

LETTER OF AMENDMENT #01 TO:

MTN-041

Qualitative Assessment of Acceptability of Vaginal Ring (VR) and Oral Pre-exposure Prophylaxis (PrEP) Use during Pregnancy and Breastfeeding

Version 1.0, dated 31 October 2017

DAIDS Protocol #38161
A Non-IND Study

Date of Letter of Amendment: 31 July 2018

Site Instruction

The following information impacts the MTN-041 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. 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 an 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. An 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-041. The primary purpose of this LoA is to clarify data management and documentation storage language for the in-depth interview (IDI) and focus group discussion (FGD) source data/documents. This LoA also adds required consent form language referring to posting of study description and results on ClinicalTrials.gov, corrects a typo in the study description, clarifies that participants in the key informant IDIs and grandmother FGDs will only complete demographic questionnaires, and updates the Investigator Signature Page and Protocol Team Roster.

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

Detailed Listing of Revisions

The following revisions (#1-3) clarify/specify data management and documentation storage for the IDI and FGD source data, including audio recordings:

1. Section 11.1, Data Management Responsibilities, second paragraph, second sentence has been revised, to clarify the source data management process:

~~Interview~~ **Source documents include audio files, transcripts and notes taken during FGDs and IDIs. Transcripts of interviews and group discussions files will be generated in the field using the audio recordings. The transcripts will be electronically transferred to RTI International using a secure File Transfer Protocol (SFTP) site, where they will be uploaded and analyzed managed using a qualitative software package. Interview and group discussion audio files and notes will be kept at the site in a secure, locked location.**

2. Appendix I, Screening and Enrollment Sample Informed Consent Form – Focus Group Discussions, Risks and/or Discomforts, second paragraph, last sentence has been added to disclose to participants how long the audio recordings and other source data will be stored:

[Sites to modify with their site-specific source documentation storage duration requirements if required by their IRBs/IECs: The audio recordings, notes, and analyses from these materials will be kept for a minimum of at least three years after completion of this research.]

3. Appendix II, Screening and Enrollment Sample Informed Consent Form – Key Informant Interviews, Risks and/or Discomforts, second paragraph, last sentence has been added to disclose to participants how long the audio recordings and other source data will be stored:

[Sites to modify with their site-specific source documentation storage duration requirements if required by their IRBs/IECs: The audio recordings, notes, and analyses from these materials will be kept for a minimum of at least three years after completion of this research.]

The following revisions (#4-5) add required consent form language referring to posting of study description and results on ClinicalTrials.gov:

4. Appendix I, Screening and Enrollment Sample Informed Consent Form – Focus Group Discussions, ClinicalTrials.gov section has been added after Research-Related Injury:

CLINICALTRIALS.GOV

A description of this research study will be available on <http://www.ClinicalTrials.gov>. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

5. Appendix II, Screening and Enrollment Sample Informed Consent Form – Key Informant Interviews, ClinicalTrials.gov section has been added after Research-Related Injury:

CLINICALTRIALS.GOV

A description of this research study will be available on <http://www.ClinicalTrials.gov>. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

The following revision updates the Investigator Signature Form language describing the investigators' responsibilities as per DAIDS requirements (see Appendix at the end of this LoA for the updated Investigator Signature Form):

6. Investigator Signature Form, first and second paragraphs:

I, the Investigator of Record (IoR), agree to conduct this study in full accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); standards of the International Conference for Harmonization ~~Conference for~~ **Council for Harmonisation (ICH)** Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., NIH, DAIDS) and institutional policies.

I agree to maintain all study documentation for a minimum of three years after submission of the site's final Financial Status Report to DAIDS, unless otherwise specified by DAIDS or the Microbicide Trials Network (MTN) Leadership and Operations Center (LOC). These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by an agreement with the sponsor. **MTN study records in accordance with protocol-specified protections of participants' confidentiality and with site IRB/IEC policies and procedures. Study records must be maintained on-site for the entire implementation period of the study and a minimum of at least three years after completion of research as per 45 CFR 46.115 (b).** DAIDS/designee will inform the investigator/institution as to when these documents no longer need to be retained.

The following revision corrects a typo in the description of the study:

7. Section 4.1, Identification of Study Design, first sentence:

The MTN-041 ~~trial~~ **study** is a multi-site exploratory study using FGDs and IDIs to identify individual, interpersonal, social and cultural factors that may affect potential uptake of two safe and effective HIV prevention products, the monthly dapivirine VR and daily oral PrEP, by pregnant and breastfeeding women in Africa.

The following revisions (#8-9) clarify that participants in the key informant IDIs and grandmother FGDs will only complete demographic questionnaires:

8. Section 7.1.1, Screening and Enrollment (Focus Group Discussions) – Administrative, Behavioral and Regulatory Procedures, Table 1 - Screening and Enrollment Procedures – Focus Group Discussions, Behavioral component:

Behavioral	• Administer demographic and behavioral questionnaire(s) *
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* **Grandmother group will only complete the demographic questionnaire(s)**

9. Section 7.2.1, Screening and Enrollment (Key Informant Interviews) – Administrative, Behavioral and Regulatory Procedures, Table 2 - Screening and Enrollment Procedures – Key Informant Interviews, Behavioral component:

Behavioral	• Administer demographic and behavioral questionnaire(s)
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Additional modifications include:

10. Section 1.4, Data Centers:

Women's Global Health Imperative Program
Research Triangle Institute (RTI) International
351 California Street, Suite 500
San Francisco, CA 94104 USA

11. Protocol Team Roster

Update:

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

APPENDIX: MTN-041 INVESTIGATOR SIGNATURE FORM

MTN-041

Qualitative Assessment of Acceptability of Vaginal Ring (VR) and Oral Pre-exposure Prophylaxis (PrEP) Use during Pregnancy and Breastfeeding

INVESTIGATOR SIGNATURE FORM

Version 1.0; October 31, 2017

Letter of Amendment #01; July 31, 2018

A Study of the Microbicide Trials Network

Funded by:

Division of AIDS (DAIDS), US National Institute of Allergy and Infectious Diseases
US Eunice Kennedy Shriver National Institute of Child Health and Human Development
US National Institute of Mental Health
US National Institutes of Health (NIH)

IND Sponsor:

A Non-IND Study (DAIDS Protocol ID: 38161)

I, the Investigator of Record (IoR), agree to conduct this study in full accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); standards of the International Council for Harmonisation (ICH) Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., NIH, DAIDS) and institutional policies.

I agree to maintain MTN study records in accordance with protocol-specified protections of participants' confidentiality and with site IRB/IEC policies and procedures. Study records must be maintained on-site for the entire implementation period of the study and a minimum of at least three years after completion of research as per 45 CFR 46.115 (b). DAIDS/designee will inform the investigator/institution as to when these documents no longer need to be retained.

I have read and understand the information in this protocol and will ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about the obligations incurred by their contribution to the study.

Name of Investigator of Record (print)

Signature of Investigator of Record

Date