Microbicide Trials Network
CLARIFICATION MEMO #02 TO:

MTN-003
DAIDS Document ID #10622

Phase 2B Safety and Effectiveness Study of Tenofovir 1% Gel, Tenofovir Disoproxil Fumarate Tablet and Emtricitabine/Tenofovir Disoproxil Fumarate Tablet for the Prevention of HIV Infection in Women

Version 1.0 / 22 May 2008
IND #: 55,690

Date of Clarification Memorandum: 25 August 2009

Section 1: Summary of Clarifications and Rationale

The items clarified in this Clarification Memorandum (CM) have been approved by the NIAID Medical Officer and are to be implemented immediately upon issuance. IRB/EC approval of this CM is not required by the sponsor; however, investigators may submit the CM to the IRB/EC overseeing the study at their site for information. This CM is official MTN-003 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-003. No change in informed consent is necessitated by or included in this CM.

This CM provides clarification on the following items:

- Updates to the Protocol Team Roster
- Anticipated bleeding associated with speculum insertion and specimen collection
- Product hold following positive HIV test results
- Schedule of dipstick urinalysis testing
- Product hold related to hypophosphatemia
- Elimination of discrepancy between Appendix I: Schedule of Study Visits and Evaluations and the protocol

---

Section 2: Implementation

With the exception of the modifications to the Protocol Team Roster, text to be deleted is noted by ~~strikethrough~~ and text to be added is noted below in **bold**.

1. The Protocol Team Roster is updated to reflect updates to contact information.

Nicola Coumi, MMed Sci
Site Investigator
MRC – HPRU
P.O. Box 70380
Overport, KwaZulu-Natal 4067 South Africa
Phone: 27-31-242-3709
Fax: 27-31-242-3800
Email: nicola.coumi@mrc.ac.za

Vijayanand Guddera, PhD
Site Investigator
MRC – HPRU
P.O. Box 70380
Overport, KwaZulu-Natal 4067 South Africa
Phone: 27-31-242-3703
Fax: 27-31-242-3800
Email: Vijananand.Guddera@mrc.ac.za

Nozizwe Dladla-Qwabe, MSoc Sci
Site Investigator
MRC – HPRU
P.O. Box 70380
Overport, KwaZulu-Natal 4067 South Africa
Phone: 27-31-242-3671
Fax: 27-31-242-3800
Email: Nozizwe.Dladla@mrc.ac.za

Sarita Naidoo, B Sci
Site Investigator
MRC – HPRU
P.O. Box 70380
Overport, KwaZulu-Natal 4067 South Africa
Phone: 27-31-242-3667
Fax: 27-31-242-3800
Email: Sarita.Naidoo@mrc.ac.za

Shayhana Ganesh, MBCHB, Dip HIV Man
Site Investigator
South African Medical Research Council
P. O. Box 70380
Overport, KwaZulu-Natal 4067 South Africa
Phone: 27-31-242-3600
Fax: 27-31-242-3800
Email: sganesh@mrc.ac.za

Yuki Sookrajh, MBChB
Site Investigator
MRC – HPRU
P.O. Box 70380
Overport, KwaZulu-Natal 4067 South Africa
Phone: 27-83-781-1027
Fax: 27-31-902-7938
Email: yuki.sookrajh@mrc.ac.za

Sharika Gappoo, MMed Sci
Site Investigator
MRC – HPRU
P.O. Box 70380
Overport, KwaZulu-Natal 4067 South Africa
Phone: 27-31-242-3645
Fax: 27-31-242-3800
Email: Sharika.Gappoo@mrc.ac.za

Molly Swenson, RN, MSN, MPH
MTN SDMC Clinical Affairs Safety Associate
FHCRC – SCHARP
1100 Fairview Ave. North, LE-400, PO Box 19024
Seattle, WA 98109-1024 USA
Phone: 206-667-5410
Fax: 206-667-4812
Email: mollys@fhcrc.org

The following individuals have been removed from the Protocol Team Roster: Roshini Govinden and Missy Cianciola.

2. Section 5.3 of the protocol has been clarified to reflect the fact that cervical bleeding associated with speculum insertion and/or specimen collection judged to be within the range of normal according to the IoR/designee is not exclusionary.

Section 5.3, Exclusion Criteria, note to item 7:

Note: Cervical ~~friability~~ ***bleeding associated with speculum insertion and/or specimen collection*** *judged to be within the range of normal according to the clinical judgment of the IoR/designee* ***is considered expected non-menstrual bleeding and*** *is not exclusionary.*

3. Section 6.6, Retrieval of Unused Study Products, Table 5: Retrieval of Temporarily Held or Permanently Discontinued Study Product, first row is updated to clarify product hold guidelines:

	Retrieve Oral Study Product	Retrieve Vaginal Study Product
Permanent discontinuation **or temporary hold** due to **potential** HIV seroconversion	Within 24 hours	Within 24 hours

4. Section 7.5, Follow-up Visits, third paragraph, second sentence is updated to clarify that dipstick urinalysis (UA) testing should be done at the participants' next visit in the event of a missed visit:

However, for participants who miss visits at which pelvic exams, complete blood counts, serum chemistries, **dipstick UA for protein and glucose,** and/or plasma archive are specified to take place, these procedures must be conducted at the participants' next visit.

5. Section 7.5.3, Laboratory Procedures, Dipstick urinalysis subsection is updated to clarify the dipstick UA schedule. Appendix I: Schedule of Study Visits and Evaluations is updated accordingly:

- Dipstick urinalysis for protein~~,~~ **and** glucose~~, nitrites, and/or leukocyte esterase~~:
    - Month 1
    - Quarterly
    - At PUEV
    - When clinically indicated

- **Dipstick urinalysis for nitrites and leukocyte esterase (LE):**
    - **When urine protein is 1+ or greater, or when otherwise clinically indicated**

Appendix I: Schedule of Study Visits and Evaluations:

UA **(protein and glucose)**	X	▲	+	■	X	X	X	X	▲
UA (nitrites and LE)	**X**	▲	+	▲	▲	▲	▲	▲	▲

6. Product hold rules are further clarified in Section 9.5.6, Hypophosphatemia, Grades 3 and 4 subsection, last sentence:

If improvement to ≤ Grade 2 can not be documented within one week of the receipt of the **confirmed** Grade 3 or 4 result, study product must be permanently discontinued.

7. Appendix I: Schedule of Study Visits and Evaluations is updated to maintain consistency with the protocol.

Physical Exam		X		■	X	X	X	X	~~X~~▲

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