# Section 4. Informed Assent and Consent



## 4. Introduction

This section provides information on informed assent and consent procedures for MTN-034. The study involves two types of informed assent/consent:

- Informed Assent & Parent/Guardian Permission Form for Screening, Enrollment, and Long-term Storage [for participants who are minors at the start of the study and unable to provide informed consent, and their parent/guardians]
- Informed Consent for Screening, Enrollment and Long-term Storage [for participants who are of legal age or minors legally able to provide informed consent at the start of the study and those participants who become legal to provide informed consent while enrolled in the study]

This section contains general and MTN-034 specific information and instructions for providing informed assent/consent and parent/guardian permission. In addition, detailed guidance is provided for the standardized approach to the informed assent/consent process that must be followed at all sites. For the purpose of this document, ICF will refer broadly to the informed assent form, the parent/guardian permission form, and the adult informed consent form.

## 4.1 Overview of Informed Consent Requirements and Procedures

Informed consent is a process by which an individual voluntarily expresses her willingness to participate in research, after having been informed of all aspects of the research that are relevant to her decision. It is not merely a form or a signature, but a process, involving information exchange, comprehension, voluntariness, and documentation. Please also refer to Section 4.8 of the *International Conference on Harmonization (ICH) Consolidated Guidance for Good Clinical Practice* (GCP) and the informed consent of participants section of the Division of AIDS (DAIDS) Site Clinical Operations and Research Essentials (SCORE) Manual for further guidance on the informed consent process and documentation requirements.

Prior to Screening Visit Procedures:

- Written informed assent or informed consent will be obtained from study participants as applicable per site IRB/EC requirements and participant age
- Parent/guardian permission will be obtained from parents/guardians (as applicable, per site IRB/EC requirements)

- If a site is required by its IRB/EC to obtain signatures from both parents/guardians, only one is needed if the other parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. Details on the availability of the second parent/guardian, if needed, should be documented in chart notes.
- If two parents/guardians must provide permission, this can be done separately or together and they can sign the same or different forms. The site process for this should be detailed in the site Informed Consent (IC) SOP and in accordance with IRB/EC requirements.

For MTN-034, the ICF for screening, enrollment and long-term specimen storage is obtained at one time point at Screening. Some sites may conduct a separate consent at Enrollment, as per IRB/EC requirements and specified in their Informed Consent SOP. In addition, participants that turn 18 during study follow-up will need to reconsent using the Informed Consent form at their next regularly scheduled visit. Regardless of when written consent is obtained, informed assent/consent is an ongoing process that continues throughout the study follow-up period through open dialog between study staff and the participant.

For participants who do not provide assent or consent, or those with a parent/guardian who does not provide permission to screen and enroll, no procedures should be performed and no data that can be linked to the participant's name or other personal identifier(s) should be recorded.

Participant informed assent/consent for future long-term storage and possible testing of urine, blood specimens, and vaginal and cervical fluids collected during the study is optional. The participant or her parent/guardian(s) may choose to not have the specimens stored for future research testing and the participant may still enroll/remain in the study. For participants or parent/guardians who do not consent to long-term 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 done. Thereafter, any remaining specimens collected from these participants will be destroyed.

For this study, participants are selected to participate in focus group discussions (FGD) or in-depth interviews (IDI) after enrollment and, therefore, consent for their possible participation is imbedded within the main consent. No additional signatures are needed for this component of the study.

US regulations (45 CFR 46) 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 by delegation of all study staff involved in the informed consent process, to deliver all required information to potential study participants and their parent/guardians.

It also is the responsibility of the IoR and designated study staff to:

- Deliver all required information in a manner that is understandable to the potential study participant and her parents/guardians
- Assure that informed assent/consent is obtained in a setting free of coercion and undue influence
    - To assure the assent/consent is done free of coercion, it is strongly recommended that sites meet with both the participant and parent/guardian (if applicable) alone at some point during the consenting process to independently confirm interest and willingness to participate
- Confirm that the participant and/or her parent/guardian comprehend the information
- Document the process

Per protocol, an illiterate participant can be consented and enrolled in MTN-034, providing she is otherwise willing and eligible, and if independent consent/assent is ensured. If a participant and/or parent/guardian(s) of the participant is illiterate, an impartial witness should also be present for the informed consent process.

## 4.2 Informed Consent/Assent SOP

As a condition of study activation, each study site must establish an SOP for obtaining informed consent and assent from potential participants and permission from the parent/guardian of potential participants where applicable. It is recommended that the SOP contain the following elements:

- Procedures for determining participant identity and age
- Procedures for determining participant literacy
- Procedures for providing all information required for informed assent/consent to the participant and her parent/guardian where applicable
- Procedures for determining participant/guardian comprehension of the required information
- Procedures to ensure that informed consent/assent is obtained in a setting free of coercion and undue influence
- Procedures for documenting the informed assent/consent and parent/guardian permission process
- Procedures for obtaining permission from second parent, if applicable, understanding and determining reasonable availability of second parent, including the procedures for determining if the second parent is reasonably available to provide permission
- Procedures to re-consent participants once they turn the age of 18 or legal age for providing informed consent per local IRB/EC) or become emancipated. (Sites may also obtain input from their IRB/EC on whether their original signature form is sufficient)
- Storage locations for blank ICFs
- Storage locations for completed ICFs
- Procedures (e.g., color-coding) to ensure that the different study ICFs and related forms are easily distinguished and used appropriately, if applicable
- Procedures for implementing a change in the versions of the ICFs used
- Staff responsibilities for all the above (direct and supervisory)
- QC/QA procedures related to the above (if not specified elsewhere)

At each site, the informed assent/consent process will be conducted per site informed consent SOPs. Where parental permission is necessary, the process may be conducted with the participant and her parent/guardian/s together or separately, per participant request and site procedures. The order of consenting procedures is likewise flexible; it is not required that parent/guardian permission be obtained prior to conducing informed assent procedures with minors. However, both consenting processes must be completed prior to conducting any other screening procedures.

Additional details related to key steps in the process are provided in the remainder of this section.

## 4.3 Site Specific Informed Assent/Consent and Parent/Guardian Permission Forms

Sample ICFs are provided in the MTN-034 study protocol. Sites are responsible for adapting the samples as needed for local use. Local adaptation may include reformatting the ICFs in accordance with local IRB/EC requirements, as well as translating the forms into applicable participant languages. Sites are responsible for following the procedures in the MTN Manual of Operational Procedures (MOP) Section 9 and the DAIDS protocol registration guidance when adapting and translating site-specific ICFs (see also SSP Section 2.8 regarding translations). Unless waived by the IRB/EC, all adapted ICFs must still contain the eight required elements of informed consent as defined in 45 CFR 46.116. All ICFs (English, translated, and back-translations) must be reviewed and approved by MTN LOC (FHI 360) prior to IRB/EC submission. After ethics approval, ICFs must be submitted to the DAIDS PRO prior to their initial use.

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

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

## 4.4 Informed Consent Support Materials

### 4.4.1 Fact Sheets and Informed Consent Flip Chart

Fact sheets and an Informed Consent Flip Chart have been developed for MTN-034 and are available on the MTN-034 web page (http://www.mtnstopshiv.org/node/6826) for use with participants, partners, and community members, as study staff deem appropriate. These documents include information on the REACH study, the dapivirine vaginal ring and the Truvada tablets. Materials used for participant education in the consent process should be translated into local languages as appropriate and IRB/EC approved before use. These materials can be used during the informed consent process, or any other time throughout the study once they are approved for use.

### 4.4.2 Other Informed Consent Visual Aids

Use of visual aids, in addition to the fact sheets, 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. Sample study products and supplemental study illustrations have been provided to each site to use as visual aids. 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 may not be 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. Sites are encouraged to have the following items available in the clinic for demonstrations with participants:

- Calendar
- Male and female condoms
- Sample vaginal ring and packaging
- Sample Truvada tablets and packaging
- Urine specimen cup
- Blood collection tubes
- Vaginal/cervical swabs
- 4 L jug (to demonstrate the total blood volume in the human body)
- Vaginal and/or pelvic model or illustrations
- Speculum
- Randomization explanation visual aids (e.g., sack or box containing two items of different colors)

When using vaginal and pelvic models, remember that participants may not be familiar with such models. Introduce the models in a sensitive manner and use information, rapport, and humor to help make the participant feel comfortable with the models. If using a pelvic model to demonstrate ring placement, it may be necessary to first orient the participant to the model and the anatomical parts shown. Point out that the vaginal opening starts at the outside edge of the plastic model. Be sure that all staff members that may use the model are able to explain what each part is and, if demonstrating ring use, are able to insert and remove the ring with ease using the model.

Regardless of use of the vaginal and pelvic models, study staff who take part in informed consent discussions should be prepared to demonstrate the various insertion positions and "mime" the insertion of the ring.

## 4.5 Comprehension Assessment

Study staff are responsible for determining whether each potential participant and, when indicated, her parent/guardian(s) understand all information provided to them to ensure they can make an informed decision about study participation. This assessment of informed assent/consent comprehension may be administered separately for the participant and her parents/guardians. The participant and/or her parent/guardian(s) must not be asked to agree to take part in the study, or sign the ICF, until they fully understand the study.

It is expected that study staff administering the ICF and informed assent/consent assessment will be sufficiently knowledgeable about MTN-034 to make good judgments about potential participants' comprehension of the required information. Study staff should ask questions that indicate if the participant and parent/guardian(s) understand significant points of the study. If the participant and/or parent/guardian(s) do not mention one or more of the main points, study staff should follow-up with another open-ended question to elicit a response about that point. Study staff should use an Informed Consent (IC) comprehension assessment form to assist with this assessment. A sample IC comprehension assessment form, to be used for participants and parents/guardians (if applicable), with open ended questions is available on the MTN-034 website under Study Implementation Materials. All comprehension assessment forms used should be submitted to local IRB/ECs for approval prior to use.

### 4.5.1 Administration of the IC Comprehension Assessment

The comprehension assessment must be administered to each potential participant and/or her parent/guardian(s), as necessary, after they have completed the informed assent/consent discussions with site staff as described above but before they are asked to sign the ICF. The comprehension assessment should not be presented to participants as a "test," but rather as a way of assuring 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. If any misinformation is reported back, study staff should explain the correct information before proceeding to another question.

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

Comments may be recorded in a designated area on the form (and on the back of the form if additional space is needed) or on an informed consent coversheet; however, this is not required. All required points must be satisfactorily addressed by the participant, before proceeding to the final informed consent decision and signing of the ICF.

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

## 4.6 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, sites should comply with the guidance provided in the DAIDS guidance document on Source Documentation. Complete all signature and date lines on the ICF in dark ink. Legal names should be used. Fabricated/falsified names should not be used. Initials may not be used

in place of a participant's full surname, and it is strongly recommended that initials not be used in place of a participant's full first name. However, if a participant commonly signs 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 a participant signs her name in a form that deviates from the specifications listed above (e.g. she uses initials for both her first and last names, or signs only using her first name), document in the research record that the name/initials/mark as written deviates from the DAIDS guidance but represents her signature as she wrote it. Sites may choose to use a standard memo to document these deviations, provided the memo has been approved for use by the site's OCSO representative.

On the ICF, in addition to completing signature requirements as described above, the participant and parent/guardian if needed, must indicate on the form whether they agree to the storage and future testing of biological specimens, if applicable (unless the site has chosen to create stand-alone ICF for this topic, in which case the form should be completed separately). The participant or parent/guardian may decline this option and the participant may still enroll in MTN-034.

If the participant and/or her parent/guardian(s) is not literate, the witness who was present during the informed consent discussion must sign and date the ICF to attest that the information in the ICF and any other written information was accurately explained to, and apparently understood by, the participant, in the participant's language of fluency, and that informed consent was freely given by the participant and/or parent/guardian(s). The participant's printed name, signature, and signature date lines on the ICF should be completed as described and illustrated in Figure 4-1. Following these procedures fulfills the protocol requirement for obtaining written informed consent from all study participants.

**Figure 4-1: Informed Consent/Assent Form Signature Lines for Illiterate Participants and/or Parent/guardians**

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

**SIGNATURES**

| Participant Name | Participant Signature | Date |
|---|---|---|
| **Mary Phiri** | | **25 NOV 2019** |

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

| | | |
|---|---|---|
| **Martha Moore** | | **25 NOV 2019** |
| Name of Staff Person Conducting Consent Discussion | Study Staff Signature | Date |

| | | |
|---|---|---|
| **Debra Ross** | | **25 NOV 2019** |
| Witness Name | Witness Signature | Date |

The DAIDS guidance in the SCORE Manual on Source Documentation details requirements and suggestions for documenting the informed consent process. All requirements listed in the DAIDS guidance must be met each time an ICF is signed. In order to also meet some of the suggestions listed in the SCORE Manual, site staff are strongly encouraged to use an Informed Consent (IC) Coversheet. Sites choosing to use a coversheet should list the coversheet as a source document in their SOPs for source documentation for MTN-034 and should use the coversheet consistently to document informed consent processes with all participants. A sample IC coversheet template is available on the MTN-034 web page. If used, an IC coversheet should be completed for each ICF completed (i.e. for participants and parents/guardians (if applicable)), The first section of the coversheet should be completed at the start of the informed consent session. The remainder should be completed at the end of the informed consent session. If a site chooses not to utilize an IC coversheet, all elements of each informed consent process must be documented in a signed and dated chart note as well as detailed in the site Informed Consent SOP.

It is essential that all informed consent documentation (e.g., the ICFs, the coversheet, IC comprehension assessment form) record that informed consent from the participant and/or her parent/guardian(s) was obtained before any study procedures were conducted.

Regulations require that participants be given a signed copy of the ICF. If a participant opts not to receive a copy, document this on the coversheet or 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.

## 4.7 Reconsenting Requirements

There may be times when site staff have to reconsent participants, due to minor modifications, Letter of Amendments (LoAs), or protocol amendments. Reconsenting must also be done for participants who reach legal age of consent during study follow-up as required by site IRBs/ECs.

When reconsenting of participants is required due to minor modifications or 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 and/or her parent/guardian(s) but does not need to read or review the entire ICF again.

Similar procedures should be conducted for participants who change their mind about participating in the optional components of the MTN-034 study, namely long-term specimen storage. Using the most current version of the appropriate ICF, review the information pertinent to the participant's decision (e.g. If a participant who previously declined long-term specimen storage later indicates that she would like to agree to storage, review the information on long-term specimen storage contained in the ICF). If the current ICF differs in any way from the version the participant originally signed, these changes should be reviewed with her as well. Note that any time reconsenting procedures are being conducted using an ICF that contains signature blocks for specimen storage, all items should be reviewed and re-signed based on the participant's current preferences. The signature lines at the end of the consent for participant, staff, and witness or parent/guardian (if applicable) must also be completed in full.

Although an IC comprehension assessment form does not need to be completed in the circumstances described above, participant and/or parent/guardian understanding should be assessed and all questions should be answered prior to signing the new ICF(s). Once comprehension has been evaluated and ensured, documentation of informed consent should be conducted per SSP section 4.6. The participant should be offered an updated, signed copy of the ICF to take home.

If reconsenting of participants and/or parent/guardians is required due to a protocol version change, a complete review of the ICF must be conducted. When changes to the ICF have been made as a result of protocol version changes, a new IC comprehension assessment form must be completed. Documentation of informed consent should be conducted per SSP section 4.6 and participants should be offered an updated, signed copy of the ICF to take home.

For participants who reach the legal age of consent or otherwise become legally able to consent during the study period, a complete informed consent process must be conducted and documented as outlined above. A full review of the ICF must occur and a new IC comprehension assessment completed, and the participant should be offered a signed copy of the ICF.

## 4.8 Informed Consent Process for Participants Who Resume Participation After Terminating Early

In the event a participant is terminated from the study early or withdraws consent and decides to rejoin the study, she must undergo a re-consenting process which includes a complete review of the ICF to restart participation in the study regardless of any previously documented written informed consent.

For participants resuming study participation, written informed consent from the participant and her parent/guardian, if indicated, must be obtained prior to any study procedures, including clinical procedures, and prior to any procedures to determine product use eligibility (see SSP section 5). Participants rejoining the study should also undergo informed consent procedures for long-term specimen storage and possible future research testing however, they may decline participation in this optional procedure and still re-join the study.

The documentation requirements for the new written informed consent documents are the same as the requirements for participants joining the study for the first time (See SSP section 4.6).

## 4.9 Ongoing Assessment of Participant Comprehension

For enrolled participants, informed consent also must be understood as an ongoing process that continues throughout the study follow-up period. Periodically, at study visits, staff should assess participants' comprehension using a discussion style similar to the screening assessment. The key elements of informed consent also should be reviewed at study follow-up visits. Sites may choose to review key elements of informed consent with individual participants, or in group sessions. Elements of informed consent can be reviewed at every visit, or periodically, as per site SOPs. Reviewing key elements of informed consent during follow-up visits may focus on the remainder of study participation and descriptions of the study phases. Should gaps in participant understanding about the study be identified, staff should provide counseling or additional education as needed to clarify potential misunderstandings, especially those that impact participant safety.

For example, at study month 1, the discussion might focus on the fact that the participant has completed the first month, and to see if she has any concerns so far with the study procedures or study requirements. Study staff might review that this visit will include a check-in on her experiences with the study product(s), that each study visit will include an HIV test, and that the participant should feel free to express questions or concerns about the study at any time. Informal assessments will help to identify aspects of the informed consent process that are, and are not, optimally effective for study participants. The assessments also may identify rumors or misperceptions about the study that require a response by the Protocol Team, either across sites or on a site-by-site basis. This discussion should be noted in the participant's chart note for that visit date.