

Microbicide Trials Network

CLARIFICATION MEMO #02 TO:

MTN-044/IPM 053/CCN019 Version 2.0 dated June 7, 2018

A Randomized, Phase 1, Open-Label Study in Healthy HIV-Negative Women to Evaluate the Pharmacokinetics, Safety and Bleeding Patterns Associated with 90-Day Use of Matrix Vaginal Rings Containing 200 mg Dapivirine and 320 mg Levonorgestrel

IND #: 126907

Date of Clarification Memorandum: 20 November 2018

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Section 1: Summary of Clarifications and Rationale

The procedures clarified in this Clarification Memorandum (CM) have been approved by the IPM, NICHD and DAIDS Medical Officer and are to be implemented immediately upon issuance. IRB approval of this CM is not required; however, investigators should submit the CM to the IRB overseeing the study at their site for information. This CM is official MTN-044/IPM 053/CCN019 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-044/IPM 053/CCN019. No change in informed consent is necessitated by or included in this CM.

This CM clarifies the guidelines for ring removal at the time of cervical biopsy sample collection at Visit 11 (Day 90, PUEV/Early termination).

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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**.

- The following revisions were made to the body and footnote of Table 14 in Section 7.4.5:
  - Cervical biopsies for DPV concentration and PD ■ ∞
  - To be collected prior to ring removal unless ring needs to be removed to collect biopsy samples**
- The following revisions were made to the body and footnote of Table 17 in Section 7.8, *Pharmacokinetics*:

Study Visit	Specimens collected for PK & PD			Specimens collected for vaginal environment
Visit 11 - PUEV/Early Study Termination Visit (Day 90) ∞	<ul style="list-style-type: none"><li>Blood for DPV ∞</li><li>Blood for LNG ∞</li></ul>	<ul style="list-style-type: none"><li>CVF for DPV ∞</li><li>CVF for LNG ∞</li></ul>	<ul style="list-style-type: none"><li>Cervical tissue for DPV and PD ■</li></ul>	

- To be collected prior to ring removal unless ring needs to be removed to collect biopsy samples**

3. The following revisions were made to the body and footnote of Appendix 1:

	Visit 1 SCR	Visit 2 ENR (Day 0)	Visits 3, 4 (Day 2,14)	Visits 5, 8 (Day 28, 58)	Visits 6, 9 (Day 30, 60)	Visits 7,10 (Day 44, 74)	Visit 11 PUEV/Early Termination (Day 90)	Visits 12- 14 (Day 91, 92, 93 or 94)	Visits 15-18 Final Phone Calls (1, 4, 8, 12 wks after ring removal)
Cervical biopsies for DPV concentration and PD			X Day 14 only		X♦ Day 30 only		■ ∞		

■ **To be collected prior to ring removal unless ring needs to be removed to collect biopsy samples**

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