

**Microbicide Trials Network**

**LETTER OF AMENDMENT #03 TO:**

**MTN-024/ IPM 031  
Phase 2a Safety Study of a Vaginal Matrix Ring Containing Dapivirine in a Postmenopausal  
Female Population**

**Version 1.0 dated 21 March 2013**

**DAIDS Protocol ID: 11915**

**IND #: 108,743**

**Date of Letter of Amendment: 20 January 2015**

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*Site Instruction*

The following information impacts the MTN-024/IPM 031 study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) as soon as possible for their information and review. This must be approved by your IRB/EC before implementation. The following information also impacts the sample informed consent. Your IRB/EC will be responsible for determining the process of informing participants of the contents of this Letter of Amendment (LoA).

*Implementation*

Upon receiving final IRB/EC and any other applicable Regulatory Entity (RE) approval(s) for this LoA, sites should implement the LoA immediately. Sites are still required to submit a LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). Sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. A LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with this letter and any IRB/EC correspondence should be retained in the site's regulatory files.

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*Summary of Revisions*

The purpose of this LoA is to update the listing of risks and/or discomforts associated with dapivirine vaginal rings (VRs) as reflected in the updated *International Partnership for Microbicides (IPM) Investigator's Brochure for Dapivirine Vaginal Ring, Version 9.0, 03 December 2014*.

Text to be deleted is noted by ~~strikethrough~~ and text to be added is noted below in **bold**.

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1. Modifications have been made to Section 13.4.1, *RISKS, General*, fifth paragraph, bulleted list, to reflect issuance of the updated *International Partnership for Microbicides (IPM) Investigator's Brochure, Dapivirine Vaginal Ring, Version 9.0, 03 December 2014*:

Based on AEs reported among female participants in previous studies, dapivirine VRs may be associated with:

- Vaginal candidiasis
- **Vaginitis bacterial**
- **Metrorrhagia**
- ~~Vaginal bleeding~~
- ~~Headache~~
- ~~Fatigue~~
- ~~Vulvovaginal or genital itching~~

- ~~Abdominal discomfort~~
- ~~Abdominal pain~~
- Urinary incontinence **tract infection**
- ~~Nausea~~
- Vaginal ~~or genital~~ discharge

2. *APPENDIX III: SAMPLE INFORMED CONSENT FORM (SCREENING, ENROLLMENT, LONG-TERM STORAGE AND FUTURE TESTING)*, Risks and/or Discomforts, Risks of Study Drug, bulleted list, has been modified to reflect issuance of the updated *Dapivirine Ring IB* and for clarity:

Based on side effects reported among women in previous studies, dapivirine ~~VRs~~ **vaginal rings** may be associated with:

- ~~Vaginal~~ Yeast infection
- Vaginal bleeding **at irregular intervals, particularly between your expected menstrual periods**
- ~~Headache~~
- ~~Fatigue~~
- ~~Vulvovaginal or genital itching~~
- ~~Abdominal discomfort~~
- ~~Abdominal pain~~
- Urinary incontinence **tract infection**
- ~~Nausea~~
- Vaginal discharge

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