

Section 5. Informed Consent

This section provides information on informed consent procedures for MTN-016. Sites may choose to enroll each woman-infant pair using a single consent form; alternatively, each woman and infant may be enrolled under a separate consent. A separate informed consent for off-site visits has also been developed. Sites may choose to incorporate this consent as a signature block within the screening and enrollment consent(s), if they prefer. For sites that wish to incorporate the off-site visit language into an existing ICF and have separate woman and infant screening and enrollment consent forms, an off-site visit signature block should appear on both ICFs. For all sites, there will be a separate informed consent form for infant testing which covers HIV testing of HIV-exposed infants, and further resistance testing if infants are HIV-infected. Therefore, each site will have between 2 and 4 total informed consent forms:

Templates for all types of informed consent forms are available in the Protocol, Appendices IV-VIII.

All potential study participants/guardians must provide written informed consent before undergoing any protocol-specified procedures as outlined in the protocol. This section contains general information and instructions applicable to required informed consent procedures for MTN-016.

5.1 Overview of Informed Consent Requirements and Procedures

Informed consent is a process by which an individual voluntarily expresses her willingness to participate in research and/or to have her infant 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, involving information exchange, comprehension, voluntariness, and documentation. Each of these aspects of the process is described in greater detail below. Please also refer to Section 4.8 of the ICH GCP guideline and the informed consent section of the DAIDS SOP for Source Documentation for further guidance on the informed consent process and documentation requirements. The process is detailed in Figure 5-1.

US regulations (45 CFR 46) specify the elements of informed consent must be conveyed to research participants through the informed consent process. It is the responsibility of the Investigator of Record (IoR) to ensure that all potential study participants receive the required information during the informed consent process before any study procedures are completed; The IoR may delegate this responsibility to other study staff.

Because of the reviews that are completed as part of the MTN protocol development and study activation processes, there is adequate assurance that once a site has been “activated” for study implementation, the site-specific informed consent form specifies 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:

- 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.
- Ensure that confidentiality is protected.

Figure 5-1
Overview of MTN-016 Screening and Enrollment Informed Consent Process

Briefly **describe the steps** in the consent process and tell the potential participant and/or guardian the how long it takes to complete.

 Does she have time to complete this today?

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

 Is she ready to have the **informed consent form** read to her or read it herself?

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

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

 Does she feel comfortable that she understands all aspects of the study?

- If yes, proceed.
- If not, determine what she needs and provide more information at that time or schedule return appointment.
- If participant demonstrates comprehension of all required topics, proceed
- If not discuss misunderstandings and probe problem areas with open-ended questions.
- If participant is fatigued or requests more time, or if study staff judge that participant needs more time, schedule return appointment and repeat steps in the process as needed.

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

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

If the participant is illiterate, 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 given freely 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 MTN CORE 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 the site. Please refer to Section Appendix 5-1 for a summary of considerations for obtaining informed consent from illiterate participants.

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.

As a condition for study activation, the study site must establish an SOP for obtaining informed consent from potential study participants that ensures that all of the above-listed requirements are met. The SOP must be consistent with the DAIDS SOP for Source Documentation. It is recommended that the SOP contain the elements listed below and that the site seek FHI 360 review and approval of the SOP.

- The minimum legal age to provide independent informed consent for research 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 (direct and supervisory).
- Staff training requirements (if not specified elsewhere).
- QC/QA procedures related to the above (if not specified elsewhere).

5.2 Informed Consent for Screening and Enrollment

The informed consent process for screening and enrollment will be conducted according to site SOPs and instructions. Informed consent for screening and enrollment should always occur at a woman’s first study visit, regardless of what stage she is in her pregnancy. This process will include informed consent for screening and enrollment of the infant if sites are using a single informed consent form. The father of the child being consented for study participation may be

included in the informed consent process and sign the consent form, if reasonably available.

Sites are advised to pay close attention to those situations in which the woman and infant are to be consented at different time points. If consent for infant participation is not obtained at the same time as maternal consent, it should be sought as soon as possible after labor and delivery. Note that consent of the woman allows for collection of infant data that are recorded on the labor and delivery notes such as apgars, length and weight, head and abdominal circumferences, and gestational age (see Pregnancy Outcome CRF, section 13). No other data on an infant may be collected and recorded until consent has been obtained for the participation of that infant.

MTN-016 informed consent forms will have an option for declining or accepting photography of infants with identified or suspected major malformations. Women (and the infant's father, if participating in the consent process) should understand that declining infant photographs will not exclude them or their infant's ability to participate in the study. Refer to SSP section 10 for a description of the major malformation assessment and photography process.

5.2.1 Informed Consent Support Materials

Site-specific informed consent forms: The informed consent forms used at the site must be reviewed and approved by FHI 360 prior to submission to the site's IRBs/EC and DAIDS, and before implementation.. After the forms are approved, the site is responsible for preparing supplies of their approved forms and for using only the currently approved versions of the forms at all times during the study. Use of an Informed Consent Version Control Log is strongly encouraged (see Appendix 5.2). Note that if sites use separate Woman/Infant Informed Consent Forms, the Version Control Log should be modified to reflect appropriate site process.

5.2.2 Comprehension Assessment

The staff person conducting the informed consent process with a potential participant is responsible for determining whether the participant comprehends the information provided to her. Comprehension should be confirmed with the administration of an Informed Consent Comprehension Survey. Samples of the survey(s) that may be used to assess comprehension of the consent process may be found in Appendices 5-4 through 5-7.

When responding to the various questions, potential participants may report back more information than is necessary. This is acceptable, as long as the required information is reported back. If any misinformation is reported back, study staff may explain the correct information.

It is expected that study staff assessing informed consent comprehension will be sufficiently knowledgeable about MTN-016 to make good judgments about potential participants' understanding of the study and help participants grasp protocol information. It is possible that a participant might repeat the correct information, yet the staff member may not be convinced that she really understands 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 may be suggested/scheduled.

5.3 Informed Consent for Infant Testing

Women who are diagnosed with HIV infection may elect to have their infants tested for HIV infection. Infants diagnosed with HIV infection will be offered HIV-1 drug resistance testing. No blood may be drawn on infants who meet the criteria for HIV testing or HIV resistance testing prior to obtaining an informed consent for that testing from the infant's parent/guardian.

5.4 Documenting the Informed Consent Process

US regulations require that informed consent be documented by "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, ensure completion of all signature and date blocks on the informed consent form in black (preferable) or blue 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/guardian commonly signs his/her name using an initial as the first name, the initial may be used, provided this practice is acceptable per the policies of the study site institution(s).

If the participant/guardian is illiterate, 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/guardian, and that informed consent was freely given by the participant/guardian. The participant's 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/guardian should make his/her mark in the appropriate block on the informed consent.
- 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 SOP for Source Documentation lists 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 use an informed consent "coversheet" similar to the example included in Appendix 5-3. If the site chooses to use a coversheet, the coversheet should be listed as a source document in their SOPs for Source Documentation for MTN-016 and should use the coversheet consistently to document all informed consent processes with all participants.

In addition to completing the documentation requirements on the informed consent form itself, each informed consent process must be documented in a signed and dated chart note. It is essential that the note (as well as the dates on the informed consent form itself) documents that informed consent was obtained prior to the initiation of any study procedures. The note should also document adherence to the requirements of the informed consent section of the DAIDS SOP for Source Documentation. 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/guardian be given a signed copy of the informed consent forms. If a participant/guardian opts not to receive a copy, document this in a chart note and offer the participant/guardian an alternate form of study contact information (e.g., a contact card or appointment card) in lieu of the full informed consent form.

5.5 Reconsenting Requirements and Procedures

If updates to the ICFs are required at any time throughout the study, revisions should be submitted to MTN CORE (FHI 360) for review and approval prior to IRB/EC submission. If ICF changes are made, the study management team and IRB/EC will help determine whether reconsenting is required. Regulatory files should be updated to reflect any determinations made regarding reconsenting requirements.

5.5.1 Reconsenting Requirements for Minor Modifications and LoAs

When reconsenting of participants is required due to minor modifications or new information contained in an LoA, the consenting procedures may be abbreviated. The staff member conducting the informed consent session should review the changes made to the ICF with the participant, but does not need to read or review the entire consent form again.

Although a comprehension checklist does not need to be completed in the circumstances described above, participant understanding should be assessed and all participant questions should be answered prior to signing the new consent form. Once comprehension has been evaluated and ensured, documentation of informed consent should be conducted per SSP section 5.4. The participant should be offered an updated, signed copy of the ICF to take home.

5.10.2 Reconsenting Requirements for Protocol Version Changes

If reconsenting of participants is required due to a protocol version change, a complete review of the ICF must be conducted. When changes to the enrollment ICF have been made as a result of protocol version changes, a new comprehension checklist must be completed. Documentation of informed consent should be conducted per SSP section 5.4 and participants should be offered an updated, signed copy of the ICF to take home.

Section Appendix 5-1
Summary of Considerations for Obtaining Informed Consent from Illiterate Persons

- The 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 the site seek IRB/EC review and approval of these procedures.
- If the participant is illiterate, an impartial witness must be present during the entire informed consent discussion. 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 ICH GCP guideline and the informed consent section of the DAIDS SOP for Source Documentation for additional information.

Section Appendix 5-2

Informed Consent Version Control Log

Woman/ Infant Screening and Enrollment Informed Consent-English

Version #/ Date of Form	IRB Approval Date	Summary of Changes from previous form
		N/A- Initial Form

Woman/ Infant Screening and Enrollment Informed Consent-Shona (site to replace with actual translation languages used; 1 tracker for each language)

Version #/ Date of Form	IRB Approval Date	Summary of Changes from previous form
		N/A- Initial Form

Infant Testing Informed Consent-English

Version #/ Date of Form	IRB Approval Date	Summary of Changes from previous form
		N/A-Initial Form

Infant Testing Informed Consent-Shona (site to replace with actual translation languages used; 1 tracker for each language)

Version #/ Date of Form	IRB Approval Date	Summary of Changes from previous form
		N/A-Initial Form

Section Appendix 5-3
Sample Informed Consent Coversheet for MTN-016

Type of Informed Consent: _____

PTID:	
Name of study staff person completing informed consent process/discussion (and this coversheet):	
Date of informed consent process/discussion:	
Start time of informed consent process/discussion:	
Language of informed consent process/discussion:	
Is the participant/guardian comfortable/fluent in other language(s) that are used at this CRS for ASPIRE?	<input type="checkbox"/> Yes: (List) _____ <input type="checkbox"/> No
Is the participant/guardian of legal age to provide independent informed consent for research?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ STOP. Participant/infant is not eligible for MTN-016.
Can the participant/guardian 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.
Version number/date of informed consent form used during informed consent process/discussion:	
Did the participant comprehend all information required to make an informed decision?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Explain in comments section.
Were all participant/guardian questions answered?	<input type="checkbox"/> N/A (participant/guardian had no questions) <input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Explain in comments section.
Was the participant/guardian given adequate time/opportunity to consider all options, in a setting free of coercion and undue influence, before making her informed decision?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Explain in comments section.
Did the participant choose to provide written informed consent?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Did the participant/guardian accept a copy of the informed consent form?	<input type="checkbox"/> NA (participant/guardian chose not to provide informed consent) <input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ Offer alternative form of study contact information to participant/guardian.
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 5-4
Sample MTN-016 Informed Consent Comprehension Survey: Woman and Infant

1. Women may enroll in MTN-016 if they became pregnant while enrolled on an HIV prevention trial. (TRUE)
2. The main purpose of this study is to see if using a medication being studied for the prevention of HIV affects the health of pregnant women and their babies. (TRUE)
3. You will have blood drawn at every study visit. (FALSE)
4. As part of this study, photographs of your baby may be taken without your permission. (FALSE)
5. You will come back for study visits each month until you give birth. (FALSE)
6. Infants enrolled in this study will return for visits for up to one year. (TRUE)
7. There is no cost to you for study visits, exams, or ultrasounds performed as a part of the study. (TRUE)
8. Once you enroll, you may not withdraw from this study at any time. (FALSE)
9. There is no direct benefit to you for participating in this study. (TRUE)
10. Your visits will be conducted to protect your privacy. (TRUE)

- Study participant passed the assessment by answering all questions correctly → proceed to signing informed consent document

- Study participant missed at least one question → complete the following:
 - Review the question(s) that were answered incorrectly with the participant.
 - Review the necessary sections of the informed consent with the participant to ensure understanding.
 - If the participant can demonstrate understanding of the questions she had previously answered incorrectly on the 2nd attempt, document and proceed with signing the informed consent document.
 - If after the second attempt, the participant is still unable to answer the questions correctly, participant is ineligible. End informed consent process and document fully.

Notes _____

Staff signature _____ Date _____

Section Appendix 5-5
Sample MTN-016 Informed Consent Comprehension Survey: Infant

1. Some of the infants enrolled in this study were born to women who became pregnant while enrolled on an HIV prevention trial. (TRUE)
2. The main purpose of this study is to see if using a medication being studied for the prevention HIV affects the health of pregnant women and their babies. (TRUE)
3. Infants will have blood drawn at every study visit. (FALSE)
4. As part of this study, photographs of your baby may be taken without your permission. (FALSE)
5. Participants in this study may experience no direct benefit. (TRUE)
6. Infants enrolled in this study will return for visits for one year. (TRUE)
7. This study will not provide or pay for others to provide routine infant care. (TRUE)
8. You will be told any new information learned during this study that might affect your willingness to let your baby stay in the study. (TRUE)
9. You may contact research staff at any time during the study if you have concerns or questions about the health of your baby. (TRUE)

- Study participant passed the assessment by answering all questions correctly → proceed to signing informed consent document
- Study participant missed at least one question → complete the following:
 - Review the question(s) that were answered incorrectly with the participant.
 - Review the necessary sections of the informed consent with the participant to ensure understanding.
 - If the participant can demonstrate understanding of the questions she had previously answered incorrectly on the 2nd attempt, document and proceed with signing the informed consent document.
 - If after the second attempt, the participant is still unable to answer the questions correctly, participant is ineligible. End informed consent process and document fully.

Notes _____

Staff signature _____ Date _____

Section Appendix 5-6
Sample MTN-016 Informed Consent Comprehension Survey: Woman

1. Women may enroll in MTN-016 if they became pregnant while enrolled on an HIV prevention trial. (TRUE)
2. The main purpose of this study is to see if using a medication being studied for the prevention HIV affects the health of pregnant women and their babies. (TRUE)
3. You will have blood drawn at every study visit. (FALSE)
4. There is no cost to you for study visits, exams, or ultrasounds performed as a part of the study. (TRUE)
5. You will come back for study visits each month until you give birth. (FALSE)
6. You may have an ultrasound as part of this study. (TRUE)
7. Once you enroll, you may not withdraw from this study at any time. (FALSE)
8. You may contact research staff at any time during the study if you have concerns or questions about the health of your baby. (TRUE)
9. There is no direct benefit to you for participating in this study. (TRUE)

- Study participant passed the assessment by answering all questions correctly → proceed to signing informed consent document
- Study participant missed at least one question → complete the following:
 - Review the question(s) that were answered incorrectly with the participant.
 - Review the necessary sections of the informed consent with the participant to ensure understanding.
 - If the participant can demonstrate understanding of the questions she had previously answered incorrectly on the 2nd attempt, document and proceed with signing the informed consent document.
 - If after the second attempt, the participant is still unable to answer the questions correctly, participant is ineligible. End informed consent process and document fully.

Notes _____

Staff signature _____ Date _____

Section Appendix 5-7
Sample MTN-016 Informed Consent Comprehension Survey: Infant Testing

1. A baby of an HIV-infected woman is at risk of getting the HIV infection through the womb, at the time of labor and delivery, or through breast milk. (TRUE)
2. In MTN-016, infants will have a needle stick for blood to test for HIV [*sites may insert other alternative*]. (TRUE)
3. It may be necessary to test the baby more than once, depending on the results of the first tests and on whether the baby is being breastfed. (TRUE)
4. If your baby is HIV infected, another test will be done to see whether the HIV virus in your baby has any resistance to the medications used to treat HIV. (TRUE)
5. HIV Care and Treatment is not provided through MTN-016. (TRUE)
6. Babies will be tested for many diseases in addition to HIV. (FALSE)
7. Knowledge gained from this study may help in the development of medications for the prevention of HIV infection. (TRUE)
8. You may contact research staff at any time during the study if you have concerns or questions about the health of your baby. (TRUE)

- Study participant passed the assessment by answering all questions correctly → proceed to signing informed consent document
- Study participant missed at least one question → complete the following:
 - Review the question(s) that were answered incorrectly with the participant.
 - Review the necessary sections of the informed consent with the participant to ensure understanding.
 - If the participant can demonstrate understanding of the questions she had previously answered incorrectly on the 2nd attempt, document and proceed with signing the informed consent document.
 - If after the second attempt, the participant is still unable to answer the questions correctly, participant is ineligible. End informed consent process and document fully.

Notes _____

Staff signature _____ Date _____