

CLARIFICATION MEMO #01 TO:

MTN-029/IPM 039

Phase 1 Pharmacokinetic Study of the Dapivirine
Vaginal Ring in Lactating Women

DAIDS Protocol #: 12036

IND#: 108,743

Version 1.0 / 30 June 2015

Clarification Memo Date: 16 February 2016

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 approval of this CM is not required by the sponsor; however, investigators may submit the CM to the IRB overseeing the study at their site for information. This CM is official MTN-029/IPM 039 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-029/IPM 039. No change in informed consent is necessitated by or included in this CM.

This document clarifies language regarding the number of breast milk samples to be collected by participants on specific clinic visit days.

Section 2: Implementation

Text to be added is in **bold**.

- 1.) Section 7.8, *Pharmacokinetic and Pharmacodynamic Measures and Specimen Collection*: Table 8, *PK Specimen Collection Schedule* has been modified to include a footnote to clarify breast milk sample collection by participants at home, on clinic visit days 1, 7, and 14, see bolded text below:

Table 8: PK Specimen Collection Schedule

STUDY VISIT	PK and PD Specimen Collection
Visit 1: Screening	<ul style="list-style-type: none"> Breast milk for baseline
Visit 2: Enrollment (Day 0)	<ul style="list-style-type: none"> Blood (Target: pre-insertion, hr 3 and hr 6) CVF (Target: pre-insertion, hr 3 and hr 6) Breast milk for DPV level and lipids (Target: pre-insertion, hr 3 and hr 6) Breast milk for anti-viral activity (Target: pre-insertion, hr 3 and hr 6)
Visit 3: Day 1*	<ul style="list-style-type: none"> Blood (Target: 24 hours) CVF (Target: 24 hours) Breast milk for DPV level and lipids (Target: 24 hours) Breast milk for anti-viral activity (Target: 24 hours)
HOME COLLECTION (DAY 2-6)	<i>Participants are to ideally collect a minimum of 2 daily samples of breast milk- all samples may not be analyzed</i>
Visit 4: Day 7*	<ul style="list-style-type: none"> Blood CVF Breast milk for DPV level and lipids Breast milk for anti-viral activity
HOME COLLECTION (DAY 8-13)	<i>Participants are to ideally collect a minimum of 2 daily samples of breast milk- all samples may not be analyzed</i>
Visit 5: Day 14*	<ul style="list-style-type: none"> Blood (Target: At ring removal) CVF (Target: At ring removal) Breast milk for DPV level and lipids (Target: At ring removal) Breast milk for anti-viral activity (Target: At ring removal)
HOME COLLECTION (Day 15)	<i>Participants are to ideally collect a minimum of 2 samples of breast milk- all samples may not be analyzed</i>

STUDY VISIT	PK and PD Specimen Collection
Visit 6: Day 16	<ul style="list-style-type: none"> • Blood (Target: 48 hours after ring removal) • CVF (Target: 48 hours after ring removal) • Breast milk for DPV level and lipids (Target: 48 hours after ring removal) • Breast milk for anti-viral activity (Target: 48 hours after ring removal)

***= Participants are to ideally collect one additional sample at home on Visit Days 1, 7, and 14 in order to maintain at least twice daily milk collection.**

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