

Section 5. Informed Consent

This section provides information on informed consent procedures for MTN-007. MTN-007 involves three types of informed consent:

- Informed consent for screening
- Informed consent for enrollment
- Informed consent for long term specimen storage and possible future research testing

Potential study participants must provide written informed consent for screening in order to undergo protocol-specified procedures for determining eligibility for study participation. Potential participants who are found to be eligible for the study must then provide written informed consent to enroll in the study and undergo protocol-specified “on study” procedures, including random assignment, use of study products and completion of follow-up visits and procedures. For enrolled participants, informed consent for long term specimen storage and possible future research is optional. Participants may choose not to consent to long term specimen storage and possible future research testing and still be enrolled in the study. Consenting to long term storage is to be completed at the enrollment visit and at the completion of the enrollment consent process.

5.1 Overview of Informed Consent for Screening and Enrollment

Written informed consent must be obtained for all MTN participants prior to the performance of any protocol-specified screening or enrollment procedures and assessments. (See overview in Section Appendix 5-1)

Informed consent is a process by which an individual voluntarily expresses the willingness to participate in research, after having been informed of all aspects of the research that are relevant to the participant’s 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, each of which is described below. See Section 4.8 of the ICH GCP guideline and the informed consent section of the DAIDS SOP for Source Documentation for detailed guidance on the informed consent process and documentation requirements.

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 Investigator of Record (IoR) and his/her staff to deliver complete and accurate information to potential research participants.

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:

- 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

5.1.1 Deliver Required Information in an Understandable Manner

As a starting point at the screening visit, assess participant literacy. If the participant is literate, give him/her a copy of the informed consent form to read. Also provide the participant with other IRB approved informational materials developed to complement the informed consent form. If the participant is not literate, read the materials to him/her verbatim. Because many of the research concepts and terms may be unfamiliar, even to literate people, the consent form must be reviewed very carefully with each potential volunteer. It is suggested that each paragraph be read by the study staff member conducting the consent discussion and that the key points be emphasized, pausing after each paragraph to allow for questions and to probe for understanding. A checklist highlighting key points may serve as a useful guide for reviewing the consent with the potential volunteer. 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 them thoroughly. Take as much time as needed to address each question and concern.

Remember: If the participant is not literate, an impartial witness must be present during the entire informed consent discussion. 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. The ICH GCP guideline 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 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’ who would be available at each site.” Each site must specify its procedures for obtaining informed consent from illiterate persons in its SOP for obtaining informed consent. The SOP should define who may serve as the witness to the informed consent process. It is recommended that each site seek IRB review and approval of these procedures.

5.1.2 Obtain Consent in a Setting Free of Coercion

During the informed consent discussion, take care not to 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 recruitment site and/or research institution will not be affected by the volunteer’s decision whether or not to take part in the study. Encourage the participant to take as much time as he/she needs and to talk about his/her potential participation with others, if he/she chooses, before making a decision.

NOTE: If the participant is not literate, and therefore a witness is present during the entire informed consent discussion, 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 for the study.

5.1.3 Confirm Participant Comprehension

The participant must not be asked to agree to take part in the screening/study or to sign or make his/her mark on the informed consent form until he/she fully understands the screening process/study.

Study staff are responsible for implementing procedures to ensure that each participant understands the screening process and the study prior to signing/marketing the informed consent forms and undertaking any screening or study procedures. Study staff should emphasize with potential volunteers aspects of the study that may be most challenging for them. It is critical that volunteers fully understand what the screening procedures are or participation in the study entails before agreeing to participate.

One suggested approach to assessing comprehension is to use a “quiz” (either oral or written) or other assessment tool which participants must complete prior to signing/marketing the informed consent form. A sample assessment is included at the end of this section. Another approach is to use open-ended questions to ascertain participant understanding during the informed consent discussion. For sites that choose to adopt tools such as those included at the end of this section, detailed use instructions must be specified in the site SOP for obtaining informed consent.

Regardless of the method used to assess comprehension, if the assessment results indicate misunderstanding of certain 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 him/her to sign/mark the informed consent form or continue screening for the study. Similarly, if the participant has concerns about possible adverse impacts on him/her or indicates that he/she may have difficulty adhering to the study requirements, do not ask him/her to sign the informed consent form. If the participant has serious concerns about family members or others learning that he/she is in the study and the participant is not willing to discuss this with them in advance, the volunteer should not be asked to sign the consent.

5.1.4 Document the Process

US regulations 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.”

It is essential that the date documented on the consent form either precedes or coincides with the (first) study screening date. In addition, enter a note in the participant chart documenting that informed consent was obtained prior to the initiation of any study procedures (Section Appendix 5-2 gives an example of an informed consent coversheet). Finally, regulations require that participants be given a signed copy of the informed consent form. If a participant opts not to receive a copy, document this in a chart note.

Signatures on the consent forms must be the legal name of the participant and not include fabricated or falsified names or nicknames. Sites are not required to verify a person’s legal name; however, if the site becomes aware that a person had not used his/her legal name, then the instructions provided for this situation in the DAIDS SOP for Source Documentation must be followed.

Initials cannot be used for the family name (last name). Use of initials for first names is discouraged, but not prohibited as long as it is acceptable per the policy of the local institution. The consent must be dated by the person signing the form; it is not acceptable for study staff to complete the date for another signer. All entries must be in ink.

NOTE: 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. If the participant cannot write her name or the date, this should be documented in the research record, in a chart note and/or on a face sheet or other documentation tool. In addition, the participant printed name, signature and signature date blocks on the informed consent form should be completed as follows:

- The “participant’s printed name” block should be left blank and the name should be recorded below the line by the person conducting the consent discussion, and initialed and dated. The participant chart should include documentation that the participant could not sign for himself/herself (e.g., documentation on the informed consent coversheet).
- The participant should make his/her mark in the “participant’s signature” block.
- The “participant signature date” block should be left blank and the date should be recorded below the line by the person conducting the consent discussion, and initialed and dated.

Section appendices 5-3 and 5-4 give an overview and example of this process.

5.2 Informed Consent for Specimen Storage

Storage of specimens remaining after trial completion is optional for each site. If a site chooses to store leftover biological specimens after all of the protocol-specified assessments and quality control procedures are completed, separate written informed consent must be obtained from each participant. This consent may be obtained at the Enrollment visit. Participants may choose not to have their specimens stored for possible future research testing and still enroll/remain in the study. To facilitate completion of CRFs at the end of the study and management of specimens, sites should keep a record that can be used to ascertain and verify who signed the consent for storage and future testing of specimens. For participants who do not consent to specimen storage and possible future research testing, specimens collected and stored on-site per protocol will be retained until the study is completed and all protocol-specified testing has been completed. Thereafter, any remaining specimens collected from these participants will be destroyed.

5.3 Informed Consent SOP

The DAIDS SOP for Source Documentation provides detailed requirements and suggestions for documenting the informed consent process. All requirements listed in the DAIDS SOP must be met. In order to also meet some of the suggestions listed in the DAIDS SOP, site staff may consider the use of an informed consent “coversheet” similar to the example included in Section Appendix 5-2.

The above describes aspects of obtaining informed consent from study participants prior to initiating their involvement in the study. Given the ongoing nature of informed consent, key elements of informed consent also should be reviewed at all study follow-up visits. At these visits, study staff should review key elements of informed consent with the participant, focusing on the remainder of their study participation.

As a condition of study activation, each study 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:

- 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 specifications of who may serve as a witness to the informed consent process
- Storage locations for blank informed consent forms
- Storage location of completed informed consent forms
- Procedures (e.g., color-coding) to ensure that the three study informed consent forms are easily distinguished and used appropriately
- Procedures for implementing a change in the version of the informed consent form
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements
- QA/QC procedures related to the above (if not specified elsewhere)
- Attached copies and instructions for use of all forms, worksheets, checklists, etc., to be used during the informed consent process

5.4 Storage of Consent Forms

All consent forms completed during the screening and enrollment process must be retained even if the participant was not enrolled in the study. It is acceptable for sites to maintain consents in a file separate from a subject's research record and to separate those for enrolled participants from those screened but not enrolled, provided that the sites do this consistently for all subjects. Sites should maintain any subsequent versions of the consent in the same manner.

5.5 Informed Consent Support Materials

Site-specific informed consent forms: The informed consent forms used at all sites must be reviewed and approved by study site IRBs and DAIDS prior to their use. After the forms are approved, each site is responsible for preparing bulk supplies of their approved forms and for only using the currently approved versions of the forms at all times during the study.

It is recommended that all sites consider the use of color-coding or other techniques to ensure that the various study informed consent forms are easily distinguished and used appropriately (such as a yellow cover sheet for screening, blue for enrollment, etc.). At the beginning of the study, bulk supplies of the screening and enrollment informed consent forms should be prepared. Care must be taken to use the correct forms for long term specimen storage and possible future research testing.

Visual Aids: Use of visual aids is encouraged throughout the informed consent process to facilitate participant comprehension. Each site should determine the most appropriate visual aids for its study population and ensure that a “kit” containing each of these aids is available in each room where informed consent discussions take place. In addition to the visual aids decided upon at each site, it may be helpful to point out such things as a locked file cabinet, a referral clinic across the way, or a calendar on the wall. It is not necessary to use each visual aid with each participant. Study staff should use their best judgment of each participant’s information needs and how best to address those needs.

Suggested visual aids for each site to consider using are as follows:

- Calendar
- Sample gel applicator
- Rectal Insertion Diagram/Pictures (see Section 9 of this SSP)
- Sample randomization envelopes
- Other randomization explanation visual aids (e.g., sack or box containing four items of different colors)

Comprehension Assessment: The staff person conducting the enrollment informed consent process with a potential participant is responsible for determining whether the participant comprehends the information provided to him/her. The sample MTN-007 Enrollment Informed Consent Comprehension Checklist (see Section Appendix 5-5) will assist staff in assessing participant comprehension and targeting follow-up educational efforts to ensure that participants understand all information required to make an informed decision about whether to enroll in the study. Sites may choose to adapt the checklist; however all checklists require approval from the MTN CORE (FHI) prior to use.

The comprehension checklist will be administered to each potential participant after they have completed the informed consent discussions described above and before asked to sign or mark on the enrollment informed consent form. The checklist should not be presented to participants as a “test,” but rather as a way of double-checking that study staff have fulfilled their responsibility to provide all information needed for the participant to make an informed decision about enrolling in the study.

It is expected that the checklist will be administered by the same staff member who conducted the enrollment informed consent discussion with the participant, however this is not a requirement per se. If more than one staff member spent time with the potential participant during the informed consent process, the checklist should be administered by the person who most recently spoke with him/her or who spent the most time with the participant.

The checklist is structured around open-ended questions that correspond with the required elements of informed consent for research. Each question should be read to the potential participant, 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 checklist specifies particular points that must eventually be included in the participant's response. When the potential participant mentions one of the required points, study staff should check off that point. If the participant does not mention one or more of the required points, study staff should follow-up with another open-ended question to elicit a response about that point. For example, one of the required points in the sample checklist (Question 1) is "study is testing four gels." If the potential participant does not mention this in his/her initial response to Question 1, the study staff member may then ask "Can you tell me how many products are being tested in this study?" If the participant responds correctly, the point may then be checked off. All required points must be satisfactorily addressed by the participant, and checked off, before proceeding to the final informed consent decision and signing or marking of the enrollment informed consent form.

When responding to the various questions, potential participants may report back more information than is included on the checklist. This is acceptable, as long as the required information is reported back. If the additional information reported by the participant applies to another question on the checklist, study staff may go ahead and check off that point. If any misinformation is reported back, study staff may explain the correct information before proceeding to another question, or defer explanation of the correct information until after the entire checklist has been administered.

Once administration of the comprehension checklist discussion begins, it is possible that the participant may spontaneously mention many of the required points, without each separate question being asked. In these cases, study staff should check off the relevant points on the checklist and then ask the remaining questions, or probe about the remaining points. It doesn't hurt to ask a question that a participant may have already answered in his/her response to a previous question. However, if staff is confident that a previous response was adequate, the specific question and/or point do not need to be repeated.

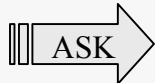
It is expected that study staff administering the informed consent process and checklist will be sufficiently knowledgeable about MTN-007 to make good judgments about potential participants' understanding of the required information. It is possible that a participant might repeat the correct information, yet the staff member may not be convinced that they really understand it. In these cases the staff should decide if further explanation or discussion is needed before proceeding to the final informed consent discussion and signing or marking of the informed consent form. The further explanation or discussion could take place at the same visit or another visit might be suggested/scheduled.

Whenever additional information or explanation is needed, all the informed consent support materials may be used. Study staff should decide which materials may be most helpful to each participant. Some potential participants may be more comfortable interacting with the same study staff person throughout the informed consent process. However, another staff member may be consulted, if necessary or desired, to help explain problematic concepts and/or respond to participant questions or concerns.


The comprehension checklist is considered a study source document that should be completed, handled, and retained in the participant's study chart like any other source document. After administering the checklist, study staff should carefully review the checklist to verify that all required points have been satisfactorily addressed by the participant and that this is adequately documented on the checklist (i.e., with a check mark beside each point). Failure to document participant comprehension of all required points on the checklist will be considered an informed consent and enrollment violation. Comments may be recorded in the designated column on the checklist (and on the back of the checklist if additional space is needed), however this is not required. Lastly, after the enrollment consent process is completed, the final outcome of the process should be recorded in the bottom left corner of the checklist and the staff member who completed the checklist should ensure his/her signature in the space provided.

Section Appendix 5-1
Overview of MTN-007 Enrollment Informed Consent Process

Briefly **describe the steps** in the enrollment consent process and tell the participant how long it takes to complete.


 Do they have time to complete this today?

- If yes, proceed.
- If no, schedule return appointment.

 Are they ready to have the **informed consent form** read to them or read it him/herself?


- If yes, proceed.
- If not, determine what is needed and provide information or schedule return appointment.

Read consent form, section by section, asking if the participant has questions and discussing as you go along.

 Do they feel comfortable that they understands all aspects of the study?

- If yes, proceed.
- If not, determine what is needed and provide more information at that time or schedule return appointment.

Administer **comprehension checklist**.

 All questions/topics on the checklist.

REQUIRES 100% COMPREHENSION

- If participant demonstrates comprehension of all required topics, proceed.
- If not, discuss misunderstandings and probe problem areas with open-ended questions. Provide information and any other materials as needed to resolve misunderstandings. Continue discussing until comprehension of all required topics is demonstrated.
- If participant is fatigued or requests more time, or if staff judge that participant needs more time, schedule return appointment and repeat steps in the process as needed.

Complete all name, signature, and date blocks on the enrollment informed consent form. Offer participant a copy of the form. Document the process per site and DAIDS SOPs.

- Proceed with enrollment procedures (per protocol and this manual).




Section Appendix 5-2
Sample Informed Consent Coversheet for MTN-007

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-007.
Date of informed consent process/discussion:	
Start time of informed consent process/discussion:	
Language of informed consent process/discussion:	English
Was the informed consent process/discussion conducted according to site SOPs for MTN-007?	<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 site and DAIDS 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 his/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):	

Section Appendix 5-3
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 SOP for Source Documentation 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 on the consent form, 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 ICH GCP guideline and the informed consent section of the DAIDS SOP for Source Documentation for additional information.

Section Appendix 5-4
Example of Completion of Informed Consent Form Signature Lines
for Illiterate Participants

SIGNATURES		
		
Participant Name (print) Jane Doe	Participant Signature/Mark	Date 25 July 2009
<i>Participant name and date written by Suzy Coordinator. SC 25JUL 09</i>		
Suzy Coordinator		25 July 2009
Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date
Mary Witness		25 July 2009
Witness Name (print)	Witness Signature	Date

Section Appendix 5-5
MTN-007 Enrollment Informed Consent Comprehension Checklist

PTID:

Date:

Open-Ended Question/Statement	Required Points of Comprehension	✓	Comments
1 Please describe your understanding of the purpose of the study.	Study is testing an experimental gel		
	Testing to learn if men and women like using the gel rectally		
	Testing to learn if the gel products are safe		
2 What do you understand that you are being asked to do in this study?	Use condoms and rectally applied study gel as required		
	Have rectal exams		
	Not get pregnant in the next 21 weeks		
3 What do you understand are possible risks to being in this study?	Possibility of social harms		
	Gel may have side effects		
4 What will happen if you do not join the study?	No effect on access to care		
5 Please tell me about the different groups in the study.	Free to make own decision about joining		
6 How will the information about you be protected?	There will be 3 different gels tested in the study (3 gel groups) and 1 no gel group; 4 groups total		
	Participant information kept under lock and key		
7 What are the benefits to participating in the study?	Only people working on study have access to my information		
8 What should you do if you have any questions about the study?	HIV/STD Counseling, HIV/STI Risk Reduction Counseling, tests, clinical care, benefit to science or community		
	Must articulate how to contact staff		
<p>Outcome:</p> <p><input type="checkbox"/> Demonstrated comprehension of all required points, decided to enroll in study.</p> <p><input type="checkbox"/> Demonstrated comprehension of all required points, decided not to enroll in study.</p> <p><input type="checkbox"/> Demonstrated comprehension of all required points, deferred enrollment decision</p> <p><input type="checkbox"/> Did not demonstrate comprehension of all required points (yet), needs more time/discussion.</p> <p><input type="checkbox"/> Unable to demonstrate comprehension of all required points, consent process discontinued.</p> <p><input type="checkbox"/> Other (specify): _____</p> <p>Staff Signature:</p>			<p>Optional Comment Categories:</p> <p>a. Answered correctly on first try</p> <p>b. Could not answer at first, but answered correctly after probing</p> <p>c. Answered incorrectly at first, but answered correctly after discussion</p> <p>d. Not able to answer correctly at this time</p> <p>e. Other (describe)</p>