

Letter of Amendment # 4 to:

**HPTN 069: A Phase II Randomized, Double-Blind, Study of the Safety and Tolerability of Maraviroc (MVC), Maraviroc + Emtricitibine (MVC+FTC), Maraviroc + Tenofovir disoproxil fumarate (MVC+TDF), or Tenofovir disoproxil fumarate + Emtricitibine (TDF+FTC) for Pre-Exposure Prophylaxis (PrEP) to Prevent HIV Transmission in At-Risk Men Who Have Sex with Men and in At-Risk Women, Version 3.0, January 3, 2013, DAIDS Document ID: 11789
IND # 113,655**

FINAL Version of LoA # 4: 14 July 2014

The following information impacts the HPTN 069 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 069 protocol is amended in the future, this Letter of Amendment will be incorporated into the next version.

Summary of Revisions and Rationale

This Letter of Amendment contains the following two additions to the protocol procedures at the Week 48 visit in order to expand on attitudes among women regarding taking the study medications and potential relationships with sexual behavior, as well as to expand on potential gender-specific aspects of study regimen adherence: 1) All women still active in the study will be asked to complete a very brief (5-item) computer-assisted structured interview (CASI)-delivered survey after they complete the existing main study CASI survey scheduled at the Week 48 visit; and 2) Women at selected HPTN 069 sites will be asked to participate in one semi-structured interview irrespective of assigned study arm (as sites will still be blinded to randomized arm). No more than 30 interested women total will complete the interview at the Week 48 visit or within 4 weeks after the Week 48 visit.

These additional procedures are covered by the existing protocol objectives, specifically the following secondary objectives:

Secondary:

“Assess adherence in each of the four study arms as measured by electronic drug monitoring device (EDM) and self report.”

“Assess and characterize sexual behavior over time as measured by computer-assisted self-interview (CASI).”

“Assess quality of life in each of the four study arms.”

All additions are in **bold** type. There are no deletions included in this amendment.

IMPLEMENTATION

Revision 1

Section 5.5 Weeks 24 and 48

Administrative, Behavioral, and Regulatory Procedures

- HIV counseling (pre- and post-test), including risk-reduction counseling
- Condom distribution
- Confirm locator information
- Adherence education and follow-up counseling (Week 24 only)
- Behavioral/adherence/QOL assessment using computer-assisted structured interviewing
- **For women on-study, complete brief (5-item) CASI after completion of the behavioral/adherence/QOL assessment CASI (Week 48 only)**
- **At selected sites in up to 30 women who provide consent, semi-structured interview (Week 48 only – may be completed at the Week 48 visit or within 4 weeks after the Week 48 visit)**
- Reminder and review of SMS assessment of sexual exposure

Revision 2 A and B

A. APPENDIX I: SCHEDULE OF PROCEDURES AND EVALUATIONS

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	Screening	Enr	Wk 2	Wk4	Wk 8, 16, 32, 40	Wk 24, 48	Wk 49
ADMINISTRATIVE, BEHAVIORAL, REGULATORY							
Informed consent (including consent for the Drug Interaction Subset [all sites] and the Tissue Subset [designated sites])	X						
Randomization ²⁸		X					
Demographic information		X					
HIV counseling (pre-and post-test), including risk-reduction counseling	X	X	X	X	X	X	X
Condom distribution	X	X	X	X	X	X	X
Locator information	X	X	X	X	X	X	
Behavioral/adherence/QOL assessment/Beliefs (PREMIS) ³ (CASI)		X		X	X	X	
Brief (5-item) CASI add in for women³⁰						X	
Semi-structured Interview³⁰						X	
SMS assessment ⁴	Random sampling at 12-13 different time points up to Week 48						
Adherence education and follow-up counseling		X	X	X	X	X ¹²	

B. FOOTNOTES FOR APPENDIX I

²⁹ These swab collections pertain to the main study participants (not the Tissue Subset participants) for GC/CT testing. Rectal swabs will be collected in all men, and in women who report having had anal sex in the last year (from the time the swab is collected). At sites that have the clinical and laboratory capacity to collect and test cervical or vaginal swabs for GC/CT, this swab should be collected. A woman may opt to self-collect a vaginal swab specimen; if she does, this must be done at the study clinic. For sites that cannot collect and test vaginal or cervical swabs for GC/CT testing, urine should be collected for this purpose.

³⁰ **Week 48 only. The brief CASI survey is only for women after completion of the main study CASI at the Week 48 visit. The semi-structured interview is conducted only with a subset of women at selected participating sites and must be conducted on or within 4 weeks after the Week 48 visit. See SSP for detailed information.**

Revision 3 A - C: Appendix V – Sample Screening and Enrollment Informed Consent Form

A. Week 24 and 48 Visits

This visit will last about 2-3 hours. During these visits, the study staff will:

- Confirm where you live and how to contact you.
- Ask you to answer questions on a computer about your sexual practices, your experiences taking your study pills, and how you feel about how your life is going.
- **[Sites participating in the semi-structured interviews to add this here:] If you are a**

woman we will ask you at your Week 48 visit if you are willing to participate in an interview that asks women about their experiences with the study pills and trying to take them. The interviews will be one-on-one with an interviewer who is not part of the study team you normally meet with here. The interview will take about an hour. The interview will occur either at your Week 48 visit or any time that is convenient to you a month after your Week 48 visit. All interviews are recorded. These recordings will be used to make a written transcript of the interview. The transcript will only have a Participant ID number on it. Your name and any other identifying information that you mention during the interview will be removed and will not get written into those transcripts. The recording will be used to summarize your experiences with the study drug and then it will be destroyed after all of the interview results are final. You do not have to participate in these interviews.

B. REIMBURSEMENT

You will receive [\$xx] for your time, effort, and travel to and from the clinic at each scheduled visit. [Sites to insert information about local reimbursement for the study. In addition, note that reimbursement for the SMS component needs to be standardized across all sites. Sites should insert here the following: Each participant will receive \$2.00 per day (for completing all of the questions for that single day) for 7 days, and an \$11.00 bonus for fully completing and answering all questions for all 7 days, for a total of \$25.00]. Additional note to sites: It is up to each site as to how they want to manage this payment scheme, e.g., it may be folded into the site's overall participant reimbursement schedule, but participants should be notified of the amount they will get each day for this component plus the bonus. **Note to sites conducting semi-structured interviews in women: Insert information here about local reimbursement for participation in the one interview.**

C. SIGNATURE PAGE

SCREENING AND ENROLLMENT CONSENT

Insert signature blocks as required by the local IRB: If you have read this consent form, or had it read and explained to you, and you understand the information, and you voluntarily agree to join the study, please sign your name or make your mark below. Also, please indicate by providing your initials in the spaces below the additional sample collection, genetic testing, or long-term storage that you agree to.

_____ I agree to take part in this study.

_____ I agree to take part in the Drug Interaction Subset, where I will have an additional blood draw at the Week 2 visit.

_____ Site staff to fill in "N/A" here (and initial and date) if the slots for the Drug Interaction Subset are filled.

_____ I agree to have samples of my blood stored and used for future testing related to HIV infection.

_____ I do not agree to have samples of my blood stored and used for future testing related to HIV infection.

- _____ I agree to allow my blood to be tested to see if my genes make the CCR5 protein.
- _____ I do not agree to allow my blood to be tested to see if my genes make the CCR5 protein.
- _____ I agree to allow my blood to be tested to see how my genes make the drugs work in my body.
- _____ I do not agree to allow my blood to be tested to see how my genes make the drugs work in my body.

[Selected sites participating in qualitative interviews to add]:

- _____ I agree to participate in an interview where I will be asked questions about this research, and the interview will be recorded.
- _____ I do not agree to participate in an interview where I will be asked questions about this research, and the interview will be recorded.

[Selected sites participating in the semi-structured interviews for women to add]:

For women participating in the semi-structured interviews, please mark one of the options below:

- _____ **I agree to participate in an interview where I will be asked questions about my experiences in this study and taking study pills, and the interview will be recorded.**
- _____ **I do not agree to participate in an interview where I will be asked questions about my experiences in this study and taking study pills, and the interview will be recorded.**