

**LETTER OF AMENDMENT #1 TO:
MTN-037**

A Phase 1 Safety and Pharmacokinetic Study of PC-1005 (MIV-150/Zinc Acetate/Carrageenan Gel) Administered Rectally to HIV-1 Seronegative Adults

Version 1.0, dated 9 November 2017

**DAIDS Protocol #35122
IND #138101**

Date of Letter of Amendment: 26 July 2018

Site Instruction

The following information impacts the MTN-037 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-037. The primary purpose of this LoA is to clarify data management and documentation storage information for the in-depth interview (IDI) source data. Other changes include adding the IND number to the protocol, updating web links in the protocol, clarifying that the ♀ symbol refers to participants with female anatomy at birth, modifying an exploratory endpoint, and updating both Appendix II, Algorithm for HIV Testing for Screening And Follow-up and the Protocol Roster.

Unless otherwise noted, text to be deleted is noted by ~~strike through~~ and text to be added is noted below in **bold**.

Detailed Listing of Revisions

The following revisions (#1-3) have been made to identify IDI source data and clarify source data storage:

1. Section 7.9, Behavioral Assessments, third paragraph:

The in-depth interviews will include, among other topics, questions on user acceptability of the product, user-centered suggestions for product design and delivery, and experiences during the volume escalation trial, including reactions to the BD™ Luer-Lok™ Tip syringe with cap and rectal administration tip, and administration method. **The interview notes, recording and transcript from the in-depth interview will be considered as source documentation.**

2. Section 11.1, *Data Management Responsibilities*, second paragraph:

Transcriptions of interviews will be generated using the audio files recorded at University of Pennsylvania. Both the audio files and the transcripts will be uploaded and managed using a qualitative software package. Interview notes will be kept at the University of Pennsylvania in the participant files.

3. Appendix III, 24-Hour Post-dosing Visits (Visits 4, 6, and 8) section, the 4th bullet point:

Have a computer-administered interview **at Visit 8**. This interview may take approximately 30-45 minutes and will occur over video chat, e.g., Google Hangout, Skype, FaceTime, etc. This conversation will be recorded, but your responses will be kept private and confidential, ~~and the audio recording will be destroyed after it has been transcribed and checked.~~ **[Sites to modify with their site-specific source documentation storage duration requirements if longer than what is stated here: The audio recording, notes, and analyses from these materials will be kept for at least two years after the gel is approved for marketing or two years after all developmental research on the gel is stopped.]**

The following revisions (#4, 5) have been made to update the website address of the Study Specific Procedures (SSP) Manual:

4. Section 7, *Study Procedures*, first paragraph, last sentence:

Detailed instructions to guide and standardize procedures as well as information regarding the study visit windows are provided in the MTN-037 SSP Manual available at <http://www.mtnstopshiv.org/studies>.

5. Section 7.12, *Specimen Management*, first paragraph, first sentence:

Study sites will adhere to the standards of good clinical laboratory practice (<https://www.niaid.nih.gov/sites/default/files/gclp.pdf>), in accordance with current DAIDS Laboratory Requirements, MTN-037 SSP Manual (<http://www.mtnstopshiv.org/studies>) and site SOPs for proper collection, processing, labeling, transport, and storage of specimens to standardize procedures.

The following revisions (#6-7) have been made to an exploratory endpoint to better reflect planned analyses:

6. The Protocol Summary and Section 4.2:

- Changes in HIV-1 p24 levels in colorectal explant culture supernatant

7. Section 10.7.2, Pharmacokinetic/Pharmacodynamic Analysis section:

Ex vivo HIV explant data will use ~~cumulative~~ **p24 virus levels** to compare baseline with study product.

Other revisions:

8. Page 1 has been revised to add the IND number to the protocol title page:

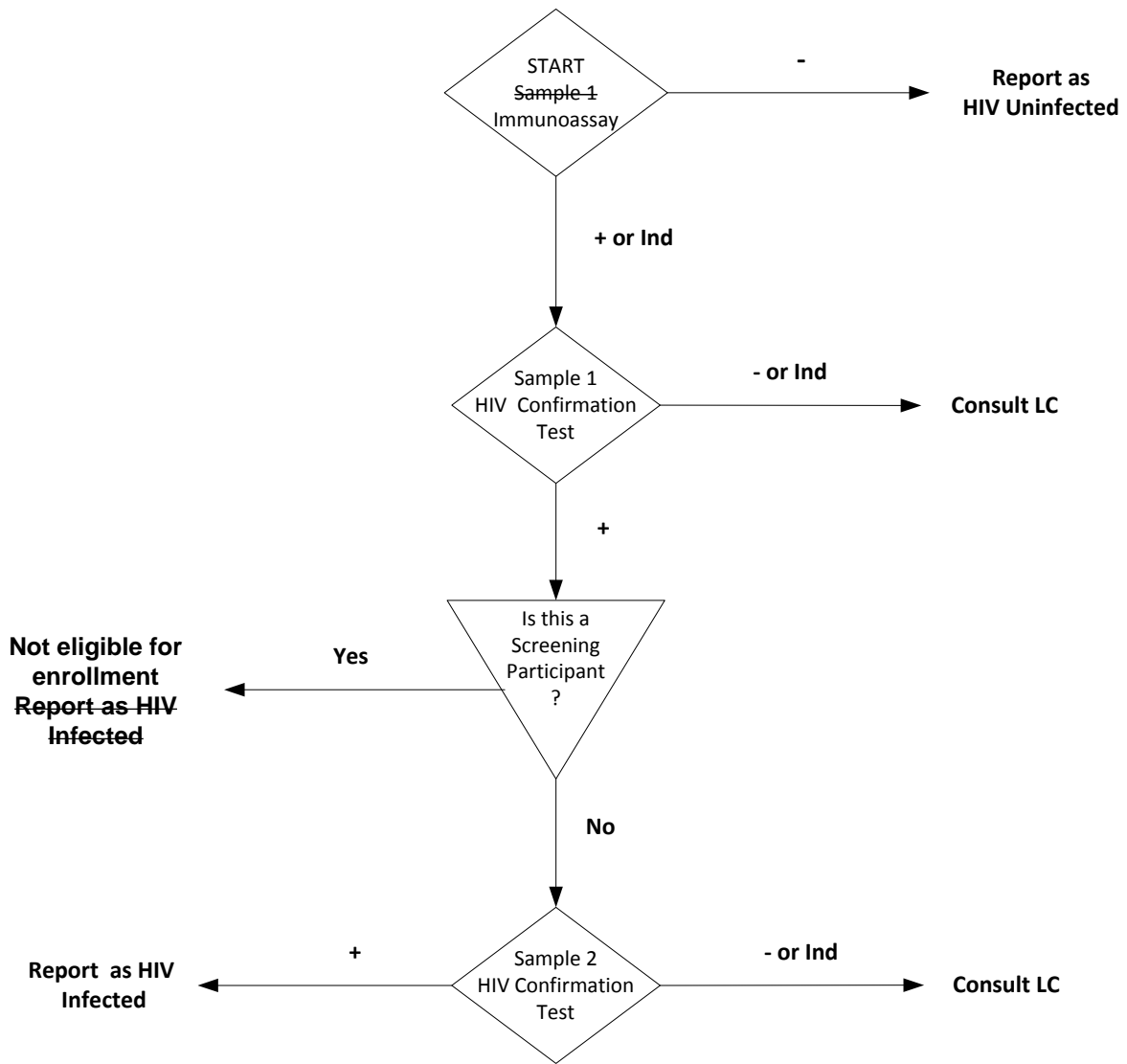
IND#: ~~XXXXX~~ **138101**

9. The following revision was made to the footnotes of Table 11 to Table 17 in Section 7 of the protocol and in the footnotes of Appendix I:

~~♀ Female participants~~ **Participants assigned female sex at birth**

10. Appendix II, Algorithm for HIV Testing for Screening And Follow-up, has been updated as below:

- In the top decision diamond, the text “Sample 1” has been deleted;
- In the step pointed to by the first left-pointing connector arrow, the text “Report as HIV Infected” has been deleted.



Ind: Indeterminate test results
LC: Laboratory Center

11. Protocol Team Roster

Removal: Sherri Johnson

Additions:

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12. 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-037

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INVESTIGATOR SIGNATURE FORM

Version 1.0; November 9, 2017
Letter of Amendment #01, July 26, 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 Holder:

DAIDS (DAIDS Protocol ID: 35122)

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