Section 1: Summary of Clarifications and Rationale

The items clarified in this Clarification Memorandum (CM) have been approved by the NIAID Medical Officer and are to be implemented immediately upon issuance. IRB/EC 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. This CM is official MTN-003 documentation and is effective immediately. A copy of this CM must be retained in each study site’s Essential Documents file for MTN-003C. No change in informed consent is necessitated by or included in this CM.

This CM provides clarification on the following items:

- Updates to the Protocol Team Roster
- Coenrollment
- Timing of Focus Group Discussions with CAB members
- Entities that may audit VOICE C

Section 2: Implementation

1. The following modifications are made to the Protocol Team Roster:

   The following individuals are removed from the roster: Mala Shah and Daniel Gondwe

   The following individual is added to the roster:

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2. Section 5.10, Co-enrollment Guidelines, is updated to clarify that VOICE-C participants may enroll in one group:

For this substudy, all participants in Group 1 will be participants in the VOICE trial. Therefore, the VOICE guidelines for co-enrollment into other studies apply to this substudy.

There are no co-enrollment restrictions regarding enrollment into other trials for participants in Groups 2, 3 and 4. Participants in Groups 1, 2, 3, and 4 may only be enrolled into one VOICE-C group.

3. Section 7.2.3, Focus Group Discussion Procedures, third paragraph, first full sentence the timing of the focus group discussion is updated.

CAB Members

FGDs with CAB members will occur approximately every six months for the duration of the study.

4. Section 13, Human Subjects Protections, is updated to allow for an audit of VOICE C by the FDA.

Site investigators will make efforts to minimize risks to participants. Participants and study staff members will take part in a thorough informed consent process. Before beginning the study, the IoR will have obtained IRB/EC approval. The IoR will permit audits by the FDA, NIH or any of their appointed agents.