

HIV Prevention Trials Network

LETTER OF AMENDMENT #4 TO:

HPTN 071

**Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART):
A cluster-randomized trial of the impact of a combination prevention package on population-
level HIV incidence in Zambia and South Africa**

Protocol Version 3.0 dated 16 November 2015

DAIDS Protocol ID: 11865

Date of Letter of Amendment: 27 September 2017

Information/Instructions to Study Sites from the Division of AIDS

The information contained in this Letter of Amendment (LoA) impacts the HPTN 071 (PopART) study and must be forwarded to your Institutional Review Board (IRB) and/or Ethics Committee (EC) as soon as possible for their review and approval. This LoA must be approved by all responsible IRBs/ECs before implementation.

The information in this LoA affects the Sample Informed Consent Forms.

Upon receiving final IRB/EC and any other applicable regulatory entity approval(s) for this LoA, your site may implement immediately any activities included in the LoA that do not require consent, or that only require revision to consent forms you have previously registered with the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). For any activities included in this LoA that require the participant to sign a consent form that is newly introduced with this LoA (that is, that your site has not previously registered with PRO), your site must first submit the LoA registration packet to PRO, including any new consents, and receive notification of successful registration prior to commencing those activities. A copy of the LoA registration notification along with this letter and any IRB/EC correspondence should be retained in the site's regulatory files. Note that a signed investigator signature page must be included in the registration packet sent to PRO.

If the HPTN 071 (PopART) protocol is amended in the future, this LoA will be incorporated into the next version.

HPTN 071
Population Effects of Antiretroviral Therapy to Reduce HIV Transmission (PopART):
A cluster-randomized trial of the impact of a combination prevention package on
population-level HIV incidence in Zambia and South Africa

DAIDS ID:
11865

Final Version 3.0
16 November 2015

Letter of Amendment 4
27 September 2017

INVESTIGATOR SIGNATURE PAGE

A Study of the HIV Prevention Trials Network (HPTN)

Sponsored by:

Division of AIDS, National Institute of Allergy and Infectious Diseases
U.S. National Institutes of Health

Funded by:

National Institute of Allergy and Infectious Diseases
National Institute of Mental Health
Office of the United States Global AIDS Coordinator
Bill and Melinda Gates Foundation
US National Institutes of Health

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.

Name of Investigator of Record

Signature of Investigator of Record

Date

Summary of Revision and Rationale

The HPTN 071 protocol v3.0, 16 November 2015 has been updated to reflect the changes listed in this Summary of Revisions and Rationale. All changes made are indicated in the next section, Implementation of the Protocol Modifications.

- 1) The protocol has been modified to increase the sample size of the *Adolescent Cross-Sectional Survey* from approximately 1,400 participants to between approximately 1,400 and 2,800 participants.

As noted in Letter of Amendment #3 to this protocol, the goal of the *Adolescent Cross-Sectional Survey* is to allow the field teams to collect data in Arm C that will complement similar data collected by Community HIV-care Providers (CHiPs) in the intervention arms of the study (Arms A & B). The original enrollment target for this survey was 200 participants from each of the seven Arm C communities. The sampling strategy, based on estimates of adolescents' prevalence in visited households and willingness to participate, predicted that study staff would need to enroll all consenting adolescents from ten or more randomly-selected blocks of houses in the community to obtain 200 participants. In fact, recruitment went more quickly than expected in Zambia, and in some cases, was completed from only eight blocks of houses. The current letter of amendment will allow field staff to enroll more adolescents into the study, from a larger number of randomly-selected blocks of houses, which will improve study power and the representativeness of the sample. It is not known if South African field teams, which are just entering the field, will also find recruitment as rapid, and so those teams may adopt the higher target (400 participants) or may not.

For the following sections, colored strikethrough (example) indicates text that has been deleted from the protocol. Colored underline (example) indicates text that has been added to the protocol. Ellipses within brackets ([...]) indicate areas where text from the protocol has not been shown, to reduce the length of this document. In the sample informed consent forms, bold text in brackets ([example]) indicates language that sites may alter, or not include, in their locally-adapted consent forms, depending on local requirements.

Revision - Sample Size Increase for the *Adolescent Cross-Sectional Survey*

SCHEMA

Study Size: The combined population of all 21 clusters is approximately 1.2 million individuals. The interventions will be implemented in 14 of the 21 clusters with a combined population of approximately 800,000 individuals (adults and children) in the intervention arms. The approximate sizes of the randomly-selected groups for main study outcome assessments are:

- *Population Cohort:* 52,500 individuals
- *Case-Control Studies:* 1,600 individuals
- *Qualitative Studies:* about 2,000 individuals
- *Adolescent Cross-Sectional Survey, Arm C:* between 1,400 and 2,800 individuals
- *Population Cross-Sectional Survey:* 10,500 individuals (if funded)

Note: Final sample sizes for surveys pending funding may change and will be described in separate protocol.

[...]

2.3 Study Design

[...]

For the Adolescent Cross-Sectional Survey, a target of approximately 200-400 participants aged 15-19 years will be enrolled in each of the seven control communities. [...]

Section 5.6 Adolescent Cross-Sectional Survey, Arm C

5.6.1 Sampling/Recruitment of Adolescent Cross-Sectional Survey

There are seven Arm C communities. The recruitment goal of the cross-sectional survey is to enroll approximately 200-400 adolescents aged 15-19 years per community, for a total of approximately 1,400-2,800 participants.

Appendix VII – - Sample Informed Consent Form –Adolescent Cross-sectional survey

Why am I being asked to participate?

We are asking you to participate because you are aged between 15 and 19 years and live in a randomly-selected block of houses in one of the seven study communities receiving the standard of care package in the HPTN 071 study. In total, we plan to conduct this survey with approximately 200-400 young people aged 15-19 years in each of these seven communities – between approximately 1400 and 2800 overall.