

LETTER OF AMENDMENT #01 TO:

MTN-039

A Phase 1 Open Label Safety and Pharmacokinetic Study of Rectal Administration of a Tenofovir Alafenamide/Elvitegravir Insert at Two Dose Levels

Version 1.0, dated March 6, 2019

**DAIDS Protocol #38470
IND #145334**

Date of Letter of Amendment: 20 September 2019

Site Instruction

The following information impacts the MTN-039 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

This LoA does not impact the overall design or the study visit schedule for MTN-039. The purpose of this LoA is to add an exclusion criterion for hepatitis B infection, specify that participants who have been administered approved or other investigational pre-exposure prophylaxis (PrEP) for HIV prevention within 3 months of enrollment will be excluded, and correct the use of rectal insert to refer to the insert used in this study.

Unless otherwise noted, 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 addition was made to exclusion criterion #1 in Section 5.3, *Exclusion Criteria*, to add hepatitis B infection to the list of laboratory results that would lead to potential participants being excluded from the study:

g) Positive hepatitis B surface antigen (HBsAg) test result.

The following revisions (2-5) were made to add a hepatitis B surface antigen test to the Screening Visit.

2. Laboratory-Blood section of Table 10: Screening Visit in Section 7.2, *Screening Visit*:

- **HBsAg**

3. Local Laboratory-Blood specimens list of bullet points in Section 7.11, Laboratory Evaluations:

- **HBsAg**

4. Laboratory-Blood section of table in Appendix I, Schedule of Study Visits and Evaluations:

HBsAg	X					
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5. Second sub-bullet of eighth bullet point in Screening Visit section of Appendix III, Sample Informed Consent Form (Screening, Enrollment, Long-term Storage and Future Testing):

- To test for infections that typically are passed through sex, including HIV, **hepatitis B** and syphilis

6. The following revision was made to exclusion criterion #4 in Section 5.3, *Exclusion Criteria*, to specify that participants who have been administered approved or other investigational PrEP for HIV prevention within 3 months of enrollment will be excluded:

Use of **approved or other investigational** pre-exposure prophylaxis (PrEP) for HIV prevention within 3 months prior to Enrollment, and/or anticipated use and/or unwillingness to abstain from PrEP during trial participation.

The following revisions (7-10) were made to correct the use of rectal insert to refer to the insert used in this study

7. Section 6.4.1, the first sentence:

CONRAD (the organization that supplies the ~~rectal insert~~ **TAF/EVG Insert**) will oversee the manufacture and analysis/release (Patheon, Whitby, ON, Canada) of the study product under current Good Manufacturing Practices (cGMP).

8. Sample Informed Consent, under Is it possible that I may be taken out of the study without my consent, first bullet point:

- The study is cancelled by the US FDA, US NIH, CONRAD (the organization that supplies the ~~rectal~~ **study** insert), the US Office for Human Research Protections (OHRP), MTN, the local or other government or regulatory agency, or the Institutional Review Board (IRB).

9. Sample Informed Consent, under (If applicable) If You Become Pregnant, first sentence in second paragraph:

We do not know what effect TAF/EVG Insert has on pregnancy, including its effect on the fetuses of women who use the ~~rectal~~ **study** insert when pregnant, or the babies of women who use the insert when breastfeeding.

10. Sample Informed Consent, under Who will know about my participation in this research study, fourth bullet point in third paragraph:

- Representatives of CONRAD, the nonprofit organization that supplies the study ~~rectal~~ insert

11. Protocol Signature Page was updated to include Letter of Amendment #1; it is appended to the end of this document.

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

MTN-039

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a Tenofovir Alafenamide/Elvitegravir Insert at Two Dose Levels**

INVESTIGATOR SIGNATURE FORM

Version 1.0; March 6, 2019

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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 Holder:

DAIDS (DAIDS Protocol ID: 38470)

I, the Investigator of Record, 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); applicable U.S. Food and Drug Administration regulations; standards of the International Conference for Harmonization 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 at least two years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by an agreement with the sponsor. DAIDS will inform the investigator/institution as to when these documents no longer need to be retained

I have read and understand the information in the Investigator's Brochure(s), including the potential risks and side effects of the products under investigation, 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