

Microbicide Trials Network

CLARIFICATION MEMO #01 TO:

MTN-028

Phase 1 Pharmacokinetic Trial of Two Intravaginal Rings (IVRs) Containing Different Dose Strengths of Vicriviroc (MK-4176) and MK-2048

DAIDS Protocol #: 12022

IND#: 123,134

Version 1.0 / 12 February 2015

Clarification Memo Date: 5 August 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 overseeing the study at their site for information. This CM is official MTN-028 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-028. No change in informed consent is necessitated by or included in this CM.

This document clarifies the general criteria for permanent discontinuation of study product, clarifies language regarding the timing of menses and scheduling of Study Visits 2-6, and provides additional guidance regarding the procedures to omit at the Early Termination Visit in the event the vaginal ring has been out of the vagina for 3 or more days.

Section 2: Implementation

Text to be deleted is noted with a ~~strike through~~ and text to be added is in **bold**.

- 1.) Section 9.3, *General Criteria for Temporary Hold and Permanent Discontinuation of Study Product, Permanent Discontinuation* section now provides additional information regarding the maximum number of days the ring can be out of the vagina before permanent discontinuation of study product is warranted:

Participant is unable or unwilling to comply with required study procedures, or otherwise might be put at undue risk to their safety and well-being by continuing product use (**including lack of ring use for 3 or more days for any reason**), according to the judgment of the IoR/designee.

- 2.) Language within Section 7.3, Visit 2- Enrollment (Day 0), has been clarified:

Ideally Menses ~~must~~**does** not coincide with Study Visits 2-6 (Days 0, 1, 2, 3, 7), therefore participant's menstrual cycle must be considered when scheduling Visit 2- Enrollment Visit (Day 0).

3.) A footnote has been added to Table 15: *Visit 13 (Day 35) Final Clinic/Early Termination Visit* within Section 7.4.4., *Visit 13 (Day 35) Final Clinic/Early Termination Visit* to clarify which procedures should be omitted in case of an Early Termination Visit:

Table 15: Visit 13 (Day 35) Final Clinic/Early Termination Visit

Visit 14 (Day 35) Final Clinic/ Early Termination Visit		
Component		Procedures
Laboratory	Blood	<ul style="list-style-type: none"> • Collect blood <ul style="list-style-type: none"> – CBC with differential and platelets* – HIV-1 serology – Chemistries – PK Ⓞ – Syphilis serology*
	Genital	<ul style="list-style-type: none"> • Collect pelvic specimens <ul style="list-style-type: none"> – Vaginal fluid pH* – Vaginal fluid for PK analysis Ⓞ – Gram stain – Rapid test for Trichomonas* – KOH wet mount for candidiasis* – Saline wet mount for BV* – NAAT for GC/CT*

* If indicated, ▲ If Early Termination Visit and not already performed, Ⓞ If Early Termination and the study VR has been out of the vagina for 3 or more days, omit.

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