

**Microbicide Trials Network
LETTER OF AMMENDMENT #01 TO:**

**MTN-003C
DAIDS Document ID #10746**

**Household and Community Level Factors Associated with Study Product Adherence in VOICE: A
Substudy of MTN-003**

Version 1.0 / 15 July 2009

Date of Letter of Amendment: 5 May 2011

Instructions to Study Sites from the Division of AIDS

The following information impacts the MTN-003C study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) as soon as possible for their information and review. This must be approved by your IRB/EC before implementation. The following information may also impact the sample informed consent. Your IRB/EC will be responsible for determining the process of informing subjects of the contents of this letter of amendment.

Summary of Revisions and Rationale

This LoA does not impact the overall design and study visit schedule for MTN-003C. In addition to incorporating the two previously issued Clarification Memos, this LoA includes the following items:

- 1.) Updates to Group 1 have been added to allow for up to 4 ethnographic interviews to occur
 - 2.) Updates to Group 2 have been included to allow for an approximate number of IDIs involving male partners of VOICE-C participants
 - 3.) Modifications to Group 3 allow for 3-5 Focus Group Discussions to occur as deemed necessary by the protocol team and notes that approximately 20 CAB members over time will be involved. Given the nominal increase, the total study sample size of approximately 275 has not been modified. In addition, the protocol has been clarified to distinguish the initial Group 3 Focus Group Discussion from the other Focus Group Discussions.
 - 4.) Modifications to Group 4 have been made to clarify details regarding Key Community Stakeholder accrual.
 - 5.) Updates to Section 10.5.1, *Study Monitoring Committee (SMC)* to remove the formal SMC for this protocol and to allow for a team review of study progress, including rates of participant accrual.
 - 6.) Updates to Section 10.5.2, *Data Analysis, Qualitative Analysis: Data Types* subsection, to more accurately describe the qualitative data to be generated from VOICE-C
 - 7.) Section 2.1, *The VOICE Study*, has been updated to accommodate for changes incorporated into Version 2.0 of the VOICE protocol, including sample size and maximum length of time on study product.
 - 8.) Section 12.0, *Clinical Site Monitoring* has been updated to remove PPD as the monitor, study monitoring will not occur during this observational study:
 - 9.) Updates to the Protocol Team Roster.
 - 10.) List of Abbreviations and Acronyms has been updated.
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Implementation

Upon receiving final IRB/EC and any other applicable Regulatory Entity (RE) approval(s) for this LoA, sites should implement the LoA immediately. Sites are still required to submit an LoA registration packet

to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). Sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. An LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with this letter and any IRB/EC correspondence should be retained in the site's regulatory files.

Except for modifications to the Protocol Team Roster, text to be deleted is generally noted by ~~strikethrough~~ and text to be added is noted below in **bold**.

**Detailed Listing of Revisions Included in Clarification Memo #01
Dated June 17, 2010**

Group	One-time IDI	Ethnography	FGD
1b: VOICE Participants			One-time exit FGD offered to each VOICE participant randomly pre-selected and eligible to participate in VOICE-C* after the VOICE study participation-Product Use End Visit (PUEV)
2a: Male Partners of VOICE Participants			One-time exit FGD offered to current male sexual partners of VOICE participants systematically selected and eligible to participate, and whose female partners consent for him to be contacted after the completion of VOICE PUEV trial*

Section 2.4.2, *Rationale for Study Design*, fifth paragraph, last sentence:

Note that in VOICE-C, the term “study exit” refers to the Product Use End Visit (PUEV) in VOICE, which indicates the point when participants have completed study product use.

Section 4.1, *Identification of Study Design*, first paragraph, third sentence, clarifies when VOICE participants will be offered participation in VOICE-C:

VOICE female participants (Group 1) who have ~~been in the trial for at least 12 weeks~~ **reached the Month 3 Visit and have been randomly pre-selected by the Statistical Data Management Center (SDMC)**, will be offered participation in VOICE-C which will involve one of the following three activities: a) a single visit during which they will participate in a FGD (conducted at study exit, after completing their time **on study product** in the trial) b) a single visit during which they will participate in an IDI (conducted as the trial is unfolding) or c) long term (1 year for a total of approximately 4 visits) ethnographic research.

Section 5.1, *Selection of the Study Population and Recruitment, Group 1 (VOICE participants)*, first sentence:

Group 1 (VOICE participants), first sentence:

As described in Sections 4.3 and 10.4, at each VOICE-C site, every **randomly pre-selected** woman who has ~~been enrolled~~ **reached the 3 Month Visit** in VOICE ~~for at least 12 weeks~~ will be invited to participate in VOICE-C.

Section 5.1, *Selection of the Study Population and Recruitment, Group 1 (VOICE participants)*, *Ethnography and In-Depth-Interview* subsections:

Ethnography, first sentence:

Randomly **pre-selected** women who have ~~been participating in~~ **reached the Month 3 Visit** in VOICE for ~~at least 12 weeks~~ will be approached and invited to participate in the ethnographic component of the VOICE- C study.

In-Depth Interviews, first sentence:

As described above, **randomly pre-selected** women who have ~~been enrolled~~ **reached the Month 3 Visit** in VOICE for ~~at least 12 weeks~~, will be approached and will be invited to join VOICE-C.

Section 5.1, *Selection of the Study Population and Recruitment, Group 2 (Male partners)*, second and third sentences:

Women who are randomly **pre-selected** to participate in IDIs (sampling described above) will be asked to provide permission for study staff to invite their primary male partner for an IDI, which will be scheduled at a mutually convenient time. Similarly, women randomly **pre-selected** for FGDs will be asked to provide permission to contact their partner to join an FGD (after the trial).

Section 5.2, *Inclusion Criteria #1:*

Enrolled in VOICE, ~~and randomized to study product~~ **and reached the Month 3 Visit** in VOICE ~~at least 12 weeks~~ prior to enrollment in the VOICE-C Substudy

1. The following sections are updated to clarify the number of Group 1 FGD participants:

Section 5.1, *Selection of the Study Population and Recruitment, Group 1 (VOICE participants), Exit Focus Group* subsection:

The allowable number of FGD participants per group will be **approximately** 6-15 participants.

2. Section 8, *Assessment of Safety*, fourth paragraph is updated to reflect the revised Manual for Expedited Reporting of Adverse Events to DAIDS:
 - ~~Definitely r~~Related: ~~unanticipated problem and study participation/procedures are related in time, and a direct association can be demonstrated with study participation/procedures~~ **There is a reasonable possibility that the social harm is related to study participation**
 - ~~Probably related:~~ ~~unanticipated problem and study participation/procedures are reasonably related in time, and the unanticipated problem is more likely explained by study participation/procedures than by other causes~~
 - ~~Possibly related:~~ ~~unanticipated problem and study participation/procedures are reasonably related in time, and the unanticipated problem could be explained equally well by causes other than study participation/procedures~~
 - ~~Probably not related:~~ ~~A potential relationship between an unanticipated problem and study participation/procedures could exist (i.e., the possibility cannot be excluded), but the unanticipated problem is most likely explained by causes other than study participation/procedures~~
 - ~~Definitely n~~Not related: ~~The unanticipated problem is clearly explained by another cause not related to study participation/procedures~~ **There is not a reasonable possibility that the social harm is related to study participation**
3. Section 7.2.2, *Ethnographic Research Procedures, Table 3: Enrollment Visits for Ethnographic Research Component*, is deleted as it no longer accurately reflects the duration of the substudy.

4. Section 13.2, *Protocol Registration*, third and last sentences are updated to reflect the change from the DAIDS Regulatory Compliance Center to the DAIDS Regulatory Support Center:

Third sentence:

For additional information, refer to the protocol registration documents located at <http://resc.tech-res.com/forms.htm>.

Last sentence:

All protocol amendments must be submitted to and approved by the relevant IRB/EC(s) and the **Regulatory Support Center (RCSC)** prior to implementing the amendment.

5. The following minor changes and clarifications are made to the protocol:

The List of Abbreviations and Acronyms is updated:

RCSC	Regulatory Compliance Center Support Center
SDMC	Statistical Data Management Center

The Protocol Team Roster is updated to reflect modifications to the Protocol Team and updates to contact information:

The following additions are made to the Protocol Team Roster:

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The following listings have updated contact information:

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The following individuals have been removed from the Protocol Team Roster: Anne Coletti, Nancy Connolly, and Ayana Moore.

Section 5.1, *Selection of the Study Population and Recruitment, Group 2 (Male partners)* subsection, eleventh sentence, is updated to clarify the number of FGDs for Group 2 participants:

These partners will be systematically contacted by staff for IDIs during the accrual phase of the trial (one partner IDI per quarter per treatment group, for a total of approximately of 12 per site), or after the woman has exited the trial (approximately 48 male partners for **approximately** 4 FGDs, with **approximately** 2 FGDs per treatment group per site).

Section 7.2.5, section header and first sentence is updated to maintain consistency with site-specific VOICE activities:

7.2.5 Participant Observation Procedures at Male Partner **and Community** Activities During the VOICE Trial

As described above at each VOICE trial site, it is expected that VOICE participants, ~~and/or~~ their male partners, **and/or community members** will be invited to attend regularly scheduled VOICE-sponsored informational/educational meetings.

Section 10.4, *Number of Participants*, last paragraph, first sentence, further clarifies that Group 2 participants will not be randomized:

No random selection of participants will be performed for **Group 2**, Group 3 and 4.

Section 10.5.2, *Data Analysis, Qualitative Analysis: Data Types, Data Types* subsection, first sentence is clarified to reflect the data types that may be collected during the substudy:

The qualitative data from VOICE-C ~~will~~ **may** include several data types:

**Detailed Listing of Revisions Included in Clarification Memo #02,
Dated November 24, 2010**

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.

Detailed Listing of Revisions New to LoA #01

1.) Modifications to Group 1: VOICE PARTICIPANTS

- Section 4.1, *Identification of Study Design*, Section 4.4, *Time to Complete Accrual*, Section 4.6, *Expected Duration of Participation*, Section 5.1, *Selection of the Study Population and Recruitment*, Section 7.2.2, *Ethnographic Research Procedures*, Section 10.4, *Number of participants*, and APPENDIX I: *Sample Informed Consent Document (Ethnographic Visit-VOICE-C Participants)*, have been clarified to allow for up to 4 Ethnographic Interviews per Group 1 participant to occur:

Please note, the changes detailed below involve a modification to the protocol mandated number of Ethnographic Interviews to be conducted. Rationale regarding this modification is provided below:

The goal for data collection for Group 1 participants randomized to EI is to conduct up to 4 visits per participants in the EI. However, the team realizes that some participants will be "better" informants than others, and some will provide more insightful information into change over time, than others. Therefore, if saturation is reached with a particular participant after her second interview, (i.e. no new information is generated, that is, new data collected is redundant to previously collected data), the team may opt to not pursue the full 4 EIs. Two visits per participant is sufficient to cover the objectives of the study and provide a sufficient longitudinal perspective to participants' experiences. Additional details regarding the minimum of 2 visits will be supplied in the SSP.

Section 4.1, *Identification of Study Design*, first paragraph, third sentence:

VOICE female participants (Group 1) who have reached the Month 3 Visit and have been randomly pre-selected by the Statistical Data Management Center (SDMC), will be offered participation in VOICE-C which will involve one of the following three activities: a) a single visit

during which they will participate in a FGD (conducted at study exit, after completing their time on study product in the trial) b) a single visit during which they will participate in an IDI (conducted as the trial is unfolding) or c) long term (1 year for ~~a total of approximately up to~~ **up to** 4 visits) ethnographic research.

Section 4.4, *Time to Complete Accrual*, fifth sentence:

Each participant in this component of the study ~~will~~ **may** receive a home visit **as frequently as** every 3 months for one year.

Section 4.6, *Expected Duration of Participation*, second sentence:

Informal interviews for the ethnographic visit will not last more than 3 hours, and ~~will~~**may** be repeated up to 4 times (over one year) with each participant.

Section 5.1, *Selection of the Study Population and Recruitment*, Ethnography subsection, fourth sentence:

The participants will be followed up for a year, ~~with a total of~~ **and complete up to** four visits.

Section 7.2.2, *Ethnographic Research Procedures*, first paragraph, sixth sentence:

Participants will be asked to participate in **up to** four ethnographic visits.

Section 7.2.2, *Ethnographic Research Procedures*, second paragraph, second sentence:

~~The second and s~~Subsequent meetings will monitor the following issues: significant events in the community (for example political disturbances), physical experiences related to gel use or pill use; barriers to gel use or pill use; rumors about the trial; neighborhood conversations about their participation in the trial; gossip overheard in the clinic waiting room.

Section 10.4, *Number of participants*, Table 4: *Target Number of Participants Per Group and Site*, Row 2 and Row 4 updated:

Group	Description	Number of Participants per Site	Details per Site
1a	VOICE participants ethnography	~30	Cohort totaling 30 participants; enrolled after month 3 of study participation in VOICE. Up to One visit per quarter over a 12 month period
1c	VOICE participants IDIs	~30	1-2 participants/month (from month 3 to ~month 21 of VOICE) ~30 IDIs

APPENDIX I: *Sample Informed Consent Document* (Ethnographic Visit-VOICE-C Participants), Study Procedures subsection, first bullet:

- You will participate in an informal conversation with a research staff member(s) at your home, or at an alternative venue of your choosing. These interactions will last no more than three hours and ~~will~~**may** take place **approximately** every three months for one year

2.) Modifications to Group 2: MALE PARTNERS OF VOICE-C PARTICIPANTS

- Section 5.1, *Selection of the Study Population and Recruitment* and Section 10.1, *Overview and Summary of the Data*, have been updated to allow for an approximate number of IDIs involving male partners of VOICE-C participants.

Section 5.1, *Selection of the Study Population and Recruitment*, Group 2 (Male Partners) subsection, 4th sentence to the end of the paragraph

These partners will be systematically contacted by staff for IDIs during the accrual phase of the trial (**approximately** one partner IDI per quarter per treatment group, for a total of approximately 12 per site), or after the woman has exited the trial (approximately 48 male partners for approximately 4 FGDs, with approximately 2 FGDs per treatment group per site).

Section 10.1, *Overview and Summary of the Data*, second sentence:

Data collection will occur at various time points at selected sites during VOICE trial implementation with four groups of informants: VOICE participants (randomly assigned to three subgroups: ethnography, exit FGDs, and IDIs), male partners of VOICE-C participants (systematically selected in **approximately** equal numbers as partners of VOICE-C participants in oral and vaginal groups), CAB members (purposively selected) and Key Community Stakeholders (purposively selected).

3.) Modifications to Group 3: CAB MEMBERS

- Protocol Summary, *Study Population*; Section 4.3, *Description of Study Population*; and Section 4-4, *Time to Complete Accrual*, Section 4.5, *Study Groups*, Table 2: *Voice Accrual Plan*; Section 4.6, *Expected Duration of Participation*, Section 7.2.3, *Focus Group Discussion*, Section 10.4, *Number of Participants*, Table 4, Appendix IV, *Purpose of Study* Section and *Study Procedures* Section are updated to allow for 3-5 Focus Group Discussions to occur as deemed necessary by the protocol team and notes that approximately 20 CAB members over time will be involved. Given the nominal increase, the total study sample size of approximately 275 has not been modified. In addition, the protocol has been clarified to distinguish the initial Group 3 Focus Group Discussion from the other Focus Group Discussions.

Protocol Summary, Study Population, third bullet:

- *Group 3: Members of Community Advisory Boards (CABs) at VOICE-C site(s) (approximately 1520 per site)*

Section 4.3, Description of Study Population, third paragraph:

CAB Members (Up to ~1520 per site)

CAB members are those individuals who have been affiliated with VOICE-C sites for a minimum of 3 months. Eligible CAB members will be purposively selected and invited to join the VOICE-C Substudy, until **approximately** 1520 individuals accept to participate. As participating CAB members **may** participate in **one or more** several bi-annual FGDs, ~~in case one~~ **if an enrolled** individual has to terminate early his/her participation into VOICE-C, he or she will be replaced by another eligible CAB member.

Section 4.4, Time to Complete Accrual:

Data collection with Group 1 participants randomized to the ethnographic component will begin after Month 3 as well. Each participant in this component of the study will receive **up to four** home visits ~~every 3 months for~~ **over the course of** one year. At study exit, FGDs will be conducted with Group 1 participants (separately for oral and vaginal product administration groups) and separate FGDs will be conducted with male partners of exited VOICE participants.

~~Data collection~~FGDs with CABs **will be conducted as deemed necessary by the protocol team (no fewer than three and no more than five will be held)**. FGDs with ~~and~~ key community stakeholders will be on an approximately semi-annual schedule for the duration of the study.

Section 4.5, *Study Groups*, third bullet:

- Group 3: Members of the CABs at VOICE-C sites: Approximately **1520** CAB members who have been serving for at least 3 months will be invited to attend **3-5** consecutive FGDs, **including as well as** a FGD at the outset of the substudy.

Section 4.5, *Study Groups*, Table 2: *Voice Accrual Plan*, Row 4:

Group	Voice Accrual Period	Voice Follow-up Period
3	Up to 15~20 participants	N/A

Section 4.6, *Expected Duration of Participation*:

Group 1 and Group 2 participants will partake in an exit FGD or an IDI only once for a duration of up to 2 hours for an IDI or 2-3 hours for a FGD. Informal interviews for the ethnographic visit will not last more than 3 hours, and will be repeated up to 4 times (over one year) with each participant. Key community stakeholders will participate in a FGD only once for a duration of up to 2-3 hours. CAB members will be invited to attend up to five successive FGDs that will last up to 2-3 hours each, ~~which includes an~~ **additional** FGD at the outset of the substudy **will occur** to discuss topics that the VOICE-C team may want to consider exploring in the context of the IDIs.

Section 7.2.3, *Focus Group Discussion Procedures*, *CAB Members* subsection:

CAB Members

FGDs with CAB members will occur ~~approximately every six months for the duration of the study~~ **as deemed necessary by the protocol team**. Factors that would affect the scheduling of a Group 3 FGD include the release of trial results, the implementation of a new component of VOICE procedures, to learn more about specific rumors or trends identified by the VOICE study team. CAB members who have been active members of the CAB for at least three months will be invited to attend, and will be asked to provide written informed consent. FGDs with CAB members will explore the ongoing relationship of the community and the trial. Additionally a **baseline** FGD with CAB members will be conducted at the outset of the substudy to discuss topics that the VOICE-C protocol team should consider exploring in the context of the IDIs. Issues of adherence and challenges to adherence will be discussed. This is the only group of **community** informants that will be interviewed at several time points, and thus it will be important to provide information on perceived changes over time in community outlook and external factors affecting adherence. The procedures will follow those outlined above, although the informed consent process will only be conducted one time per individual.

Section 10.1, *Overview and Summary of Design*, third sentence:

Aside from CAB members who **will may** participate in **several more than one** (~~approximately five-monthly~~) FGDs throughout the duration of the VOICE trial and those participants who are randomized to the ethnographic portion of the study, all other informants will only be interviewed once.

Section 10.4, *Number of participants*, Table 4: *Target Number of Participants Per Group and Site*, Row 7:

Group	Description	Number of Participants per Site	Details per Site
3	CAB FGDs	Up to Approximately 15-20 maximum	5 groups, same ~1520 participants each per site*

Section 10.4, *Number of Participants*, last sentence:

No random selection of participants will be performed for Group 2, Group 3 and 4. All CAB members **will be invited to participate** and key community stakeholders will be invited to participate.

Appendix IV, Sample Informed Consent Document (FGDs-CAB Members), *Purpose of Study* section, second paragraph, third sentence:

If you agree to participate, you will take part in **3-5** focus group discussions.

Appendix IV, Sample Informed Consent Document (FGDs-CAB Members), *Study Procedures* section, second bullet, second sentence:

~~The~~**Each** discussion will last up to two to three hours and will take place ~~approximately every six months for~~ **over** the duration of the study, facilitated by a trained staff member.

4.) Modifications to Group 4: KEY COMMUNITY STAKEHOLDERS

- Section 4.4, *Time to Complete Accrual*, Section 4.5, *Study Groups* and Section 10.4, *Number of Participants* have been modified clarify details regarding Key Community Stakeholder accrual.

Section 4.4, *Time to Complete Accrual*, last sentence has been modified.

FGDs with CABs will be conducted as deemed necessary by the protocol team (no fewer than three and no more than five will be held). **Up to 5** FGDs with key community stakeholders will ~~be on an approximately semi-annual schedule~~ **occur for throughout** the duration of the study.

Section 4.5, Study Groups

- Group 4: Key community stakeholders: CAB members, community-group members (i.e. women's groups, church groups, market groups) and site staff will help identify and purposively select ~~approximately 50~~ key community stakeholders at each site **to attend, between 3-5** FGDs ~~(with 10 members each) conducted throughout trial implementation with this group~~ **the duration of the study. No more than 50 key community stakeholders will be enrolled; each enrollee will attend one focus group discussion.**

Section 4.5, Study Groups, Table 2: VOICE-C Accrual Plan, Row 5 has been updated:

Group	VOICE Accrual Period	VOICE Follow-up Period
4	40	10
4	Up to 50 participants will be accrued during the VOICE accrual and follow-up periods	

Section 10.4, *Number of Participants*, last sentence:

No random selection of participants will be performed for Group 2, Group 3 and 4. All CAB members **will be invited to participate** and key community stakeholders will be ~~invited to participate~~ **selected by study staff** for participation.

- 5.) Section 10.5.1, Study Monitoring Committee (SMC) has been modified to remove the formal SMC for this protocol and to allow for a team review of study progress, including rates of participant accrual:

Section 10.5.1, *Study Monitoring Committee (SMC)*

No Data and Safety Monitoring Board (DSMB) oversight **or MTN Study Monitoring Review** ~~are~~ planned for this observational study. The ~~MTN SMC protocol team~~ will conduct periodic **internal** reviews of study progress including rates of participant accrual. These reviews will take place approximately every 12 months or as needed. ~~At the time of these reviews, or at any other time, the SMC may recommend that the study proceed as designed, proceed with design modifications, or be discontinued. The SMC may consider recommending termination of this study if recruitment is lower than targeted.~~ If the **SMC protocol team** deems that accrual targets are not being met for male partners of VOICE-C participants, recruitment of this population will be extended to male partners of other VOICE participants, who were previously not selected to participate in VOICE-C.

- 6.) Section 10.5.2, *Data Analysis, Qualitative Analysis: Data Types* subsection has been modified to more accurately describe the qualitative data to be generated from VOICE-C:

Data types

The qualitative data from VOICE-C may include several data types:

- Transcripts from audio recorded IDIs or FGDs
- **Transcripts from H**handwritten notes (brief field notes, summary notes, debriefing reports) from ethnographic field notes **interviews**, FGDs, and IDIs
- ~~List of terms generated through free listing and pile sorting exercises during IDIs~~
- Participant observation notes or summary reports from male partner **or community** meetings, if available

- 7.) Section 2.1, *The VOICE Study*, has been updated to accommodate for changes incorporated into Version 2.0 of the VOICE protocol, including sample size and maximum length of time on study product.

Section 2.1, *The VOICE Study*, second paragraph, second sentence:

Approximately ~~4200~~ **5000** participants will be randomized to the five study arms in a 1:1:1:1:1 ratio.

Section 2.1, *The VOICE Study*, third paragraph, second sentence:

All participants will complete monthly follow-up visits for a period of 12 to ~~33~~ **36** months, and will receive ongoing HIV risk reduction counseling, condoms, and diagnosis and treatment of STIs throughout the course of study participation.

- 8.) Section 12.0, Clinical Site Monitoring has been updated to remove PPD as the monitor, study monitoring will not occur for this observational study:

Study monitoring **is not planned for MTN-003C** and will be **not be** carried out **for this study**. ~~by PPD (Wilmington, NC) in accordance with all applicable DAIDS guidance for monitoring of substudies. Please refer to the VOICE (DAIDS Protocol #10622) Clinical Site Monitoring Section (Section 12) for additional applicable details.~~

- 9.) The following updates are made to the Protocol Team Roster:

The following individual is added to the roster:

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10.) The List of Abbreviations and Acronyms is updated:

FHI	Family Health International
RCC	Regulatory Compliance Center
SMC	Study Monitoring Committee
PPD	Pharmaceutical Product Development, Inc.
RE	regulatory entity
RSC	Regulatory Support Center

Other minor updates include the following: Regulatory Compliance Center (RCC) is now Regulatory Support Center (RSC) and the acronym *FHI* no longer stands for Family Health International. Any references to RCC or Family Health International have been removed throughout the protocol.

The above information will be incorporated into the next version of the protocol if it is amended.