**Microbicide Trials Network**

**CLARIFICATION MEMO #01 TO:**

**MTN-003C**
**Household and Community Level Factors Associated with Study Product Adherence in VOICE: A Substudy of MTN-003**
**Version 1.0/15 July 2009**

**DAIDS Document ID 10746**

**Date of Clarification Memorandum: 17 June 2010**

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*Section 1: Summary of Clarifications and Rationale*

The procedures clarified in this Clarification Memorandum (CM) have been approved by the NIAID Medical Officer and are to be implemented immediately upon issuance. IRB approval of this CM is not required by the sponsor; however, investigators may submit the CM to the IRB overseeing the study at their site for information. This CM is official MTN-003C 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.

The primary goals for this CM are to clarify within the protocol that the "study exit" in MTN-003C refers to the Product Use End Visit (PUEV) in VOICE and to clarify the point at which VOICE participants are invited to participate in VOICE-C. This CM also updates the number of allowable participants in Group 1 Focus Group Discussions (FGD). A clarification is made to Section 8, Assessment of Safety to reflect recent updates for Expedited Adverse Event Reporting to the US NIH Division of AIDS. Additionally, this CM removes the accrual plan for the ethnographic component since the VOICE-C timeline no longer reflects the duration of VOICE at the VOICE-C study site(s). Minor clarifications and updates are also included in this CM.

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*Section 2: Implementation*

With the exception of the changes to the Protocol Team Roster, text to be deleted is noted by ~~strikethrough~~ and text to be added is noted below in **bold.**

1. The following sections are updated to clarify that "study exit" in VOICE-C refers to the Product Use End Visit (PUEV) in the main VOICE trial and to further clarify the point at which VOICE participants are invited to participate in VOICE-C:

*Protocol Summary, Study Regimen for Participants* table, row 1b VOICE Participants and row 2a Male Partners of VOICE Participants:

| 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

2. 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.

3. Section 8, *Assessment of Safety*, fourth paragraph is updated to reflect the revised Manual for Expedited Reporting of Adverse Events to DAIDS:

- ~~Definitely r~~**R**elated: ~~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~~**N**ot 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**

4. 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.

5. 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://r~~c~~**s**c.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 (**R~~C~~**S**C**)** prior to implementing the amendment.

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

The List of Abbreviations and Acronyms is updated:

| | |
|---|---|
| R~~C~~**S**C | Regulatory ~~Compliance~~ **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 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:

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