Microbicide Trials Network

CLARIFICATION MEMO #01 TO:

MTN-042

Phase 3b, Randomized, Open Label Safety Trial of Dapivirine Vaginal Ring and Oral TRUVADA® Use in Pregnancy

DAIDS Protocol #: 38544

IND#: 139,598

Version 2.0 / 20 May 2021

Clarification Memo Date: 29 April 2022

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-042 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-042. No change in informed consent is necessitated by or included in this CM.

This document clarifies the language in the protocol regarding the timing of the phone contact, bi-weekly visit and 4-week visit that are indicated for participants during their 36th week of gestation; clarifies that study procedures such as prescreening and screening may be conducted for the next scheduled cohort during the interim review of the previous cohort. This CM also 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.

The following clarifications (1-5) were made regarding the timing of the phone contact, bi-weekly and 4-week visit that are indicated for participants during their 36th week of gestation:

1. Figure 2 in *Protocol Summary* and Figure 6 of Section 7, *Study Procedures*:

   Every odd-numbered week ~~after~~ **starting from** 36th week of gestation (e.g., follow-up weeks 5, 7, 9) until pregnancy outcome (phone, home or clinic as needed per local standard of care)

2. Figure 3 in *Protocol Summary* and Figure 7 of Section 7, *Study Procedures*:

   4-week and every 4 weeks ~~until~~ **through** 36th week of gestation

   Every odd-numbered week ~~after~~ **starting from** 36th week of gestation (e.g., follow-up weeks 19, 21, 23) until pregnancy outcome (phone, home or clinic as needed per local standard of care)

3. Section title, the first sentence and title of Table 5 of Section 7.4.2, *Bi-weekly Visits After 36th Week of Gestation:*

   7.4.2 Bi-weekly Visits **Starting from** ~~After~~ 36th Week of Gestation

This visit will occur for all participants every two weeks (i.e., approximately 14 days) ~~following~~ **starting from** their 36th week ~~(inclusive – the visit should occur in the 36th week)~~ of gestation until pregnancy outcome**.**

Table 1: Bi-weekly Visits **Starting from** ~~After~~ 36th Week of Gestation

Bi-weekly Visits **Starting from** ~~After~~ 36th Week ~~(inclusive)~~ of Gestation	
Component	Procedures

4. Second sentence of Section 7.4.4, *4-week Visit(s) (Cohorts 2-3):*

   For Cohort 3, this visit will also occur every 4 weeks after their first 4-week Visit ~~until~~ **through** their 36th week ~~(inclusive – this visit should occur in the 36th week)~~ of gestation. **If both a bi-weekly and 4-week visit are indicated in the 36th week for a participant, the 4-week visit should be conducted.**

5. Title of columns of Appendix 1: *Table of Visits and Study Procedures – Mothers:*

	Visit 1 SCR	Visit 2 ENR	Phone Contacts Prior to Pregnancy Outcome	Cohorts 2-3 only	Bi-weekly Visits **Starting from** ~~After~~ 36th Week	PPO Visit	1-week PPO Phone Contact	6-week PPO Visit/SEV/ Early SEV

The following additions (6-7) were made to clarify that the word accrual refers to the act of enrollment:

6. First sentence of Section 4.4, *Time to Complete Accrual*:

   Time to complete accrual will be approximately 4 to 9 months for recruitment and enrollment of each Cohort, with accrual **(enrollment)** pauses of approximately 3 to 8 months between Cohorts to allow all enrolled participants to give birth and for interim safety analyses to be conducted before continuing to the next Cohort, for a study duration of approximately 37-45 months.

7. From the second to the sixth sentence of Section 10.5, *Participant accrual, Follow-up, and Retention*:

   The accrual **(enrollment)** period for Cohorts 1-2 will be approximately 4-5 months, while the accrual period for Cohort 3 will be approximately 7-9 months… Cohort 1 accrual began in February 2020 and is expected to finish in May 2021.

The following edits (8-9) were made to clarify that study procedures such as prescreening and screening may be conducted for the next scheduled cohort during the interim review of the previous cohort:

8. Ninth sentence of Section 7.1, *Pre-Screening:*

   Potential participants may be pre-screened **or screened** for the currently enrolling group or for the subsequent group not yet open for enrollment, with attention to the participant's gestational age and the screening window.

9. Last sentence in the second paragraph of Section 10.7, *Data and Safety Monitoring Procedures*:

   However, an interim review of the safety data by the IRP is planned after each cohort completes scheduled participation and prior to beginning accrual **(enrollment)** in the next scheduled cohort. **Study procedures (e.g., prescreening and screening) prior to the act of enrollment may be conducted during the interim review.**

10. Protocol Team Roster – Removals: Luis Duran, Johntraye Davis, Tanya Harrell

11. Protocol Team Roster – Addition:

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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.