

Microbicide Trials Network

CLARIFICATION MEMO #01 TO:

MTN-026 Version 2.0 dated July 21, 2017

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 #136,320

Date of Clarification Memorandum: 13 October 2017

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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 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-026. No change in informed consent is necessitated by or included in this CM.

This CM corrects reference numbering starting from Section 2.3.4, *Animal Studies of Universal Placebo Gel*, and also corrects typos in Section 10.4.1, *Safety Endpoints*, and *Appendix I*.

This CM also notes that an IND number (IND#136,320) has been assigned to the MTN-026 study, and that the IND number will be incorporated into the next version of the protocol at a later time if it is amended.

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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 revisions were made to Section 2.3.4, *Animal Studies of Universal Placebo Gel*, first sentence of "Local Tolerance" sub-section, and to the Reference List, respectively:

A 10-day rabbit vaginal irritation study (10 per arm, 2 arms, placebo gel vs. 0.9% saline control) found the HEC-based placebo gel was not irritating to the vaginal mucosa of rabbits when dosed daily for 10 days.<sup>5-7</sup>

~~7. Gilead Sciences. Investigator's Brochure: Tenofovir Gel (GS-1278). Second Edition. 3-31-2005.~~

- 2) The following revisions were made to Section 2.4.1, *Clinical Studies of Dapivirine Gel*, second sentence of first paragraph, and to the Reference List, respectively:

In addition, one Phase 1 clinical trial has been conducted in 48 male participants to evaluate the safety and tolerability of dapivirine vaginal gel (Gel 4759) following multiple topical penile exposures.<sup>1, 9 10, 11</sup>

~~11. International Partnership for Microbicides (IPM). Investigator's Brochure: Dapivirine Vaginal Gel (Version 7.0 Final). Version 7.0. 8-28-2013.~~

- 3) Reference numbering for citations #8-10 were revised to citations #7-9 and reference numbering for citations #12-35 were revised to citations #10-33 throughout the protocol text and Reference List.

- 4) The following revisions were made to Section 10.4.1, *Safety Endpoints*, last sentence of fourth paragraph:

Hence, while comparisons will be made between the drug containing ~~V~~R arm of the study and the placebo ~~V~~R arm, the study will only have power to detect very large differences in safety event rates.

- 5) The following revision was made to Appendix I: *Schedule of Study Visits and Evaluations*, fifth row of *Clinical* section:

	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
<b>CLINICAL</b>								
Perform rectal examination	X	X	X	Φ (Visit 4, 5 or 6)	▲ (Visits 7 & 8 only)	X	Φ (Visit 14, 15 or 16)	

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