LETTER OF AMENDMENT #02 TO:
MTN-026

A Randomized, Double Blind, Placebo-Controlled, Phase 1 Safety and Pharmacokinetic Study of Dapivirine Gel (0.05%) Administered Rectally to HIV-1 Seronegative Adults

Version 2.0, dated 21 July 2017

DAIDS Protocol #12021
IND #136320

Date of Letter of Amendment: 6 July 2018

Site Instruction

The following information impacts the MTN-026 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-026. The purposes of this LoA are to add language to describe the inclusion of study data on ClinicalTrials.gov web site in the sample informed consent, modify the language of an exploratory endpoint, and update a link to DAIDS laboratory policy.

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. In Appendix III (Sample Informed Consent form), under the section "NEW INFORMATION", the following language has been added after the first paragraph:

   A description of this clinical trial 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.

2. An Exploratory Endpoint has been modified throughout the protocol to better reflect planned analyses:
   Changes in HIV-1 ~~p24~~ levels in colorectal explant culture supernatant

3. In Section 7.17, a link to DAIDS laboratory policy has been updated:

   The study site will adhere to the standards of good clinical laboratory practice (~~https://www.niaid.nih.gov/sites/default/files/gclp.pdf~~ **https://www.niaid.nih.gov/sites/default/files/laboratorypolicy1.pdf**) in accordance with current DAIDS Laboratory Requirements…

4. The Protocol Signature Page was updated to include Letter of Amendment #02; 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-026

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INVESTIGATOR SIGNATURE FORM

Version 2.0; July 21, 2017
Letter of Amendment #01, March 22, 2018
Letter of Amendment #02, July 6, 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

IND Sponsor:

DAIDS (DAIDS Protocol ID: 12021)

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