

Section 4. Informed Assent and Consent

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This section provides information on informed assent and consent procedures for MTN 023/IPM 030. MTN 023/IPM 030 involves two types of informed assent/consent:

- Informed Assent & Parent/Guardian Permission Form for Screening, Enrollment, and Long-term Storage [for participants not of legal age to provide Informed Consent and their parent/guardians]
- Informed Consent for Screening, Enrollment and Long-term Storage [for participants that reach legal age to provide Informed Consent based on state regulations while enrolled in the study; or for emancipated minors]

This section contains general information and instructions applicable to providing informed assent/consent and parent/guardian permission required for MTN 023/IPM 030. 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 to the informed assent/consent and parent/guardian 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 section of the DAIDS policy on *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials* for further guidance on the informed consent process and documentation requirements.

Prior to Screening Visit Procedures:

- Written informed assent will be obtained from each study participant
- Informed consent will be obtained from parents/guardians (as applicable, per site IRB requirements)
 - If a site is required by its IRB 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 2nd parent/guardian should be documented in chart notes.

- If two parents/guardians provide informed consent this can be done separately or together and they can sign the same form or different forms. The site process for this should be detailed in the site IC SOP and in accordance with IRB requirements.
- For emancipated minors, written informed consent may be obtained from the participant herself, and not from her parent/guardian; however sites should follow local IRB policies

For MTN 023/IPM 030, the ICF for screening, enrollment and long term specimen storage is obtained at one time point at Screening. For participants or their parent/guardian who do not provide assent or 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. The Screening and Enrollment visits will occur on separate days due to the need to wait for screening laboratory results and confirmation of study eligibility at the Enrollment visit. Informed assent/consent is an ongoing process that continues throughout the study follow-up period through open dialog between study staff and the participant.

Participant informed assent/consent for future storage and testing of blood specimens and vaginal and cervical fluids is optional. The participant or her 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 guardians 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 done. Thereafter, any remaining specimens collected from these participants will be destroyed.

For this study, participants are randomized to the in-depth interview (IDI) 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 Investigator of Record (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 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 potential study participants and their parents/guardians
- Assure that informed assent/consent is obtained in a setting free of coercion and undue influence
- Confirm that the participant and her guardian comprehend the information
- Document the process

Per protocol, potential participants must be literate in English as an eligibility criterion for MTN 023/IPM 030. However, if a parent/guardian of the participant is illiterate, then an impartial witness should be present for the parental permission process.

4.2 Informed Consent/Assent SOP

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

- 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
- Procedures for determining participant/guardian comprehension of the required information
- Procedures to ensure that ICF 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 state regulations). Sites may also obtain input from their IRB 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 forms are easily distinguished and used appropriately, if applicable
- Procedures for implementing a change in the version of the ICFs used
- Staff responsibilities for all of 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 according to site SOPs. The consent process may be conducted with the participant and her guardian/s together or separately, per participant request and site 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

A sample ICF is provided in the MTN 023/IPM 030 study protocol. Sites are responsible for adapting the sample as needed for local use. Local adaptation may include reformatting the ICF in accordance with local IRB/EC requirements. Unless waived by the IRB, the adapted ICF must still contain the eight required elements of informed consent as defined in 44 CFR 46.116. It is recommended that all ICF forms are reviewed and approved by MTN LOC (FHI 360) and/or Westat prior to IRB/EC submission. After IRB/EC approval, the ICF must be submitted to the DAIDS Protocol Registration Office (DAIDS PRO) for MTN sites or Westat for ATN sites prior to its initial use.

Each site is responsible for preparing bulk supplies of the approved ICF and for only using the currently approved version of the ICF 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 ICFs are easily distinguished and used appropriately. A system for tracking version control and approvals of the ICF is also recommended. Upon receiving final IRB/EC and any other applicable regulatory approval(s) for an amendment to the ICF, MTN sites should implement the ICF immediately and submit the updated version to DAIDS PRO per the timelines outlined in the protocol registration manual. ATN sites should implement and submit the amended ICF per the ATN Manual of General Operations (MOGO).

4.4 Informed Consent Support Materials

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. Sample study products will be 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. Suggested visual aids for each site to consider using are as follows:

- Calendar
- Male condoms
- Sample vaginal ring and packaging
- Urine specimen cup
- Blood collection tubes
- 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)
- Placebo explanation visual aids (e.g., sugar with and without vitamin A, hair gels with and without straightener, food flavoring sauces in sweet and non-sweet versions). Visual aids to explain placebos should look identical to each other.

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 their parents/guardians understand all information provided to them to ensure they are able to make an informed decision about study participation. This assessment of IC comprehension may be administered separately for the participant and her guardians. The participant and her parents/guardians must not be asked to agree to take part in the study, or sign the ICF, until they fully understand the study.

Study staff should ask some questions that indicate if the participant and guardians understand significant points of the study. If the participant and guardians 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. Sample tools to assist with this assessment are available on the MTN-023/IPM 030 website under Study Implementation Materials. The sample IC assessment “open ended questions” tool may be administered to both the participant and her guardian. The “true/false” assessment tools have been separated for participant understanding and parent/guardian understanding. Instructions to administer the assessment should be included in the site SOP for obtaining informed consent. The comprehension assessment must be administered to each potential participant and her parent/guardian(s) individually after they have completed the informed assent/consent discussions with site staff as described above but before they are asked to sign the ICF.

4.5.1 Administration of Comprehension Assessment Tool

A comprehension assessment tool should be administered to each potential participant and guardians after they have completed the informed consent discussions described above and before they are asked to sign the ICF. It is expected that study staff administering the ICF and assessment will be sufficiently knowledgeable about MTN 023/IPM 030 to make good judgments about potential participants’ comprehension of the required information. The comprehension assessment tool 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 comprehension assessment tool 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 assessment tool, study staff should carefully review the assessment to verify that all required points have been satisfactorily addressed by the participant and 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 final outcome of the process should be recorded directly on the assessment tool (or in a chart note) and the staff member who completed the assessment tool should ensure his/her signature is recorded in the space provided. All comprehension assessment tools utilized should be submitted to local IRB/ECs for approval prior to use. Detailed information for how comprehension will be assessed must be specified in the site SOP for obtaining informed consent.

4.6 Documenting the Informed Consent Process

US FDA regulations and ICH E6 guidelines 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, 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).

In addition to completing signature requirements as described above, the participant and her guardian(s) must indicate on the form whether she agrees to storage and future testing of biological specimens. The participant may decline and still enroll in MTN 023/IPM 030.

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 some of the suggestions listed in the DAIDS policy, site staff are strongly encouraged to use an Informed Consent Coversheet similar to the sample included on the MTN 023/IPM 030 webpage under Study Implementation Materials. Sites choosing to use a coversheet (one for the participant and one for each guardian) should list the coversheet as a source document in their SOPs for source documentation and should use the coversheet consistently to document all informed consent processes with all participants. The first half of the coversheet (items up to and including "Version number/date of informed consent form used during informed consent process/discussion") should be completed at the start of the IC session. The remainder should be completed at the end of the informed consent session. If a site chooses not to utilize the Informed Consent Coversheet, all elements of each informed consent process must be documented in detail in a signed and dated chart note.

It is essential that all informed consent documentation (e.g., the informed consent form, the coversheet) document that informed consent 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 in source documents (for example, on the cover sheet 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 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 initial assessment. 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. These informal assessments will help to identify aspects of the informed consent process that are, and are not, optimally effective for study participants. This discussion should be noted in the participant's chart note for that visit date.