.) will comprise the third group. This includes those who have declined additional injections but agree to additional follow-up and those lost to follow-up. Those who wish to withdraw from the main trial may be invited to participate in this group as well, if participation in the sub-study can be offered at the time the participant expresses their desire to withdraw from the main study. Participants who wish to withdraw from the main study will be asked to remain in the main study until their participation in the qualitative study (a one-time interview) is complete. We will not attempt to re-contact participants who have previously withdrawn their consent or who leave the study before the qualitative sub-study is activated at that site~~.

4) **Participants who received oral PrEP during the blinded phase of the main study (placebo injection) and wish to receive open-label injectable PrEP after unblinding.**

~~Participants who move from "adherent" to "non-adherent" or vice versa will not be excluded from participation in interviews for the other group if they are selected for participation upon the change in classification. However, participants who are classified as part of group three will be excluded from participating in the Step 3 interviews to avoid duplication of data. Participants will be selected for participation during years 1-3 of the qualitative study. In order to sample across the study population, we will aim to recruit approximately 12-13 participants per month for qualitative interviews.~~ Our total N will be determined by achieving thematic saturation of data by site, or the point at which new information is unlikely to be obtained by completing additional interviews.[10] ~~We anticipate interviewing approximately 10-15 individuals in each category at each of the 5 sites for a total N of 150-225 for Step 2.~~

~~For Step 3 (open label phase), we anticipate interviewing approximately 10-15 individuals at each of the 5 study sites to explore opinions and preferences about the two study products. This is a total N of 50-75 participants for Step 3.~~

Participants will be selected via purposive sampling, whereby study staff members attempt to find representative participants from the various groups we are sampling. We will aim to have TGW comprise approximately 25% of the total sample for the qualitative study.

Revision 5: Section 3.1- Inclusion Criteria

Inclusion criteria will mirror those of the parent study, but for specific enrollment purposes they are:

- Properly enrolled and consenting participant in **Step 2 or 3 of** the HPTN 083 parent study and at one of the study sites for this qualitative sub-study
- **Has been unblinded to the treatment regimen they received during the blinded phase of the main trial and has indicated a desire to continue with open-label, study-provided PrEP**
- ~~From Step 2 of the trial, meets one of the three criteria:~~
    1. ~~The "adherent "group will be comprised of individuals who receive at least two consecutive injections within 10 weeks of their prior injection (the timeline of which will begin once injections are scheduled every eight weeks), at any point in Step 2.~~
    2. ~~The "imperfectly" adherent or "non-adherent" group will consist of individuals who receive any injection outside of the aforementioned window of 10 weeks for the adherent group at any point in Step 2, but have not been lost to follow-up or prematurely left the trial.~~
    3. ~~Those who have discontinued their randomized blinded study product after getting at least 1 injection.~~
- ~~From Step 3 of the trial: any participant in Step 3 of the trial may be selected to participate except those participants who are classified as part of group three in Step 2 (those who may not be active participants or otherwise as described above) who will be excluded to avoid duplication of data.~~

Revision 6: Section 3.2- Exclusion Criteria

Exclusion criteria will mirror those of the parent study **with the addition of this criterion:**

- **Participants who were interviewed prior to main study unblinding**~~;~~ ~~participants who seroconvert will not be excluded from participation.~~

Revision 7: Section 6.2- Sample Size

This sample size will be refined by achieving thematic saturation of data by site, or the point at which new information is unlikely to be obtained by completing additional interviews.[10] We anticipate interviewing approximately ~~150-225~~40-60 participants from ~~for~~ Step**s** 2~~,~~ and ~~50-75 participants for Step~~ 3 **at each site**, for a total N of 200-300 participants for this sub-study.