

## HIV Prevention Trials Network

### 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 3.0, dated 12 August 2021**

**DAIDS Document ID: 38070**

**Date of FINAL Clarification Memo: 7Dec2021**

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### **Implementation**

The items clarified in this Clarification Memorandum (CM) have been approved by the Division of AIDS (DAIDS) Medical Officer and are to be implemented immediately upon issuance. Institutional Review Boards/Ethics Committees (IRBs/ECs) approval of this CM is not required by the sponsor; however, investigators may submit the CM to the IRB/EC overseeing the study at their site for information.

No change in the informed consent forms is necessitated by or included in this CM.

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

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### **Summary of Revisions and Rationale**

**1.** Text has been added to the protocol to specifically clarify the following participants may transition to v3.0 of the protocol and that the CMC must be contacted for participant management:

- participants who were on the Contraceptive Sub-Study during the v2.0 protocol, and who have not completed their Sub-Study activities when the site transitions to the v3.0 protocol.

participants who had been transitioned to 48 weeks of open-label TDF/FTC during the v2.0 protocol for safety reasons, and who have not completed that 48-week period when the site transitions to the v3.0 protocol.

- participants who became HIV-infected during the v2.0 protocol and have not completed that 48-week period when the site transitions to the v3.0 protocol.
- participants who became pregnant during the v2.0 protocol and who are pregnant when the site transitions to the v3.0 protocol.

The v3.0 protocol specifically states: “Contact the CMC (084cmc@hptn.org) for guidance if there are other scenarios for a discussion about choice and obtaining informed consent that are not outlined here.” The intention all along was for sites to contact the CMC for guidance. However, during protocol training it became evident that sites would appreciate specific guidance so we created this CM to assist them in implementation of v3.0.

**2.** Clarified that participants who become pregnant during Step 4 and who received at least one CAB LA injection during HPTN 084 are eligible to participate in the Pregnancy and Infant Sub-Study.

Again, the v3.0 protocol specifically states: “Contact the CMC (084cmc@hptn.org) for guidance if there are other scenarios for a discussion about choice and obtaining informed consent that are not outlined here.” The intention all along was for sites to contact the CMC for guidance. However, during protocol training it became evident that sites would appreciate specific guidance on currently pregnant participants, so we created this CM to assist them in implementation of v3.0.

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<b>Revision 1-Related Changes:</b> Clarified Text Regarding Participants who are in the Midst of the Protocol v2.0, Contraceptive Sub-Study Schedule of Events at Implementation of the v3.0 Protocol
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**Revision 1, Change 1)** Added text in Section 3.1, “Overview”

“Contact the CMC (084cmc@hptn.org) for guidance if there are other scenarios for a discussion about choice and obtaining informed consent that are not outlined here. **Scenarios that the CMC should be contacted for include, but are not limited to, the following:**

- **participants who were on the Contraceptive Sub-Study during the v2.0 protocol, and who have not completed their sub-study activities when the site transitions to the v3.0 protocol.**
- **participants who had been transitioned to 48 weeks of open-label TDF/FTC during the v2.0 protocol for safety reasons, and who have not completed that 48-week period when the site transitions to the v3.0 protocol.**
- **participants who became HIV infected during the v2.0 protocol and have not completed that 48-week period when the site transitions to the v3.0 protocol.**
- **participants who became pregnant during the v2.0 protocol and who are pregnant when the site transitions to the v3.0 protocol.”**

<b>Revision 2-Related Changes:</b> Clarified Text Regarding Participants who are Pregnant at Implementation of the v3.0 Protocol
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**Revision 2, Change 1)** Added text in Section 3.1, “d. Step 4d”

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Participants who become pregnant during Step 4 and who received at least one CAB LA injection during HPTN 084 are eligible to participate in the Pregnancy and Infant Sub-Study. In addition, participants in Step 5 who received a CAB LA injection within 8 weeks of pregnancy confirmation may join the Pregnancy and Infant Sub-Study. All participants interested in participating in Step 4d will be provided informed consent for this Step prior to any study activities.

**Note: Participants who had at least one CAB LA injection under v2.0 of the protocol and who are pregnant at the transition to the v3.0 protocol are eligible for Step 4d. The site must consult with the CMC for PPT management instruction.”**