Section 4. Participant Accrual

This section provides information on requirements and procedures for recruiting, screening, and enrolling participants in MTN-009.

4.1. Study Accrual Plan

MTN-009 will enroll approximately 1000 study participants in order to achieve the enrollment target of 350 evaluable HIV-positive women. Accrual of all 1000 participants is targeted to be completed within two years.

For each site, accrual will begin after the MTN Coordinating and Operations Center (CORE) at FHI issues a written site-specific, study activation notice. Once the study is initiated, accrual will be closely monitored. On a weekly basis, the site will report the number of participants screened (participants who sign the IC but are not enrolled) and enrolled (participants who are assigned a PTID, see section 4.2) in the study to CORE (FHI). CORE (FHI) will then distribute a weekly, consolidated, cross-site accrual report to the Protocol Team. The MTN Statistical and Data Management Center (SDMC) will post reports on the ATLAS portal listing the number of participants enrolled in the study based on data received and entered into the study database. Please see Section 11 of this manual for more information on the study reporting plan.

Since the target population for MTN-009 is women who present to the study site for an HIV prevention trial, MTN-009 study staff will not independently recruit women for MTN-009. Rather, MTN-009 study staff will rely on recruitment efforts in the HIV prevention trial(s) occurring at the site, and will recruit for MTN-009 those women who present to the study site for an HIV prevention trial. If a woman who presents for prescreening or screening for an HIV prevention trial meets eligibility criteria for MTN-009, she will first be offered the option of joining the MTN-009 study prior to prescreening or screening for the HIV prevention trial.

Eligibility determination, enrollment and study procedures at the Screening and Enrollment Visit are anticipated to take place on the same day. However, if for some reason blood for HIV testing is not drawn on the day of enrollment, sites have one week from the day of enrollment to complete the blood draw. If a repeat blood draw is required to meet protocol requirements, then the repeat blood draw must be done no later than one week after the date of enrollment. If the initial or repeat blood draw cannot be done within one week of the enrollment date, then sites will cease efforts to schedule the blood draw and the data will be considered lost.

4.2 Screening and Enrollment: Definition and Procedures

The term “screening” refers to procedures performed to determine whether a potential participant is eligible to take part in MTN-009. The study eligibility criteria are defined in protocol Section 5 and listed in Figure 4-1.

Figure 4-1
MTN-009 Eligibility Criteria

Inclusion Criteria

Women must meet all of the following criteria to be eligible for inclusion in MTN-009

- Present to an MTN-009 study site to pre-screen or screen for an HIV prevention trial
- Age 18-40 years, verified per site SOPs
- Able and willing to provide written informed consent for participation in MTN-009
- Able and willing to provide adequate locator information, as defined in site SOPs

Exclusion Criteria

Women who meet the following criterion will be excluded from the study:

- Any condition that, in the investigator's opinion, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achievement of the study objectives

It is the responsibility of the MTN-009 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
- Staff responsibilities for all of the above

Should site staff identify that an ineligible participant has inadvertently been enrolled in MTN-009, the IoR or designee should contact the MTN-009 management alias list (mtn009mgmt@mtnstopshiv.org) immediately for guidance on subsequent action to be taken.

Once it is determined that a participant is eligible for MTN-009, study staff may enroll the participant. Participants will be considered enrolled in MTN-009 when they have been assigned an MTN-009 Participant ID number (PTID). The order of procedures for the screening/enrollment visit is listed in Figure 4-2.

The MTN SDMC will provide each study site with a listing of PTIDs for use in MTN-009. As shown in Figure 4-3, the listing will be formatted such that it may be used as the log linking MTN-009 PTIDs to participant names, at each site. Further information on the structure of PTIDs for MTN-009 can be found in Section 9 of this manual.

Figure 4-2: Order of Screening and Enrollment Procedures

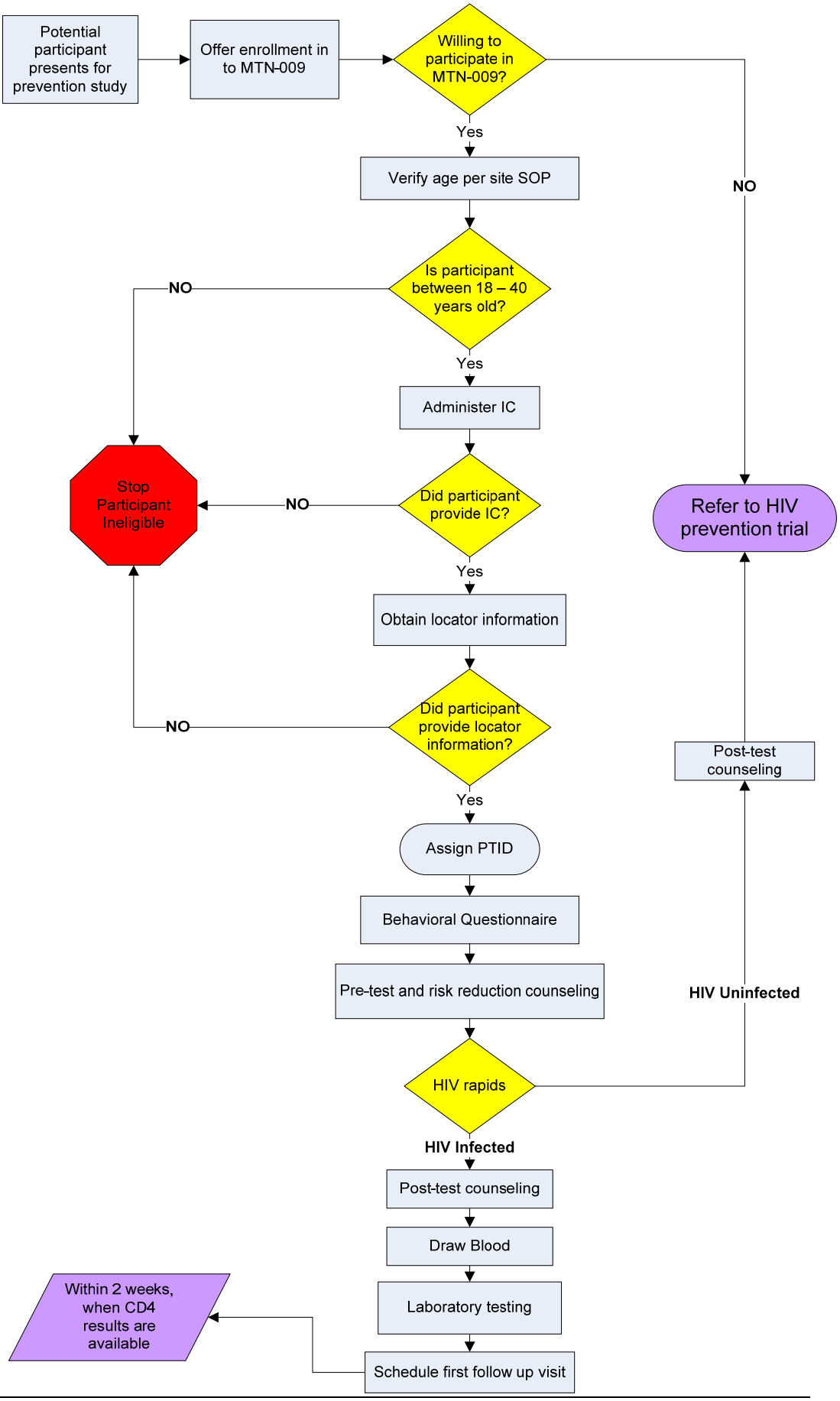

Figure 4-3
Sample PTID List and PTID-Name Link Log for MTN-009

MTN-009 Participant ID	Participant Name	Date	Staff Initials
XXX- 00001-C			
XXX- 00002-C			
XXX- 00003-C			
XXX- 00004-C			
XXX- 00005-C			

PTIDs should only be assigned to consenting participants who have met the MTN-009 eligibility criteria, as determined by the IoR or designee. PTIDs should be assigned after eligibility has been confirmed and participants have signed the informed consent. Site staff are responsible for establishing procedures and staff responsibilities for proper storage, handling, and maintenance of the PTID list so 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.

4.2.1 Screening and Enrollment HIV Testing

Screening and Enrollment HIV testing will be performed using two different rapid HIV tests per the algorithm in protocol Appendix II. At least one of the two rapid tests must be FDA approved and each site's test kit selections must be validated and approved by the MTN Network Laboratory (NL). Always contact the NL in cases of unusual test results or problems with testing methods.

HIV testing will be performed at the Screening and Enrollment visit after administration of the behavioral questionnaire:

- Blood for rapid tests will be collected via fingerstick
- If both rapid tests are negative, the participant will be considered HIV-uninfected; no further testing is required. Refer participant to HIV prevention trial.
- If both rapid tests are positive, the participant will be considered HIV-infected and blood will be drawn for additional laboratory testing.
- If the two rapid tests are discordant, collect blood via venipuncture and perform an FDA-approved Genetic Systems Western blot (WB) test, manufactured by Bio-Rad Laboratories.
    - If the WB is negative, the participant will be considered HIV-uninfected; no further testing is required. You may refer participant to HIV prevention trial at that time or you may consult the NL before referring participant to HIV prevention trial in cases where site may be concerned of a natural reactivity to the rapid tests.
    - If the WB is positive, the participant will be considered HIV-infected. Send plasma samples for additional laboratory testing. Contact the participant to schedule the first follow up visit.
    - If the WB is indeterminate, the participant will be asked to present to the study site in approximately one month for re-testing. At that time, the two rapid tests will be repeated and the above-described algorithm will be followed.

All sites should notify the NL in the event that discordant rapid HIV test results are obtained. This notification is for informational purposes; while the NL may provide technical guidance to the site if needed, WB testing at the local lab should proceed immediately upon identification of the discordant rapid test results.

Guidelines for performing HIV tests during screening and enrollment are provided in Section 8 of this manual. All tests must be documented on local laboratory log sheets or other laboratory source documents; such documents must capture the start and end/read times for each test. A second independent clinic or laboratory staff member trained in proper HIV testing and result recording procedures must review, verify, and sign-off on test results within the specified timeframes for the tests and prior to disclosure of results to participants. In addition to initialing or signing the testing logs to document review and verification of the results, the second staff member must also record the time at which the results were reviewed and verified.

The administrative, clinical, behavioral, and laboratory procedures to be performed at screening and enrollment are specified in Section 7.1 of the MTN-009 protocol. These procedures also are listed on the Screening and Enrollment visit checklist in Section 7 of this manual. Further guidance on counseling and laboratory procedures is provided in Sections 6 and 8 of this manual, respectively.

Follow-up visits are only required for participants who are found to be HIV infected. These participants will be asked to return to the clinic for at least two follow-up visits to obtain their test results, receive clinically relevant post-test counseling, and additional referrals. However, no additional clinical procedures will take place during these follow-up visits. Given the nature of the study, and to ensure participant confidentiality, all study visit procedures must take place at the study clinic. Like all study visits, all contacts should be documented in participant study records.

4.3 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-009 is shown in Figure 4-4.

Figure 4-4
Sample Screening and Enrollment Log for MTN-009

	Screening and Enrollment Date	**MTN-009 PTID or NA if participant not enrolled**	**Reason participant was not enrolled (NA if enrolled)**
1			
2			
3			
4			
5			

4.4 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 that includes: informed consent for screening and enrollment, and informed consent for storage and future research testing of biological specimens (blood). Participants must document their consent for specimen storage separate from their consent for screening and enrollment by writing their initial or making their mark to indicate whether or not they give their permission to the use and future testing of leftover blood samples. Consent for each is obtained separately, as participants may choose not to consent to specimen storage and still enroll in the study. Participants also may choose whether to have their test results communicated to non-study clinicians. Participants may choose not to consent to communicating test results 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 CORE (FHI) 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 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

4.4.1 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 has 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 CORE (FHI) 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.

4.4.2 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 of 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, take care 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.

4.4.3 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 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 and the tools should be submitted to the IRB for approval.

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).

4.4.4 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, the participant should print her name, sign, and date the informed consent form 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 participant should print her own name. If she is unable to do so, 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 participant should write the date of signature herself. If she is unable to do so, then 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-009 and should use the coversheet consistently to document the informed consent process conducted with each participant.

The 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) 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.

GCP 4.8.11 requires that participants are 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.

4.4.5 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, specifying 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

4.5 Obtaining Locator Information

Each study site is encouraged to develop an exhaustive locator form to maximize contact effectiveness. Sites also may wish to consider having outreach workers accompany participants to their homes or other community based locations to verify or further clarify their locator details. Potential locator items include:

- Participant's full name, alias, and/or nickname; government-issued identification number; home address; home phone number; mobile phone number; pager number; work address; work phone number; fax number; e-mail address; daytime and nighttime locations, meeting places, hangouts.

- Walking/driving/public transport directions and/or pictorial map to the participant's home, workplace, etc.

- Name, address, telephone number, and/or other contact information for stable community contacts (i.e., participant family members and friends) who typically know the whereabouts of the participant.

- Name, address, telephone number, and/or other contact information for the participant's health care provider; school or training program; church or other place of worship; social service case worker; counselor, rehabilitation provider, etc; participant's child's school and health care provider.

- Name, address, telephone number, and/or other contact information for support groups, shelters, food pantries, and other social service organizations used by the participant.

During the informed consent process and when collecting locator information, study participants must be informed that their locator sources will be contacted if study staff are unable to locate the participant directly. Study staff will negotiate with the participant how they will identify themselves when locator sources are contacted. Arrangements agreed upon with the participant should be documented on the locator form.

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. Each site should 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.

- If the participant is unable to write her own name, the study staff member who completes the informed consent process/discussion with the participant should then 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.

- If the participant is unable to write the date herself, the study staff member who completes the informed consent process/discussion with the participant should then 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-009

		True	False
1	The main purpose of this study is to find out if women who test HIV-positive have resistance to HIV medications.	☒	☐
2	Each woman will be in this study for two years	☐	☒
3	Study participants will have blood tests at the enrollment visit to test for HIV.	☒	☐
4	Study participants must agree to have blood and vaginal fluids stored for future testing in order to join this study.	☐	☒
5	If the study staff finds that you have HIV, they will refer you to available sources of medical care.	☒	☐
6	If the study staff finds that you have HIV, they will give you medication to treat your HIV infection ("ARVs").	☐	☒
7	Study participants could become worried or anxious while talking about HIV or waiting for test results.	☒	☐
8	Participants' study records will be available to everyone at the [name of site institution].	☐	☒
9	Being in this study could cause problems for study participants with their partners, family members, or community contacts (e.g., neighbors).	☒	☐
10	If you decide not to join this study, you can still come to the [name of site institution] for medical care.	☒	☐

Section Appendix 4-3
Sample Open-Ended Discussion Questions for Assessing Comprehension of MTN-009

1. **Please describe your understanding about this study.**
   - ☐ Study objectives
   - ☐ Overall study design: duration, visit schedule, procedures done, options for specimen storage

2. **What do you think you will get out of being in this study?**
   - ☐ HIV/STI education, counseling, and testing
   - ☐ Lab tests
   - ☐ Referrals for care/treatment
   - ☐ Personal satisfaction

3. **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
   - ☐ Risks to privacy and possible social harms

4. **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

5. **What are some reasons why the study staff might end your participation in the study?**
   - ☐ The study is stopped or cancelled
   - ☐ The staff feels it would be harmful for the participant to stay in the study

6. **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

7. **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-009

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?	☐ Yes ☐ No ⇒ STOP. Participant is not eligible for MTN-009.
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-009?	☐ Yes ☐ No ⇒ Record and explain departures from site SOPs below.
Can the participant read?	☐ Yes ☐ 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?	☐ Yes ☐ No ⇒ Explain below.
Were all participant questions answered?	☐ Yes ☐ No ⇒ Explain below.
Did the participant comprehend all information required to make an informed decision?	☐ Yes ☐ No ⇒ Explain below.
Was the participant given adequate time/opportunity to consider all options before making her informed decision?	☐ Yes ☐ No ⇒ Explain below.
Did the participant accept a copy of the informed consent form?	☐ NA (participant chose not to provide informed consent) ☐ Yes

	☐ 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):	