Microbicide Trials Network

Clarification Memo #02 to:

MTN-004
Phase I Study of the Safety and Acceptability of 3% w/w SPL7013 (VivaGel™) Applied Vaginally in Sexually Active Young Women, Version 2.0, Dated 15 May 2007

DAIDS PROTOCOL #10492

IND #62,482

Date of Clarification Memorandum: 03 October 2007

Section 1: Summary of Clarifications and Rationale

The procedures clarified in this memorandum have been approved by the NIAID and NICHD Medical Officers 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 IRB overseeing the study at their site for their information.

This clarification memo is official MTN-004 protocol documentation. It is effective immediately. A copy of this memo must be retained in each study site's Essential Documents file for MTN-004.

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

The primary goals for this clarification memo are to modify the format of the Protocol Safety Team Reports (PSRT) cited in Section 8.2 Clinical Data Safety Review and Section 8.2.2 Weekly Reviews. Section 7.6.4, Phone Assessment is also updated to reflect an additional day allowed for the window period. Appendix 1: Schedule of Study Visits and Evaluations is also modified to reflect this change. Two administrative changes to the protocol team roster are also noted here.

Further detail can be found in the section below.

Section 2: Implementation

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 add one team member and to indicate a change in protocol team role for another member:

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2. Section 7.6.4, last sentence has been updated to reflect a change in the window period. The window period for the Phone Assessment is changed to Study Day 2-4.

This contact may be initiated by study staff or the participant on Study Day 2~~-or 3~~**4** (Target Day 2), as agreed upon prior to the call.

3. Appendix I: Schedule of Study Visits and Evaluations, pg. 76, has been modified accordingly to reflect the window period for the Phone Assessment as Study Day 2-4.

Appendix I: Schedule of Study Visits and Evaluations

	Screen 1	Screen 2	Enroll	Phone Call	1-Week Clinic Visit	2-Week Clinic Visit	3-Week Clinic Visit	Inter./ Safety Visit
Target Day	≤30 Days		Day 0	Day 2	Day 7	Day 14	Day 21	PRN
Window Period	≤36 Days		Day 0	Day 2-~~34~~	Day 6 – 8	Day 13 – 15	Day 20 – 24	
Study Communications								
Informed Consent	X		X					
Assign Participant ID	X							
Eligibility Assessment	X	X	▲					
Collect Demographics	X							
HIV Pre- & Post-Test Counseling	X							
Screening Results (as available)	X	X	X					
Treatment or Referral	▲	▲	▲		▲	▲	▲	▲
Record/Update Medical and Menstrual History	X	X	X		X	X	X	X
Baseline Behavioral Questionnaire			X					
Record/Update Con. Meds.			X		X	X	X	▲
Record Adverse Events					X	X	X	▲
Vaginal Product History			X					
Acceptability Assessment						X		
Adherence Assessment					X	X		
Male Condom Counseling	X		X		X	X		▲
Record/Update Contacts	X	X	X		X	X	X	X
Schedule Next Visit	X	▲	X		X	X	▲	▲
Obtain Random Assignment			X					
Phone Assessment				X				
Study Burden Questionnaire							X	
Reimbursement	X	X	X		X	X	X	
Laboratory								
Qual. Urine Pregnancy Test	X	X	▲		X	X	X	X
Urinalysis	X		▲		▲	▲	▲	▲
Urine Culture & Sensitivity	▲		▲		▲	▲	▲	▲
CBC, Liver Function Panel, Creatinine Level, Coag. Panel	X		X		X	X	▲	▲
RPR (Syphilis)	X		▲		▲	▲	▲	▲
Confirmatory Tests for Syphilis	▲		▲		▲	▲	▲	▲
HIV Antibody Screen	X							▲
HIV Confirmatory Testing	▲							▲
SPL7013 Level			X			X		
Plasma Archive			X			X		
Vaginal pH	X		X		X	X	X	▲
Quantitative Vaginal Cultures			X		X	X	X	▲
Vaginal Wet Prep Slide	X		X		X	X	X	▲
Gram-Stained Vaginal Smears	X		X		X	X	X	▲
Cervical Swabs for Cytokines and Innate Factors			X		X	X	X	▲
Urine SDA for Gonorrhea & Chlamydia	X		▲					
Genprobe Aptima					▲	▲	▲	▲
Pap Smear of Cervix	X							▲
Herpes Culture	▲				▲	▲	▲	▲
Clinical								
Colposcopy			X		▲	X	▲	▲
Vital Signs	X		X		X	X	X	▲
Abdominal/Pelvic Exam	X		X		X	X	X	▲

4. Section 8.2, Clinical Data Safety Review, fourth (with exception of 1st sentence) and fifth paragraphs have been removed to allow for a change in the MTN-004 PSRT report format.

Routine safety review occurs at the start of enrollment, and then daily, weekly, monthly, and every 4 months during the study. ~~Reviews proceed from a standardized set of protocol-specific safety data reports. These reports are produced by the SDMC and are annotated with queries that are sent to the MTN study sites as needed with any additional notes. Events are tracked by the internal reports until resolution. Other reports, containing queries and notes, are distributed to the MTN-004 PSRT.~~

~~The following reports are produced:~~

~~• Clinical quality control~~
~~• Safety review~~
~~• Pre-existing conditions~~
~~• Adverse events (AEs) requiring review~~
~~• Adverse event/concomitant medication~~
~~• Safety summary~~

~~More detailed information regarding the contents and distribution of these reports can be found in the MTN MOP~~.

5. Section 8.2.2, Weekly Review, first sentence, first paragraph, has been modified to be consistent with the changes made to Section 8.2 Clinical Data Safety Review regarding the MTN-004 PSRT report format.

The SDMC Clinical Affairs staff reviews internal reports of all clinical values that fall outside of the ~~standard~~ MTN safety parameters ~~(see MTN MOP)~~.