Microbicide Trials Network

Clarification Memorandum #01 to:

MTN-001
Phase 2 Adherence and Pharmacokinetics Study of Oral and Vaginal Preparations of Tenofovir, Version 2.0, dated 03 September 2008

DAIDS PROTOCOL #10617

IND # 55,690

Date of Clarification Memorandum: 03 February 2009

Section 1: Summary of Clarifications and Rationale

The procedures in this Clarification Memorandum (CM) have been approved by the NIAID Medical Officer and are to be implemented immediately upon issuance. IRB approval of this CM is not required by the sponsor; however, investigators may submit the CM to the IRB overseeing the study at their site for information. This CM is official MTN-001 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-001. No change in informed consent is necessitated by or included in this CM.

The goal of this CM is to clarify the assessments to be done during periods of temporary product hold and following permanent discontinuation in Sections 7.4. Sections 7.8.3 and 10.5 are updated to correct the number of US sites participating in the Intensive PK portion of the study. Section 10.5 is further updated to reflect that Intensive PK cohort will be at US sites.

Section 2: Implementation

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

1. In Section 7.4, Follow up Procedures for Participants who Discontinue Study Product, the following clarification is made at the end of the first paragraph:

During periods of temporary study product hold or permanent discontinuation, documentation of the last three doses of study product is not required. In addition, the procedures below will be performed as specified within the 6-week study period in which the hold/discontinuation is implemented. These procedures will then be discontinued until study product use resumes (in the case of a temporary hold):

- **Adherence, behavioral, and intravaginal practices assessment will be performed at the next Mid-study or End-of-Study Period Visit, whichever comes first**

- **Acceptability assessment and study product sharing assessment will be performed at the End-of-study Period Visit**

2. In Section 7.8.3, Pharmacokinetic Procedures: Intensive PK Participants (US Sites), third paragraph, first sentence clarifies that the second randomization will be done within all of the US sites participating in Intensive PK portion of the study:

   For the Intensive PK cohorts at US sites, the End of Study Period sample timing will require a second randomization which will be stratified within each of the ~~two~~ **four** sites.

3. In Section 10.5, Randomization Procedures, the second paragraph, last sentence, clarifies that the second randomization will be done within all of the US sites participating in Intensive PK portion of the study and is updated to specify that the Intensive PK cohort will be at the US sites to maintain consistency within the protocol:

   For the intensive PK cohorts at ~~domestic~~ **US** sites, the end of study period sample timing will require a second randomization which will be stratified within each of the ~~two~~ **four** sites.