

HIV Prevention Trials Network

Clarification Memorandum # 02 to:

HPTN 059, Phase II Expanded Safety and Acceptability Study of the Vaginal Microbicide 1% Tenofovir Gel, Version# 2.0, Dated 13 March 2006

IND #55, 690

Date of Clarification Memorandum: 22 September 2006

Section 1: Addition to the HPTN059 Protocol Team Roster

Protocol Team Roster (Page vi) to be updated to include:

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Section 2: Summary of Clarifications and Rationale

The procedures clarified in this memorandum have been approved by the NIAID Medical Officer and are to be implemented immediately upon issuance. IRB approval of this Clarification Memorandum is not required by the sponsor; however, investigators may submit the clarification memo to the IRBs/ECs overseeing the study at their site for their information.

This clarification memo is official HPTN 059 protocol documentation. It is effective immediately. A copy of this memo must be retained in each study site's Essential Documents file for HPTN 059.

No change in the informed consent form are necessitated by or included in this Clarification Memo.

The primary goal for this clarification memo is:

- to provide clarification and detail on "Intermenstrual Bleeding/Spotting" in Appendix II: Outcomes, Diagnostics, and Follow Up Evaluations
- to clarify Protocol Section 5.0 with regards to Laboratory Procedures and collection and preparation of cervical and vaginal swabs

Section 3: Implementation

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

1. Protocol Appendix II: Outcomes Diagnostics, and Follow Up Evaluations will be slightly modified. In the revision the word, "**Unexpected**" will be added to Intermenstrual Bleeding/Spotting to further clarify the type of genital bleeding that would require study gel to be held until evaluation. This will result in the following:

From:

Condition	Study gel Use	Evaluation	Follow up and Treatment Action
Intermenstrual Bleeding/Spotting	Hold study Gel (until evaluated)	Naked eye evaluation and/or colposcopy	If determined to be endometrial bleeding with no other source, continue study gel use. Re-evaluate in 48 - 72 hours if the participant reports the bleeding/spotting has not resolved.

To:

Condition	Study gel Use	Evaluation	Follow up and Treatment Action
Unexpected Intermenstrual Bleeding/Spotting	Hold study Gel (until evaluated)	Naked eye evaluation and/or colposcopy	If determined to be endometrial bleeding with no other source, continue study gel use. Re-evaluate in 48 - 72 hours if the participant reports the bleeding/spotting has not resolved.

2. Protocol Section 5.0, Clinical and Laboratory Procedures for Final Screening/Enrollment and all Follow Up Visits will be revised to the following:

- 5.2.1 *Clinical Procedures* (Final Screening/Enrollment, Page 31 of 65)
Additionally for Baseline Procedures:
 - collection of one cervical swab for ~~one~~ **two** dried smears for detection of neutrophils (Gram stain assessment at the HPTN CL)
 - **collection of genital ulcer swab for multiplex polymerase chain reaction (PCR) (at the HPTN CL) if ulcer or other anogenital finding thought to be herpetic is identified**

- 5.3.1 *Clinical Procedures* (Weeks 4, 12 Visits, Page 33 of 65)
 - Perform pelvic exam including:
 - collection of one cervical swab for ~~one~~ **two** dried smears for detection of neutrophils (Gram stain assessment at the HPTN CL)

- collection of swab specimen from the lateral vaginal wall for two dried smears (~~Gram stain assessment at the HPTN CL~~) (NOTE: removed due to duplicate entry)

5.3.2 *Laboratory Procedures* (Weeks 4, 12 Visits, Page 34 of 65)

- Prepare HBV viral load for analysis (at the HPTN CL at Week 12 only for CHVB **CHBV** participants)

ADD

- **prepare quantitative vaginal specimen for shipment to HPTN CL (US sites only)**

ADD

- when clinically indicated only, perform the following procedures:
 - **prepare blood specimens for plasma and serum archive**
 - **perform urine NAAT for GC and CT**
 - **record results of dipstick urinalysis for protein, glucose and blood (perform microscopy and culture if dipstick is positive for leukocyte esterase or nitrates)**

5.4.2 *Laboratory Procedures* (Weeks 8, 16, 20 Visits, Page 35 of 65)

- when clinically indicated only, perform the following procedures:
 - **prepare blood specimens for plasma and serum archive**

5.5.1 *Clinical Procedures* (Week 24/Early Termination Visit, Page 36 of 65)

- Perform pelvic exam including:
 - collection of **two** cervical swabs for cytokine and chemokine testing (for analysis at HPTN CL)
 - collection of one cervical swab for ~~one~~ **two** dried smear for detection of neutrophils (Gram stain assessment at the HPTN CL)

5.5.2 *Laboratory Procedures* (Week 24/Early Termination Visit, Page 37 of 65)

- **prepare quantitative vaginal specimen for shipment to HPTN CL (US sites only)**