

LETTER OF AMENDMENT #02 TO:

MTN-032

Assessment of ASPIRE and HOPE Adherence

Version 2.0, dated 5 September 2017

**DAIDS Protocol #12058
A Non-IND Study**

Date of Letter of Amendment: 21 August 2018

Site Instruction

The following information impacts the MTN-032 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 a 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. 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-032. The primary purpose of this LoA is to include language allowing international regulatory authority review of study records in both the protocol and informed consent. This LoA also clarifies data management and documentation storage language for the in-depth interview (IDI) and focus group discussion (FGD) source data/documents, adds required consent form language referring to the Network's Certificate of Confidentiality (CoC) as well as to posting of study description and results on ClinicalTrials.gov, 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 (#1-6) allow international regulatory authority review of study records:

1. Section 12, Clinical Site Monitoring, last paragraph, second sentence:

The IoR/designee also will allow inspection of all study-related documentation by authorized representatives of the US OHRP, NIH, NIAID, and/or contractors of the NIH, and other local, ~~or~~ **US or international** regulatory authorities, and representatives of the MTN, as needed.

2. Section 13.1, Institutional Review Boards/Ethics Committees, first paragraph, last sentence:

The IoR/**designee** will permit audits by the NIH, local authorities, site IRBs/ECs, the MTN, OHRP, **other local, US, or international regulatory authorities**, or any of their appointed agents.

3. Section 13.6, Participant Confidentiality, first bullet point:

Representatives of the US Federal Government, including the US OHRP, NIH, and/or contractors of the NIH, and other local, ~~and~~ **US, or international** regulatory authorities

4. Appendix I, Screening and Enrollment Sample Informed Consent Form – Phase 1 (ASPIRE) Participants, Confidentiality, fourth bullet point:

Representatives of the US Federal Government, including the US OHRP, NIH and/or contractors of NIH, and other local, ~~and-US,~~ **or international** regulatory authorities

5. Appendix II, Screening and Enrollment Sample Informed Consent Form – Phase 2 (HOPE) Participants, Confidentiality, fourth bullet point:

Representatives of the US Federal Government, including the US OHRP, NIH and/or contractors of NIH, and other local, ~~and-US,~~ **or international** regulatory authorities

6. Appendix III, Screening and Enrollment Sample Informed Consent Form – HOPE Participants' Male Partners, Confidentiality, fourth bullet point:

Representatives of the US Federal Government, including the US OHRP, NIH and/or contractors of NIH, and other local, ~~and-US,~~ **or international** regulatory authorities

The following revisions (#7-10) clarify/specify data management and documentation storage for the IDI and FGD source data, including audio recordings:

7. 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 (FTP) site, where they will be uploaded and managed analyzed using a qualitative software package. Interview and group discussion audio files and notes will be kept at the site in the participant or group discussion files, respectively.**

8. Appendix I, Screening and Enrollment Sample Informed Consent Form – Phase 1 (ASPIRE) Participants, Risks and/or Discomforts, second paragraph, sixth sentence has been revised and last sentence has been added, to disclose to participants how long the audio recordings and other source data will be stored:

~~Your audio recordings and any other~~ **The information that links you to the research materials will be kept in a secure location that will be accessed only by members of the MTN-032 study team for the purposes of this research. Your voice recordings will also be kept in a secure location and only people involved with the study will have access to these recordings. Study leaders will make sure this happens. [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.]**

9. Appendix II, Screening and Enrollment Sample Informed Consent Form – Phase 2 (HOPE) Participants, Risks and/or Discomforts, second paragraph, sixth sentence has been revised and last sentence has been added, to disclose to participants how long the audio recordings and other source data will be stored:

~~Your audio recordings and any other~~ **The information that links you to the research materials will be kept in a secure location that will be accessed only by members of the MTN-032 study team for the purposes of this research. Your voice recordings will also be kept in a secure location and only people involved with the study will have access to these recordings. Study leaders will make sure this happens. [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.]**

10. Appendix III, Screening and Enrollment Sample Informed Consent Form – HOPE Participants' Male Partners, Risks and/or Discomforts, second paragraph, sixth sentence has been revised and last sentence has been added, to disclose to participants how long the audio recordings and other source data will be stored:

Your audio recordings and any other The information that links you to the research materials will be kept in a secure location that will be accessed only by members of the MTN-032 study team for the purposes of this research. ~~Your voice recordings will also be kept in a secure location and only people involved with the study will have access to these recordings. Study leaders will make sure this happens.~~ **[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 (#11-13) add required consent form language referring to posting of study description and results on ClinicalTrials.gov:

11. Appendix I, Screening and Enrollment Sample Informed Consent Form – Phase 1 (ASPIRE) Participants, 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.

12. Appendix II, Screening and Enrollment Sample Informed Consent Form – Phase 2 (HOPE) Participants, 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.

13. Appendix III, Screening and Enrollment Sample Informed Consent Form – HOPE Participants' Male Partners, 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 revisions (#14-16) add required consent form language disclosing to participants the Network's CoC and its limitations:

14. Appendix I, Screening and Enrollment Sample Informed Consent Form – Phase 1 (ASPIRE) Participants, Confidentiality section, final sentence:

[Sites to remove/amend the following if instructed by their local IRB/IEC:]

The researchers will do everything they can to protect your privacy. **In addition to the efforts of the study staff to help keep your personal information private, we have obtained a Certificate of Confidentiality from the US Federal Government. This Certificate protects study investigators from being forced to tell people who are not connected with this study, such as the court system, about your participation or information you give for study purposes. With limited exceptions, researchers may not disclose names, information or documents containing information you give for study purposes. This Certificate does not expire.**

However, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, they will be required to tell the proper authorities. Also, we may have to release your information if the organization that is funding this study, *[Funding Agency]*, requests the information, or if the FDA, EMA or other regulatory body tells us to release this information. This Certificate does not prevent you from releasing information about yourself and your participation in the study.

15. Appendix II, Screening and Enrollment Sample Informed Consent Form – Phase 2 (HOPE) Participants, Confidentiality section, final sentence:

[Sites to remove/amend the following if instructed by their local IRB/IEC:]

The researchers will do everything they can to protect your privacy. In addition to the efforts of the study staff to help keep your personal information private, we have obtained a Certificate of Confidentiality from the US Federal Government. This Certificate protects study investigators from being forced to tell people who are not connected with this study, such as the court system, about your participation or information you give for study purposes. With limited exceptions, researchers may not disclose names, information or documents containing information you give for study purposes. This Certificate does not expire.

However, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, they will be required to tell the proper authorities. Also, we may have to release your information if the organization that is funding this study, [*Funding Agency*], requests the information, or if the FDA, EMA or other regulatory body tells us to release this information. This Certificate does not prevent you from releasing information about yourself and your participation in the study.

16. Appendix III, Screening and Enrollment Sample Informed Consent Form – HOPE Participants’ Male Partners, Confidentiality section, final sentence:

[Sites to remove/amend the following if instructed by their local IRB/IEC:]

The researchers will do everything they can to protect your privacy. In addition to the efforts of the study staff to help keep your personal information private, we have obtained a Certificate of Confidentiality from the US Federal Government. This Certificate protects study investigators from being forced to tell people who are not connected with this study, such as the court system, about your participation or information you give for study purposes. With limited exceptions, researchers may not disclose names, information or documents containing information you give for study purposes. This Certificate does not expire.

However, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, they will be required to tell the proper authorities. Also, we may have to release your information if the organization that is funding this study, [*Funding Agency*], requests the information, or if the FDA, EMA or other regulatory body tells us to release this information. This Certificate does not prevent you from releasing information about yourself and your participation in the study.

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):

17. 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); applicable U.S. Food and Drug Administration (FDA) regulations; standards of the International Conference for Harmonization **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. DAIDS will inform the investigator/institution as to when these documents no longer need to be retained **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.**

Additional minor modifications include:

18. Section 1.4, Data Centers, Qualitative Data Center:

Women’s Global Health Imperative Program

Research Triangle Institute (RTI) International
351 California Street, Suite 500
San Francisco, CA 94104 USA

19. Protocol Team Roster – Updates:

~~Research Triangle Institute (RTI) International~~ **MTN Qualitative Data Management Center (QDMC)**

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20. Protocol Team Roster – Additions:

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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-032 INVESTIGATOR SIGNATURE FORM

MTN-032

Assessment of ASPIRE and HOPE Adherence

INVESTIGATOR SIGNATURE FORM

Version 2.0; September 5, 2017
Letter of Amendment #01; March 28, 2018
Letter of Amendment #02; August 21, 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: 12058)

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