IPCP Rectal Microbicide Program/ Microbicide Trials Network
CLARIFICATION MEMO #03 TO:

RMP-02/MTN-006
A two-site, Phase 1, partially-blinded, placebo-controlled safety, acceptability, and pharmacokinetic trial of topical, vaginally-formulated tenofovir 1% gel applied rectally compared with oral 300 mg tenofovir disoproxil fumarate in HIV-1 seronegative adults

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Date of Clarification Memorandum: 16 November 2009

Section 1: Summary of Clarifications and Rationale

The items clarified 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 RMP-02/MTN-006 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for RMP-02/MTN-006. No change in informed consent is necessitated by or included in this CM.

The primary goal for this CM is to modify the protocol to reflect the allowable windows for post-dose specimen collection timepoints at Visits 3, 7, and 12. Note that efforts will be made to collect the specimens in approximately the same order detailed in the RMP-02/MTN-006 SSP. The goal will be to collect the last sample (tissue biopsies) by the target collection timepoint. A change previously noted in RMP-02/MTN-006, CM #02 is also included in this CM. The Protocol Team Roster is also updated.

Section 2: Implementation

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

1. The following sections of the protocol are updated to reflect allowable windows for post-dose specimen collection timepoints **(+/- 15 minutes** for the 30 minute timepoint and **+/- 30 minutes** for 2- and 4-hour timepoints).

Table 15: Visit 3 and 7 (Study Product #1; Study Product #2 and 30' Sampling for each), Female Pelvic Specimens row, note to first bullet, and *Rectal Specimens* row, notes to fourth and seventh bullets

Table 19: Visit 12 (Sampling Following Once Daily Exposure for 7 Days (7th dose given in clinic)), Female Pelvic Specimens row, note to first bullet, and *Rectal Specimens* row, notes to fourth and seventh bullets

Section 7.11.1, Pharmacokinetic Procedures: Single Oral Dose

Section 7.11.2, Pharmacokinetic Procedures: Single Rectally Applied Dose

*Section 7.~~10~~**11**.3, Pharmacokinetic Procedures: Following 7-Day Rectally Applied Dose*

2. The following individual has been removed from the Protocol Team Roster: Nancy Connolly

3. The following item was previously noted in RMP-02/MTN-006, CM #02, dated 23 September 09:

The protocol is updated to reflect that PK testing will be performed for all compartments at all PK Visits 2, 5, 6, and 9 have been updated to reflect this:

Appendix 1: Schedule of Study Visits and Evaluations is modified accordingly:

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13/Early Term	F/U Call	Interim
Histology		X	X		X	**X**	X		X	**X**		X			

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