Section 4: Informed Consent

4. Introduction

This section provides information on informed consent procedures for MTN-045. MTN-045 uses one consolidated Informed Consent Form (ICF) for Screening and Enrollment. For this study, consent for possible participation in in-depth interviews (IDI) is imbedded within the main consent form. No additional signatures are needed for this component of the study.

Depending on IRB/EC requirements, sites may choose to separate consent for any of these components. If this is done, each separate ICF must contain all required elements of informed consent.

This section contains general and specific information and instructions for administering ICFs. In addition, detailed guidance is provided on standardized approaches to the informed consent process that all sites must follow.

4.1 Overview of Informed Consent Requirements and Procedures

Informed consent is a process whereby an individual voluntarily expresses their willingness to participate in research, after having been informed of all aspects of the research that are relevant to their decision. Informed consent is rooted in the ethical principle of respect for persons. It is not merely a form or a signature, but a process, involving information exchange, comprehension, voluntariness, and documentation. Each of these aspects of the process is described in greater detail below. Please refer to the ICH E6 Section 4.8 and the informed consent section of the DAIDS policy on Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials for further guidance on the informed consent process and documentation requirements.

US regulations (45 CFR 46.116) specify the elements of informed consent that must be conveyed to research participants through the informed consent process. It is the responsibility of the IoR, and all delegated study staff involved in the informed consent process, to provide all required information to potential study participants.

Based on the technical and regulatory reviews that are completed as part of the MTN protocol development and study activation processes, there is adequate assurance that once the MTN LOC (FHI 360) has activated a site for study implementation, site-specific ICFs specify all

information required by the regulations. However, responsibility for informed consent does not end with preparation of adequate ICFs.

It is the responsibility of the IoR or designated study staff to perform the following:

- Deliver all required information in a manner that is understandable to potential study participants
- Assure that informed consent is obtained in a setting free of coercion and undue influence
- Confirm that the participant comprehends the information
- Document each step of the process

4.2 Site-Specific Informed Consent Forms

A sample ICF is provided in protocol Appendix I. Sites are responsible for adapting the sample as needed for local use. Local adaptation may include reformatting the consent form in accordance with local IRB/EC requirements.

Sites are responsible for following procedures outlined in the MTN MOP and DAIDS Protocol Registration Manual when drafting and translating their site-specific ICFs. Unless waived by the local IRB/EC, site-specific ICFs must address the eight required elements of informed consent, as required by U.S. federal regulations at 45 CFR 46.116. All ICFs (English and translations and back-translations) must be reviewed and approved by MTN LOC (FHI 360) prior to IRB/EC submission. After ethics approval, ICFs must be submitted to and approved by the DAIDS PRO prior to their initial use.

Each site is responsible for preparing bulk supplies of its approved ICFs and for only using the currently-approved ICF version(s) during the study. It is recommended that sites consider the use of color-coding or other techniques to ensure that the various study ICFs be easily distinguishable and used appropriately. A system for tracking version control and approvals of ICFs is also recommended and should include, at a minimum, the version number and date of the ICF, as well as the implementation dates (start and end) indicating when a particular version was in use. If additional guidance on version control tracking is needed, sites are encouraged to ask the MTN LOC (FHI 360) for assistance.

Upon receiving final IRB/EC and any other applicable regulatory approval(s) for an amendment to the ICF(s), sites should implement the ICF(s) immediately and submit updated versions to DAIDS PRO per the timelines outlined in the Protocol Registration Manual.

4.3 SOP for Obtaining Informed Consent

As a condition for study activation, each site must establish an SOP describing the steps for conducting the IC process and obtaining informed consent from potential study participants. This SOP should contain, at minimum, the following:

- Information about applicable local laws, regulations and institutional policies pertaining to the IC process
- The minimum legal age to provide independent IC for research at the study site
- Procedures for determining participant identity and age
- Procedures for determining participant literacy
- Procedures for providing all information required for IC to the participant
- Procedures for determining participant comprehension of the required information
- Procedures to ensure that IC is obtained in a setting free of coercion and undue influence

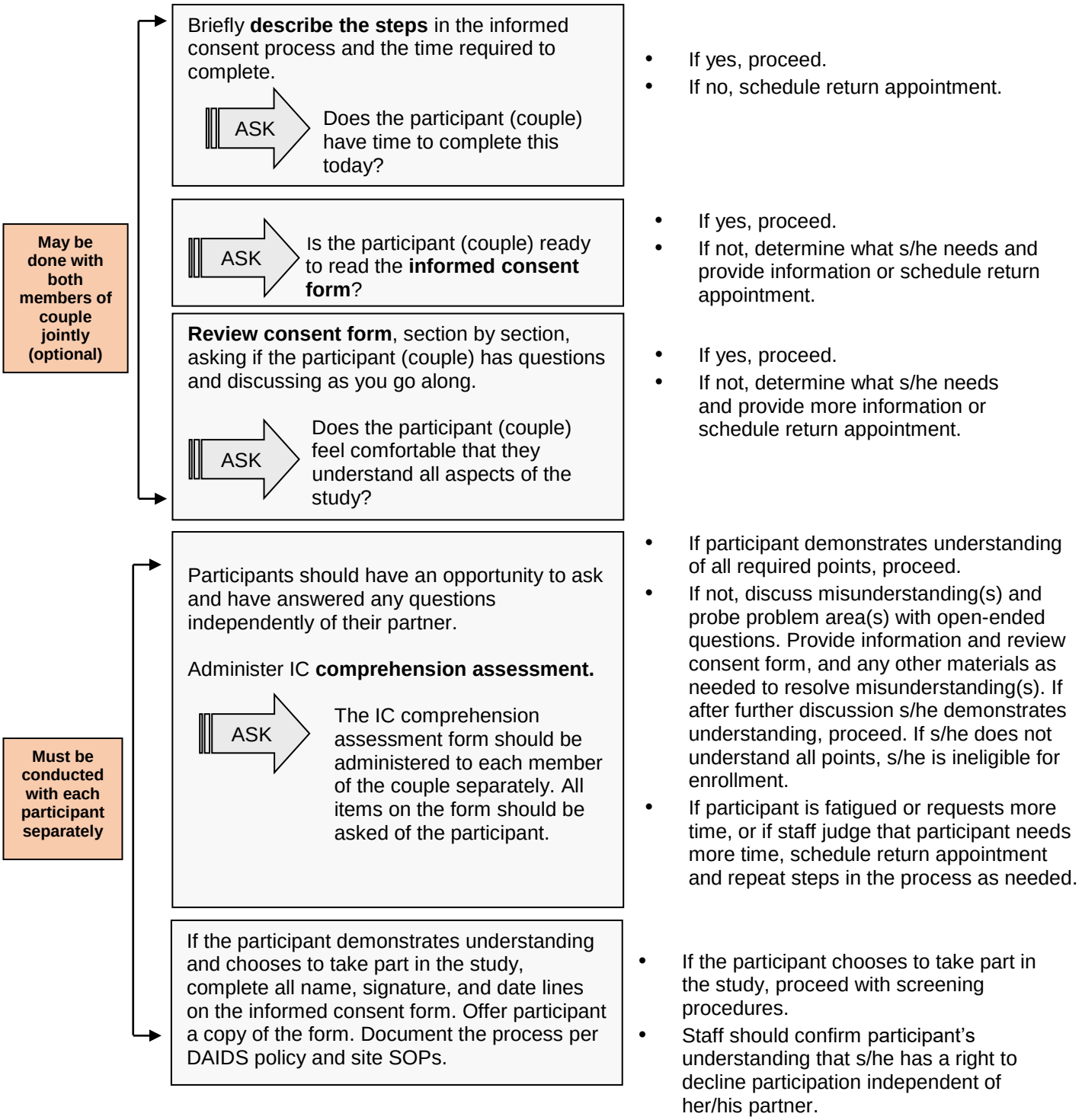
- Procedures for documenting the IC process
- Procedures for conducting part of the IC process with couples together, if applicable
- Storage locations for blank ICFs
- Storage locations for completed ICFs
- Procedures (e.g., color-coding) to ensure that different versions of the study ICF are easily distinguishable and used appropriately
- Procedures for implementing a change in version of the ICF used
- Staff training requirements
- Staff responsibilities for all the above (direct and supervisory)
- QC/QA procedures related to the above (if not specified elsewhere)

4.4 Informed Consent for Screening and Enrollment

Informed consent must be obtained before performing any “on-study” procedures at the Screening and Enrollment Visit. For participants who do not consent to study participation, no procedures should be performed and no data that can be linked to their name or other personal identifier(s) should be recorded.

An overview of the standardized approach to the informed consent process is provided in Figure 4-1 below. Additional details related to key steps in the process are provided in the remainder of this section.

Figure 4-1
Overview of MTN-045 Informed Consent Process



4.4.1 Informed Consent Procedures for Illiterate Participants

Illiterate participants may be consented and enrolled in MTN-045, providing they are otherwise willing and eligible and if independent consent is ensured. Site SOPs must outline the process for assessing participants for literacy and how independent consent is ensured for participants who are not literate. If the participant is illiterate (not able to read), an impartial literate witness who speaks the language of the participant must be present during the entire informed consent process/discussion with the participant. ICH GCP guidance identifies an “impartial” witness as a person who is independent of the study, who cannot be unfairly influenced by people involved with the study. The MTN CORE has received guidance from the US Food and Drug Administration’s GCP office stating that the witness need not be “totally unaffiliated with the study.” It may be possible, for example, to designate a "subject advocate." The site SOP for obtaining informed consent should define who may serve as the witness to the informed consent process. It should be noted, however, that a participant’s partner may not serve as their impartial witness.

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.

This witness must sign and date the informed consent form to attest that the information therein and any other written information was accurately explained to, and apparently understood by, the participant, in the participant’s language of fluency, and that informed consent was freely given by the participant. The participant’s printed name, signature, and signature date lines on the informed consent form should be completed as described and illustrated in Figure 4-2 below. Following these procedures fulfills the protocol requirement for obtaining written informed consent from all study participants.

Figure 4-2
Informed Consent Form Signature Lines for Illiterate Participants

- Unless other conventions that have been endorsed by DAIDS are specified in site SOPs, the study staff member who completes the informed consent process/discussion with the participant should print the participant's name and date of informed consent below the "participant's printed name" and "date" line, respectively, together with a signed and dated note documenting the name of the person who made the entry and the date of the entry.
- The participant should add his or her fingerprint or make his or her mark above the "participant's signature" line.
- The witness will print, sign, and date in the section designated for "Witness"

SIGNATURES

Participant Name	Participant Signature	Date
Mary Phiri		**25 NOV 2009**

Participant name and date written by Martha Moore. MM 25 NOV 09

Martha Moore		**25 NOV 2009**
Name of Staff Person Conducting Consent Discussion	Study Staff Signature	Date

Debra Ross		**25 NOV 2009**
Witness Name	Witness Signature	Date

4.4.2 Couples Informed Consent Considerations

Study staff will explain the study to both members of the couple and determine their presumptive eligibility to participate in the study; both of these informed consent process components may be done with the potential participants either separately or together as a couple. However, to reduce the potential for coercion by one partner of the other, study staff will assess each participant's willingness to be in the study and confirm their eligibility separately from their partner (see SSP Manual Section 3 regarding eligibility assessment). This will be presented as a standard procedure so as not to raise concerns from either member of the couple. Participants will also sign individual consent forms, undergo comprehension assessment, and have an opportunity to ask questions about the study separately from their partner. As part of the individual consent process, study staff should confirm with the participant that their participation in the study is voluntary and their choice alone. Should the participant decline to partake for matters related to their relationship (such as coercion), staff should discuss this with the participant and come to an agreement with them about how study staff will communicate the couple's ineligibility to their partner.

4.5 Comprehension Assessment

The participant must not sign the ICF until s/he fully understands the information contained therein, including that pertaining to visit procedures. Site SOPs should explain the procedures that study staff are responsible for implementing to ensure that each participant understands the screening process and the study prior to signing the ICF and undertaking any study procedures, respectively.

A comprehension assessment should be conducted and documented prior to a participant signing the ICF. This assessment should occur with individual members of the couple after the participant has completed the informed consent discussion described above, but before s/he is asked to sign the ICF. It is expected that staff administering the informed consent and assessing comprehension be sufficiently knowledgeable about MTN-045 to make good judgments about the potential participant's understanding of the required information and their willingness to participate independent of their partner.

4.5.1 Comprehension Assessment Checklist

A sample open-ended enrollment informed consent comprehension assessment checklist is available on the Study Implementation Materials section of the MTN-045 webpage.

This tool is structured around open-ended questions that correspond with the required elements of informed consent for research. Each question should be read to potential participants, giving them time to respond to each one. Each question should be satisfactorily answered by the participant before moving to the next question. For each question, the assessment specifies points that must be included in the participant's response. These are identified on the tool as "Required Points of Comprehension."

Regardless of the method used to assess comprehension, if the assessment results indicate misunderstanding of any aspect of the study, staff should review those until the participant fully understands them.

If, after all possible efforts are exhausted, the participant is not able to demonstrate adequate understanding of the study, do not ask him/her to sign the ICF to screen/enroll in the study. Similarly, if the participant has concerns about possible adverse effects of participating in the study, including on his/her relationship, or indicates that s/he is being coerced to participate by his/her partner or may have difficulty adhering to the study requirements, do not ask him/her to sign the ICF.

4.5.2 Documenting the Comprehension Assessment

The comprehension assessment checklist tool is considered a study source document that should be completed, handled, and retained in the participant's study file like any other source document. After administering the assessment tool, staff should carefully review the form to verify that all required points have been satisfactorily addressed by the participant and that this is adequately documented. Consideration should be given to having two study staff members complete this verification because failure to document comprehension of all required points will be considered an informed consent process protocol deviation.

Comments may be recorded in a designated area on the form (and on the back of the form if additional space is needed) or on an Informed Consent Coversheet, a template of which is available on the MTN-045 webpage under Study Implementation Materials. All required points

must be satisfactorily addressed by the participant before proceeding to the final informed consent decision and signing of the ICF.

After the informed consent process is completed, the outcome of the process should be recorded directly on the comprehension assessment form (or in a chart note) and the staff member who completed the form should record his/her signature in the space provided. Detailed information on how comprehension will be assessed must be specified in the site Informed Consent SOP.

4.6 Documenting the Informed Consent Process

It is essential that all informed consent documentation (i.e. ICFs, IC coversheet, IC comprehension assessment tool) indicate that participant informed consent was obtained before any study procedures were conducted.

US FDA regulations and ICH E6 guidelines require that informed consent be documented by "the use of a written informed consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent."

To fulfill this requirement, complete all signature and date lines on the ICF in dark ink. Legal names should be used. Fabricated/falsified names should not be used. Initials may not be used in place of a participant's full surname, and it is strongly recommended that initials not be used in place of a participant's full first name. However, if a participant commonly signs his/her name using an initial for first name, the initial may be used, provided this practice is acceptable per the policies of the study site institution(s).

The DAIDS policy on Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials lists detailed requirements and suggestions for documenting the informed consent process. All requirements listed in the DAIDS policy must be met. To meet the suggestions listed in the DAIDS policy, sites are strongly encouraged to use an Informed Consent Coversheet similar to the template provided on the MTN-045 webpage under Study Implementation Materials. Sites choosing to use a coversheet should list the coversheet as a source document in their Data Management SOP and should use the coversheet consistently to document all informed consent procedures undertaken with participants. The sample IC Coversheet indicates the items to be completed at the start of the informed consent session. The remainder should be completed at the end of the informed consent session.

If a site chooses not to utilize the IC Coversheet, all elements of the informed consent process must be adequately described in the site SOP for obtaining Informed Consent and documented in detail in a signed and dated chart note.

Regulations require that participants be given a signed copy of the ICF(s). If a participant opts not to receive a copy or if site IRB/EC policy mandates that a blank ICF be provided, document this on the IC coversheet or visit note and ensure that an alternative form of study contact information (e.g., a contact card or appointment card) is provided in lieu of the full signed/dated ICF.