HIV Prevention Trials Network

Clarification Memorandum # 01 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: 03 August 2006

Section 1: 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 is necessitated by or included in this Clarification Memo.

The primary goal for this clarification memo is to provide clarification and detail on three laboratory procedures, and, one administrative change to update the protocol team roster. Further detail can be found in the section below.

Section 2: Implementation

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

1. The Protocol Team Roster is updated to remove the following protocol team member:

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2. Protocol Section 5.1: Clinical Procedures [for Screening] – Deleting third bullet to clarify that comprehension test will not be administered at Screening (the comprehension test will only be administered at the Final Screening/Enrollment Visit):

5.1.1 Clinical Procedures

- assign participant ID
- explain study requirements to the participant
- ~~administer comprehension test according to site SOPs~~
- obtain written informed consent(s)

3. Protocol Section 6.2 "Clinical Data Safety Review" – Third paragraph will be modified to state that PSRT calls will occur on a monthly basis:

At the beginning of the study, the PSRT will aim to meet via conference call ~~every two weeks~~ **on a monthly basis** during the period of study implementation, to review clinical and laboratory data reports (blinded by study treatment) generated by the HPTN SDMC.

4. Protocol Appendix I Schedule of Study Visits and Evaluations will be modified to the following (changes made are indicated in the highlighted rows):

EVALUATIONS	Screening (up to –56 days)	Final Screening	Enrollment Visit (Day 0)	Weeks 4, 12,	Weeks 8, 16, 20	Week 24 or Early Termination
PERFORM LABORATORY EVALUATIONS:						
urine pregnancy test – LL	X	X	X	X	X	X
urine NAAT for GC and CT – LL **or CL**	X		X	▲	▲	X
dipstick urinalysis-LL	X		X	▲	▲	X
urine microscopy and culture - LL	▲		▲	▲	▲	▲
HIV serology (EIA/WB when indicated) - LL	X	▲	X	▲	▲	X
HBsAg – LL	X		X	▲	▲	X
HBV viral load – CL			●	●[b]		●
***PK sampling – CL				X	X[c]	
***HBV serum archive (if participant provides consent) – LL			●	●[b]		●
Syphilis serology – LL	X		X	▲	▲	X
***HSV-2 serology – LL or CL	X		X	▲	▲	X
***plasma and serum archive[i] - LL	X[i]		X	▲	▲	X
CBC – LL	X		X	X	▲	X
LFT and RFP - LL	X		X	X	▲	X

***** - Items marked with ***** indicates those specimens will be batched for shipment
X - Protocol specific evaluation for all participants
▲- If clinically indicated
● - CHBV participants only

a - Unless documentation of a normal Pap test result in the 90 days prior to screening
b - Assessment will be performed at Week 12 only
c - Assessment will be performed at Week 20 only
d - ~~RFP~~ **LFT** only
e - When available
f - Behavioral assessment done only at the Enrollment Visit
g - Non-CHBV participants only
h - Assessment will be performed at Week 36 only
i – For HSV-2 serology, only plasma archive will be drawn

LL – at the Local Lab

CL – at the HPTN CL for assay

Urine NAAT for GC and CT – LL **or CL:** Because the Bronx Lebanon Hospital Center (BLHC) has changed laboratories from Quest to LabCorp, Urine NAAT for GC and CT will be done at the Central Lab. The appendix was revised to state urine samples for NAAT for GC and CT can be done at the Local Lab or Central Lab.

HSV-2 and Plasma Archive: HSV-2 testing will be performed from the sample drawn for the plasma archive samples. Due to an oversight, the "X" that should be captured under the screening visit for the plasma archive – LL was omitted. Since we will be conducting an HSV-2 test at Screening, the appendix has been revised to indicate that a plasma archive sample will be drawn at Screening, and an "X" has been inserted in the specified area of the table to reflect the addition. This does not result in any increase in the amount of blood required at the screening visit, as the schedule originally stated that a sample for HSV-2 serology would be collected and prepared at screening.

LFT and RFP[d] – LL: The note for this line item has been revised to match Protocol Sections 2 and 5, to state that LFT (instead of RFP) will be done for CHBV participants at Week 28, 32, and 36 Visits.

5. The following language has been added to Protocol Sections 5.1.2 (Laboratory Procedures for Screening Visit), 5.2.2 (Laboratory Procedures for Enrollment Visit), 5.5.2 (Laboratory Procedures for Week 24 Visit) to reflect the change stated above in #2 for Urine NAAT for GC and CT:

    - Perform urine NAAT for GC and CT **(India and UAB sites)**
    - **Prepare urine specimen for NAAT for GC and CT (BLHC site)**