IPCP Rectal Microbicide Program/ Microbicide Trials Network
CLARIFICATION MEMO #02 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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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 correctly reflect that PK testing will be performed in all compartments. This CM also clarifies that tenofovir levels will be measured in mucosal mononuclear cells (MMC).

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 correctly reflect that PK testing will be performed for all compartments at all PK visits. Visits 2, 5, 6, and 9 have been updated to reflect this.

Table 9: Schedule of Study Endpoints:

Visit 2: Enrollment/Baseline	Blood, fluids from sponges, stool, endoscopic lavage, biopsies (~17)***	✓***		✓			✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Visit 5 A/B: (Day 1-3, or 4-6)	Blood, fluids from sponges, stool, endoscopic lavage, biopsies (~17)			✓			✓	✓	✓	✓	✓	✓	✓	✓	✓~~*~~	✓
Visit 9A/B: (Day 1-3, or 4-6)	Blood, fluids from sponges, stool, endoscopic lavage, biopsies (~17)			✓			✓	✓	✓	✓	✓	✓	✓	✓	✓~~*~~	✓

~~*Visits 5 and 9: No flow will be done at these visits.~~

Table 14: Visit 2 (Enrollment/Baseline Evaluation Visit-All Participants), a sub-bullet is added to blood specimens to reflect specimen collection for **Plasma and PBMC tenofovir levels**. A sub-bullet is also added to the 5th bullet of the Rectal Specimens row to reflect the measurement of **Tenofovir levels in MMC** at this visit.

Table 17: Visits 5 and 6 and Visits 9 and 10 (2-Week Sampling Period), references to ~~(Visits 5 and 9 only)~~ are removed from the 4th bullet, 1st and 3rd sub-bullets.

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

Plasma tenofovir levels		**X**	X	X	X	X	X	X	X	X	X	X	X		
PBMC tenofovir levels		**X**	X	X	X	X	X	X	X	X	X	X	X		

~~CD4 cells~~ (TFV levels in MMC~~)~~		**X**	X		X	**X**	X		X	**X**		X			

Histology		X	X		X	**X**	X		X			X			

2. References to CD4 cells ~~(Tenofovir in MMC)~~ are replaced with **Tenofovir levels in MMC** in the following sections of the protocol:

   Table 15: Visit 3 and Visit 7 (Study Product #1; Study Product #2 and 30" sampling) and *Table 19: Visit 12 (Sampling Visit Following Once Daily Exposure for 7 Days (7th dose given in clinic))*, Rectal Specimens, 6th bullet, 2nd (reference to ~~tenofovir in MMC~~ is deleted) and 3rd sub-bullets (**Tenofovir levels in MMC** is added).

   Table 17: Visits 5 and 6 and Visits 9 and 10 (2-Week Sampling Period), 4th bullet, 3rd sub-bullet.

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