

Section 4. Participant Accrual

This section provides information on requirements and procedures for recruiting, screening, and enrolling participants in MTN-015.

4.1 Study Accrual Plan

MTN-015 study staff will recruit all participants who seroconvert in MTN microbicide trials. There is no time limit for accrual into MTN-015; accrual will remain open for the duration of MTN funding.

Potential participants will be referred to MTN-015 as soon as possible after identification of HIV seroconversion (per the HIV testing algorithm of the parent microbicide study). For microbicide trial participants who seroconvert prior to site-specific activation of MTN-015, study staff will retrospectively contact the participants for possible enrollment in MTN-015, unless the participants have refused further contact with study staff. For microbicide trial participants who seroconvert after activation of MTN-015, study staff will prospectively contact the participants for possible enrollment in MTN-015. Eligible participants may be enrolled in MTN-015 at any time after identification of seroconversion (per the HIV testing algorithm of the parent microbicide study).

MTN-015 recruitment efforts should include education about the MTN-015 study, including but not limited to the general study objectives, the schedule of study visits and types of visit procedures, expected duration of participation, and the risks and benefits of enrollment. To minimize visit burden, participants should be offered the opportunity to combine MTN-015 visits with ongoing parent protocol visits, if desirable to the participant. Sites should monitor reasons for decline in MTN-015 enrollment, and periodically assess whether adjustments to recruitment strategies are needed—for example, if participants are concerned about additional blood draws or potential stigma from enrollment into protocol for HIV-positive individuals, then MTN-015 education should be modified to better address these concerns upfront with participants. If participants initially decline or are undecided about MTN-015 and need more time to consider their decision to enroll, sites should have systems in place to check back in with participants periodically to see if their circumstances have changed. Sites may consider developing site-specific recruitment scripts or informational materials about MTN-015 to facilitate recruitment. A sample study information sheet/script is available on the MTN-015 website (<http://www.mtnstopshiv.org/node/468>), which sites can adapt to meet their needs as needed. Contact FHI 360 as needed for assistance with developing any necessary tools.

Per the reporting plan in Section 14 of this manual, the MTN Statistical and Data Management Center (SDMC) will provide the MTN-015 Protocol Team with progress reports via ATLAS on the status of participant accrual at each study site.

4.2 Screening: Definition and Procedures

The term “screening” refers to procedures performed to determine whether a potential participant is eligible to take part in MTN-015. The study eligibility criteria are defined in protocol Section 5 and listed in Figure 4-1

Figure 4-1
MTN-015 Eligibility Criteria

<p>Inclusion Criteria</p> <p>Participants must meet both of the following criteria to be eligible for inclusion in the study:</p> <ul style="list-style-type: none">• HIV-1 seroconversion during participation in any MTN clinical trial based on local laboratory testing and according to the HIV testing algorithm of the parent MTN trial.• Able and willing to provide written informed consent to participate in the study.
<p>Exclusion Criteria</p> <p>Participants who meet the following criterion will be excluded from the study:</p> <ul style="list-style-type: none">• Has any condition that in the opinion of the investigator or designee, would preclude provision of informed consent, make participation in the study unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives.

The MTN-015 protocol specifies three screening procedures: informed consent, review of parent study records to confirm HIV seroconversion, and eligibility determination. Written informed consent must be obtained before conducting any other procedures; see Section 4.5 below for guidance on the informed consent process.

Each of the three protocol-specified screening procedures is listed in the Screening and Enrollment visit checklist posted on the MTN-015 Study Implementation Materials webpage (<http://www.mtnstopshiv.org/node/468>), together with checkboxes that can be used to source document the outcome of assessments performed to determine participant eligibility vis-à-vis the criteria in Figure 4-1.

It is the responsibility of the MTN-015 Investigator of Record (IoR) to ensure that only participants who meet the study eligibility criteria are enrolled in the study. Each site must establish a standard operating procedure (SOP) that describes how the IoR, and designated study staff, will fulfill this responsibility. This SOP minimally should contain the following elements:

- Eligibility determination procedures (and documentation thereof)
- Eligibility verification procedures (and documentation thereof)
- PTID assignment procedures (see also Section 4.3 below)
- Staff responsibilities for all of the above

Should site staff identify that an ineligible participant has inadvertently been enrolled in MTN-015, the IoR or designee should immediately contact the MTN-015 Management Team for guidance on subsequent action to be taken.

4.3 Enrollment: Definition and Procedures

Participants will be considered enrolled in MTN-015 when they have been assigned an MTN-015 Participant ID number (PTID).

The MTN SDMC will provide each study site with a listing of PTIDs for use in MTN-015. As shown in Figure 4-2, the listing will be formatted such that it may be used as the log linking MTN-015 PTIDs, participant names, and parent study PTIDs at each site. Further information on the structure of PTIDs for MTN-015 can be found in Section 12.3.1 of this manual.

PTIDs should only be assigned to consenting participants who are determined to meet the MTN-015 eligibility criteria, after eligibility has been confirmed. Site staff are responsible for establishing procedures and staff responsibilities for proper storage, handling, and maintenance of the PTID list such that participant confidentiality is maintained, individual PTIDs are assigned to only one participant, and individual participants are assigned only one PTID. It is recommended that these procedures and responsibilities be included in site SOPs for eligibility determination; alternatively, these procedures and responsibilities may be specified in site SOPs for data management.

**Figure 4-2
Sample PTID List and PTID-Name Link Log for MTN-015**

MTN-015 Participant ID	Participant Name	Parent Study	Parent Study Participant ID	Date	Staff Initials
XXX- 00001-C					
XXX- 00002-C					
XXX- 00003-C					
XXX- 00004-C					
XXX- 00005-C					

The administrative, clinical, behavioral, and laboratory procedures to be performed at enrollment are specified in Section 7.1 of the MTN-015 protocol. These procedures also are listed on the Screening and Enrollment visit checklist. Further guidance on clinical, counseling, and laboratory procedures is provided in Sections 8-10 of this manual.

Because enrollment visit procedures involve laboratory testing, a contact is required after the Screening and Enrollment visit to provide participants with their test results, clinically relevant post-test counseling, and/or clinically indicated treatment. Study staff may complete these contacts at the study site or at community-based locations, depending on site capacities and site and participant preferences. Like all study visits, all contacts should be documented in participant study records.

4.4 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 sample screening and enrollment log suitable for use in MTN-015 is shown in Figure 4-3.

**Figure 4-3
Sample Screening and Enrollment Log for MTN-015**

	Screening Date	Parent Study PTID	Enrollment Date (NA if not enrolled)	MTN-015 PTID (or NA)	Screening Failure Date (NA if enrolled)	Reason for Screening Failure (NA if enrolled)
1						
2						
3						
4						
5						

4.5 Informed Consent

Informed consent is a process by which an individual voluntarily expresses her willingness to participate in research, after having been informed of all aspects of the research that are relevant to her 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, with four key considerations — information exchange, comprehension, voluntariness, and documentation — each of which is described below. See Section 4.8 of the International Conference on Harmonization Good Clinical Practice (GCP) Consolidated Guidance (ICH-E6) and the informed consent section of the DAIDS policy on *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials* for detailed guidance on the informed consent process and associated documentation requirements.

This study involves one informed consent form: informed consent for screening and enrollment. Informed consent for storage and future research testing of biological specimens is included in the Screening and Enrollment consent form. Study sites may choose to use one informed consent form to present all relevant screening, enrollment, and specimen storage information to participants, or to use one form for screening and enrollment and a second form for specimen storage. With either approach, participants must document their consent for specimen storage separate from their consent for screening and enrollment. Participants may choose not to consent to specimen storage and still enroll in the study.

US regulations 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 designated study staff, to deliver all required information to potential research 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 informed consent forms specify all information required by the regulations. However, responsibility for informed consent does not end with preparation of an adequate informed consent form. It also is the responsibility of the IoR and 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 the process

Each of these requirements is described below.

4.5.1 Deliver all required information in a manner that is understandable to potential participants

As a starting point, if the participant is literate, give her a copy of the informed consent form to read. Also provide her with other informational materials developed to complement the informed consent form, if any. If the participant is not literate, read the materials to her. After the participant has read the written material (or had it read to her), verbally review the information provided. A checklist or the informed consent form itself may serve as a useful guide for this. For example, you may note the main points described in each paragraph of the informed consent form, and ask if the participant has questions or concerns about each point. Listen carefully to the questions and/or concerns expressed by the participant, and discuss these thoroughly. Take as much time as needed to address each question and concern.

If the participant is not literate, an impartial literate witness must be present during the entire informed consent process/discussion with the participant. As part of the documentation steps detailed below, the witness will be asked to sign and date the informed consent form to attest that the information in the consent form was accurately explained to, and apparently understood by, the participant, and that informed consent was freely given by the participant. ICH-E6 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 LOC (FHI 360) has previously 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" who would be available at each site ...” Please refer to Section Appendix 4-1 for a summary of considerations for obtaining informed consent from illiterate participants.

4.5.2 Assure that informed consent is obtained in a setting free of coercion and undue influence

During the informed consent discussion, take care to not overstate the possible benefits of the study, nor to understate the risks. Also emphasize to the participant that the availability of medical care and other services routinely obtained from the study site institution will not be affected by her decision whether or not to take part in the study. Encourage the participant to take as much time as she needs — and to talk about her potential participation with others, if she chooses — before making a decision.

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.

4.5.3 Confirm that the participant comprehends the information

The participant must not be asked to agree to take part in the study, or to sign or make her mark on the informed consent form, until she fully understands the study. Study staff are responsible for implementing procedures to ensure that each participant understands all aspects of study participation before signing or marking the informed consent form.

One approach to assessing comprehension is to use a “quiz” (either oral or written) or other assessment tool which participants must complete prior to signing or marking the informed consent form. A sample assessment tool of this type is included in Section Appendix 4-2. Another approach is to use open-ended questions to ascertain participant understanding during the informed consent discussion; some sample open-ended questions that may be used for this study are included in Section Appendix 4-3. For sites that choose to adopt tools such as the samples included in the section appendices, use instructions should be included in the site SOP for obtaining informed consent.

Regardless of the method used to assess comprehension, if the assessment indicates misunderstanding of aspects of the study, review those aspects again 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 her to sign or mark the informed consent form or to enroll in the study. Similarly, if the participant has concerns about possible adverse impacts on her if she were to take part in the study, or indicates that she may have difficulty adhering to the study requirements, do not ask her to sign the informed consent form or enroll in the study unless or until such issues can be resolved to the satisfaction of the participant and the IoR (or designee).

4.5.4 Document the process

US regulations require that informed consent be documented through “the use of a written informed consent form approved by the IRB/EC and signed and dated by the subject or the subject's legally authorized representative at the time of consent.”

To fulfill this requirement, all signature and date blocks on the informed consent form should be completed in 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 her name using an initial for her first name, the initial may be used, provided this practice is acceptable per the policies of the study site institution(s).

If the participant is not literate, the witness who was present during the informed consent discussion must sign and date the informed consent form to attest that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant, and that informed consent was freely given by the participant. The participant printed name, signature, and signature date blocks on the informed consent form should be completed as follows:

- The study staff member who completes the informed consent process/discussion with the participant should enter the participant's name below the “participant's printed name” block, 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 make her mark in the “participant's signature” block.
- The study staff member who completes the informed consent process/discussion with the participant should enter the date upon which the participant made her mark on the informed consent form below the “participant signature date” block, together with a signed and dated note documenting the name of the person who made the entry and the date of the entry.

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. In order to also meet many of the suggestions listed in the DAIDS policy, site staff may use an informed consent coversheet similar to the example included in Section Appendix 4-4. Sites choosing to use a coversheet should list the coversheet as a source document in their SOPs for Source Documentation for MTN-015 and should use the coversheet consistently to document the informed consent process conducted with each participant.

In addition to completing the documentation requirements on the informed consent form itself, each informed consent process should be documented in a signed and dated chart note. The note (as well as the dates on the informed consent form itself) should document that informed consent was obtained before conducting any study procedures. The note also should document adherence to the requirements of the informed consent section of the DAIDS policy on *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials*. However, if an informed consent coversheet is used, it is not necessary to transcribe information recorded on the coversheet into the chart note.

Finally, regulations require that participants be given a signed copy of the informed consent forms. If a participant opts not to receive a copy, document this in a chart note and offer the participant an alternate form of study contact information (e.g., a contact card or appointment card) in lieu of the full informed consent form.

4.5.5 SOP for Obtaining Informed Consent

As a condition for study activation, each site must establish an SOP for obtaining informed consent from potential study participants. This SOP should reflect all of the information provided in this section and minimally should contain the following elements:

- The minimum legal age to provide independent informed consent at the study site
- Procedures for ascertaining participant identity and age
- Procedures for ascertaining participant literacy
- Procedures for providing all information required for informed consent to the participant
- Procedures for ascertaining participant comprehension of the required information
- Procedures to ensure that informed consent is obtained in a setting free of coercion and undue influence
- Procedures for documenting the informed consent process
- Considerations and requirements for illiterate participants, including specification of who may serve as a witness to the informed consent process
- Storage locations for blank informed consent forms
- Storage locations for completed informed consent forms
- Procedures for implementing a change in the version of the informed consent form used
- Staff responsibilities for all of the above

Section Appendix 4-1
Summary of Considerations for Obtaining Informed Consent from Illiterate Persons

- Each site must specify procedures for obtaining and documenting informed consent from illiterate persons in its SOP for obtaining informed consent. These procedures must be consistent with the DAIDS policy on *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials* and must be followed each time informed consent is obtained. It is recommended that each site seek IRB/EC review and approval of these procedures.
- An impartial witness must be present during the entire informed consent discussion with an illiterate participant. The witness must sign and date the informed consent form to attest that the information in the consent form was accurately explained to, and apparently understood by, the participant, and that informed consent was freely given by the participant.
- The site SOP for obtaining informed consent should define who may serve as the witness to the informed consent process.
- Take care to minimize the perception of coercion due to the presence of the witness.
- The study staff member who completes the informed consent process/discussion with the participant should enter the participant's name below the "participant's printed name" block, 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 make her mark in the "participant's signature" block.
- The study staff member who completes the informed consent process/discussion with the participant should enter the date upon which the participant made her mark on the informed consent form below the "participant signature date" block, together with a signed and dated note documenting the name of the person who made the entry and the date of the entry.
- Refer to Section 4.8 of the Good Clinical Practice Consolidated Guidance (ICH-E6) and the informed consent section of the DAIDS policy on *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials* for additional information.

Section Appendix 4-2
Sample Informed Consent Comprehension Assessment Tool for MTN-015

		True	False
1	This study is part of the regular medical care offered here at [clinic name].	<input type="checkbox"/>	<input checked="" type="checkbox"/>
2	The main purpose of this study is to find out if using a microbicide affects the health of women after they become infected with HIV.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
3	Each woman will be in this study for two years	<input type="checkbox"/>	<input checked="" type="checkbox"/>
4	Study participants will have study visits every month.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
5	Study participants will have blood tests and pelvic exams at every visit.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
6	Study participants are not allowed to bring their male partners to the study clinic.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
7	Study participants can get condoms and HIV/AIDS counseling from the study staff at any time.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
8	Study participants must agree to have blood and vaginal fluids stored for future testing in order to join this study.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
9	If you join this study, you must stay in the study for as long as the study nurse says.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
10	If the study staff find that you have any medical problems, they will refer you to available sources of medical care for those problems.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
11	If you join this study, the study staff will give you medication to treat your HIV infection (“ARVs”).	<input type="checkbox"/>	<input checked="" type="checkbox"/>
12	Study participants could become worried or anxious while talking about HIV or waiting for test results.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
13	Participants’ study records will be available to everyone at the [name of site institution].	<input type="checkbox"/>	<input checked="" type="checkbox"/>
14	Being in this study could cause problems for study participants with their partners, family members, or community contacts (e.g., neighbors).	<input checked="" type="checkbox"/>	<input type="checkbox"/>
15	If you decide not to join this study, you can still come to the [name of site institution] for medical care.	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Section Appendix 4-3
Sample Open-Ended Discussion Questions for Assessing Comprehension of MTN-015

1. **If you wanted to tell a friend or family member about this study, how would you describe it to them?**
 - Study objectives
 - Study population
 - Overall study design: duration, visit schedule, procedures done, options for specimen storage

2. **How do you think it would affect your day-to-day life to be in this study?**
 - Study duration
 - Study visit schedule and visit duration (1-2 hours)
 - Services provided — and not provided — by the study
 - Perceived risks and benefits of study participation (including potential social harms)
 - No costs to participants

3. **What do you think you will get out of being in this study?**
 - HIV/STI education, counseling, and testing
 - Condoms
 - Physical exams and lab tests
 - STI treatment
 - Referrals for other care/treatment
 - Personal satisfaction

4. **Are there aspects of being in this study that concern you?**
 - Embarrassment/worry/anxiety when discussing HIV/AIDS and risk behaviors
 - Worry/anxiety while waiting for test results
 - Discomfort/pain during blood draw and pelvic exams
 - Risks to privacy and possible social harms

5. **What might the study staff do if you miss a study visit?**
 - Mail, phone, other contacts to re-schedule the visit
 - Home visits or other community-based contacts to re-schedule the visit
 - Work through locator contacts to reach the participant

6. **What are some reasons why the study staff might end your participation in the study?**
 - The study is stopped or cancelled
 - The staff feel it would be harmful for the participant to stay in the study
 - The participant is unable to keep appointments for study visits

7. **What will the study staff do to protect your privacy and confidentiality during the study?**
 - Conduct visits in private
 - Keep information about study participation and all study records confidential
 - Maintain privacy and confidentiality when conducting locator activities
 - However some “outsiders” may review records

8. **What would you do if you joined the study and then you didn't feel comfortable about the way you were treated in the study?**
 - Role of IRB/EC and human subjects contact person
 - Voluntary participation — can leave the study at any time
 - Voluntary participation — can continue to receive other services at the study site institution

Section Appendix 4-4
Sample Informed Consent Coversheet for MTN-015

Participant Name (or PTID):	
Name of study staff person completing informed consent process/discussion (and this coversheet):	
Is the participant of legal age to provide independent informed consent for research?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ STOP. Participant is not eligible for MTN-015.
Date of informed consent process/discussion:	
Start time of informed consent process/discussion:	
Language of informed consent process/discussion:	
Was the informed consent process/discussion conducted according to site SOPs for MTN-015?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Record and explain departures from site SOPs below.
Can the participant read?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ A literate impartial witness should be present during the entire informed consent process/discussion. Refer to DAIDS policies and site SOPs for specific instructions. Record name of witness here: Record relationship of witness to participant here:
Version number/date of informed consent form used during informed consent process/discussion:	
Was all information required for the participant to make an informed decision provided in a language that was understandable to the participant?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Explain below.
Were all participant questions answered?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Explain below.
Did the participant comprehend all information required to make an informed decision?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Explain below.
Was the participant given adequate time/opportunity to consider all options before making her informed decision?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Explain below.
Did the participant accept a copy of the informed consent form?	<input type="checkbox"/> NA (participant chose not to provide informed consent) <input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Offer alternative form of study contact information to participant.
End time of informed consent process/discussion:	
Notes/Comments (continue on back if needed):	
Signature of study staff person completing informed consent process/discussion (and this coversheet):	