Microbicide Trials Network

CLARIFICATION MEMO #01 TO:

MTN-043

A Phase 3B, Randomized, Open-Label, Safety, and Drug Detection Study of Dapivirine Vaginal Ring and Oral TRUVADA® in Breastfeeding Mother-Infant Pairs

DAIDS Protocol #: 38591

IND#: 139,598

Version 1.0 / 24 July 2019

Clarification Memo Date: 28 May 2020

Section 1: Summary of Clarifications and Rationale

The procedures clarified in this Clarification Memorandum (CM) have been approved by the NIAID Medical Officer and are to be implemented immediately upon issuance. IRB/IEC approval of this CM is not required by the sponsor; however, investigators may submit the CM to the IRB/IEC overseeing the study at their site for information. This CM is official MTN-043 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-043. No change in informed consent is necessitated by or included in this CM.

This document includes information related to COVID-19's impact on study implementation. This document clarifies that the content of the planned behavioral assessments may include questions related to the impact of the COVID-19 pandemic on the participants' behavioral context for study product use. This document also clarifies that the overall study duration may be affected by COVID-19 closures, and that changes to procedures may be implemented for immediate hazards to participants or for public health emergencies. This CM also corrects an error in the Study Visit Schedule Figure and updates the Protocol Team Roster.

Section 2: Implementation

With the exception of updates to the protocol team roster, text to be deleted is noted below with a ~~strikethrough~~, text to be added is in **bold**, and text in ***bold italics*** is not to be added, but to serve as a clarification of the implementation item in question. This information will be included in the protocol the next time the protocol is updated.

1.) The following clarification applies to Section 7.11, *Behavioral Evaluations*:

At the Enrollment Visit and Product Use End Visit (Visit 7), additional questions may be asked related to COVID-19's potential influence on the context of participants' study product use, in order to explore the impact of the pandemic on study product adherence and acceptability.

2.) The following clarification applies to Protocol Summary, *Study Duration;* Section 4.4., *Time to Complete Accrual*; and Section 10.6, *Participant Accrual, Follow-up and Retention:*

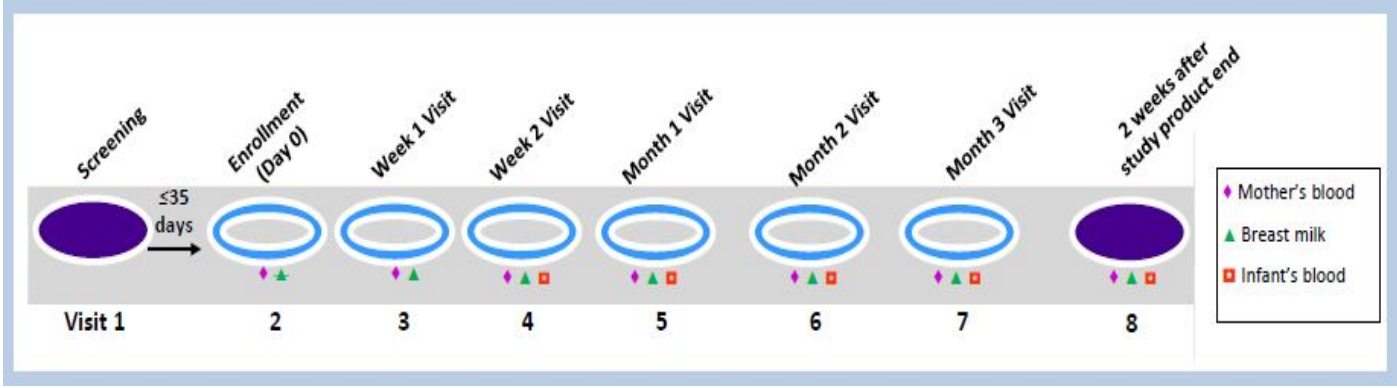
Overall study duration - from first enrollment through closure of all follow-up - may be longer than planned if temporary site closures due to the COVID-19 pandemic cause a delay or pause in enrolling participants at one or more research sites.

3.) The following clarification applies to Section 13, *Human Subjects Protections:*

Changes to this protocol may be implemented by investigators prior to IRB/IEC approval, if those changes are required to eliminate apparent immediate hazards to the study participant. [See 45 CFR 46.108(a)(3)(iii) under the 2018 Requirements and 45 CFR 46.103(b)(4)(iii) under the pre-2018 Requirements.] These changes must be documented as Protocol Deviations and reported to the Protocol Team and IRB/IEC as soon as possible [see ICH E6(R2), Good Clinical Practice, Section 4.5.4]. In the event of a public health emergency, investigators should adhere to the recommendations of their local institutions, IRB/IEC and local health departments. When conflicts exist between local directives, MTN,

Protocol Team and/or DAIDS policies or guidance, sites should follow the requirement that is most protective of study participants and site staff. [See DAIDS Guidance, Coronavirus Disease (COVID-19) and DAIDS HIV/AIDS Network Clinical Research Studies, Page 3, dated March 13, 2020.]

4.) The following clarification removes the collection of breast milk symbol (the green triangle) from the Enrollment Visit in the Study Visit Schedule Figure 1 and Figure 2 in both Protocol Summary and Section 7, Study Procedures to be consistent with the protocol text in Section 7 and Appendix I:



5.) Protocol Team Roster – Removals: Jennifer Berthiaume, Karen Patterson, Felix G. Muhlanga

6.) 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.