



# MTN-017

# Letter of Amendment #01

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MTN Annual Meeting   o   Bethesda, MD   o   February 10, 2013



# Overview

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- Letter of Amendment #01
  - Review the summary of changes to MTN-017
- Open the floor to questions and discussion
- Review the anticipated timeline for LoA approval



# Section 6.0, Study Product

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- Product use instructions for the proper administration of FTC/TDF 200mg/300mg Tablet (Truvada®) and TFV RG 1% Gel (daily and RAI-associated) are provided within Section 6.0
- Details regarding the planned participant-centered discussion of strategies to enhance adherence within Section 6.5, *Adherence Counseling* have been moved to Section 7.10.2, *Adherence*

This change required additional modifications to Section 7.0, Study Procedures and Appendix I:

- Product use instructions and adherence counseling
- **Product adherence counseling/interview**

# Section 6.6, Concomitant Medications and Practices

- Per protocol, concomitant use of locally approved effective HIV prevention agents is not restricted.
- During the Oral (Daily FTC/TDF) Period, participants are to use study product rather than their prescribed PrEP medication.

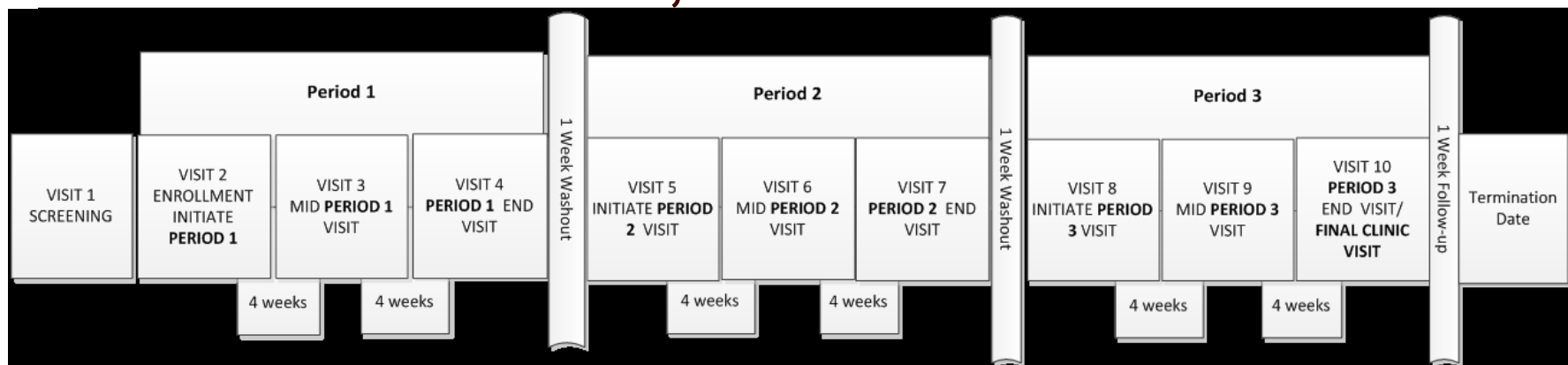
Section 6.6, *Concomitant Medications and Practices*:

During the Oral (Daily FTC/TDF) Period, participants will use the study provided product and refrain from using the prescribed PrEP medication, FTC/TDF. Prescription medications, over-the-counter preparations, vitamins and nutritional supplements, and herbal preparations will be recorded as concomitant medications.



Image Source:  
<http://www.healthcommunities.com/hiv-aids/daily-combination-drug-and-hiv-prevention.shtml>

# Section 7.2.1, Period 1- Visit 2, Period 2 – Visit 5, Period 3- Visit 8



- Per protocol Version 1.0, all AEs needed to have resolved or stabilized prior to study product initiation during Periods 2 and 3.
- The protocol has been modified to delay of study product initiation if a grade 2 or higher and judged to be related to study product AE is present.

See edits to Section 7.2.1, *Period 1- Visit 2, Period 2 – Visit 5, Period 3- Visit 8*

At Visit 5 and Visit 8, prior to the initiation of study product, all AEs **grade 2 or higher judged to be related to study product** need to have resolved or stabilized.

# Pharmacokinetic Sample Collection Schedule

Mid-Period Visits Period 1- Visit 3 (Week 4), Period 2- Visit 6 (Week 13), Period 3- Visit 9 (Week 22)		
Component		Procedures
Laboratory	Blood	<ul style="list-style-type: none"><li>• <b>Blood for PK (Plasma)</b></li></ul>

This change is reflected in Section 7.8, *Pharmacokinetics and Pharmacodynamics*, Table 10: *PK and PD Sample Collection Schedule* and Appendix I: *Schedule of Study Visits and Evaluations*.

# Section 7.8, Pharmacokinetics and Pharmacodynamics

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The required amount of blood volume for PK will not to exceed 34 mLs at any given visit.

See edits below:

- All participants will have blood (plasma and/or PMBCs) collected for PK. ~~It is anticipated that a~~**When blood is collected for PK, a volume not to exceed** ~~maximum of 24 mL~~**34 mL (3 8-mL CPTs) will be drawn** ~~will be required for PK each time point (Period 1 End, Period 2 End, and Period 3 End).~~ In addition, rectal fluid will be collected via sponge for PK and PD. **See the sample collection schedule below.**



## Section 7.10.2, Adherence

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- Updated to include a Product Adherence Counseling/ Interview Section, this includes:
  - A description of the adherence counseling planned (i.e., text from Section 6).
  - A description of the adherence interview (the data convergence interview).

*Please note: The protocol now requires to recording of Adherence Counseling/Interview sessions.*

This change required additional modifications to Section 7.0, *Study Procedures* and Appendix I:

~~Product use instructions and adherence counseling~~

~~Data Convergence Interviews~~

Product adherence counseling/interview

# Data Convergence Interview

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## 1. SMS Diary & CASI

- Text messages will collect data on study product use only
- Participants will no longer report their sexual activity and condom use via text message
- Participants will now receive a bonus if they respond to 85% (vs. previous 90%) of the messages or more. (1/week)
- CASI data will not be reviewed during the Data Convergence Interview

Revisions to reflect the above information have been made throughout the protocol.

# Data Convergence Interview

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1. SMS  
Diary &  
CAS!

2.  
Applicator &  
Tablet  
Counts

# Data Convergence Interview

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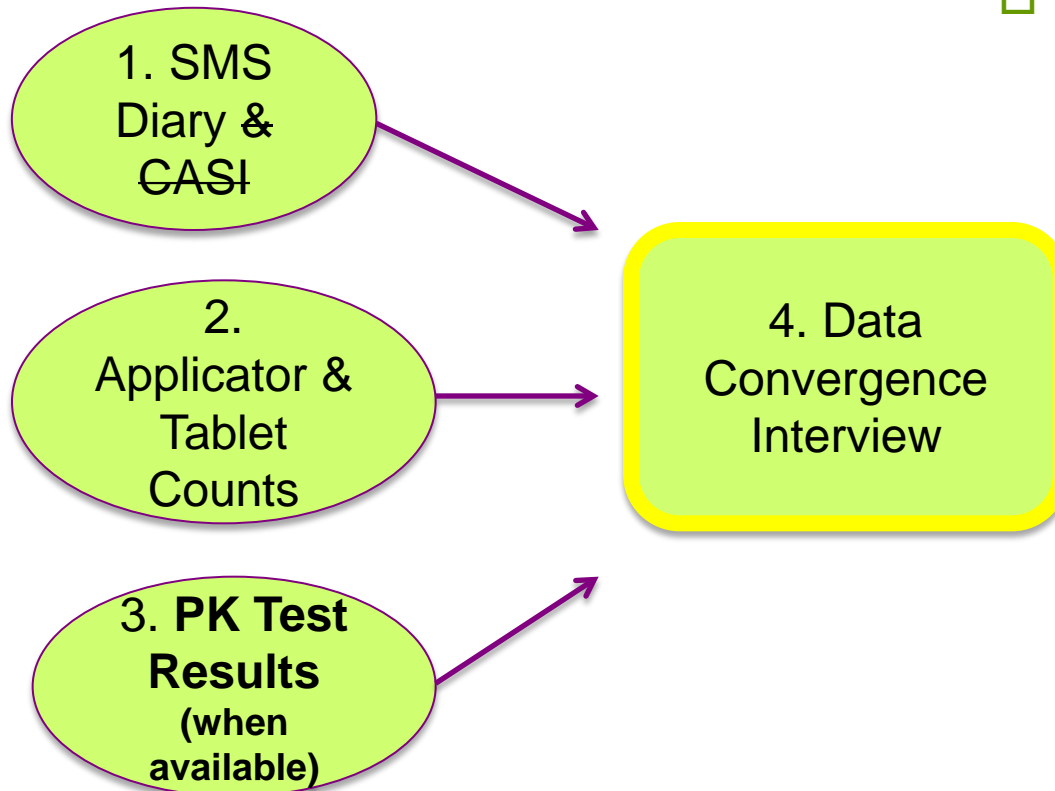
1. SMS  
Diary &  
CAS!

2.  
Applicator &  
Tablet  
Counts

3. **PK Test  
Results**  
(when  
available)

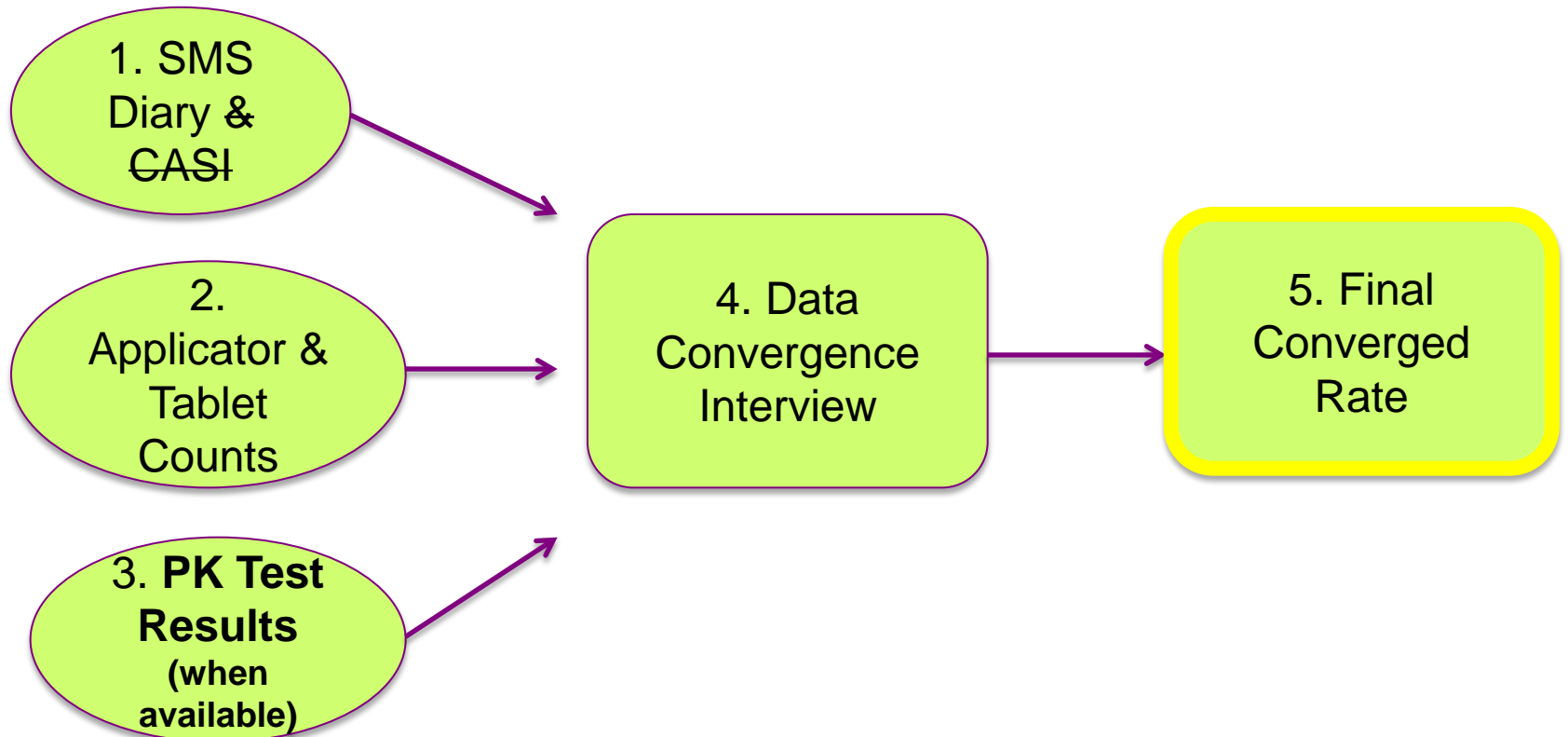
- Section 7.10.2, *Adherence*, has been updated to describe when PK test results are to be discussed with participants
- Revisions to the informed consent include informing participants that blood will be collected at Mid- and End- Period Visits for PK, that levels of tenofovir will be used to check adherence to study product, and that a discussion will take place to review these results

# Data Convergence Interviews



- The sessions will be recorded to ensure quality and consistency. In addition, new to LoA #01, study staff will have the ability to content analyze the audio in order to identify potential patterns of use.

# Data Convergence Interviews



Adapted from Pool R, Montgomery CM, Morar NS, et al. A mixed methods and triangulation model for increasing the accuracy of adherence and sexual behaviour data: The Microbicides Development Programme. Plos One 2010;5(7):e11600.



# Final Converged Rate

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## ~~Summary Database~~ Final Converged Rate

The **BRWG** will review the data from each data comparison form and will assign each interview a ~~together with the~~ **final converged rate, which represents an estimate of the result of most likely adherence to product use will constitute the summary database on adherence, sexual behavior and condom use during the study number of doses taken based on the available data from SMS, product counts and PK data.**

# Appendix III: Sample Informed Consent Form

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- *What are the possible risks, side effects, and discomforts of this research study?* Section, *Other Possible Risks* sub-Section, first full paragraph, new fourth and fifth sentence:
- [...] You will be shown how to erase the text message sessions from your mobile phone by study staff. **However, as with all text messages sent from and received on your phone, it is possible that others may see your personal messages. Protections have been made to ensure that questions asked via text message are vague and will not directly convey information about your participation in this research study.**



# Other Modifications

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- Update the protocol to reflect the most recent Investigator's Brochure
  
- Protocol Roster Additions:
  - Anupong Chitwarakorn
  - Karen Liu
  - Vanessa Njoku
  
- Study product protocol deviation reporting requirements will likely be added to Section 6.5, *Retrieval of Unused Study Product*.
  
- Other consistency issues were addressed.

# Questions?

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Image source- <http://www.dfid.gov.uk/Stories/Case-Studies/2012/Kenya-WAD-case-study/>





# Timeline

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- 15 February 2013-
  - Circulate final version for sign-off by study leadership
- 19 February 2013-
  - Submit to the IND Sponsor, CONRAD
- 22 February 2013-
  - DAIDS Submission
- First or Second Week in March
  - LoA approval 1-2 weeks after submission

# Acknowledgements

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