HIV Prevention Trials Network

Letter of Amendment # 2 to:

HPTN 091

Integrating HIV Prevention, Gender-Affirmative Medical Care, and Peer Health Navigation for Transgender Women in the Americas: A Vanguard Study

DAIDS Study ID: 38695

Version 1.0, dated 13 April 2020

Date of Letter of Amendment: 27 July 2021
Final Version

The following information impacts the HPTN 091 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 Investigatory 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. A 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 091 protocol is amended in the future, the changes in this LoA will be incorporated into the next version. Text appearing below in highlighted **bold** will be added, and text appearing in highlighted strike-through will be deleted.

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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)

Summary of Revisions and Rationale

1. Section 6.1, Implementation Testing, is being removed. The implementation testing will not provide a reliable measure of retention or information to optimize procedures as originally intended. We consulted with the chair of the HPTN 091 Study Monitoring Committee (SMC), who agreed with removing the implementation testing. Implementation data will be reviewed by the SMC as described in Section 8.9 of the protocol. The implementation testing and its timeline will be removed from the protocol and informed consent templates.
   See revision 1-4
2. Section 6.9.2 was added to provide additional information regarding safety follow up for participants who are GAHT-naïve.
   See revision 5-6.

Revision 1: Section 6.1: Implementation Testing

~~A run-in period will be performed by enrolling a small number of participants at each participating site prior to full study rollout. The purpose is to fully capacitate the peer navigators and the clinicians providing integrated clinical services in the intervention.~~

~~The run-in period will follow the same study design (refer to Section 3.0) and schedule of events as the full study (refer to Sections 6.2 – 6.4, 6.6 – 6.8, and Appendix Ia – Ic), with the exception of the Qualitative Data Collection sub-study, but with limited enrollment and follow-up. Accordingly, up to 10% of site's target sample size will enroll, ideally over a 3-month period. At each site, the Implementation Testing period will be completed after the last participant enrolled as part of this group completes their 6-month follow-up visit. While the Implementation Testing period is happening at the site, no additional participant may be enrolled as part of the full protocol. There will not be a separate consent for participants in the run-in period since all study procedures and relevant consent information will be the same independently if they enroll in the Implementation Testing part of the study or the full study, with the exception of the option to participate in the Qualitative Data Collection sub-study.~~

~~The run-in period will allow the study sites an opportunity to optimize local study procedures before the full study proceeds. As such, for each study site a study conduct review will take place after the last participant enrolled has completed their 6-month follow-up visit. This review will be conducted in part by the study leadership. The review will involve an evaluation of key operational components of the study, such as fidelity to intervention and referral procedures, data management procedures, and laboratory procedures, all in accordance with Good Clinical Practice (GCP). The review may also include evaluation of screening, enrollment, and retention data. Follow-up of the~~

~~participants enrolled in the run-in period will continue uninterrupted during the time the run-in period is being evaluated. This provides for continuity of study operations at the study sites should the full study proceed.~~

Revision 2: SCHEMA: Study Duration

For each individual site, the duration of the study is approximately 3**0**~~6~~ months from the time of site activation. Accrual will require approximately ~~15~~ **12** months ~~(3 months for Implementation testing and 12 months for general study~~); and individual participants will be followed for 18 months. Once enrolled, each participant will complete eight follow-up visits.

Revision 3: 3.4 Study Duration

Once a site is activated, the total study duration is anticipated to be approximately **30~~6~~** months: accrual will require approximately ~~15~~ **12** months ~~(3 months for Implementation testing, and 12 months for general study)~~, with 18 months of follow-up per participant. ~~The total study duration is dependent on the timeframe to complete the run-in phase.~~ Participants will complete 8 scheduled study visits: Screening, Enrollment, Week 13 (Month 3), Week 26 (Month 6), Week 39 (Month 9), Week 52 (Month 12), Week 65 (Month 15), Week 78 (Month 18). In addition, an GAHT initiation visit will be scheduled up to 10 days following the collection of samples for estradiol and total testosterone testing for initiation/re-initiation of GAHT. Additional visits may be done between scheduled study visits, please refer to Section 6.9.

Revision 4: Sample Informed Consent Forms for the US and Brazil sites

All mention of implementation testing will be removed from the body of the consent form and the signature page.

Interviews with a subgroup ~~[*Not applicable for participants enrolled in the Implementation Testing part of the study*]~~

I agree to participate in an interview where I will be asked questions about this research, and the interview will be recorded. ~~[*Not applicable for participants enrolled in the Implementation Testing part of the study]*~~
I do not agree to participate in an interview where I will be asked questions about this research, and the interview will be recorded. ~~[Not applicable for participants enrolled in the Implementation Testing part of the study]~~

Revision 5: New **Section 6.9.2: Post GAHT Initiation Safety Visit for GAHT-Naïve Participants**

Participants who are initiating GAHT for the first time AND their medications include either spironolactone or cyproterone should have an ad-hoc safety visit approximately one month following GAHT initiation. At this visit, sites should do a clinical evaluation, including vital signs and review of medical history. In addition, the following safety laboratory samples should be collected:

- **ALT, AST, CBC (if taking cyproterone)**
- **Potassium (if taking spironolactone)**

Please note, this safety visit is done only if deemed necessary by IoR or designee.

Revision 6: Appendix III: Informed Consent Templates, Sample Informed Consent Forms for Sites in Brazil and the United States: BEING IN THE STUDY: Once you enroll in the study, you will have 6 visits over one and a half (1½) years.

You may have more study visits if needed; for example, you may come to the site to get medications, if you are sick, or we need to check on your health, or to meet with a Peer Health Navigator. If you choose to start Gender-Affirming Hormonal Therapy **(GAHT)**, an extra study visit will be scheuled within ten (10) days after the collection of estradiol and total testosterone testing **to pick-up your GAHT. Also, if this is the first time you are using GAHT AND you are taking either spironolactone or cyproterone, you may have an additional study visit approximately one month following GAHT initiation to check on your health. The study staff will let you know which GAHT you are using, address any questions you may have, and let you know if this visit is necessary.**