

**SUMMARY OF CHANGES
INCLUDED IN THE FULL VERSION PROTOCOL AMENDMENT OF
MTN-026**

**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 # [XXXXXX]

THE AMENDED PROTOCOL IS IDENTIFIED AS: Version 2.0/ 21 July 2017

Information/Instructions to Study Sites

The information contained in this protocol amendment impacts the MTN-026 study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) as soon as possible for their information and review. IRB approval is required before implementation of the modifications contained in this amendment. All IRB requirements must be followed.

Please file this Summary of Changes, Version 2.0 of the protocol and all associated IRB correspondence in your essential documents files for MTN-026.

Summary of Revisions

A summary of revisions is provided below:

1. The IND holder changed from International Partnership for Microbicides (IPM) to DAIDS, resulting in several consequent changes in the document, including, for example, each place the IND Sponsor was mentioned, a change in study designation from MTN-026/IPM 038 to MTN-026, a change in IND# from 69,022 to [XXXXXX], limitation of IPM's protocol-designated role to publication review, and addition of informed consent form review to DAIDS's protocol-designated responsibilities.
2. New, clarified, or updated data regarding DPV rings, films and gels was added, including data from FAME-02B, recently released data from MTN-020 (ASPIRE) and IPM 027 (The Ring Study), and updated Investigator's Brochure (IB) data.
3. The Male Genital Grading Table for Use in Microbicide Studies (Addendum 2 to the DAIDS AE Grading Table) was added to the list of Grading Tables to be used for AE determination in this study.
4. Eligibility criteria was edited for clarity as follows:
 - Participants to meet age eligibility as of Screening date, not Enrollment.
 - Rectal product studies added to list of prohibited co-enrollment studies.
 - "Unprotected RAI" changed to "RAI without a condom".
5. Study visit procedure language was edited for clarity and consistency as follows:

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MTN-026 (continued)**

- Cervicovaginal lavage (CVL) and rectal enema effluent samples will be collected for pharmacokinetics (PK) as well as pharmacodynamics (PD) at the same visits.
 - Added asterisk (*) to physical exam weight assessment in Section 7.13.
6. Edits to Section 11.1 were made to change the data management system used in this study from DataFax to Medidata Rave EDC, an electronic data capture system compliant with US-EU Safe Harbor, the EU Data Protection Directive 95/46/EC, ICH GCP and CFR requirements.
 7. The Site Investigator for the University of Pittsburgh Clinical Research Site (CRS) was changed from Ross Cranston to Ken Ho, among a number of other updates to the Protocol Team Roster.
 8. The Investigator Signature Form (p. 18) was edited to include newly required language as per DAIDS's updated policy.
 9. The protocol has been updated to refer to the most recent revision of the DAIDS Table for Grading Adult and Pediatric Adverse Events (now Corrected Version 2.1, July 2017)
 10. Other information has been added or updated for clarity and/or consistency:
 - It was clarified that sexual lubricant data may be recorded on a separate form in Section 6.9.
 - “Mucosal immunology” changed to “mucosal safety” in Section 7 tables and Appendix I to be consistent with secondary objective wording.
 - Evaluations performed at the Local Laboratory as listed in Section 7.16 were updated.
 - “Anogenital STIs” changed to “Anorectal STIs” in Section 9.3.
 - Risk language for phlebotomy and rectal biopsy collection was updated in Section 13.4.1.
 - Participant confidentiality language was updated in Section 13.6.
 - Language regarding blood clots was added to Appendix III.

Other minor updates, corrections, and clarifications are also incorporated into the document, including update of website addresses for NIAID and DAIDS and formatting of the protocol document to meet DAIDS-preferred Electronic Common Technical Document (eCTD) guidelines.