Letter of Amendment # 5

HPTN 052: A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 In Serodiscordant Couples, Version 3.0, November 20, 2006, DAIDS Document ID: 10068

Final Version: 10 May 2011

Instructions to the Study Sites from the Sponsor

The following information impacts the HPTN 052 study and must be forwarded to all responsible Institutional Review Boards (IRBs)/Ethics Committees (ECs) and any other locally required regulatory agencies IMMEDIATELY for their information and review. Because important new information learned from a pre-planned efficacy and safety review by an independent Data and Safety Monitoring Board may impact study participants and alters the risk/benefit ratio of study participation, the changes to the HPTN 052 study specified in this Letter of Amendment (LoA) are considered effective and must be implemented by each study site within 10 working days of receipt of this LoA by the IRB/ECs, unless the IRB/EC directs otherwise in writing.

This Letter of Amendment has appended to it a Participant Letter for all study participants (See Appendix I).

Your site is still required to submit a LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). Your site 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. This Memorandum and all related IRB/EC correspondence, including documentation of verbal communication, must be retained in the site regulatory file and in other pertinent files.

The HPTN 052 protocol will be fully amended in the near future, and will include the changes outlined in this Letter of Amendment.

Summary of Revisions and Rationale

All modifications included in this Letter of Amendment are based on results of a pre-planned efficacy and safety review by the National Institute of Allergy and Infectious Diseases (NIAID) Multinational Data and Safety Monitoring Board (MDSMB). On 28 April 2011, the NIAID Multinational DSMB was in agreement that the primary question of whether immediate antiretroviral therapy (ART) given to an HIV-infected person reduces transmission of HIV to their HIV negative partner has been answered in the affirmative, and was highly statistically significant (See Appendix II, Final Summary of MDSMB). Clinical events in the HIV-infected individual (Index Case) were in the beneficial direction for the immediate ART arm, but were not statistically

significant. Because of these results, the DSMB recommended that the trial results be made available as soon as possible. The study's sponsor (NIAID), accepted the Board's recommendation, and requires that all HIV-infected participants in the trial who are not already on ART be offered it as soon as possible. A full protocol amendment is currently being developed; however, the modifications specified below reflect an interim approach to be employed until that amendment is finalized and approved by the sponsor and the IRBs/ECs.

The immediate modification is summarized as:

- All HIV-infected participants on the delayed ART arm that have not already initiated ART will be offered to do so as soon as possible.

No other changes in follow-up or assessment schedules and procedures are to be made at this time. All participants randomized to the immediate ART arm will remain on treatment. Instructions to the investigators, study clinicians and site pharmacists are being provided by the sponsor and study team leadership.