LETTER OF AMENDMENT #02 TO:

MTN-008

DAIDS Document ID 10805

Expanded Safety Investigation of Tenofovir 1% Gel in Pregnancy and Lactation
Version 1.0/29 March 2010
IND # 55,690

Letter of Amendment Date: February 23, 2011

Instructions to Study Sites from the Division of AIDS

The following information impacts the MTN-008 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 may also impact the sample informed consent. Your IRB/EC will be responsible for determining the process of informing subjects of the contents of this letter of amendment.

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 an 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. An LoA registration notification from the DAIDS PRO is <u>not</u> 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 and Rationale

The primary reason for this LoA is to update the informed consent documents to include additional information regarding the risks and benefits of participation in MTN-008. This LoA does not impact the overall design and study visit schedule for MTN-008. This LoA provides updates/clarification on the following items:

1. Sample Informed Consent documents updated to describe the level of risk and possible benefits associate associated with participation in MTN-008.
2. Clarifying language was added to APPENDIX VI: Sample Informed Consent Document for Pregnancy Cohort- Mothers and Infants (Enrollment), Study Procedures, to note that the storage of blood for plasma archive will be limited to the length of study participation, unless a participant consents to long-term storage and future testing.

Implementation

Except for modifications to the Protocol Team Roster, text to be deleted is generally noted by ~~strikethrough~~ and text to be added is noted below in **bold**.

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Detailed Listing of Revisions

1. APPENDIX IV: Sample Informed Consent (Screening- Pregnancy Cohort) and APPENDIX V: Sample Informed Consent (Screening- Lactation Cohort), APPENDIX VI: Sample Informed Consent for Pregnancy Cohort- Mothers and Infants (Enrollment), and APPENDIX VII: Sample Informed Consent for Lactation Cohort (Enrollment), are updated to include language regarding the level of risk and possible benefits associated with participation in MTN-008:

   In APPENDIX IV: Sample Informed Consent (Screening- Pregnancy Cohort), the following edits are made to the *Introduction*, first and second (new) paragraphs:

You are being asked to screen for the research study named above. This study is for healthy women **between 18-40 years of age** who are pregnant or breastfeeding and their babies **(after they are born)**. **Research in pregnancy is allowed if it is of minimal risk (for example, no more risk than a routine clinic visit or a blood draw), or if there is the possibility of direct benefit for the mother or fetus. Your use of tenofovir gel as part of this study may expose your fetus to greater than minimal risk. However, if you are sexually active during this study there is a possibility that tenofovir gel may protect you from contracting HIV and genital herpes, and since these infections can be passed to your baby, this may therefore also protect your baby from contracting these infections. If you do not expect to be sexually active during the seven day period that you would use tenofovir gel, then do not enroll in this study.**

Before you decide whether to be screened for this study, we would like to explain ~~the screening procedures~~**its purpose,** review ~~their~~**its** risks and benefits, discuss what is expected of you **and your baby,** and help you understand what you can expect from the study site. The United States National Institutes of Health is funding this study.

In APPENDIX V: Sample Informed Consent (Screening- Lactation Cohort), the following edits are made to the *Introduction*, first and second (new) paragraphs:

You are being asked to screen for the research study named above. This study is for healthy women **between 18-40 years of age** who are pregnant or breastfeeding and their babies **(after they are born)**. **Research in children is allowed if it is of minimal risk (for example, no more risk than a routine clinic visit or a blood draw), or if there is the possibility of direct benefit for the child. Your use of tenofovir gel as part of this study may expose your infant to greater than minimal risk. However, if you are sexually active during this study there is a possibility that tenofovir gel may protect you from contracting HIV and genital herpes, and since these infections can be passed to your baby, this may therefore also protect your baby from contracting these infections. If you do not expect to be sexually active during the seven day period that you would use tenofovir gel, then do not enroll in this study.**

Before you decide whether to be screened for this study, we would like to explain ~~the screening procedures~~**its purpose,** review ~~their~~**its** risks and benefits, discuss what is expected of you **and your baby,** and help you understand what you can expect from the study site. The United States National Institutes of Health is funding this study.

In APPENDIX VI: Sample Informed Consent for Pregnancy Cohort- Mothers and Infants (Enrollment), the following edits are made to the *Introduction*, first and second (new) paragraphs:

You are being asked to volunteer for the research study named above. This study is for healthy women **between 18-40 years of age** who are pregnant or breastfeeding ~~a~~nd their babies (after they are born). **Research in pregnancy is allowed if it is of minimal risk (for example, no more risk than a routine clinic visit or a blood draw), or if there is the possibility of direct benefit for the mother or fetus. Your use of tenofovir gel as part of this study may expose your fetus to greater than minimal risk. However, if you are sexually active during this study there is a possibility that tenofovir gel may protect you from contracting HIV and genital herpes, and since these infections can be passed to your baby, this may therefore also protect your baby from contracting these infections. If you do not expect to be sexually active during the seven day period that you would use tenofovir gel, then do not enroll in this study.**

Before you decide whether to be in this study, we would like to explain its purpose, review its risks and benefits, discuss what is expected of you and your baby, and help you understand what you can expect from the study site. The United States National Institutes of Health is funding this study.

In APPENDIX VII: Sample Informed Consent for Lactation Cohort (Enrollment), the following edits are made to the *Introduction*, first, second (new) and third (new) paragraphs:

You are being asked to volunteer for the research study named above. This study is for **healthy** women **between 18-40 years of age** who are pregnant **or** breastfeeding and their babies **(after they are born). Research in children is allowed if it is of minimal risk (for example, no more risk than a routine clinic visit or a blood draw), or if there is the possibility of direct benefit for the child. Your use of tenofovir gel as part of this study may expose your infant to greater than minimal risk. However, if you are sexually active during this study there is a possibility that tenofovir gel may protect you from contracting HIV and genital herpes, and since these infections can be passed to your baby, this may therefore also protect your baby from contracting these infections. If you do not expect to be sexually active during the seven day period that you would use tenofovir gel, then do not enroll in this study.**

This part of the study will include mother-infant pairs. This means that both you and your baby will be asked to join this study together.

Before you decide whether to be in this study, we would like to explain its purpose, review its risks and benefits, discuss what is expected of you and **your baby, and** help you understand what you can expect from the study site. ~~This part of the study will include mother-infant pairs. This means that both you and your baby will be asked to join this study together.~~ The United States National Institutes of Health is funding this study.

In APPENDIX VI: Sample Informed Consent for Pregnancy Cohort- Mothers and Infants (Enrollment), Risks and/or Discomforts, fourth paragraph, first sentence and in APPENDIX VII: Sample Informed Consent for Lactation Cohort (Enrollment), Risks and/or Discomforts, fifth paragraph, first sentence the following edits are made:

A small amount of tenofovir may pass from the vaginal gel into your blood or breast milk~~.~~**; your use of tenofovir gel as part of this study may expose your baby to greater than minimal risk.**

In APPENDIX VI: Sample Informed Consent for Pregnancy Cohort- Mothers and Infants (Enrollment) and APPENDIX VII: Sample Informed Consent for Lactation Cohort (Enrollment), BENEFITS, the following text is added, third paragraph (new):

I**f you are sexually active during this study there is a possibility that tenofovir gel may protect you from contracting HIV and genital herpes, and since these infections can be passed to your baby, this may therefore also protect your baby from contracting these infections.**

2. In APPENDIX VI: Sample Informed Consent Document for Pregnancy Cohort- Mothers and Infants (Enrollment), Study Procedures, 3rd paragraph, 3rd bullet, previously modified language is further clarified:

- Give blood] [site to insert amount] to check the health of your blood, liver and kidneys; some of this blood will be saved **for the duration of your participation in MTN-008** and may also be tested for HIV, if you have a positive HIV test while you are in the study. **If you consent to the long-term storage and future testing of specimens you will be asked to sign a separate consent document and these leftover blood samples may be stored for a period beyond your participation in MTN-008, but only if you provide your permission.**

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