LETTER OF AMENDMENT #01 TO:

MTN-023/IPM 030

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

Version 2.0, dated 14 January 2015

DAIDS Protocol #11927

IND #108,743

Date of Letter of Amendment: 16 February 2016

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 impacts both the sample informed assent and 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. DAIDS sites are still required to submit a LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). ATN sites are required to submit IRB approval of this LoA to Westat, who will submit required approval documentation to the DAIDS PRO on the sites' behalf. 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 for MTN-023/IPM 030. The primary purpose of this LoA is to discontinue in-depth interviews (IDIs) and short-message service (SMS) activities related to the secondary and exploratory endpoints of acceptability and adherence due to unforeseen funding constraints, which take effect mid-February 2016. It is important to note that all IDIs and SMS data collected to date will be analyzed to address the secondary and exploratory objectives.

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

Detailed Listing of Revisions

1. Section 7.4.5, Visit 9: 24-Week Final Clinic Visit/Early Termination Visit, Table 9, last bullet under Behavioral/Counseling, has been revised to allow the discontinuation of IDIs:

   - Administer In-depth Interview (subset of participants only)
     Note: As of February 2016, In-Depth Interviews are discontinued.

2. Section 7.8.1, Behavioral Evaluations has been updated to discontinue weekly SMS for adherence data collection:

Adherence will be measured at all monthly visits, including the 24-Week Final Clinic Visit/Early Termination Visit, via questions about the duration that the ring was out of the vagina and reasons for expulsion and removal. In addition, participants will receive and reply to weekly text messages during their product use periods about expulsion and removal. **Note: As of February 2016, text messages are discontinued.** Text messaging may ~~also~~ **still** be used as a reminder to adhere to the monthly study visits.

3. Section 7.8.1, Behavioral Evaluations, In-Depth Interview sub-section has been updated to discontinue IDIs:

   Approximately 6 participants per site will be randomized to complete an in-depth qualitative interview that addresses use of study product during the trial. **Note: As of February 2016, In-Depth Interviews are discontinued. The following text describes the In-Depth Interviews that occurred prior to this date.** This interview will be conducted by a trained study interviewer and will follow a structured interview guide. Participants will be asked about their experience with the ring, including questions about their home settings that may have affected ring adherence, social/partner networks that may have affected ring adherence, intercourse experience, partner response to ring use, removal timing, vaginal hygiene, condom use behavior, SMS and image-based ACASI for ease of use, privacy, adherence support and feasibility. The interview will take approximately one hour in duration and will be conducted at the 24-Week Final Clinic Visit/Early Termination Visit.

4. Appendix I: Schedule of Study Visits and Evaluations, last row under Behavioral/Counseling, has been updated to discontinue IDIs:

   In-Depth Interview
   Note: As of February 2016, In-Depth Interviews are discontinued.

5. *New* **Appendix V: Addendum to the Sample Informed Assent & Parent Permission Form and to the Sample Informed Consent Form, Enrollment and Follow-up Procedures Update**, has been added to the protocol to inform participants of the discontinuation of SMS and In-Depth Interview activities:

   [Sites to adapt/format the following text as required. Signatures of participants and their guardians regarding acknowledgement of this protocol modification may or may not be necessary and will be at the discretion of the local Institutional Review Boards (IRBs).]

   As you know, several study procedures aim to assess your overall experience using the vaginal ring. For example, text messages are sent about your ring use. In addition, you were told at the beginning of the study that you might have been selected to take part in an interview at your 24-Week Final Clinic Visit/Early Termination Visit.

   This note is to inform you that text messages and interviews will no longer be completed as part of the MTN-023/IPM 030 study. Study staff may still send you text messages to remind you about study visits but they will no longer ask you questions about using the ring. *[Sites to insert information about reimbursement:]* **This protocol change *[will/will not affect]* the amount of money you receive for the study.**

   It is important that you know that researchers will still review all of the text messages you have already answered about your ring use. Further, interviews that have already been conducted will be analyzed. This information will help researchers to better understand young women's experience using the vaginal ring.

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