

Clarification Memo # 1 to:

HPTN 083: A Phase 2b/3 Double Blind Safety and Efficacy Study of Injectable Cabotegravir Compared to Daily Oral Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC), For Pre-Exposure Prophylaxis in HIV-Uninfected Cisgender Men and Transgender Women who have Sex with Men

Version 1.0, February 2, 2016

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Summary of Revision and Rationale

Currently, Protocol Section 3.1 indicates that randomization may not occur until at least one HIV test from the Enrollment visit has been resulted and is non-reactive. In direct conflict, Section 5.2 indicates that study product should not be provided until at least one HIV test from the Enrollment visit has been resulted and non-reactive. Therefore, Section 3.1 has been revised to specify that study product should not be provided until at least one HIV test has been performed and deemed non-reactive or negative from the Enrollment visit. This revision also harmonizes the language already included in the accompanying Study Specific Procedures (SSP) Manual for the Enrollment visit, which also states that study product should not be provided to a participant until the HIV testing requirements are performed and the participant is deemed eligible to participate in the study.

Implementation

The clarifications included in this memorandum have been approved by the Division of AIDS (DAIDS) Medical Officers and are to be implemented immediately upon receipt or upon local Investigational Review Board (IRB)/Ethics Committee (EC)/other regulatory entity approval if required. IRB/EC approval of Clarification Memo # 1 to HPTN 083 Version 1.0 is not required by DAIDS.

None of the clarifications being made impact the sample informed consent forms, and the benefit-to-risk ratio for participants is not affected in any way.

The modifications included in this Clarification Memo will be incorporated into the next letter of amendment or full protocol amendment. Text appearing below in highlighted **bold** will be added, and text appearing in highlighted **strike-through** will be deleted.

Section 3.1: Inclusion Criteria

Note: Only one sub bullet is impacted by this clarification in this section, and only the corresponding main bullet to which the sub bullet is under is included below.

- In general good health, as evidenced by the following laboratory values, which must be from specimens obtained within 45 days prior to study enrollment:

- Non-reactive / negative HIV test results*
- Hemoglobin > 11 g/dL,
- Absolute neutrophil count > 750 cells/mm³
- Platelet count ≥ 100,000/mm³
- Calculated creatinine clearance ≥ 60 mL/minute using the Cockcroft-Gault equation
- Alanine aminotransferase (ALT) < 2 times the upper limit of normal (ULN)
- Total bilirubin ≤ 2.5 times ULN
- Hepatitis B virus (HBV) surface antigen (HBsAg) negative
- HCV Ab negative
- No Grade 3 or higher laboratory abnormalities

*HIV uninfected, based on HIV test results obtained at Screening and just prior to randomization at the Enrollment visit. All HIV test results from the Screening visit must be obtained and must all be negative/non-reactive. This includes testing for acute HIV infection, which must be performed within 14 days of Enrollment. In addition, at least one HIV test result obtained at the Enrollment visit must be obtained prior to **randomization in to the study provision of study product** and must be negative/non-reactive. Individuals who have one or more reactive or positive HIV test results will not be enrolled, even if subsequent confirmatory testing indicates that they are not HIV-infected (see SSP Manual).

- No medical condition that, in the opinion of the study investigator, would interfere with the conduct of the study (e.g., provided by self-report, or found upon medical history and examination or in available medical records)
- Willing to undergo all required study procedures