

HIV Prevention Trials Network

LETTER OF AMENDMENT #5 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: 17 April 2018

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.

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 5
17 April 2018

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 are indicated below and organized by protocol section.

- 1) To change the assessment period for the primary outcome from PC0–PC36 to PC12–PC36.

During the October 2016 DSMB meeting, the HPTN 071 protocol team requested to change the assessment period for the primary outcome from PC0–PC36 to PC12–PC36 which is intended to provide information about the effectiveness of the intervention once it was up and running. This proposal, as well as the Board’s consideration, was based on the modeling results and not interim data on effectiveness. The minutes from this meeting reflect that the DSMB had no objection to the study team’s proposal.

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.

OVERVIEW OF STUDY DESIGN AND RANDOMIZATION SCHEME

HIV incidence measured over 3 years in the Population Cohort, with the primary analysis including HIV incidence measured between Months 12 and 36 of the study.

7.1.2 Primary Endpoint – HIV Incidence Over 36 Months

The incidence of HIV infection among initially HIV-uninfected *Population Cohort* members will be measured during the follow-up period of 36 months, with the primary analysis including HIV incidence measured between PC12 and PC36.

7.3 Statistical Analysis

The primary analysis will be based on a comparison of the incidence of HIV infection during the follow-up period between PC12 and PC36 ~~of 3 years~~ between Arms A and C, Arms B and C, and Arms A and B. This will be carried out using appropriate analytical methods for cluster-randomized trials.

Table 10 - Summary of Study Objectives and Related Outcomes

Objectives and Outcome Measures	Research Participants						
	PC at baseline	PC at 12m	PC at 24m	PC at 36m	PX at 36m ^a	Uptake Ca-Co	Qualitative Research
<i>Effect of the interventions on...</i>							
HIV incidence							
<i>HIV infection between 12 and 36 months among those testing HIV negative at enrollment-PC12 or enrolled and negative at PC12N or PC24N (primary objective)</i>	X	X	X	X			