Microbicide Trials Network

LETTER OF AMENDMENT #01 TO:

MTN-024/ IPM 031
Phase 2a Safety Study of a Vaginal Matrix Ring Containing Dapivirine in a Postmenopausal Female Population

Version 1.0 dated 21 March 2013
DAIDS Protocol ID: 11915
IND #: 108,743
Date of Letter of Amendment: 30 May 2013

Site Instruction

The following information impacts the MTN-024/IPM 031 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 impacts the sample informed consent. Your IRB/EC will be responsible for determining the process of informing participants of the contents of this Letter of Amendment (LoA).

Implementation

Upon receiving final IRB/EC and any other applicable Regulatory Entity (RE) approval(s) for this LoA, sites should implement the LoA immediately. Sites are still required to submit a LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). 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

The purpose of this LoA is to update the roster, remove the mode by which vaginal fluid is collected for pharmacokinetics (PK), modify the formatting of the Menopausal Rating Scale and the Urogenital Distress Inventory (UDI-6 Short Form) within the tables, as well as the administration schedule for the UDI-6 Short Form, clarify the title of the Product Preference/Acceptability Assessment, allow for the use of a computer or phone to conduct the in-depth interviews, clarify that when the in-depth interview is conducted it may be audio and/or video recorded, and remove the prescriptive text that requires records containing names or other personal identifiers be stored separately from study records marked by code number.

Except for modifications to the Protocol Team Roster, text to be deleted is noted by strikethrough and text to be added is noted below in **bold**.

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1. Contact information for the following individual has been updated in the Protocol Team Roster:

   Ariane van der Straten, PhD, MPH
   BRWG Representative
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   San Francisco, CA 94104 USA
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2. Modifications have been made to Table 6: *4-Week and 8-Week Study Visits*, Table 7: *12-Week Final Clinic Visit/Early Termination*, Section 7.7, *Pharmacokinetics*, Section 10.4.2*, Secondary Endpoints,* Appendix I and Appendix III to allow for greater flexibility regarding the method of vaginal fluid collection:

Table 6: *4-Week and 8-Week Study Visits* and Table 7: *12-Week Final Clinic Visit/Early Termination*

Component		Procedures
Laboratory	Samples	• Pelvic Sample Collection o ~~Tear test strips~~**Vaginal fluid** for PK on a subset of participants (See Section 7.7)

Section 7.7, *Pharmacokinetics,* second through fourth paragraphs have been modified:

A subset of approximately 30 participants across MTN-024/IPM 031 sites will be asked to provide vaginal fluid ~~via tear test strip(s)~~ at Visits 3, 4 and 5. These participants will be asked to opt-in to the PK subset.

An additional 15 participants will be asked to provide vaginal fluid ~~via tear test strip(s)~~ at Visits 3, 4 and 5 and will also provide two cervical tissue biopsy samples at a single time point, Visit 5. These participants will be asked to opt-in to the intensive PK subset.

A total of 96 participants will provide plasma, 45 participants will provide vaginal fluid ~~via tear test strip(s)~~ and 15 will provide cervical tissue.

Table 1: *PK Specimen Collection Schedule*

Visit	Specimens Collected for PK
Visit 3: 4-Week	• Vaginal fluid ~~via tear test strip(s)~~ (n= 45)
Visit 4: 8-Week	• Vaginal fluid ~~via tear test strip(s)~~ (n= 45)
Visit 5: 12-Week	• Vaginal fluid ~~via tear test strip(s)~~ (n= 45)

Section 10.4.2, *Secondary Endpoints, Pharmacokinetic Endpoints, first paragraph, fourth sentence:*

The vaginal fluid will be collected by ~~tear strip~~**an absorptive device** and the cervical tissue will be collected by biopsy in only a subset of women, 45 for ~~tear strip~~**vaginal fluid** and 15 for biopsy.

Appendix I*: Schedule of Study Visits and Evaluations*

	SCR	ENR	4-Wk Visit	8-Wk Visit	12-Wk Final Clinic Visit/Early Termination Visit	1-Wk and 13- Wk Termination Phone Call
LABORATORY (vaginal and cervical swabs as required)						
Vaginal ~~tear test strips~~ **fluid** for PK (subset only)			X	X	X	

Appendix III, *Sample Informed Consent*, *Optional Procedures: Vaginal Fluid and Cervical Tissue Samples* section, second paragraph:

If you agree to provide extra samples, you will have an exam of your vagina using a speculum. To collect the vaginal fluid, study clinicians will ~~insert a strip of special paper to~~ collect fluid from your vagina. ~~These strips~~**This** will be collected at weeks 4, 8, and 12, and used to see how much of the study drug is present in your vaginal fluid**.** You do not need to agree to the collection of this fluid to participate in this study.

3. To allow for more flexible administration of the Menopausal Rating Scale and the Urogenital Distress Inventory (UDI-6 Short Form) Table 5: *Enrollment Visit* and Table 7: *12-Week Final Clinic Visit/ Early Termination Visit* have been modified. In addition, in Table 6: *4-Week and 8-Week Study Visits* and Appendix I the urogenital distress inventory schedule has been modified:

Table 5: Enrollment Visit and Table 7: 12-Week Final Clinic Visit/ Early Termination Visit

Component	Procedures
Clinical	• Review medical history~~, to include:~~ ~~o~~ • Menopausal Rating Scale ~~o~~ • Urogenital Distress Inventory (UDI-6 Short Form)

Table 6: 4-Week and 8-Week Study Visits

Component	Procedures
Clinical	• Review medical history~~, to include:~~ ~~o~~ • ~~Urogenital Distress Inventory (UDI-6 Short Form)~~

Appendix I: Schedule of Study Visits and Evaluations

	SCR	ENR	4-Wk Visit	8-Wk Visit	12-Wk Final Clinic Visit/Early Termination Visit	1-Wk and 13- Wk Termination Phone Call
Urogenital Distress Inventory (UDI-6 Short Form)		X	~~X~~	~~X~~	X	

4. To maintain consistency with Appendix I: *Schedule of Study Visits and Evaluations* the Preference/Acceptability Assessment has been retitled ~~Product Preference/~~Acceptability Assessment, modifications have been made to Table 5: *Enrollment Visit*, Table 6: *4-Week and 8-Week Study Visits*, Table 7: *12-Week Final Clinic Visit/ Early Termination Visit*, and Section 7.8, *Behavioral Measures*.

5. Modifications have been made to allow for in-depth interviews to be conducted via computer or phone and may be audio and video recorded in Section 7.8, *Behavioral Measures*, subsection *In-depth Interview*, first paragraph and *Appendix III*, *Enrollment and Follow-up Procedures: At <u>most</u> study visits you will*, bullet twelve:

   Section 7.8, *Behavioral Measures*, *In-depth Interview*

   A subset of approximately 24 randomized participants across sites will complete an in-depth interview at the 12-Week Final Clinic Visit. The interview will address study VR use and acceptability during the trial. These interviews will be conducted by a trained qualitative interviewer and will follow a semi-structured questionnaire guide and are anticipated to last approximately 45-60 minutes. Participants will be compensated for the completion of the in-depth interview. These interviews may be conducted over the computer **or phone**. The ~~audio from the~~ interview will be recorded and transcribed for analysis.

   Appendix III, *Enrollment and Follow-up Procedures: At <u>most</u> study visits you will*

   - Answer questions about your experience using the VR, including whether or not the ring was removed from or fell out of your vagina, and about any menopausal or bladder symptoms that you may be experiencing. You may use a computer **or phone** to answer these questions or a staff member may ask you these questions. You may also be selected to be interviewed by **a trained** study staff member **who may not work at this facility** at your week 12 clinic visit to talk about your experience using the VR in this clinical trial. This interview may take approximately 45-60 minutes. This conversation will be recorded, but your responses will be kept private and confidential~~,~~**.**~~and~~ **Only** the audio-recording will be **used for data purposes and all recordings will be** destroyed~~ after they have been transcribed~~.

6. Modifications have been made to Section 13.6, *Participant Confidentiality*, second paragraph, fourth and sixth sentences have been removed:

   All study-related information will be stored securely. All participant information will be stored in locked areas with access limited to study staff. All laboratory specimens, study data collection, and administrative forms will be identified by coded number only to maintain participant confidentiality. ~~All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored separately from study records identified by code number~~. All local databases will be secured with password protected access systems. ~~Forms, lists, logbooks, appointment books, and any other listings that link participants' ID numbers to identifying information will be stored in a separate, locked file in an area with limited access.~~ After receiving appropriate approval, all study documents/data will be properly disposed of, including the proper destruction and/or deletion of paper files, electronic study data, and electronic documents. Audio files will be transcribed and destroyed as soon as transcription and analyses are completed. A member of the MTN Behavioral Research Working Group (BRWG) or designee is responsible for ensuring that these files have been destroyed. Participants' study information will not be released without their written permission, except as necessary for review, monitoring, and/or auditing by the following.

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