

Microbicide Trials Network

CLARIFICATION MEMO #01 TO:

MTN-026/IPM 038

A Randomized, Double Blind, Placebo-Controlled, Phase 1 Safety and Pharmacokinetic Study of Dapivirine Gel (0.05%) Administered Rectally to HIV-1 Seronegative Adults

DAIDS Protocol #12021
IND #69,022

Date of Clarification Memorandum: 30 November 2015

Section 1: Summary of Clarifications and Rationale

The procedures 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/EC overseeing the study at their site for information. This CM is official MTN-026/IPM 038 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-026/IPM 038. No change in informed consent is necessitated by or included in this CM.

This CM updates the protocol team roster, clarifies the specific anorectal samples that will be used to assess mucosal safety to satisfy the secondary objective. Clarifications for protocol consistency have also been made within Section 10.4.1, *Safety Endpoints* and *Appendix I*.

Section 2: Implementation

With the exception of updates to the protocol team roster, text to be deleted is noted below with a ~~strike through~~ and text to be added is in **bold**.

- 1) The following individual has been added to the Protocol Team Roster:

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- 2) Within the *Table of Contents* and *Table of Figures*, the titles of Section 7.15 and Table 15 were updated:

7.15 Pharmacokinetics, Pharmacodynamics and Mucosal ~~immunology~~ **Safety**

Table 15: PK, PD, and Mucosal ~~immunology~~ **Safety** Sampling Table

- 3) Within Section 7, *Study Procedures*, procedure names in the following tables (*Laboratory* section) have been updated:

Table 8: Visit 2: Enrollment (Day 0)

Anorectal Samples	<ul style="list-style-type: none">• Rectal tissue for mucosal immunology safety baseline• Rectal fluid for mucosal immunology safety baseline
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Table 9: Visit 3: Single Dose Administration Visit

Anorectal Samples	<ul style="list-style-type: none">• Collect rectal specimens<ul style="list-style-type: none">– Rectal fluid for mucosal immunology safety •– Rectal tissue for mucosal immunology safety •
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Table 12: Visit 13: Last Study Product Administration Visit/Early Termination Visit

Anorectal Samples	<ul style="list-style-type: none"> • Collect rectal specimens <ul style="list-style-type: none"> - Rectal fluid for immunology safety • - Rectal tissue for immunology safety •
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4) Section 7.15, *Pharmacokinetics, Pharmacodynamics and Mucosal Immunology*: The section name, the title of its corresponding table (Table 15), and the name of the table's 4th column (at right) were updated:

7.15 Pharmacokinetics, Pharmacodynamics and Mucosal ~~Immunology~~ **Safety**

Table 15: PK, PD, and Mucosal ~~Immunology~~ **Safety** Sampling Table

Visit	Specimens Collected to Assess Drug Concentrations (PK)	Specimens Collected for Anti-HIV Activity (PD)	Specimens Collected for Mucosal Immunology Safety
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5) Section 7.16, *Laboratory Evaluations, Laboratory Center (LC)*, 2nd bullet (*Anorectal specimens*), wording was updated in two sub-bulleted locations:

- Anorectal specimens
 - Rectal fluids and/or lavage for:
 - Mucosal ~~immunology~~ **safety**
 - Rectal tissue for:
 - Mucosal ~~immunology~~ **safety**

6) Section 10.4.1, *Safety Endpoints*, fourth paragraph has been updated for consistency:

[...] For example, if the true rate of a given toxicity endpoint in the placebo gel arm is 11.1% (1 of 9 ~~women~~ **participants** experiencing a safety event), the proposed sample size provides 85% power to exclude safety endpoint rates greater than 67% (61% with $\alpha=0.10$) which translates to at least 12 of 18 participants in the active arm. Hence, while comparisons will be made between the drug containing ~~VR~~ arms of the study and the placebo ~~VR~~ arm, the study will only have power to detect very large differences in safety event rates.

7) Appendix 1: *Schedule of Study Visits and Evaluations, Anorectal Samples* section, wording was updated in Rows 4 & 5:

	Visit 1 SCR	Visit 2 ENR	Visit 3 Dosing Visit	Visit 4, 5, 6 (Sampling Assigned 4, 5, or 6)	Visit 7, 8, 9, 10, 11, 12: Dosing Visits*	Visit 13 (Final Dose)/ Early Term	Visit 14, 15, 16, (Sampling Assigned 14, 15 or 16)	Visit 17 F/U Contact
CLINICAL								
Perform pelvic examination	♀	♀	♀▲	♀♂ (Visit 4, or 5 or 6)	♀▲	♀	♀♂ (Visit 14, or 15 or 16)	
Perform rectal examination	X	X	X	♂ (Visit 4, or 5 or 6)	▲ (Visits 7 & 8 only)	X	♂ (Visit 14, or 15 or 16)	
ANORECTAL SAMPLES								
Rectal fluid for mucosal immunology safety (Visits 3 and 13 at either 30-60 or 120 minutes)		X	♂			♂		
Rectal tissue for mucosal immunology safety (Visits 3 and 13 at 30-60 min or 120 minutes)		X	♂			♂		

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