

**DATE:** March 31, 2009  
**FROM:** Z. Mike Chirenje, MD, FRCOG and Jeanne Marrazzo, MD, MPH  
**TO:** MTN-003 Clinical Research Sites  
**SUBJECT:** MTN-003 Letter of Amendment #01, dated March 31, 2009

The information contained in the accompanying Letter of Amendment (LoA) impacts the MTN-003 study and must be forwarded to your Institutional Review Board (IRB) and/or Ethics Committee (EC) as soon as possible for their information and review. Site IRBs/ECs are responsible for assessing whether and how the changes included in the LoA are communicated to study participants. All IRB/EC requirements must be followed. As this LoA does not impact the overall risk-to-benefit profile of study participation or the informed consent documents, re-consenting is unnecessary. This LoA and all associated IRB/EC correspondence should be filed in essential documents files for MTN-003.

One purpose of the LoA is to eliminate a discrepancy between the MTN-003 protocol Version 1.0 and the Sample Informed Consent Form (Enrollment) regarding PBMC extraction from blood samples. Although the protocol includes a laboratory procedure for PBMC extraction from blood, the consent does not include reference to this procedure; therefore, blood cannot be collected for PBMC extraction. PBMC extraction is being removed from the protocol through this LoA to eliminate this discrepancy. Even prior to IRB/EC approval of this LoA, it is important that you do not collect any blood for PBMC extraction because the participants will not have consented to this.

Another purpose of this LoA is to allow site discretion to defer the informed consent process for specimen storage and possible future research testing from the Enrollment Visit to a subsequent visit to reduce burden on participants. Version 1.0 of the protocol states that consent for specimen storage will be obtained at the Enrollment Visit. Until the LoA has been approved by your IRB/EC, if a participant appears to be too tired or is otherwise unable to complete the stored specimen consent process at her Enrollment Visit, please document that in her record and defer the process until her next visit.

The LoA also clarifies the product use and adherence assessments that can be discontinued during periods of time when the participant is on product hold or discontinuation. There will be a separate ACASI questionnaire that site staff can select for participants with a product hold/discontinuation of 4 weeks or more prior to the visit at which ACASI is administered. Appropriate adherence assessment is addressed by the current Case Report Forms and ACASI instruments. Therefore, no additional action is required on the part of site staff.

Another item being addressed in the LoA is the elimination of reporting of fetal losses as adverse events (AEs) and expedited adverse events (EAEs). Prior to IRB/EC approval of this LoA, fetal losses must be reported as AEs and EAEs per Version 1.0 of the protocol. After IRB/EC approval has been obtained, fetal losses will no longer be reportable as specified in this LoA.

The LoA also contains several minor clarifications and updates, including updates to the Protocol Team Roster.

Please contact the MTN CORE if you have any questions or concerns about the information contained in this memo or in the LoA.