Section 19. Household and Community Factors Associated with VOICE Product Adherence Substudy (VOICE-C)

This section describes study-specific procedures for VOICE-C, *Household and Community Factors Associated with VOICE Product Adherence*, a substudy of the VOICE study. VOICE-C will be conducted at the WRHI study site in Johannesburg, and additional sites may be added. Therefore, the WRHI site must maintain this section of the Study-Specific Procedures (SSP) Manual in its entirety. All other VOICE sites not participating in VOICE-C are not required to maintain this section of the manual. For clarity of documentation, however, all sites should maintain a reference copy of Version 1.0 of this page (19-1), dated 17 June 2010, in their SSP manuals.

19.1 Introduction

This section specifies the sources of procedural information available to VOICE-C substudy staff, the responsibilities of VOICE-C Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of VOICE-C.

19.1.1 Sources of Procedural Information

All study procedures must be conducted in accordance with the VOICE-C protocol. The purpose of this manual is to supplement the protocol, not to replace or substitute it. In the event that this manual is inconsistent with the protocol, the specifications of the protocol take precedence. Please alert the VOICE-C Study Management Team (described below) of any such inconsistencies. Study implementation questions that are not answered by the protocol or this manual should be directed to the VOICE-C Study Management Team. This group consists of representatives of the MTN Coordinating and Operations Center (CORE-PITT and CORE-FHI 360), RTI International, and the Protocol Chairs. This group can be reached using the following email address:

mtn003c-siteops@mtnstopshiv.org

19.1.2 Investigator Responsibilities

VOICE-C must be conducted in accordance with the United States Code of Federal Regulations and the International Conference on Harmonization Consolidated Guidance for Good Clinical Practice. Copies of these regulations and guidelines are referenced in the MTN Manual of Operations (MOP) which can be accessed at:

http://www.mtnstopshiv.org/node/187

The DAIDS policies on *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials* and *Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials* are useful for interpreting and operationalizing the regulations and guidelines in accordance with DAIDS expectations. These policies can be accessed at:

http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch

VOICE-C also must be conducted in accordance with all site-specific regulations, policies, and guidelines applicable to human subjects research in general and/or the conduct of study procedures in particular. Copies of all such regulations, policies, and guidelines should be maintained in on-site essential document files. Please refer to Section 3.1 of this manual as well as Section Appendix 19-2.

The IoR at each site must sign both a protocol signature page and an Investigator Agreement to formally indicate his/her agreement to conduct VOICE-C in accordance with the study protocol and all applicable regulations, policies, and guidelines. The protocol signature page can be found in Section Appendix 19-1 of this manual. The obligations and responsibilities assumed by the IoR when signing the Investigator Agreement are listed on the form. IoRs may delegate their obligations and responsibilities for conducting VOICE-C to other study staff members; however, delegation does not relieve the IoR of his/her ultimate responsibility for all study procedures performed and all study data collected. Delegation of IoR responsibilities must be formally documented throughout the period of study implementation.

Consistent with the regulations, guidelines, and policies cited above, the IoR at each site must obtain and maintain Institutional Review Board and/or Ethics Committee (IRB/EC) approval of VOICE-C throughout the period of study implementation. See Section 8.4 of the MTN Manual of Operations (MOP) for detailed information on IRB/EC submission, review, approval, and documentation requirements. All sites are encouraged to request an acknowledgement of receipt for all documents submitted to their IRBs/ECs and to request that IRBs/ECs note the effective and expiry dates of all approvals. Documentation of all correspondence to and from all responsible IRBs/ECs (i.e., complete copies of all submissions, responses, and approvals) must be maintained in on-site essential document files.

19.1.3 Study Activation Process

Prior to undertaking any study procedures, each site must obtain approval to conduct VOICE-C from all responsible regulatory authorities and IRBs/ECs. Each site also must complete protocol registration procedures with the DAIDS Regulatory Support Center Protocol Registration Office and study activation procedures with DAIDS and the MTN CORE (FHI 360). Detailed information on the requirements of these pre-implementation steps can be found in Section 10 of the MTN MOP. On a site-by-site basis, the MTN CORE (FHI 360) will issue a Site-Specific Study Activation Notice when all study activation requirements have been met. At each site, no protocol-specified study procedures may be undertaken prior to issuance of the Site-Specific Study Activation Notice.

19.2 Protocol

A complete reference copy of the VOICE-C protocol is provided in Section Appendix 19-1. Protocol Version 1.0, dated July 14, 2009 reflects current protocol specifications.

To ensure that this manual continues to reflect current protocol specifications in the future:

- Upon receipt of any protocol clarification memos, add a copy of the memo to Section Appendix 19-1.

- Upon receipt of any letters of amendment, add a copy of the letter of amendment to Section Appendix 19-1.

- Upon receipt of any full protocol amendments, replace the contents of Section Appendix 19-1 with the amended protocol. See Section 19.3.1 for filing requirements related to the protocol and other essential documents.

Further information on the content and required handling of protocol clarification memos, letters of amendment, and full amendments is available in Section 9.2 of the MTN MOP.

19.3 Documentation Requirements

Study staff are responsible for proper collection, management, storage, quality control, and quality assurance of all study-related documentation, related to the MTN VOICE-C study. A unique set of essential documents as they pertain to the VOICE-C study should be maintained separately from the parent study. This section contains information on the essential documents that each study site must maintain throughout the study. It also contains information related to establishing adequate and accurate participant research records — commonly referred to as the "participant file" — for VOICE-C.

19.3.1 Essential Documents

The DAIDS policy on *Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials* specifies the essential documents that study sites must maintain for DAIDS-sponsored studies, including VOICE-C. When required documents are modified or updated, the original and all updated versions must be maintained. Although all required documentation must be available for inspection at any time, all documents need not be stored together in one location. In its policy on *Requirements for Manual of Operational Procedures*, DAIDS requires study sites to establish a standard operating procedure (SOP) for maintaining essential documents. This SOP should be established prior to activation of VOICE-C and should be followed for VOICE-C.

Section Appendix 19-2 presents a suggested essential documents filing structure for VOICE-C. The suggested structure incorporates guidance received from the DAIDS Prevention Science Program and the DAIDS Clinical Site Monitoring Group. Study sites are not required to adopt the suggested structure, but are encouraged to consider it when developing their filing approach for VOICE-C. Three tips for the suggested filing structure are provided as clarification:

- Essential documents may be stored in files and/or in binders. The files/binders listed in Section Appendix 19-2 may be further subdivided, consolidated, and/or re-organized if desired.

- Insert a contents sheet as the first page(s) of each file/binder. File documents for each binder in ascending date order (most recent documents in front).

- The suggested filing structure assumes that VOICE-C participant files will be stored separately from the other essential documents listed in Section Appendix 19-2. Section 19.3.2 below provides information on the required contents of these files. The suggested filing structure also assumes that the Screening and Enrollment Logs (which are described in Section 19.4.6 of this manual) will be stored in the study clinic or data management area, and not necessarily with the other essential documents listed in Section Appendix 19-2.

19.3.2 Participant File Documentation

Study sites must maintain adequate and accurate participant file records containing all information pertinent to VOICE-C for each study participant.

19.3.2.1 Participant File Contents

Participant files should contain all of the following elements:

- Basic participant identifiers.

- Documentation that the participant provided oral consent to participate in screening procedures for the study prior to the conduct of any screening procedures.

- Documentation that the participant met the study's selection (eligibility) criteria.

- Documentation that the participant provided written consent to participate in the study prior to the conduct of any study procedures (outside of requirements for Screening 1 and 2).

    - Note: Any questions the participant asks during the written IC process (and responses to these questions) should be documented in file notes or on the informed consent cover sheet.

- A record of the participant's study arm assignment (Groups 1 and 2 only).

- If applicable: documentation of changes to assigned interview modality due to operational challenges or study design changes (and approval from the protocol team)

- A record of all contacts, and attempted contacts, with the participant.

- A record of all study activities and interview transcripts that take place during the conduct of the study.
    - Notes recorded on interview guides and/ or separate sheets of paper for the ethnographic interview (EI) or in-depth interview (IDI) are filed in the participant file; separate files can be created to store all FGD group information such as checklists, notes and participant lists. Copies of supplemental probing guides should be filed with the corresponding interview guides.

- Referrals made (including for social harms or adverse events (Group 1 only) reported)

- Reason for any deviation required from procedures outlined in the site SOP

- If in Group 1, record of whether permission to contact partner for Group 2 participation was granted (Permission to Contact form to be filed separately because of identifying information).

- Group 2-4, documentation of literacy if screening is conducted over the phone.

In addition to the above, DAIDS requires that all protocol deviations be documented in participant records, along with reasons for the deviations, efforts made to correct the deviations, and efforts made to prevent similar deviations in the future (see the MTN website at http://www.mtnstopshiv.org/ for the protocol deviation template used for all MTN studies). VOICE-C study sites also must report reportable protocol deviations per Section 15.4 of the MTN MOP. It is also recommended that a copy of all protocol deviations recorded at the site be maintained in one central file with the Essential Documents.

19.3.2.2 Concept of Source Data and Source Documentation

The International Conference on Harmonization Consolidated Guidance for Good Clinical Practice (ICH-E6) defines the terms source data and source documentation. Please refer to section 3.2.2 of this SSP for more detail.

Source documents are commonly referred to as the documents — paper-based or electronic — upon which source data are first recorded. As a condition for study activation, each study site must establish a Source Documentation SOP that specifies the use of the documents listed below as source documents. Although it is the responsibility of each site to determine the most appropriate source document for each required participant file element, Section Appendix 19-3 provides a guide that sites may follow.

For VOICE-C, participant files contain several source documents:

- **Narrative participant file notes**: file notes should be used to communicate any deviations from SOPs, any protocol deviations that are not recorded on other source documents, any referrals made that were not documented elsewhere, or contacts with all participants if the Participant Contact Log is not used for this purpose

- **Case Report Forms (CRFs) and non-CRF forms:** The case report forms for this study are designed for use with the RTI data management system described in Section 19.11 of this manual. RTI will provide the master versions of these forms to the site, and printing will be coordinated locally. RTI will also provide several additional study-specific forms (non-CRFs) to the site. See Section Appendix 19-3.1 for a listing of all forms for this study. All CRFs and other forms used in this study can be found on the MTN VOICE-C website.

- **Qualitative Guides for in-depth interviews and ethnographic interviews:** Individual interview guides and ethnographic field notes, supplemental probing guides, as well as any additional notes taken during qualitative data collection are source documents and must be kept in the participant file. Although the audio file is the source for the interview, transcriptions of the interview (in local language and the final translated version) must be kept in the participant file and the location of the source must be specified. Guides and notes for the focus group discussions should be filed per the site Source Documentation SOP.

- Other source documents (e.g., site-specific worksheets) as identified in the site Source Documentation SOP.

19.3.2.3 Document Organization

Study staff must make every effort to store all study records securely and confidentially. Participant files must be stored in the same manner for all participants, in areas with access limited to authorized study staff only. Study staff are responsible for purchasing file folders, binders, storage cabinets, and any other equipment or supplies needed to properly store all records.

Study-related documentation collected during the screening process should be stored in file folders (flat files) or thin folders for each potential participant. All screening documentation — for potential participants who eventually enroll in the study as well as for those who do not enroll — must be maintained and available for monitoring throughout the study. Flat files may be maintained for participants who enroll, if the files have some kind of secure mechanism (i.e. rings, clasps) to hold papers. Otherwise, documentation should be transferred to files that have secure mechanisms for holding papers. Pocket files are not adequate as loose papers may still fall out.

All documents contained in participant files must bear a participant identifier, which generally will consist of either the participant identification number (PTID) or the participant name. To maximize participant confidentiality, the PTID should be used whenever possible, and records that bear names or other personal identifiers, such as locator forms and informed consent forms, must be stored separately from records identified by PTID. Any documents transferred or transmitted to a non-study site location — including RTI or a local data management center— must be identified by PTID only. Table 19-1 gives a list of documents developed for VOICE-C and whether name, PTID, or both are used.

Table 19-1- Listing of VOICE-C CRFs and Logs

Document name	Name/ Initials only	PTID only	Name/Initials and PTID
Enrollment Status Form (Groups 1-4)		X	
Locator form (Groups 1-4)	X		
Permission to contact form (Group 1)			X
Screening and Enrollment Log (Groups 1-4)			X
Consent forms (Groups 1-4)	X		
Participant Contact Log (Groups 1-4)		X	
Case Report Forms		X	
Visit Checklists		X	

Visit Checklists: The sample checklists in Section Appendix 19-5 of this manual provide an example of convenient tools to fulfill the requirement of documenting all study activities that take place at each IDI, Ethnographic Interview or FGD with study participants. Checklists used for IDI and Ethnographic Interviews should be filed with the participant files. A single checklist used for a FGD should be filed per the site Source Documentation SOP. Every item in the left column of each checklist should be ticked or marked 'NA'. If the visit procedures deviate from what is outlined in the checklist, documentation of this should be in the comments section or at the bottom of the checklist.

All on-site databases must be secured with password-protected access systems. When in use, documents that link PTIDs to other participant identifiers should not be left unattended or otherwise accessible to study participants, other study clinic patients, or any other unauthorized persons.

As a condition for study activation, each study site must establish an SOP for Data Management. This SOP minimally should contain the following elements:

- Procedures for assigning PTIDs, and linking PTIDs to participant names
- Procedures for establishing participant files
- During-visit participant file and CRF review procedures
- Post-visit participant file and CRF review procedures and timeframes
- CRF data entry procedures, including timeframes, CRF storage locations before and after data entry, and mechanisms for identifying when forms have been entered
- Data collection using the guides (FGD, IDI and ethnography interview) and data, back-up, transcribing/translating procedures, and transmission procedures. This section should also include timeframes, and mechanisms for identifying when questionnaires have been transmitted
- Procedures and timeline for resolving data quality control notes from RTI
- Procedures and timeline for handling and filing field workers' logs, worksheets, etc.
- Storage locations for blank CRFs and guides
- Storage locations for documents identified by participant names or other personal identifiers
- Storage locations for documents identified by PTID
- Handling of participant study files for off-site contacts and visits
- Confidentiality protections
- Other ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures related to the above (if not specified elsewhere)

19.3.3 Record Retention Requirements

Please refer to Section 3.4 of this manual. The documents for VOICE-C must be maintained (at least) for the same timeframe as those for the VOICE study. No documents may be destroyed without written permission from DAIDS.

19.4 Participant Accrual

This section provides information on requirements and procedures for recruiting, screening, and enrolling participants in VOICE-C. Informed consent considerations are provided in Section 19.5.

19.4.1 Study Accrual Plan and Site-Specific Accrual Targets

Approximately 275 participants per site are targeted to be enrolled in VOICE-C, prior to the conclusion of the VOICE trial. This is anticipated to take place over a period of approximately 2.25 years (about 28 months) but will ultimately depend on the overall schedule of the VOICE trial. VOICE-C will have the following 4 participant groups with the following approximate accrual targets:

1. Group 1: VOICE participants (approximately 150 participants);
2. Group 2: Male partners of VOICE participants (approximately 60 participants);
3. Group 3: Community Advisory Board members (approximately 20 participants);
4. Group 4: Key Community Stakeholders (up to 50 participants).

Accrual Order & Timing

The order of accrual into the study for the four groups of participants is independent of the study group number (e.g. Group 1 vs. Group 3).

The first group to be screened and enrolled into the study is Group 3 (Community Advisory Board members), who will take part in the first of a series of Focus Group Discussions (FGD), beginning at the study outset. Between three and five FGDs with approximately the same cohort of Group 3 participants are conducted on an as-needed basis as determined by the Protocol Team. New CAB members may join Group 3 during the study if they meet eligibility criteria (see Section 19.4.3).

Potentially eligible Group 1 participants will be randomly pre-selected by SCHARP, and will be screened on or after their Month 3 VOICE visit.

Group 1 participants who are successfully screened and randomized will be asked to provide consent to their primary male partner being recruited for participation in Group 2. Contact and recruitment of potential Group 2 participants is dependent on this "permission to contact" process.

This permission to contact is documented on the Permission to Contact Form and on the Group 1 Enrollment Status Form (item 11) as specified in section 5.1 of this protocol. If a Group 1 participant has more than one partner, priority should be given to successfully recruit the primary male partner. The timing of contact with male partners depends on the Group 1 assignment: Male partners of Group 1 participants randomized to IDI may be contacted at any time after the female partner has provided permission to contact. Partners of Group 1 FGD participants will be contacted after the product use end visit (PUEV) and after the Group 1 participant has reviewed and updated (if applicable) her Permission to Contact Form. Partners of Group 1 EI participants should only be contacted upon prior authorization from the Study Management team. This will be based on an evaluation of recruitment levels for Group 2 by the Protocol Co-Chairs.

Accrual for Group 4 (Community Stakeholders) participants can begin anytime after study activation, and will continue throughout the duration of VOICE-C accrual and follow-up periods until four FGDs with approximately 6-15 participants each are completed.

Refer to Section Appendix 19-6 for a summary of the four groups, randomization assignments, accrual targets, and general timing.

Refer to Section 19.6 Visit Procedures for timing of study activities for each sub-group.

Randomization

In the VOICE-C study, only Group 1 participants will be randomized to an interview modality on the day of Screening 1. The randomization scheme is based on a 1:3:1 allocation to IDI, FGD and EI, respectively. Prior to the start of the study, a VOICE-C randomization assignment (not selected, IDI, FGD, EI) will be designated by SCHARP for the first 200 VOICE participant at the site on the Participant Tracking and Randomization List (PTRL). SCHARP will provide subsequent PTRL, as required.

In addition to randomization assignments, enrollment status will be recorded on the PTRL that is provided by SCHARP. A sample template of this list is pasted below in Table 19-2. The VOICE-C Study Coordinator is responsible for updating the VOICE PTIDs on this list regularly (at least weekly). Because the VOICE-C randomization assignment is linked to the enrollment sequence number into VOICE, and determined prior to the start of the study, it is critical that the corresponding VOICE-PTID is accurately recorded in the proper sequence order after the VOICE study starts. This should be done by referencing the VOICE Clinic Randomization Envelope Tracking Record.

Table 19-2: Sample Template of Participant Tracking and Randomization List

Enrollment sequence in VOICE	VOICE PTID		VOICE-C Group 1 Randomization Assignment	VOICE Month 2 Visit Date (dd-MMM-yy)	VOICE Month 3 Target Date (dd-MMM-yy)	Was Participant Enrolled in VOICE-C?	VOICE-C Participant ID	Staff Initials
1	325-		Not selected					
2	325-		Not selected					
3	325-		Not selected					
4	325-		Exit FGD					
5	325-		Not selected					
6	325-		Not selected					
7	325-		Not selected					

The interview modality assigned to a primary male partner enrolled in Group 2 is dependent on his female partner's randomized interview modality in Group 1. For example, if a Group 1 participant is randomized to the IDI modality, her primary male partner will be assigned to the IDI modality for Group 2, if eligible and willing to enroll in the VOICE-C study. If a participant in Group 1 is randomized to EI, she will also be asked for permission to contact her male partner for involvement. For women randomized to the EI modality, they should be informed that their partner may or may not be contacted for recruitment into Group 2 if she provides permission to contact – this will depend on recruitment targets for Group 2, and will only happen with authorization from the VOICE-C management team.

Ideally, once randomized, participants may not switch interview modality, i.e. an EI participant should not be scheduled to participate in an FGD or vice versa. This rule applies to Group 2 participants as well. VOICE-C staff should counsel participants in Groups 1 and 2 that they will participate in the interview method they are randomized to. If a participant does not wish to stay involved due to the randomization, or if there are logistical or other practical considerations that prevent a participant from receiving his/her assigned interview method (i.e. schedule does not permit a participant to attend a FGD, in which case it may be acceptable to have an IDI instead) staff should email the VOICE-C management team to determine whether this individual should be included in the study. Documentation of this in the participant file is required.

Both Group 3 and Group 4 have only the FGD as an interview modality option.

Note: Effective in October, 2011, participants randomized to the active tenofovir tablet arm in VOICE and randomly pre-selected for the EI group were switched to the IDI group if they had not yet enrolled in VOICE-C by the time of their VOICE PUEV. Effective November 2011, participants randomized to either gel arm in VOICE and randomly pre-selected for the EI group were switched to the IDI group if they had not yet enrolled in VOICE-C at the time of the PUEV. These modifications are a result of the VOICE DSMB meetings and are documented in a memo to file for site regulatory documentation.

VOICE-C Study Participant Accrual Plan

Each site is responsible for developing its own accrual plan that can be described in the site Accrual SOP. However, as accrual of Group 1 participants is dependent on participation in the VOICE study, it is recommended that the section of the accrual plan addressing VOICE-C Group 1 is developed in cooperation with the VOICE clinical staff. Working in collaboration with the VOICE clinical staff, the Community Working Group (CWG), and local Community Advisory Board (CAB) is encouraged. Please contact FHI 360 to help facilitate any of this process as needed.

The accrual plan should minimally contain the following elements:

- Site-specific accrual targets
- Methods for tracking actual accrual versus accrual targets
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

Study staff are responsible for updating this accrual plan if needed to meet site-specific accrual goals.

19.4.2 Assignment of Participant ID Numbers

For all VOICE-C participants, RTI will assign VOICE-C participant ID numbers (PTIDs) for Group 1 – 4. The site should assign one PTID to each participant after verbal consent to screen for the study has been obtained (see Section 19.4.3 Screening Definition and Eligibility Criteria). PTIDs are assigned in sequential order within the range of the applicable group as participants are screened for the study (Part 1 of the Enrollment Status Form). Staff should ensure that each PTID is assigned only once and may track this by using a Screening and Enrollment Log. Once a participant has received a PTID, s/he will maintain that same PTID throughout the entire study. Each participant may only enroll into one group for VOICE-C. For example, a Group 2 participant cannot enroll as a Group 3 or Group 4 participant.

For Group 1, the Enrollment Status Form (ESF) will capture both the VOICE-C PTID and the VOICE PTID of the female participant. The VOICE-C PTID should be used for all subsequent VOICE-C documentation. **For Group 2,** the ESF will also capture the VOICE-C PTID of the female participant in addition to the PTID for the Group 2 participant.

VOICE-C PTID boxes are located near the upper left corner of each CRF page. The PTIDs used for this study are four digits long and are formatted as "XYYY." The two parts of the PTID are: the group number (X) and the participant number (YYY).

For Group 1 participants, the range of IDs will be: 1001 – 1200 for participants screened and enrolled and 1901-1999 for ineligible participants
For Group 2 participants, the range of IDs will be: 2001 – 2100 for participants screened and enrolled and 2901-2999 for ineligible participants

For Group 3 participants, the range of IDs will be: 3001 – 3100 for participants screened and enrolled and 3901-3999 for ineligible participants

For Group 4 participants, the range of IDs will be: 4001 – 4100 for participants screened and enrolled and 4901-4999 for ineligible participants

19.4.3 Screening Definition and Eligibility Criteria

Screening refers to procedures undertaken to further confirm eligibility, and obtain a verbal expression of willingness to join/enroll in the study. Verbal consent for screening procedures, including eligibility determination, will most likely occur in the clinic for Group 1, and may occur over the phone for Group 2-4 participants. The screening process is formally documented on the appropriate ESF CRF for each VOICE-C study group (i.e. each study group has an ESF unique to that group), the Verbal Consent Checklist, and in participant file notes as appropriate. Any contact made with potential participants for verbal consent for screening and/or screening procedures should be documented in the Participant Contact Log and/or participant file notes. The ESF CRF is used as a source document.

Screening begins once a participant has provided verbal consent to participate in the screening process. Participants who consent to screening should then have a unique, sequential VOICE-C PTID assigned, as described above in Section 19.4.2. The screening consent process must be documented using the Verbal Consent Checklist. In the case that a participant does not provide verbal consent for screening, a numeric code of "X9XX" should be entered as the PTID on the Screening and Enrollment Log, as well as on his/her ESF in place of a "0000" code or enrollment PTID. For Group 1 this would be 19XX (the first participant who refuses screening would be PTID 1901, then 1902 etc). For Group 2 these PTIDs start at 29XX, 39XX for Group 3, and 49XX for Group 4.

After the screening verbal consent and assignment of a VOICE-C PTID, each participant will be assessed for eligibility criteria appropriate for his or her group (Screening 1 procedures as outlined on the ESF). The study eligibility criteria for each group is listed in VOICE-C Protocol Section 5 and further discussed in this section below. If it has been more than 14 days between Screening 1 and the day of enrollment it is necessary for study staff to revisit eligibility criteria for Groups 1 and 2 to ensure that participants are still eligible for VOICE-C. This process is called "Screening 2", and is documented in section 2 of the ESF. Specific procedures related to each group can be found below.

Group 1:

Screening for Group 1 begins during the Month 3 VOICE visit or later. Sites should develop reliable methods to ensure that VOICE participants who were pre-randomized to VOICE-C do not leave the clinic prior to VOICE-C screening, (i.e. file labels/ flags, referral to VOICE-C) and describe these in the site Accrual SOP. It is acceptable for a potential participant to be screened and enrolled into VOICE-C if she is early for her Month 3 visit, but still within the VOICE protocol-specified window (-14 days from her VOICE target date). A participant can be screened and enrolled into VOICE-C at any time on or after her VOICE month-3 visit date.

VOICE CRFs must be verified to determine eligibility for Group 1 VOICE-C participants each time the participant is screened. The process for retrieving this information must be outlined in the site Accrual or Eligibility Determination SOP. These CRFs from the parent study must be used as source documents for determining eligibility per the site Source Documentation SOP and certified copies of the VOICE CRFs needed to document eligibility must be maintained in the VOICE-C participant file. If the participant requires the second screening visit (more than 14 days have passed between the first screening and study enrollment) but the participant has NOT had a VOICE visit since the first VOICE-C screening was conducted, document as such in the participant file and certified copies of the VOICE CRFs do not need to be refiled. Note that a woman on temporary product hold for VOICE could be eligible for VOICE-C once she has restarted study product. If it is determined that she is on temporary product hold and is therefore not eligible for VOICE-C prior to the Screening 1 Visit, she should not have this visit until she resumes study product. If it is learned that she is on temporary product hold *during* the Screening 1 VOICE-C visit, she should be considered ineligible and her Screening 2 visit held to assess eligibility once she resumes study product.

If a participant expresses immediate unwillingness to join the VOICE-C study, her desire will be respected. Nonetheless, she should inform the VOICE-C staff of her decision.

The Screening 1 process will include the randomization assignment of an interview modality. A woman should not be informed of her randomization group prior to providing verbal consent for screening. Group 1 participants who are randomized to either the IDI or EI interview modalities and are eligible should be scheduled for these data collection activities to occur within 14 days. If data collection does not occur within 14 days of Screening 1, Screening 2 procedures are carried out and documented on the ESF prior to enrollment into the study to ensure the participant is still eligible. All Group 1 participants who are randomized to the FGD interview modality should be informed that Screening 2 will be conducted at her Product Use End Visit (PUEV) for VOICE in order to reassess her eligibility for VOICE-C. Group 1 FGDs will be scheduled during the 8 week period between eligible participants' PUEV and Termination Visit (TEV). Although in many cases more than 14 days may pass between Screening 2 (at PUEV) and enrollment (at the FGD), no new VOICE data on this participant will be collected so eligibility for VOICE-C does not need to be re-confirmed at the time of enrollment (at the FGD).

If eligible, Group 1 participants randomized to IDI or EI will be asked to consent to their primary partner being contacted for potential participation in Group 2. This consent to contact is documented on the Permission to Contact Form as specified in section 5.1 of the protocol. The Group 1 participant will provide her initialed permission to contact, and the address, phone number or other contact details with which to contact the male partner. Group 1 participants randomized to the Ethnographic Interview should be informed that her partner *may or may not* be recruited for participation. His involvement will depend on the accrual success of partners from Group 1 participants randomized to FGD or IDI. Group 1 participants randomized to FGD will be asked about permission to contact male partners at the PUEV, since partners could change between Screening 1 and the time of the exit FGD. Group 1 participants who decline this "permission to contact" may still be enrolled and continue in the VOICE-C study and may change their mind later on about permission to contact their partner. Similarly, if her primary male partner declines verbal consent for Group 2 screening, the Group 1 participant will not be withdrawn from the VOICE-C study, and may continue as scheduled. If a Screening 2 visit is needed, the permission to contact information on the ESF, as well as the Permission to Contact form should be reviewed and updated as needed.

At the time the Permission to Contact form is completed, the Group 1 participant should be provided with a VOICE Male Partner Fact Sheet to give to her partner. She should be informed that this is made available for male partners of all VOICE participants and the VOICE-C staff may also provide him with this after his VOICE-C interview if he has any questions pertaining to the VOICE study.

Inclusion and exclusion criteria for Group 1 participants are as follows:

Inclusion Criteria: Group 1 (VOICE Participants):

1. Enrolled in VOICE, randomized to study product, and reached the Month 3 visit window in VOICE prior to enrollment in the VOICE-C Substudy
2. Able and willing to provide informed consent for participation in the VOICE-C Study

Exclusion Criteria: Group 1 (VOICE Participants):

1. Permanent or long term (> 2 months) discontinuation from study product by the site Investigator of Record (IoR)/designee, per the specifications of the VOICE protocol, by the time of the scheduled ethnographic visit, IDI, or FGD
   NOTE: This criterion does not apply to participants who discontinue study product use as a result of completing VOICE protocol requirements (i.e. early study termination per DSMB recommendations, or natural end of the VOICE study). .
2. Has any condition that, in the opinion of the IoR/designee, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives
3. Has HIV-seroconverted prior to the time of the VOICE-C IDI or exit FGD or start of ethnography. Note: a participant who seroconverts after the start of her Ethnographic Interviews will be allowed to continue with the visits, and will not be withdrawn from the VOICE-C study.

<u>Group 2:</u>

For potential Group 2 participants**,** contact and recruitment is dependent on the Group 1 participant's permission, as described above. Group 2 participants who are partners of Group 1 participants assigned to FGD or IDI are automatically assigned to the same interview modality as their female partners. Male partners of Group 1 participants randomized to ethnographic interviews will only be recruited if needed to reach the desired sample size for either the FGD or IDI arm in Group 2. Male partners randomized to IDI may be screened and enrolled any time after the woman has been randomized and provided consent to contact her male partner. Thus, it is possible that a male partner may be enrolled in the VOICE-C study even if his female partner does not end up being fully enrolled in the VOICE-C. For example, a male partner may enroll in Group 2 and attend a FGD, but his female partner may be unable to attend her FGD and cannot be rescheduled.

Note that male partners who are randomized to FGD should NOT be contacted until the female partners' VOICE PUEV visit. From the time of her initial Screening visit for VOICE-C to her Screening 2 visit during VOICE PUEV she may 1) have a different partner or 2) no longer wish for her partner to be contacted. This information will be gathered at her VOICE PUEV, updated on the Permission to Contact Form, and the male partner will be recruited (or not) for the FGD accordingly.

Group 2 eligibility criteria will be assessed in the Screening 1 section of ESF_G2 over the phone after verbal consent for screening is obtained. Verbal consent should be documented on the ESF_G2, on the Verbal Consent Checklist, and in participant files notes. Similar to Group 1, if a male partner does not provide verbal consent for screening, a numeric code "29XX" should be entered in the PTID field of the ESF_G2, as well as in the Group 2 Screening and Enrollment Log. Otherwise, a VOICE-C PTID should be assigned, and the partner should be screened for inclusion and exclusion criteria. His female partner's VOICE-C PTID should also be documented on his ESF.

VOICE CRFs of the female partner must be verified to determine eligibility for Group 2 VOICE-C participants. The process for retrieving this information must be outlined in the site Accrual SOP. Certified copies of the appropriate CRFs from the parent study must be used as source documents for determining eligibility of the Group 2 participant per the site Source Documentation SOP. If the participant requires the second screening visit (more than 14 days have passed between the first screening and study enrollment) but the Group 1 partner has NOT had a VOICE visit since his first VOICE-C screening was conducted, document as such in the participant file and certified copies of the VOICE CRFs do not need to be refiled.

Once eligibility is determined, the Group 2 participant should be scheduled for his IDI or FGD. If his IDI or FGD takes place more than 14 days after the Screening 1 visit, his eligibility will need to be reconfirmed in Screening 2 when he presents for the IDI/ FGD. Assuming all criteria are met and he is interested, he will provide written informed consent for enrollment at the time of the IDI/FGD.

Inclusion and exclusion criteria for Group 2 participants are as follows:

Inclusion Criteria: Group 2 (Male Partners)

1. 18 years of age or older, male, able and willing to provide informed consent for participation in the VOICE-C Substudy
2. Identified as a partner of a female VOICE or VOICE-C participant who meets eligibility criteria for VOICE-C (i.e. on product, no seroconversion)
3. Identified by a VOICE or VOICE-C participant in either arm of the trial as a current sexual partner (current is defined as a sexual partner by the VOICE or VOICE-C participant at the time she is asked permission to contact him)

4. Identified by the VOICE or VOICE-C participant as someone she is willing to have the study team to contact

Exclusion Criteria: Group 2 (Male Partners)

1. Has already participated in a VOICE-C male partner IDI (for FGDs only)
2. Has any condition that, in the opinion of the IoR/designee, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives

Group 3:

All eligible CAB members from each site should be invited to join the VOICE-C study at the start of the Group 3 accrual period (see Section 19.4.1 above). After obtaining and documenting verbal consent for screening, a VOICE-C PTID should be assigned and documented on ESF_G3 and the Group 3 Screening and Enrollment Log. Additional eligibility criteria for this group should be assessed, and the Screening 1 section on the ESF_G3 should be completed. Verbal consent for screening and Screening 1 procedures, including eligibility determination, may be conducted over the phone rather than in person. Screening should take place just prior to the FGD, however, there is not a requirement to re-screen Group 3 participants after a defined number of days.

Inclusion and exclusion criteria for Group 3 participants are as follows:

Inclusion Criteria: Group 3 (CAB Members)

1. 18 years of age or older, able and willing to provide informed consent for participation in the VOICE-C Substudy
2. At the time of enrollment, has been a member of a CAB affiliated with the site for at least 3 months as reported by the site CAB liaison
3. At the time of enrollment, is considered an active CAB member as reported by the site CAB liaison

Exclusion Criteria: Group 3 (CAB Members)

1. Has any condition that, in the opinion of the IoR or designee, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives
2. CAB members who have been involved in the VOICE-C protocol development process

If a CAB member refuses participation, document as PTID '39XX' in the Group 3 Screening and Enrollment Log, as well as on his/her ESF_G3. If a new member joins the CAB during the course of the VOICE study, s/he should be invited to join VOICE-C, and will participate in any remaining FGDs.

Group 4:

Group 4 potential participants will be identified and referred by CAB members, study staff and other Group 4 participants already enrolled in VOICE-C on an ongoing basis. FGDs with CAB members will be a primary source of referrals. VOICE-C staff will record all identified individuals, including name, institutional affiliation and title/role, contact phone number and the referencing individual in the Group 4 Referral List. The IoR or designee will determine the most suitable individuals to invite to join each FGD, based on individual characteristics (occupation, role in the community, demographics) and the composition of the focus group and previous focus groups. The IoR will aim to get a broad array of perspectives from community stakeholders. Unlike Group 3, Group 4 consists of up to 50 participants each of whom participates in only one FGD with approximately 6-15 participants.

Once a potential Group 4 participant is referred to VOICE-C staff, s/he will be asked to give verbal consent for screening. The verbal consent will be documented on ESF_G4, the Verbal Consent Checklists and in the participant file notes, and the participant will be assigned a PTID number and logged in the Group 4 Screening and Enrollment Log. Additional eligibility criteria for this group will be assessed, and the Screening 1 section on the participant's ESF_G4 should be completed. Verbal consent for screening, and Screening 1 procedures, including eligibility determination, may be conducted over the phone rather than in person Screening should take place just prior to the FGD, however, there is not a requirement to re-screen Group 4 participants after a defined number of days.

Inclusion and exclusion criteria for Group 4 participants are as follows:

Inclusion Criteria: Group 4 (Key Community Stakeholders)

1. 18 years of age or older, able and willing to provide informed consent for participation in the VOICE-C Substudy
2. Lives or works within the community in which the parent study is being conducted

Exclusion Criteria: Group 4 (Key Community Stakeholders)

1. Has any condition that, in the opinion of the IoR/designee, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives
2. Current CAB member at that site

It is the responsibility of the site Investigator of Record (IoR) and other designated staff to ensure that only participants who meet the study eligibility criteria are enrolled in VOICE-C. Each site must establish a SOP for Eligibility Determination that describes how study staff will fulfill this responsibility. This SOP minimally should contain eligibility determination procedures, eligibility verification procedures for each inclusion/exclusion criteria, QC/QA procedures, and staff responsibilities. Should study staff identify that an ineligible participant has inadvertently been enrolled in the study, the IoR or designee should contact the VOICE-C study management team (mtn003c-siteop@mtnstopshiv.org).

19.4.4 Definition of Enrollment

Participants will be considered enrolled in VOICE-C after they have provided written informed consent. Written informed consent should be obtained on the day of first qualitative data collection for all groups. Further information on the informed consent process is provided in Section 19.5.

Note: Group 1 participants will receive a randomization assignment for VOICE-C prior to confirming eligibility, but will not be considered enrolled until they provide written informed consent.

19.4.5 Screening and Enrollment Timeframe

Recruitment, accrual, and screening procedures for VOICE-C will begin upon study activation for the VOICE study and continue through the Product Use End Visit for all VOICE participants pre-selected to take part in the substudy. Thus, depending on the participant group and the randomization assignment, enrollment in VOICE-C may take place on the first day of screening at the site (for IDI) or up to 28 months (for FGD) after the first VOICE-C screening date.

A potential Group 1 participant attending her Month 3 VOICE visit on 8 July 2010 could be screened for VOICE-C, and randomized to an IDI. If the staff is able and the participant is willing, the participant could be enrolled and the IDI could be conducted that day as well. Thus the participant was screened, enrolled and terminated from VOICE-C on 8 July 2010. Alternatively, a potential Group 1 participant could be randomized to a FGD, complete Screening 1 on the ESF on 8 July 2010. She could then complete Screening 2 at her PUEV on 19 July 2012 and enroll (go through written informed consent), complete a FGD, and terminated from VOICE-C on 29 July 2012. In this example, Screening 2 had to take place at PUEV to verify eligibility.

The FGD for Groups 1 and 2 may take place more than 14 days after this screening 2 visit. Enrollment into VOICE-C for Group 1 and Group 2 participants should be completed before the VOICE participant's Termination Exit Visit (TEV) from VOICE. Ideally, the FGD is also held before the TEV from VOICE, but it is acceptable for a participant to be scheduled for an FGD after her TEV if necessary.

19.4.6 Screening and Enrollment Logs

The *DAIDS policy on Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials* requires study sites to document screening and enrollment activity on Screening and Enrollment Logs. A separate log should be maintained for each participant group. Screening and Enrollment Logs will provide a comprehensive picture of all participants screened, randomized (if applicable) and enrolled in the study. Each participant logged should also have a completed Enrolment Status form, which will indicate enrollment into VOICE-C or reasons for ineligibility. Each person who agrees to be screened is provided with the next chronological PTID; those who do not provide verbal consent for screening are provided with a PTID of 'X9XX', as described in Section 19.4.3. Examples of Screening and Enrollment Logs for each Group can be found in Section Appendix 19-8. The site is encouraged to modify these as needed.

For Group 1, randomly pre-selected VOICE-C participants who attempt to screen for VOICE-C should be documented on the Group 1 Screening and Enrollment Log. This log will include VOICE-C PTID, participant initials if not enrolled and participant name if enrolled, Screening 1 date, randomization date, study arm, Screening 2 date (if needed), enrollment date and reason for non-enrollment (if applicable). PTIDs are only assigned if the participant is approached for screening and has the opportunity to allow or refuse to be screened.

For Group 2, all primary male partners for whom "permission to contact" is allowed, VOICE-C PTID, participant initials if not enrolled and participant name if enrolled, PTID of Group 1 partner, study arm, Screening 1 date, Screening 2 date (if needed), whether he was eligible, enrollment date, and reason for non-enrollment (if applicable) should be documented in the Group 2 Screening and Enrollment Log. PTIDs are only assigned if the participant provides verbal consent to be screened.

For Groups 3 and 4, all participants should be documented in the order in which they are screened on the respective Screening and Enrollment Log. This log will include VOICE-C PTID, participant initials if not enrolled and participant name if enrolled, Screening 1 date, whether he/she was eligible, enrollment date and reason for non-enrollment (if applicable). PTIDs are only assigned if the participant provides verbal consent to be screened.

19.4.7 Weekly VOICE-C Progress Reports

Once VOICE-C accrual is initiated, study staff will report the number of participants screened and enrolled to the VOICE-C management team on a weekly basis, along with other key progress indicators.

19.5 Informed Consent

Please refer to Section 5 of this manual. The general principles, policies, instructions, and guidelines contained in that section also apply to VOICE-C.

VOICE-C involves two types of informed consent:

- Verbal consent process for screening,
- Written informed consent for enrollment in the study.

Screening procedures will be preceded by a request for verbal consent for screening. Each site is to develop a site-specific verbal consent checklist for screening, which must contain all the elements of informed consent as specified in US regulations (45 CFR 46). This form must be approved by the VOICE-C protocol co-chairs and MTN Core (FHI 360) and then approved by the relevant IRBs and DAIDS prior to implementation. Verbal consent must be obtained before performing any VOICE-C screening procedures per Informed Consent SOP and verbal consent checklist. In order to minimize the burden on participants, verbal consent for screening and Screening 1 procedures may be conducted over the phone for Group 2-4 participants, and for Group 1 participants who give permission during their VOICE visit to be called (at a later time) for this purpose. The participant must be provided with an opportunity to ask any questions he/she has. Any questions the potential participants may have regarding verbal consent and responses to these questions must be documented in file notes and per site Informed Consent SOP.

Written informed consent forms for enrollment are specific to the data collection modality and Group, thus there are 7 consent forms in the study. Written informed consent for IDIs, EI, and FGDs for all Groups must be obtained before performing any VOICE-C data collection activities (aside from establishing eligibility during screening).

Language of informed consent: All consent procedures should be conducted in the primary language of the participant (as indicated on the ESF CRF). If the written informed consent form is requested in a language that is *different* from the language the procedure was conducted in, this discrepancy should be documented on the informed consent cover sheet or in the participant file notes. For Group 1 participants, if the consent process for VOICE-C is conducted in a different language than the consent process for VOICE, this discrepancy should be similarly documented.

Documentation of informed consent: An informed consent cover sheet can be used with each informed consent form as a way to document informed consent procedures. Per DAIDS policy, each step must be documented, either using this cover sheet or an alternate method as described in the site Informed Consent SOP.

Comprehension of informed consent: Comprehension of the informed consent process must also be documented per the site Informed Consent SOP. For participants who do not consent, no VOICE-C procedures should be performed.

19.5.1 Informed Consent Procedures for a Group Setting

As participants arrive for the focus group discussion, the informed consent forms should be distributed in the language of the participant's choice for those who have not yet been consented. A staff member should read the entire informed consent document and explain it in detail to ensure that participants fully understand the FGD process. Participants should be encouraged to ask questions, and will have the opportunity for one-on-one consultations. In a private location, the staff member should determine whether the participant is literate (able to read) in the language of the selected form, per the site Informed Consent SOP. Once participants' questions regarding the study are thoroughly addressed, participants who wish to participate in the FGD should be asked to sign or make their mark on the informed consent document. Those not willing to provide consent should be reimbursed for their transport expenses only and should not participate in the FGD.

19.5.2 Informed Consent Procedures for Illiterate Participants

If a participant is not literate in English, Zulu or Sotho, an impartial literate witness must be present during the entire informed consent process/discussion with the participant. The impartial witness will be asked to sign and date the informed consent form to attest that the information in the informed consent form was accurately explained to and apparently understood by the participant. When a witness is present during the informed consent process, care should be taken to minimize the perception of coercion due to the presence of the witness. For example, the purpose of having the witness present should be clearly explained to the participant, with emphasis on the fact that the witness is there as a protection for the participant, not as an agent of the study per se. Refer to Section Appendix 5-1 for a summary of considerations for obtaining informed consent from illiterate participants.

At each site, the informed consent process for VOICE-C will be conducted according to the site Informed Consent SOP.

19.6 Visit Procedures

This section provides information on requirements and procedures for FGD, IDI and Ethnographic Interviews in VOICE-C.

19.6.1 Visit Scheduling

Ethnographic Interview (EI)

Only Group 1 participants may be randomized to the Ethnographic Interview (EI) modality. Between two and four EIs with the participant will be scheduled over the course of one year. It is recommended that the same interviewer carry out all Ethnographic Interviews for a participant so that rapport is not disrupted. The location and time of the first Ethnographic Interview will be arranged on the day of Screening 1. All Ethnographic Interviews will be held in the participant's home or surrounding community, at the study clinic or at any other location mutually agreeable to the participant and study staff, and should be scheduled to be evenly spaced over the course of one year from the date of the first scheduled interview. The next ethnographic interview should be scheduled at the end of each ethnographic interview.

It is recognized that all participants may not be appropriate candidates for the completion of all 4 interviews. Interviews with the participant may be discontinued prior to the completion of all 4 interviews if the participant is not willing to continue, or the interview data reaches a point of saturation, or if study design changes necessitate earlier-than-anticipated termination from VOICE. This decision will be made by the Protocol Chairs based upon discussion with the site staff and review of the interview transcripts. Each site should ensure that two interviews are held with each participant at a minimum. If fewer than four interviews will be held, the spacing of these interviews should be determined by the Site Investigator.

If the participant is enrolled in the EI and then is terminated from VOICE due to completing VOICE protocol requirements (e.g. early termination per DSMB recommendations or the natural end of the study), the study team may continue to conduct the EIs with the participant, provided she is willing. EIs should not extend beyond two months after her VOICE PUEV (since she will not have been on study product for two months or more). Depending on the number of EIs remaining after VOICE termination it may not be appropriate to conduct all four interviews with the participant and this is left to IoR discretion, however the minimum of two interviews should still be honored.

In-Depth Interview (IDI)

Group 1 participants randomized to an IDI may have the IDI conducted on the same day as screening into VOICE-C, or scheduled for a later, more convenient time. Again, if the IDI occurs more than 14 days after the initial Screening visit, Screening 2 procedures must be carried out and documented on the ESF. It is recommended that VOICE-C staff member who screened the participant carry out the IDI to ensure that rapport is not disrupted.

Group 2 participants who are assigned to an IDI should be scheduled for their IDI as close as possible to the IDI of their female partner. It may occur that an IDI is completed for a Group 1 participant, but the Group 2 partner misses his scheduled IDI, or vice versa. Staff may need to be flexible in scheduling IDIs, and allow for after-hours and weekend meeting times, and/or alternate venues to make the meetings convenient for the participants.

Focus Group Discussion (FGD)

Group 1 participants randomized to one-time-only FGDs will have the FGD occur after their VOICE PUEV visit, thus there will be delay between Screening 1 and Screening 2/ Enrollment of many months, or even years. For VOICE participants who are followed up for the length of the study, this product use end visit occurs at the end of the VOICE study, when all endpoints are met and study participation is over. At their VOICE PUEV visits, VOICE-C participants will be asked to see the VOICE-C staff so that they can be re-screened for eligibility and given a date for participation in an FGD. Permission to contact forms should also be updated at this time. Visit flow for VOICE PUEV should be addressed in the Accrual SOP at the site.

If there are an adequate number of VOICE-C FGD participants (approximately 6) who exit from VOICE *early* (due to voluntary withdrawal or another reason) and are eligible to continue participation in the sub-study a FGD may be scheduled to accommodate this group. It is not expected that this will happen, and should be addressed on a case by case basis through communication with the management team.

Group 2 participants assigned to FGD will only be identified at the Group 1 participant's PUEV visit, therefore the FGD with male partners will not occur until matching partners from Group 1 have completed their PUEV (or early study termination) visits.

For Groups 3 and 4, FGD scheduling should be done based on availability for the greatest number of respondents. Ideally three proposed times should be identified, all respondents should be contacted to assess their availability at each, and the final time should then be determined and communicated to the respondents.

Continued data collection with Group 3 (CAB members) will proceed on an as needed basis, as determined by the Protocol Team. Between 3-5 FGDs with approximately the same cohort of respondents will be conducted. Every effort will be made to retain the same cohort of individuals for each scheduled FGDs. However, during the course of the study, members may be added to the site CAB, and these members may participate in any remaining FGDs, provided they meet eligibility criteria. If an invited CAB member misses a scheduled FGD, the visit will be considered "missed" for that individual, and this will be documented in participant file notes, and on the Termination Form at the end of the study. CAB members who do not participate in the final CAB FGD will not be classified as lost to follow-up.

19.6.2 Preparing for the Interview

Before each data collection visit (interview or focus group discussion) the following should occur for all study groups:

- Reference the probing tables developed from previous interviews (section 19.11.11 provides more information regarding these tables). These tables outline the specific topics that should be followed up on for the next Group 1 EI, IDI, or Group 3 FGD. As transcripts become available, the tables outline general areas where additional probing would have been beneficial during previously conducted EI, IDI, or FGD for Groups 1, 2, or 4.
- Discuss with IoR and/or other team members if the probing table is unclear or more guidance is required to effectively probe on the topic.
- Ensure the correct version of the guide is ready for use and the supplemental probing guide is printed if a Group 1 or Group 2 IDI or EI is conducted.
- Call or SMS the participant(s) to remind them of the visit (per site Retention SOP).

For Group 3 FGDs and Group 1 EIs, the interviewer/facilitator should read through the Debriefing Report or Field Notes form (as applicable) to ensure that this information is fresh when going into the next interview. This should be done in addition to the review of the probing table for these groups.

19.6.3 Data Collection Procedures

All interviewer-administered CRFs and guides should be administered in the primary language of the participant (as indicated on the ESF). Any deviation from this should be documented in the participant file notes. Visit checklists should guide the order of procedures for each FGD, IDI and Ethnographic Interview. See Section 19.7 for more information.

Focus Group Discussion Procedures

If site staff determine that FGD participants (of Groups 3 and 4) would benefit from more education regarding the VOICE study, arrangements may be made to host such an educational session prior to the FGD. The relevant VOICE staff should conduct the education session in collaboration with VOICE-C staff, and use the appropriate study-provided VOICE materials.

FGD visits will take approximately 2-3 hours, including provision of informed consent (as needed), completion of Demographic form, Enrollment Status Form (ESF), and conduct of the FGD. The FGDs should be conducted in an appropriate meeting room that is conducive to

the number of participants, privacy, and the need to audio-record the session. Upon arrival at the scheduled meeting time, FGD participants should be greeted, offered refreshments, and presented with an informed consent document to review while awaiting the arrival of the remaining participants. Please refer to Section 19.5 for the informed consent procedures for FGD.

The facilitator and note-taker should then pull participants individually to the side to complete the ESF and Demographic form. At this time, the participant should choose a pseudonym and write it on a card to place in front of him or herself during the discussion. If the participant cannot write, study staff can do this for the participant. The pseudonym should be documented on the Demographic form (under 'Visit Type'). The Screening and Enrollment Log should be completed with the 'date of enrollment'.

If more than one language is used, a guide for each language should be available during the FGD to ensure that questions asked to the group are not translated on the spot. All primary questions in the guide should be read as close to verbatim as possible, to ensure consistency. Each guide used during the discussion should be filed with the FGD data collection materials.

The facilitator should initiate the FGD by first explaining that the session will be audio-recorded and later transcribed and translated. Ground rules for conduct should be described. These include a review of confidentiality requirements (use pseudonyms, do not share information outside the FGD); etiquette (do not interrupt or disrespect others opinions, turn off cell phones) and operational issues (no right or wrong answers, speak one-at-a-time, state your pseudonym before you speak).

The facilitator should then start the audio-recorder and begin the session. The facilitator may start with an ice breaker. The ice-breaker should be any light topic of interest to the participants (current events, weather, sports, etc.) and not one that is controversial, too sensitive or related to the study topic as it may negatively affect the rest of the discussion. After the ice breaker the discussion should follow the appropriate FGD guide. FGD guides are structured, but will allow opportunity for probing and exploration of spontaneously generated themes. The note-taker should take notes during the session as a back-up to the audio-recording, and to record non-verbal information. At the end of the FGD, participants should be thanked and reimbursed for their transport expenses and time.

Immediately following each FGD carried out for Group 4 the Termination form for each participant must be completed. For Group 3 participants, the Termination form is completed immediately following the last FGD for this group. The facilitator and note-takers should complete their notes in the appropriate space provided on the FGD guide, and complete their debriefing report in the Access database. The guide will request some basic statistics about the session (i.e. duration, mood of interview, number of participants, people present, etc.) as well as a summary notes related to each question in the guide. Some questions will request categorical summary responses from the facilitator. This information and any other comments by the notetaker and facilitator should be hand-written and later typed into the debriefing report database. Each debriefing report should thus represent a summary and extraction of the full data that can be used in "real-time". This will allow access to pertinent findings while the data goes through the longer process of QA, coding and more formal qualitative analysis.

Further description of the management of the audio-files, interview notes, debriefing reports, CRFs, visit checklists and transcripts of the FGDs is described in Section 19.11.11.

For Group 3 participants: This is the only group of informants who will participate in FGDs at several time points, and thus it will be important to explore perceived changes over time in community outlook and external factors affecting adherence. The procedures should follow

those outlined above, although the informed consent process and CRF completion should only be conducted one time per individual, prior to the first FGD that the participant joins. Group 3 participants should keep the same pseudonym for each FGD they participate in.

In-Depth Interview Procedures

The IDIs will be conducted in private meeting rooms that are quiet enough for audio-recording. The IDIs should be located in a confidential private location, which may be at the clinic, or another venue preferred by the participant. If requested or preferred by the participant, the IDI can be arranged at the participant's home, or at a different outside location. Upon arrival for the IDI, the participant will be greeted and offered refreshments. If more than 14 days have passed since Screening 1, the Screening 2 procedures must be carried out. Prior to conducting the interview the ESF must be updated, written informed consent performed, and the Demographic form completed.

The IDI will follow an IDI guide, but will allow for iteration, probing and digression on relevant themes. The most current versions of supplemental probing guides should also be used. IDIs will be audio-recorded and later transcribed and translated by site staff. Ideally a note-taker will be present to take notes during the session, but if only a facilitator is available, the IDI may still go on, and the facilitator will take brief notes as the interview is ongoing (these will be immediately expanded by the facilitator, after completing the IDI). Following the IDI, the participant will be thanked for his/her time and reimbursed for his/her travel and time.

Immediately following each IDI, the facilitator should complete their notes and debriefing report, and complete the Termination form, as described above.

Further description of the management of the audio-files, interview notes, debriefing reports, CRFs, visit checklists and transcripts of the IDIs is described in Section 19.11.11.

Ethnographic Interview Procedures

Ethnographic Interviews will focus on the participant's everyday life as it relates to study product adherence and the VOICE trial. The primary site for ethnographic research will be the participant's household and surrounding community. Trained and experienced researchers will first meet participants randomized to the ethnographic research after their Screening 1 visit at the clinic. They will arrange a time and place to meet for the first EI, preferably at home. However, some participants may not want to draw attention to their involvement in the trial and therefore neutral venues in the community will be used for these purposes. Participants will be asked to participate in up to four ethnographic visits. Prior to beginning the first interview the ESF must be reviewed and Screening 2 carried out if it has been more than 14 days since the first screening visit. Informed consent must be conducted and the Demographic form completed.

During the first EI the researcher will collect a life history, social and economic background, sexual biography, and reasons for enrolling in VOICE by interviewing the participant. The subsequent interviews will monitor the following issues: significant events in the community (for example political disturbances), physical experiences related to gel use or tablets use; barriers to gel use or tablets use; rumors about the trial; neighborhood conversations about their participation in the trial; gossip overheard in the clinic waiting room. In addition, observations of the household and the use of space will be recorded. At the end of the visit the participant will be reimbursed, and the subsequent meeting will be scheduled. The Ethnographic Interview guide is designed so that each subsequent visit builds upon the previous one. Therefore, if for example, a participant misses the second visit but returns for

her third visit, she will be administered those questions that follow up on her previously attended visit. The most current version of supplemental probing guides should be used, as well as specific probing issues for that participant (identified in previous interviews). Study staff should make an effort to schedule each EI participant for 4 interviews, unless fewer interviews are warranted per the discretion of the Protocol Chairs.

These discussions may be audio-recorded with the participant's permission. If the participant does not grant permission for the audio-recording or if the study staff feel that use of an audio-recording device is not appropriate given the surrounding environment, the discussions will be recorded in a notebook and field notes will be expanded and transcribed into a word processor that day or within five days of the interview to minimize lost data. Notes will be filed according to participant ID number and date of ethnographic data collected and field visit.

Further description of the management of the interview notes, debriefing reports, CRFs, and visit checklists for the Ethnographic Interviews is described in Section 19.11.11.

Participant Observation Procedures

It is expected that VOICE participants, their male partners, and/or community members will be invited to attend regularly scheduled VOICE-sponsored informational/educational meetings. These meetings will be arranged as a forum to provide information and answer questions about the main VOICE trial. When possible, VOICE-C staff should attend male partner or community-based informational/educational VOICE-initiated meetings. No individual-level data will be collected by VOICE-C staff and no personal identifiers of anyone at the meeting will be recorded. However, the VOICE-C team should complete a Field Notes Report Form (available on the MTN VOICE-C website) upon completion of each meeting attended. If more than one staff member from VOICE-C attends, field notes should be consolidated into one Report Form. This form captures the date, type of event and location, approximate number of people and key issues raised at the meeting. The forms may be uploaded into the qualitative data analysis software NVivo, coded, and analyzed as supplemental data to the FGD, IDI and EI transcripts. These reports will not be considered primary data because they are summaries of group activities. Attendance at these events should be logged in the Supplemental Data Collection Log. This log should be transmitted to RTI when new entries are added (via email or FTP), along with final Field Notes Report Forms.

19.6.4 Modified Procedures for Participants Who Miss Scheduled Data Collection Visits

Participants who miss scheduled IDIs may reschedule their visit. The EI guide is one comprehensive guide designed to have questions that build upon the previous interview. Therefore, if for example, a participant misses the second quarterly visit, she should be asked those questions if she then returns for her third quarterly visit. Participants who miss FGDs may join later FGDs if there are remaining slots available in an applicable FGD. If a FGD is scheduled and not enough participants present to the FGD, the site investigator may determine that in-depth interviews with each person may be used as a replacement, given the difficulty to ensure all scheduled participants come on the day for the group discussion. As there is already a large number of individual interviews conducted with Group 1 participants, it is preferable that this transition to IDI occur only with the Group 2 participants. Site staff should anticipate low turn-out for FGD and invite 12-20 participants to ensure adequately sized groups turn up the day of the discussion. In cases of a missed visit (IDI or first EI) eligibility must be re-confirmed on the date (or within 14 days) of data collection and documented in the comments section of the ESF.

19.7 Visit Checklists

Section Appendix 19-5 contains examples of checklists detailing the protocol-specified procedures that must be completed at VOICE-C study visits. These checklists should be modified as needed to ensure they fit with systems at the site, then reviewed by the MTN CORE (FHI 360) for approval prior to implementation. The checklists also specify the data collection forms that must be completed at each visit. See Section 19.3.2.3 for more information on visit checklists.

19.8 Participant Retention

The majority of data collection activities for VOICE-C are one-time only events, thus participant retention is not applicable. The only groups with more than one activity are Group 3 CAB members and Group 1 participants who are randomized to EI. Group 3 CAB members will be encouraged to attend as many FGDs as possible, but it is unlikely that all group members will be able to attend the pre-scheduled time for each FGD. Group 3 participants will still be considered "retained" even if they miss one or more FGDs. Group 1 participants randomized to receive Ethnographic Interviews will be enrolled at their first Ethnographic Interview, and will be scheduled to have up to 3 more interviews over the course of a year. A Group 1 EI participant will be considered "retained" if she completes at least two interviews.

Strategies for maximizing participant retention are located in Section 8 of this SSP.

19.9 Reporting of Social Harms, Adverse Events and Adherence Issues

Adverse Events and Social Harms
VOICE-C is a qualitative study with no clinical procedures and no investigational products. Nonetheless, because VOICE-C is a sub-study to an FDA-regulated trial, it is necessary to make provisions for the identification and proper reporting of adverse events (AE) experienced by Group 1 participants and social harms (SH) as reported by all VOICE-C participants.

If any AEs or SHs are reported by participants (regardless of group), the AE or SH should be fully documented in participant file notes by the VOICE-C staff and social harms related specifically to the VOICE-C study documented on the Social Harms CRF. Study staff should use as much detail as possible to describe the event, including a full description of the event, severity of the event, action/medication taken, approximate onset and resolution dates. Every effort will be made by study staff to provide appropriate referrals (including counseling referrals to VOICE staff) to the participant, and/or referral to appropriate outside resources as needed.

VOICE-C staff may disclose VOICE-C Group 1 or Group 2 participant information to VOICE staff in order for potential social harms of VOICE participants to be mitigated and/or monitored. In the event that this must occur, VOICE-C staff should ask VOICE staff to not directly discuss what was disclosed during the VOICE-C interview with the VOICE participant.

The following additional guidelines apply for Group 1:
Participants will be referred to the VOICE staff as soon as possible and not more than 48 hours if either of the following occur:

1) The participant reports an AE or SH while she is still actively enrolled in the VOICE study (i.e. during an IDI or ethnographic interview),

2) An AE or social harm is observed by the VOICE staff member during an EI visit
3) The participant has had her PUEV or Termination Visit in VOICE (i.e. during an FGD) but discusses clear clinical problems with the study product or a social harm that occurred due to the VOICE trial.

Each site will provide listings of social harms related to VOICE-C participation that are reported by study participants to the VOICE-C Protocol Team at a minimum of every 6 months per any applicable DAIDS requirements. Additionally, sites will develop a Participant Safety Monitoring SOP for emergency procedures to be used in situations of social harm and when situations that require immediate attention are identified, including domestic violence, suicidal ideation or behavior. The procedures will provide clear guidelines for VOICE-C researchers to refer participants in these situations to the relevant institution/body and to communicate the event to staff members in the main VOICE trial.

NOTE: All social harms related to VOICE-C participation will be documented and reported through VOICE-C; social harms related to VOICE participation/procedures will be documented and reported by VOICE staff and per VOICE SOPs and guidelines. Participants experiencing a social harm related to either study will be referred to VOICE staff for counseling.

Relationship to study participation or procedures will be assessed by the site IoR, or designee, based on the following definitions:

- **Related:** There is a reasonable possibility that the problem may be related to the study product.

- **Not related:** There is not a reasonable possibility that the AE is related to the study product.

Adherence Issues
A primary objective of VOICE-C is to identify issues that impede VOICE participants' ability to properly adhere to their prescribed study product regimen. VOICE-C data collected during the VOICE accrual and follow-up period may identify important product use constraints that may require the attention of the VOICE protocol team. The process of immediate transcription and electronic entry of debriefing notes and interview summaries is specifically designed to enable a rapid response to such issues. In the event that potentially important adherence-related issues are identified, the sequence of events identified in the flow chart in Section Appendix 19-7 should be followed to ensure efficient and thoughtful consideration and follow-up.

Additionally, VOICE trial staff at the VOICE-C site or a partner VOICE site may identify important adherence-related issues that would benefit from further exploration in VOICE-C data collection. A similar flow chart of information is also described for the communication between VOICE and VOICE-C staff in Section Appendix 19-7.

Similarly, important protocol- or study- related issues may emerge during VOICE-C data collection that warrant feedback to the VOICE team, or issues may emerge from the VOICE team that warrant exploration in VOICE-C. The same flow charts (Section Appendix 19-7) of communication between VOICE-C and VOICE should be followed in these circumstances. Sites will develop SOPs for communicating issues related to adherence, social harms and adverse events experienced by Group 1 participants back to VOICE staff.

19.10 Counseling Considerations

As specified in Section 8 of the VOICE-C protocol, participants may experience social harms as a result of participation in VOICE-C. If a social harm is reported by a Group 1 participant, the participant will be referred to a counselor in the VOICE trial. For social harms reported by participants in Groups 2-4, every effort will be made by VOICE-C study staff to provide referrals to appropriate resources to ensure the safety of the participant. All reports of social harms will be documented in VOICE-C participant file notes and on the Social Harms CRF.

19.11 Data Collection

Only data collection issues unique to VOICE-C are covered in this section. For more information on VOICE data collection procedures, see Section 14 of this manual.

For questions about this section or about general data collection policies, procedures, or materials for VOICE-C, please contact Liz Montgomery (emontgomery@rti.org) or Helen Cheng (hcheng@rti.org).

19.11.1 PTIDs

For Group 1 participants, there will be VOICE-C PTID distinct from the VOICE PTID of the participant. Groups 2, 3 and 4 participants will only have a VOICE-C PTID. For Group 1 and 2 participants, there will be a link to the female VOICE participant's VOICE PTID on the Demographic form. The ESF for Group 1 participants will also contain this link.

For more information on assigning PTIDs for VOICE-C, please refer to Section 19.4.2 of this manual.

19.11.2 Study Visit Timing

VOICE-C participants complete only 1 visit with two exceptions: Group 1 participants randomized to the Ethnographic Interview will be scheduled to complete up to 4 visits and Group 3 participants will be invited to participate in between 3 to 5 FGDs. The detailed breakdown is below.

Group 1 participants will complete one of the following: 1 IDI, 1 exit FGD, or up to 4 Ethnographic Interviews (over the course of a year);

Group 2 participants will complete 1 IDI or 1 exit FGD;

Group 3 participants will complete between 3-5 FGDs;

Group 4 participants will complete 1 FGD.

Target Days and Visit Windows: There are no specific target dates or visit windows for VOICE-C. Rather, there are guidelines for when qualitative data should be collected from each group, as described in the data collection timeline (Section 19.6.1).

Split Visits: If an IDI or Ethnographic Interview participant is not able to complete the interview in one day, s/he may be rescheduled to come back and complete the rest of the interview on another day. If the second part of the visit is conducted more than 14 days from the last screening visit, re-check eligibility and document this in the participant file. Because s/he was eligible at the time of the initial IDI/EI, the visit should be held upon irrespective of the participant meeting eligibility at the time of the second part of the interview. In the event of a split visit, the same visit code will be maintained on both visits. If an individual is unable to complete participation in an FGD, this should be documented in the debriefing notes for the FGD as well as in the participant file notes. S/he will not rejoin another FGD unless determined necessary by the management team. Any split visits must be documented in participant file notes.

Missed Visits: If a Group 1 Ethnographic Interview participant does not complete a scheduled EI, study staff should document this in the participant file notes and reschedule this visit as soon as possible. If more than 1 month goes by, the management team should be contacted to assess whether this visit should be rescheduled or if the study team should consider this a missed visit and also to provide guidance regarding the information to collect at the next EI. At the end of the one year period when EI participants are being terminated from the study, their attended and missed visits should be recorded on the Termination form. Group 3 participants who miss a scheduled FGD will be documented as having a missed visit(s) for that FGD on their Termination form. This should also be noted in participant file notes for the individual. In instances of missed visits for one-time interviews (IDI, one-time FGD) every effort should be made to reschedule the IDI for a convenient time for the participant or reschedule the participant into one of the remaining FGDs.

Interim Visits: Per the VOICE-C protocol, it is not expected that any interim visits will occur for VOICE-C. However, participants may come into the clinic for more information or questions related to VOICE-C. In such circumstances, this should be documented in participant file notes.

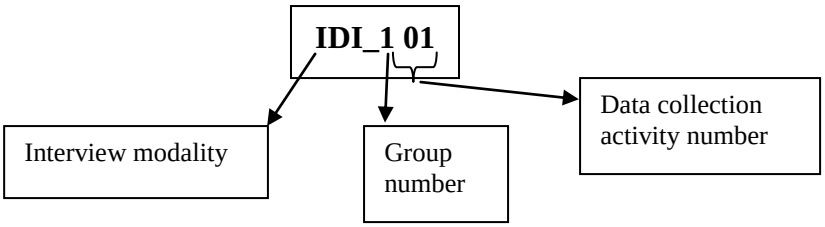
19.11.3 Visit Codes

In VOICE-C, visit codes will be assigned for each qualitative data collection activity and recorded on each page of the corresponding interview guide, checklist and notes. The visit code is a unique alpha-numeric identifier that describes the modality of interview, the participant group and the interview number. Table 19-3 and Figure 19-1 describe the VOICE-C visit codes.

Table 19-3 VOICE-C Visit Codes

Participant Group	Modality	Visit Code
Group 1	**IDIs**	IDI_101 – IDI_140
	EIs	EI_101a – EI_130a EI_101b – EI_130b EI_101c – EI_130c EI_101d – EI_130d
	FGDs	FGD_101 – FGD_108
Group 2	**IDIs**	IDI_201 – IDI_220
	FGDs	FGD_201 – FGD_204
Group 3	**FGDs**	FGD_301 – FGD_306
Group 4	**FGDs**	FGD_401 – FGD_405

Figure 19-1: Visit Code Components



9.11.4 Case Report Form Completion Schedule

Table 19-4 lists the case report forms that are required to be completed at VOICE-C visits. Additionally, a Social Harms (SH) form is required to be completed when an SH related to VOICE-C study participation is reported.

Table 19-4
VOICE-C Case Report Form Completion Schedule

Form Acronym	Form Name	Completion Schedule
DEM	MTN VOICE-C Demographic Form	On date of qualitative interview
ESF_G1	MTN VOICE-C Enrollment Status Form – Group 1	During screening and enrollment
ESF_G2	MTN VOICE-C Enrollment Status Form – Group 2	
ESF_G3	MTN VOICE-C Enrollment Status Form – Group 3	
ESF_G4	MTN VOICE-C Enrollment Status Form – Group 4	
TF	MTN VOICE-C Termination Form	At end of study completion

19.11.5 Form Supply

All master case report forms and guides needed for VOICE-C will be supplied by RTI and should be printed locally. The site is responsible for maintaining an adequate supply of the current version of CRFs (blank) and guides in all languages. One copy of previous versions of CRFs and guides should be maintained in an archive, and all other copies destroyed.

19.11.6 Form Storage

Form storage will be detailed in each site's Data Management SOP. It is recommended that for each participant study forms be stored in a flat file with either secure closures or a hard-cover binder (see also Section 19.3.2.3).

19.11.7 How to Complete Interviewer-Administered Forms

Please refer to Section 14.5 of this manual for information on completing interviewer-administered forms. For VOICE-C, the Demographic Form listed above is interviewer-administered.

19.11.8 Form Completion Instructions

Detailed form completion instructions are provided on the back of each form page. These instructions include the purpose of each form as well as how each form should be completed. Some items on forms are straightforward and do not require specific instructions. Therefore, instructions for all form items are not listed on the back of each form; rather, instructions are provided only for those items needing a detailed explanation. For the VOICE-C interviewer-administered forms instructions on how to probe for participant responses are included in the instructions on the back of each form page.

19.11.9 Case Report Forms

The current version of all case report forms (English and local language) will be kept on the MTN VOICE-C website.

19.11.10 Data Flow: Quantitative Data Management

Data for quantitative analysis will be collected manually on CRFs at the site. Data will then be double entered at the site per instructions in the Data Management Manual (Appendix A), using a CSPro database (which allows for double data entry). Following data entry the site generates a discrepancy report to check consistency between the two entries as well as other designated consistency checks. Once the reports are run, they should be printed and used to document the corrections that are made to the main database by site data entry personnel. A written note documenting the change made, staff initials and date should be provided for each finding listed on the on the discrepancy report and then the report filed. PTIDs for newly entered CRFs are recorded on a File Transfer Protocol (FTP) log (see Section Appendix 19-9). Once corrections are completed, the data file and SAS programming code are exported from CSPro to the site machine and the FTP log, data file, and SAS code is uploaded to a secure (encrypted) FTP site for retrieval by RTI data staff. .

Encrypted FTP is set by RTI's FTP department with encryption security settings dictated by VOICE-C compliance regulations. FTP use is account, username and password protected with only designated team members from RTI and the site given access. The encrypted FTP site tracks user activity and file uploads making it easy to manage precisely by whom and when new files are updated, what changes are made, and what versions are most current.

Once quantitative data is transferred to the FTP site, RTI performs additional cleaning checks on updated data using SAS. RTI will send QC reports to site staff by email. Corrections are then made to the main database as needed. Data is then transmitted back to RTI as described above until all queries are resolved. All QC reports received from RTI should be filed at the site. Changes made to the CSPro database should be documented on the QC report, as done for the site's internal discrepancy report (described above).

Staff training: Site staff who collect data on CRFs and/or who enter data onto the CSPro Database and transfer data to the FTP server will receive training at the study initiation training, and will be instructed through a Data Management Manual developed by RTI. Additional training will be available as needed at site visits made by RTI or FHI 360 staff to train and monitor quality of site data management.

Report Generation and Communication: Reports will be generated at RTI as necessary. Frequent email communication between RTI and site staff will occur to continuously address questions that emerge and ensure that RTI and the sites are in sync throughout the quantitative data management process.

See Section Appendix 19-7 for flow chart of the VOICE-C quantitative data flow.

19.11.11 Data Flow: Qualitative Data Management

Focus group Discussion (FGD):

VOICE-C qualitative data will be captured from the FGD guides. All current guides (English and local language versions) will be maintained on the MTN VOICE-C website. When the FGD is conducted at the site, it is audio-recorded. *Note*: after the interview the audio file is copied onto the password protected hard drive, and a password protected CD is burned. The audio file is also uploaded onto the FTP server.

When the FGD is conducted, FGD notes are taken during each session to supplement the audio recording. *Note*: hardcopies of all notes, guides, and checklists are stored in VOICE-C files at the site. See Section 19.3.2.1 for a description of participant file contents. CRFs are stored in VOICE-C participant data files. Participant consent forms are stored in a separate secure location.

Data storage and confidentiality: To maximize confidentiality, all storage places are locked and kept separate from VOICE files to lessen potential participant concern over general information communicated in VOICE-C affecting their participation in VOICE. It will be emphasized to Group 1 participants that only AE and social harms information obtained in VOICE-C will be communicated to VOICE staff on an individual level.

Immediately following the FGD, the site Facilitator and Note-Taker will complete columns 2 and 3 of the applicable guide by recording responses to the quantitative summary questions (col 2) and key quantitative summary points for each question (col 3) and overall notes about the session (front of guide). The final guide with completed columns, the original local language transcript and the final English transcript must all be stored in the FGD data file for the relevant FGD, or per site Data Management SOP.

Transcription-Translation: The site staff will conduct the transcription-translation process per their site specific SOP. *Note:* If a one-step transcription-translation process is used, a quality control comparison using a 2-step process will be carried out to check internal consistency. Once the accuracy of translation and transcription is approved, the FGD is uploaded onto the FTP site. During the transcript QC process (outlined below), issues identified by the protocol team requiring follow up, additional probing, or discussion with the interviewers should be added to the probing table. This could include general findings related to FGD facilitation techniques or specific issues that should be teased apart further in future FGDs. These probing tables will be discussed during team meetings and identify staff training needs.

Timeframe: As detailed in the FGD Visit Checklist (Section Appendix 19-5), within 1 week of the FGD session the facilitator/notetaker notes should be entered electronically into the Debriefing Report Database (created in Microsoft Access) to create a FGD Debriefing Report. This report is sent to RTI within 1 week of the FGD. Within 1 month of the FGD session, the site transcription and internal consistency checks are performed and external translation (and transcription) double checks are performed and conferred with the site. Then the transcript is saved and emailed to RTI for review. A VOICE-C Qualitative Data Tracking Log will be completed by RTI to maintain record of each interview that is submitted along with details regarding the submission date, query status, and finalization date.

RTI will conduct a QC review in which the transcript is reviewed for typographical errors and clarifications on the meaning and interpretation of text. Once queried, the transcript will be emailed to the site for review. The site should respond to all comments within 1 week. All clarifications must be made in the text of the transcript using [brackets] or through using the comment box in the reviewing mode of MS Word. This revised transcript then undergoes the

same process of being emailed to RTI for QC review. Once this step is approved, the English FGD transcript is fully cleaned (edits accepted and comments cleared), formatted and finalized. At that point the transcript is ready for circulation to the analysis team and uploading to the Nvivo database for coding and analysis.

Staff Training: Site staff who collect data on the guides, enter data onto the Access Report Database, and transfer data to the FTP server will be instructed through a Data Management Manual devised by RTI as well as site visits made by RTI staff to train and monitor quality of site data management. In addition to the Debriefing Report and transcript QC communication submitted to RTI, the site and RTI will be in frequent email communication to address any queries, ensure processes are moving forward appropriately, and ensure RTI and the site are in sync throughout the qualitative data management process. Internal debriefings with the Site Investigator will be held weekly to discuss transcripts and content from a previous FGD (when applicable), and to review the probing report to address team questions or training needs.

In Depth Interview (IDI):

VOICE-C qualitative data will be captured from the IDI given at the site. When the IDI is conducted at the site, it is audio-recorded. *Note*: the audio file is copied onto the password protected hard drive, and a password protected CD is burned. The audio file is uploaded onto the FTP server.

When the IDI is conducted, IDI notes are taken during each session whenever possible to supplement the audio recording. *Note*: hardcopies of all notes, guides and checklists are stored in VOICE-C files. CRFs are stored in VOICE-C participant data files. Participant consent forms are stored in a separate secure location.

Data storage and confidentiality: To maximize confidentiality, all storage places are locked and have limited access. It will be emphasized to Group 1 participants that only AE and social harms information obtained in VOICE-C will be communicated to VOICE staff on an individual level.

Immediately following the IDI, the Facilitator (or Note-Taker if involved) reviews the guide, ensures a tick for each item in the middle column, reviews the middle and right-hand column and adds comments as needed. Additionally, the Facilitator completes the Debriefing Report in the Access database by listing basic information about the session and providing a summary report of the interview that can be used in "real time". The final guide with completed columns, the original local language transcript and the final English transcript must all be stored in the IDI data file, or per site Data Management SOP.

Transcription-Translation: The site staff will conduct the transcription-translation process per their site specific SOP. *Note:* If a one-step transcription-translation process is used a quality control comparison using a 2-step process will be carried out to check internal consistency. Once the accuracy of translation and transcription is approved, the IDI is uploaded onto the FTP site. During the transcript QC process (outlined below), issues identified by the protocol team requiring follow up, additional probing, or discussion with the interviewers should be added to the probing table. This could include general findings related to IDI facilitation techniques or specific issues that should be teased apart further in future IDIs. These probing tables will be discussed during team meetings and identify staff training needs.

Timeframe: As detailed in the IDI Visit Checklist (Section Appendix 19-5), within 1 week of the IDI session, the facilitator (or notetaker if present) notes should be entered electronically into the Debriefing Report Database (created in Microsoft Access) to create a IDI Debriefing

Report. This report is sent to RTI within 1 week of the interview. Within1 month of the IDI session, the site transcription and internal consistency checks are performed and external translation (and transcription) double checks are performed and conferred with the site. Then the transcript is saved and emailed to RTI for review. A VOICE-C Qualitative Data Tracking Log will be completed by RTI to maintain record of each interview that is submitted along with details regarding the submission date, query status, and finalization date.

RTI will conduct a QC review in which the transcript is reviewed for typographical errors and clarifications on the meaning and interpretation of text. Once queried, the transcript will be emailed to the site for review. The site should respond to all comments within 1 week. All clarifications must be made in the text of the transcript using [brackets] or through using the comment box in the reviewing mode of MS Word. This revised transcript then undergoes the same process of being emailed to RTI for QC review. Once this step is approved, the English IDI transcript is fully cleaned and final. It is then uploaded to RTI's Nvivo8 Database for coding and analysis.

Staff Training: Site staff who collect data on the guides, enter data onto the Access Report Database, and transfer data to the FTP server will be instructed and in communication with RTI as described above in the FGD staff training section. Internal debriefings with the Site Investigator will be held weekly to discuss transcripts and content from previous IDIs (when applicable), and to review the probing report to address team questions or training needs.

See Section Appendix 19-7 for flow chart of the VOICE-C qualitative data flow.

Ethnographic Interview (EI):

VOICE-C qualitative data will also be captured from the Ethnographic Interviews (EIs). EI data will be recorded through written ethnographic field notes and may also be audio-recorded, depending on the participant's preferences and the surrounding environment.

Data storage and confidentiality: To maximize confidentiality, all storage places are secure and distinct from VOICE files to lessen potential participant concern over general information communicated in VOICE-C affecting their participation in VOICE. It will be emphasized to female participants that only AE and social harms information obtained in VOICE-C will be communicated to VOICE staff. The final EI guide, the original local language transcript and the final English transcript (if applicable) must all be stored in the EI data file, or per site Data Management SOP.

Transcription-Translation: If applicable, the site staff will conduct the transcription-translation process per their site specific SOP. *Note:* If a one-step transcription-translation process is used a quality control comparison using a 2-step process will be carried out to check internal consistency. Once the accuracy of translation and transcription is approved, the EI is uploaded onto the FTP site. During the transcript QC process (outlined below), issues identified by the protocol team requiring follow up, additional probing, or discussion with the interviewers should be added to the probing table. This could include general findings related to EI facilitation techniques or specific issues that should be teased apart further in future EIs. Issues that are pertinent to the next EI for that participant should be clearly identified. These probing tables will be discussed during team meetings to identify staff training needs.

Timeframe: As detailed in the sample EI Visit Checklist (Section Appendix 19-5), the facilitator should expand his or her field notes into a Word document immediately following the interview.

Within 1 month of the interview, the site transcription (based on expanded field notes and the audio files if applicable) and internal consistency checks are performed and external translation (and transcription) double checks are performed and conferred with the site. Then the transcript is saved and emailed to RTI for review for QC and completion of the VOICE-C Qualitative Data Tracking Log as described above for the FGDs and IDIs.

RTI will conduct a QC review in which the transcript is reviewed for typographical errors and clarifications on the meaning and interpretation of text. Once queried, the transcript will be emailed to the site for review. The site should respond to all comments within 1 week. All clarifications must be made in the text of the transcript using [brackets] or through using the comment box in the reviewing mode of MS Word. This revised transcript then undergoes the same process of being emailed to RTI for QC review. Once this step is approved, the English IDI transcript is fully cleaned and final. It is then uploaded to RTI's Nvivo8 Database for coding and analysis.

Staff Training: All site staff who participate in Ethnographic Interviewing will undergo training in Ethnographic field note taking. All site staff who collect data on the guides, and transfer data to the FTP server will be instructed and in regular communication with RTI as described above in the FGD staff training section. Internal debriefings with the Site Investigator will be held weekly to discuss transcripts and content from previous EIs (when applicable), and to review the probing report to address team questions or training needs.

See Section Appendix 19-7 for flow chart of the VOICE-C qualitative data flow.

Male Involvement Meetings and VOICE-sponsored Community Events:

Field Note Reports from Male Involvement Meetings and VOICE-sponsored Community Events should be consolidated and electronically summarized on the Field Note Report Form and sent to RTI within 1 week of the event. These reports will be reviewed by RTI and queried, similar to the processes described above. These reports will not be considered primary data because they are summaries of group activities. However, the notes and reports should be filed in a secure location, and report transcriptions will be included in the qualitative NVivo database and coded for analysis. All activities that have Field Notes Reports will be logged in the Supplemental Data Collection Log.