FINAL

Letter of Amendment # 2 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 # 2: July 1, 2013

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 does not impact the sample informed consents. However, some sites may be required to include the inclusion/exclusion criteria in their site-specific informed consents. In such cases, 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

Major Revision

1. In Letter of Amendment (LoA) #1, dated May 24, 2013, the allowable calculated creatinine clearance value for entry into the study was revised for female participants to ≥ 60 mL/minute (from ≥ 70 mL/minute). In a memo to the protocol team dated June 11, 2013, the FDA provided a clinical comment related to the safety of reducing the value of this criterion in females, and recommended that the value return to ≥ 70 mL/minute for females for entry into the study. The protocol team agrees with this recommendation. This change is reflected in Section 3.1.

All additions are in **bold** type and deletions are made with ~~strikethrough~~ type.

IMPLEMENTATION OF MAJOR REVISIONS

Major Revision 1 Section 3.1 – Inclusion Criteria, Seventh bullet, Fifth sub-bullet

- For men **and women,** calculated creatinine clearance ≥ 70 mL/minute using the Cockcroft-Gault equation**; ~~for women, calculated creatinine clearance ≥ 60 mL/minute using the Cockcroft-Gault equation~~**