LETTER OF AMENDMENT #01 TO:

MTN-023/IPM 030

Phase 2a Safety Study of a Vaginal Ring Containing Dapivirine in Adolescent Females

Version 1.0, dated October 23, 2013

DAIDS Protocol #11927

IND #108,743

Date of Letter of Amendment: 15 April 2014

Site Instruction

The following information impacts the MTN-023/IPM 030 study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) as soon as possible for their information and review. This must be approved by your IRB/EC before implementation. The following information does not impact the sample informed consent, however your IRB/EC will be responsible for determining the process of informing participants of the contents of this letter of amendment, if needed.

Implementation

Upon receiving final IRB/EC and any other applicable Regulatory Entity (RE) approval(s) for this LoA, sites should implement the LoA immediately. DAIDS sites are still required to submit a LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). DAIDS sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. A LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with this letter and any IRB/EC correspondence should be retained in the site's regulatory files.

Summary of Revisions

This LoA does not impact the overall design or the study visit schedule for MTN-023/IPM 030. The primary purpose of this LoA is to remove the protocol required Western Blot assay for HIV confirmation to allow for the use of alternative assays (e.g., HIV-1/-2 differentiation assays). In addition, this LoA expands the biological specimens that may be used to test for GC/CT as well as clarifies that participants are to abstain from inserting anything into their vagina prior to monthly visits for a designated period of time.

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

Detailed Listing of Revisions

1. The following revision has been made to the sixth sentence of Section 6.7, *Use of Intravaginal Medications/Products and Practices*, to clarify that participants will be instructed to abstain from inserting anything into the vagina 72 hours prior to each monthly follow-up visit:

   Please note, neither the use of tampons or sex toys, nor participant engagement in coitus is restricted, however, participants will be instructed to abstain from ~~inserting anything into the~~ **these practices and from inserting any non-study** vagina**l products** for 72 hours prior to each **monthly** follow-up visit, including abstaining from penile-vaginal intercourse.

2. A note permitting for the collection of vaginal swabs in lieu of urine for Nucleic acid amplification test (NAAT) for Neisseria gonorrhoeae and Chlamydia trachomatis (GC/CT) has been included throughout the tables in Section 7.0, *STUDY PROCEDURES*, Section 7.10, *Laboratory Evaluations,* and Appendix I: SCHEDULE OF STUDY VISITS AND EVALUATIONS:

Table 5: *Screening Visit*:

Screening Visit		
Component		Procedures
Laboratory	Urine	• Collect urine for: o human chorionic gonadotropin (hCG) o Nucleic acid amplification test (NAAT) for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (GC/CT) ***Note: A vaginal swab may be collected for GC/CT in lieu of urine test, per local standard of care*** o Dipstick UA and/or urine culture, per local standard of care*

Table 6: *Enrollment Visit*, Table 7: *2-Week Study Visit*, Table 8: *4-Week Study Visit*, and Table 9: *8-Week Study Visit,* have been modified as follows:

Component		Procedures
Laboratory	Urine	• Collect urine for: o hCG o NAAT for GC/CT* ***Note: A vaginal swab may be collected for GC/CT in lieu of urine test, per local standard of care*** o Dipstick UA and/or urine culture, per local standard of care*

Table 10: *12-Week Final Clinic Visit/Early Termination Visit*:

12-Week Final Clinic Visit/ Early Termination Visit		
Component		Procedures
Laboratory	Urine	• Collect urine for: o hCG o NAAT for GC/CT ***Note: A vaginal swab may be collected for GC/CT in lieu of urine test, per local standard of care*** o Dipstick UA and/or urine culture, per local standard of care*

Section 7.10, *Laboratory Evaluations:*

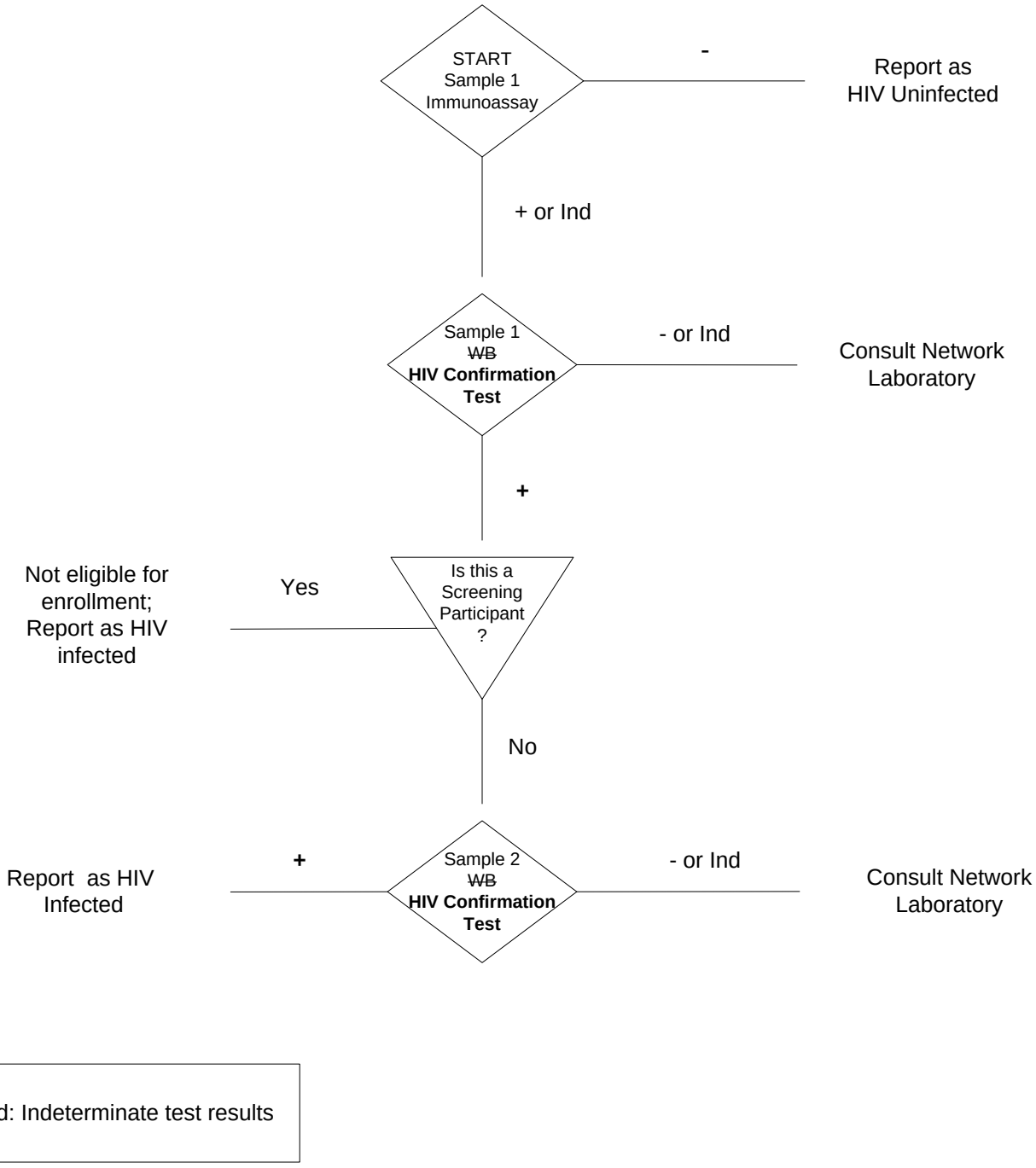
Local Laboratory

- Urine
  - o Urine hCG
  - o Urine NAAT for GC/CT
    (Note: A vaginal swab may be collected for GC/CT in lieu of urine test, per local standard of care)
  - o Dipstick UA and/or urine culture

APPENDIX I: SCHEDULE OF STUDY VISITS AND EVALUATIONS

	SCR	ENR	2-Wk Visit	4-Wk Visit	8-Wk Visit	12-Wk Final Clinic Visit/Early Termination Visit	1-Wk and 13-Wk Termination Phone Call
LABORATORY							
Urine/**Vaginal Swab** NAAT for GC/CT	X	*	*	*	*	X	

3. APPENDIX II: ALGORITHM FOR HIV ANTIBODY TESTING FOR SCREENING AND ENROLLED PARTICIPANTS, has been modified to remove the specific assay to confirm HIV serostatus to allow for the use of alternative assays:



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