

LETTER OF AMENDMENT #02 TO:

**MTN-001
DAIDS Document ID 10617**

**Phase 2 Adherence and Pharmacokinetics Study of Oral and Vaginal Preparations of
Tenofovir**

Version 2.0 /03 September 2008

IND # 55,690

Letter of Amendment Date: 07 August 2009

Information/Instructions to Study Sites from the Division of AIDS

The information contained in this Letter of Amendment (LoA) impacts the MTN-001 study and must be forwarded to your Institutional Review Board (IRB) and/or Ethics Committee (EC) as soon as possible for their information and review. IRB/EC approval is required before implementation of the revisions contained in this LoA.

The following information will also impact the sample informed consent. Site IRBs/ECs are responsible for assessing whether and how the changes included in this LoA are to be communicated to study participants. All IRB/EC requirements must be followed.

Please file this LoA and all associated IRB/EC correspondence in your essential documents files for MTN-001. You will be required to submit IRB/EC correspondence and approved informed consent forms to the DAIDS Protocol Registration Office for informational purposes; however, you will not receive an approval notification from the DAIDS Protocol Registration Office for the LoA.

Summary of Revisions and Rationale

This LoA modifies the accrual numbers for the Botha's Hill and Umkomaas Clinical Research Sites in Durban, South Africa. The number of in-depth interviews to be administered at these sites is also updated to account for the shift in enrollment slots.

Implementation

This LoA is official MTN-001 protocol documentation. Prior to implementing the revisions listed below, study sites will submit this LoA to all relevant regulatory authorities and the IRB/EC. The Division of AIDS Regulatory Affairs Branch will submit this LoA to the United States Food and Drug Administration for inclusion in Investigational New Drug (IND) application # 55,690.

Upon receipt of all required regulatory and IRB/EC approvals, the protocol revisions listed below will be implemented.

Text to be deleted is indicated by ~~strikethrough~~ and text to be added is noted below in **bold**.

Detailed Listing of Revisions

1. The following changes have been made to the protocol to account for the changes in target enrollment numbers for the Botha's Hill and Umkomaas Clinical Research Sites. Appendix VII: Sample Informed Consent Document (Enrollment) is modified accordingly.

Section 7.7, Behavioral Measures, item 2, first paragraph, first sentence:

We will identify a random sample of ~~eight~~ **about forty total** participants ~~from enrolled at~~ five sites (Umkomaas CRS, Botha's Hill CRS, Makerere University-JHU Research Collaboration CRS, Case CRS, and Pitt CRS) to complete an in-depth interview that addresses use of study drugs and male condoms during the trial.

Section 7.7, Behavioral Measures, item 2, second paragraph, first sentence:

If, at a particular site, women with differential adherence between study products are not included in the random sample of in-depth interview participants, up to two additional participants from that site, who did report differential adherence between products **(if any)**, ~~will~~ **may** be invited to complete an in-depth interview as well.

Appendix VII: Sample Informed Consent Document (Enrollment), Twenty-One Week Visit, In-Depth Interview subsection, first sentence:

This interview will take about 30 minutes (in addition to the one and a half hours for the other parts of the 21-Week Visit). About ~~eight to ten~~ **forty** participants **total at each study site** will be asked to answer extra questions at the 21-Week Visit about what they thought about the study products.

Section 10.6, Participant Accrual, Follow-up, Retention, and Replacement, first paragraph, third sentence:

~~Five of the 7 participating sites will recruit and enroll 24 evaluable participants each, and 2 of the participating sites will enroll 12 evaluable participants each for a total of~~ **Approximately 144** evaluable participants **will be enrolled across all sites**.

Appendix VII: Sample Informed Consent Document (Enrollment), How Many Women Will Take Part In This Study? subsection, first sentence:

Approximately 144 women will take part in this study. ~~about 24 each from 5 of the sites (Botha's Hill, Durban, South Africa, Umkomaas, Durban, South Africa, Cleveland, USA, Kampala, Uganda, and Pittsburgh, USA), and 12 each from Birmingham, USA and Bronx, USA.~~

The above information will be incorporated into the next version of the protocol at a later time if it is amended.