Clarification Memo # 1 to:

HPTN 084: A Phase 3 Double Blind Safety and Efficacy Study of Long-Acting Injectable Cabotegravir Compared to Daily Oral TDF/FTC for Pre-Exposure Prophylaxis in HIV-Uninfected Women
Protocol Version 1.0, dated 2 March 2017

Final Clarification Memo (CM) Version: FINAL CM#1 of 11 May 2017

Summary of Revisions and Rationale

1. Reference to the US Agency for International Development (USAID) and Office of the US Global AIDS Coordinator (OGAC) throughout the protocol has been removed.

2. A typographical error has been corrected in the diagram of the "Overview of Study Design and Randomization Scheme."

3. Typographical errors have been corrected in the Sample Screening and Enrollment Consent Form. No change in procedures or implementation were made.

4. Updated DAIDS Toxicity Tables reference to incorporate the Version 2.1, March 2017 guidelines.

5. The study roster has been updated to reflect a change in Data Managers.

6. Typographical errors have been corrected in the protocol. No change in procedures or implementation were made.

Implementation

The procedures clarified in this memorandum have been approved by the Division of AIDS (DAIDS) Medical Officer and are to be implemented immediately upon issuance. IRB approval of HPTN 084 Protocol Clarification Memo #1 to HPTN 084, Version 1.0 is not required by the sponsor; however, sites may submit the clarification memo to the responsible IRBs for their information.

No change in the informed consent forms is necessitated by or included in this Clarification Memo, aside from the corrected typographical error.

The modifications included in this Clarification Memo will be incorporated into the next full protocol amendment. Text noted below by **~~strikethrough~~** will be deleted; text appearing below in **bold** will be added.

Revision 1-Related Changes: Removed Reference to USAID and OGAC

Revision 1, Change 1) Removed USAID and OGAC from the list of study supporters on the Title page and Protocol Signature Page on page 14

> "Support Provided by:
> ViiV Healthcare
> Gilead Sciences, Inc.
> Bill & Melinda Gates Foundation (BMGF)
> ~~**US Agency for International Development (USAID)**~~
> ~~**Office of the US Global AIDS Coordinator (OGAC)**~~"

Revision 1, Change 2) Removed USAID and OGAC staff from the Roster on pages 11 and 12

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Revision 1, Change 3) Removed USAID and OGAC from Section 10.7, "Use of Information and Publications" on page 87

> "10.7 Use of Information and Publications
>
> Publication of the results of this study will be governed by HPTN policies. Any presentation, abstract, or manuscript will be submitted by the Investigator to the HPTN Manuscript Review Committee (MRC), DAIDS, ~~**OGAC,**~~ ViiV Healthcare, Gilead Sciences, Inc., ~~**USAID,**~~ and BMGF for review prior to submission."

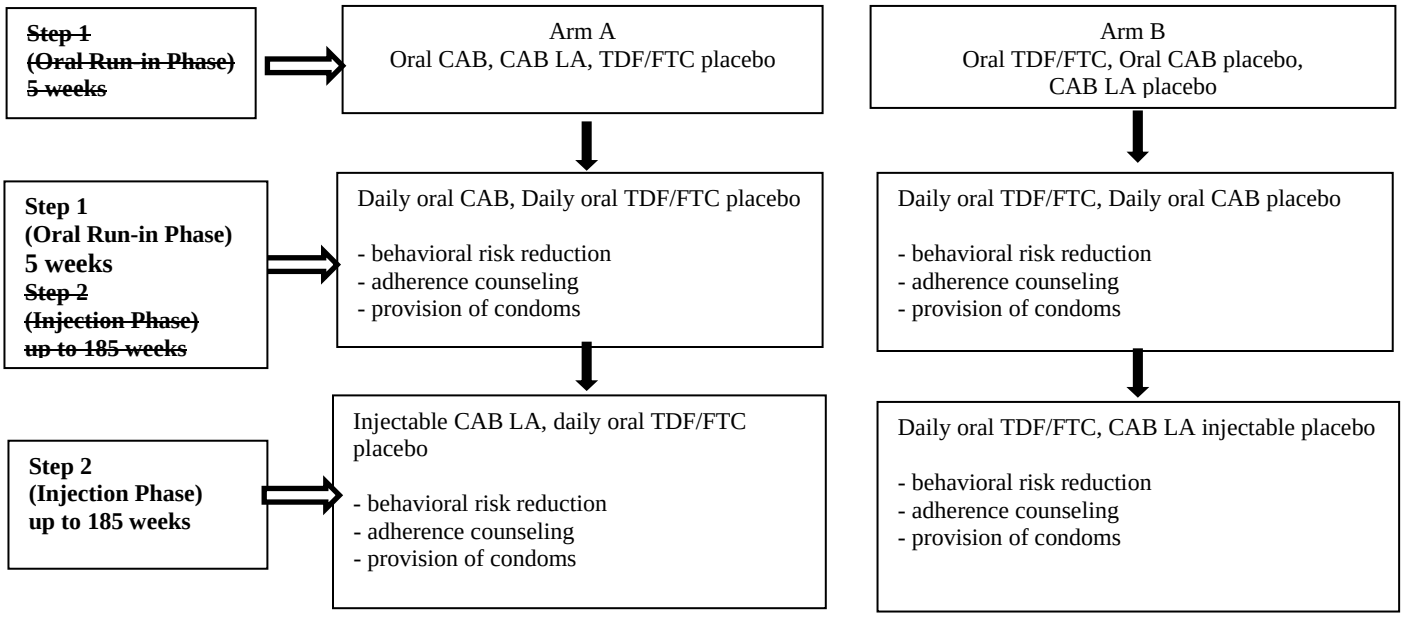
Revision 1, Change 4) Removed USAID and OGAC from the list of study supporters shown in the consent forms on pages 109, 126 and 129

> "Sponsored by: Division of AIDS, United States (US) National Institute of Allergy and Infectious Disease, US National Institutes of Health.

Study products are provided by ViiV Healthcare and Gilead Sciences, Inc. Additional support is provided by ~~**the US Agency for International Development (USAID), Office of the US Global AIDS Coordinator (OGAC), and**~~ the Bill & Melinda Gates Foundation (BMGF)."

Revision 2-Related Changes: Corrected Typographical Shift in Two Boxes of the Diagram

Revision 2, Change 1) Moved left-hand boxes for "Step 1" and "Step 2" to correct placement in the diagram of the "Overview of Study Design and Randomization Scheme" on page 19



Revision 3-Related Changes: Corrected Typographical Errors in the Sample Screening and Enrollment Consent Form

Revision 3, Change 1) Corrected sentence to make it consistent with the rest of the ICF and protocol in the "Procedures if you become infected with HIV during the study" section of the Sample Screening and Enrollment Consent Form on page 117

"You will ~~**either**~~ stop receiving the injections and stop taking study pills."

Revision 3, Change 2) Removed duplicate sentence from "HIV Infection" section of the Sample Screening and Enrollment Consent Form on page 121

" ~~**Women of reproductive potential must agree to use a reliable form of contraception during the trial and for 52 weeks after stopping injections, or for 30 days after stopping oral study product.**~~"

Revision 3, Change 3) Corrected sentence to make it consistent with the rest of the ICF and protocol in the "Benefits" section of the Sample Screening and Enrollment Consent Form on page 122

> "TDF/FTC is known to protect people from getting HIV if taken daily as directed. CAB has not been shown to protect against getting HIV, which is the reason we are doing this study. **Neither y~~Y~~ou nor we** will know which real drug you are getting in this study."

Revision 4-Related Changes: Updated Protocol Text to Incorporate New DAIDS Toxicity Tables of March, 2017

Revision 4, Change 1) Edited text in Section 6.1, "Definition and Reporting" Section on page 61

> "AE severity will be graded per the DAIDS Table for Grading Adult and Pediatric Adverse Events, Version 2.**~~0~~1**, **~~November 2014~~ March 2017**. This version will be used for the entire duration of the study."

Revision 4, Change 2) Edited text in Section 6.2.3, "Grading Severity of Events" Section on page 62

> "The Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.**~~0~~1**, **~~November 2014~~ March 2017**, will be used for the entire duration of the study for determining and reporting the severity of AEs. The DAIDS grading table is available on the DAIDS RSC website at http://rsc.tech-res.com/safetyandpharmacovigilance/.

Revision 5-Related Changes: Updated Protocol Roster

Revision 5, Change 1) Edited text in Protocol Roster to reflect a recent change in Data Managers on pages 10-12

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Revision 6-Related Changes: Typographical Errors have bee Corrected in the Protocol

Revision 6, Change 1) Edited text in Section 2.5, "Study Design and Overview" Section, Step 3, Follow-up Phase by removing extraneous period on page 41

> "All participants will be transitioned to locally-available HIV prevention services including services for PrEP, if available~~.~~ when participation in Step 3 ends."

Revision 6, Change 2) Corrected text in Section 4.1.2, "Injectable Suspension" Section on page 49

> "IM Dosing Considerations
> IM injections ~~**should**~~ **are administered** into the gluteus muscle (gluteus medius method preferred) using a needle of appropriate gauge and length (recommended 1.5" 23-gauge needle for CAB LA or placebo)."

Revision 6, Change 3) Corrected text in Section 5.11.2, "After Study Enrollment/Randomization" Section, Step 3 on page 57

> "Neither ART nor funds for provision of ART will ~~**not**~~ be provided by the study."

Revision 6, Change 4) Edited text in Section 5.17, "Planned Unblinding of Study Participants" Section on page 60

> "When the required number of incident HIV endpoints has been reached, or when the last participant completes scheduled Step 2 follow-up (meaning all participants have moved to Step 3), and when all corresponding procedures at the HPTN SDMC, LC, and LOC have been completed, including final confirmation from the **H**PTN SDMC, the study will be unblinded."

Revision 6, Change 5) Updated text in Section 10.3, "Study Coordination" Section on page 86

> "Study CRFs will be developed by the study team and HPTN SDMC. Data will be transferred to the HPTN SDMC, entered, and cleaned by the HPTN SDMC~~**. Datafax data management system. Quality control reports and q**~~**Q**ueries routinely will be generated and distributed to the study sites for verification and resolution.