

Section 3. Accrual, Eligibility Determination, & Study Procedures

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3 Introduction

MTN-041 will enroll pregnant/breastfeeding women, male partners, grandmothers and key informants. The purpose of this SSP section is twofold: 1) To provide information on requirements and procedures for recruiting participants and determining participant eligibility, and 2) to outline study procedures for each study population in MTN-041.

3.1 Study Accrual Plan and SOP

Each site is responsible for developing its own accrual plan that should be described in the site SOP for Participant Accrual and Eligibility Determination. Working in collaboration with the Community Working Group (CWG) and local Community Advisory Board (CAB) is encouraged. Participants will be recruited from selected study sites using approved recruitment plans and materials (if applicable). Community education strategies, including group sessions, may be employed as part of participant/partner outreach. At each site, and in consultation with the Research Triangle Institute (RTI) team, community advisory boards (CABs) and project staff will be responsible for identifying the KIs to be interviewed. Target KIs include: HCPs (e.g. obstetrician, nurse, pharmacist, etc.), traditional care provider (e.g. TBA, healer, midwife, etc.); social service providers (social worker, family planning counselor, etc.); and religious and community leaders.

The SOP for Participant Accrual and Eligibility Determination should minimally contain the following elements related to the site accrual plan:

- Site-specific accrual targets and timelines
- Description of any community sensitization plans
- Recruitment strategies relevant for each key study population (current/recently pregnant or breastfeeding women, male partners, grandmothers, and key informants), including:
 - Potential recruitment locations and venues
 - Plans for education about the study
 - Description of prescreening activities (as applicable)
 - Plans for referral to screening visits (and how ineligible participants will be handled)
 - Plans for recruitment materials (as applicable)
- Methods for tracking actual accrual versus accrual targets, and implementation of back-up plans as needed
- Methods for maintaining participant confidentiality during the accrual process
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

Study staff are responsible for updating this SOP as needed to meet site-specific accrual goals.

3.2 Site-Specific Accrual Targets and Timelines

Approximately 50 male and female community members for focus group discussions (FGDs) and approximately 10 key informants (KI) for IDIs per site are targeted to be enrolled in MTN-041. The total accrual time anticipated for this study is 3-6 months from initiation of enrollment at each site. The participant subgroups and approximate enrollment targets are shown in Table 3-01, by interview modality. FGDs with pregnant and breastfeeding women will focus on the recruitment of women who do not have previous microbicide/PrEP experience, however it is not prohibited for women with prior experience or knowledge of microbicides/PrEP to enroll.

Table 3-01: Approximate Enrollment Targets per Site

| Participant Group | Approximate No. of Participants/Site for KI IDI | Approximate no. of participants/ FGD (min. 4, max 12) | Target Number of FGDs |
|------------------------------|---|---|-----------------------|
| Pregnant/Breastfeeding Women | N/A | 6-10 | 2 |
| Grandmothers | N/A | 6-10 | 1-2 |
| Male Partners | N/A | 6-10 | 1-2 |
| Key Informants | 10 | N/A | N/A |

All potentially eligible community participants will be asked to complete a single FGD (with other participants in the same group assignment). Sites may ask enrolled participants to complete a single IDI instead of an FGD after consultation with the MTN-041 management team. The decision to conduct an IDI instead of an FGD will be dependent on adequate sample size and scheduling feasibility. Sites should be mindful of sample size and not exceed enrollment of 50 FGD participants or 10 KI IDI participants total, unless approved by the MTN-041 management team. Sites should aim to have FGDs with no less than 4 and no more than 12 participants across the three participant groups. **Total sample size across all sites should not exceed 200 FGD participants and 40 key informants.**

3.3 Prescreening/Recruitment Activities

Prescreening for this study primarily refers to recruitment procedures undertaken by site staff in the field, prior to scheduling potential participants for their MTN-041 screening and enrollment visit. Site teams should provide education about the MTN-041 study to potential participants as outlined in their site-specific SOPs for Accrual and Recruitment. Note that use of printed materials and/or formal prescreening checklists is not encouraged in MTN-041, but may be implemented with appropriate approvals from site IRBs. Should sites choose to develop these materials, their use should be outlined in site specific SOPs. After providing study education, potentially interested participants should be scheduled for an MTN-041 screening and enrollment visit, which will be the same date of the IDI/FGD in most cases.

Recruitment activities should be tracked on site-specific logs to monitor progress towards accrual goals. These logs should include only summary level, non-identifiable information such as: recruitment venue, total number of potential participants contacted, number of potential participants booked for screening and enrollment visits, type of interview/FGD, and date of scheduled visit. No identifiable information about potential participants should be collected prior to signing informed consent form during the screening and enrollment visit. If sites choose to assign prescreening IDs, this process should be outlined in site SOPs and the IDs should not be linked to any personally identifiable information.

3.4 Visit Location

It is important that study visits be conducted in a private location to maintain the confidentiality and safety of the participant(s). It is also important that locations are quiet enough for audio-recording. Typically, visits will be conducted at the study site. Per protocol, visits may also be conducted at an alternate location (such as the participant's home for an IDI), if agreed upon by the participant and if privacy can be maintained. In the event a visit is conducted anywhere other than the study site, staff should document participant agreement to the visit location in their participant binder.

3.5 Screening and Enrollment Visit and Procedures

MTN-041 staff will meet potential participants for their screening and enrollment visit at the designated time and venue agreed to by the participant during pre-screening/recruitment contact. Most often this will be the study clinic, however interviews may take place at other locations, if agreed upon by the participant and if the venue offers participant privacy as described in Section 3.5 of this SSP.

Ideally participants enrolled into MTN-041 will have their screening and enrollment procedures and CRFs completed and their IDI/FGD conducted on the same day. However, if that is not possible, visit procedures may be conducted over more than one day.

Details about Study Procedure design can be found in the Study Protocol Section 7. For each study visit, completion of the following procedures for each participant is required and should be documented on the applicable Study Visit Checklist:

1. **Obtain written informed consent for screening and enrollment:** Written IC must be obtained prior to conducting any protocol-specified study procedures. Details outlined in SSP Section 4 (Informed Consent).
2. **Assign a PTID Number:** See Section 3.7 of this SSP for details.
3. **Collect locator information:** Although "provision of adequate locator information" is not required inclusion criteria for MTN-041, we do ask that sufficient participant locator information be collected to allow for participant contact in the case of visit rescheduling, necessary follow-up on safety issues/social harms (expected to be rare), and/or dissemination of study results. Each site can determine the appropriate type of locator information to collect for these purposes, and suitable approaches for capturing this information.
4. **Confirm eligibility:** Eligibility confirmation must occur by designated staff, after written IC is obtained, and prior to completion of any data collection procedures (CRF, IDI/FGD). Details are outlined in Section 3.8 of this SSP.

5. **Administer CRFs:** All questionnaires should be administered individually to study participants in a location that ensures participant confidentiality. The CRFs will ideally be administered before the IDI/FGD. Additional guidance regarding form administration is as follows:
 - a. **Participant Status Form** is completed for all study participants. These CRFs are to be started by study staff when the participant is enrolled and completed once the participant has completed participation in MTN-041. The form captures information about a participant's status in the study.
 - b. **Demographic CRFs** are administered to all participants. These CRFs are provided in English only and staff are expected to ask questions in the preferred language of the participant, as appropriate, to elicit information required for form completion.
 - c. **Behavioral Assessment CRFs** are administered only to pregnant/breastfeeding women and male partners. These CRFs are available in English and local languages, and should be administered in the preferred language of the participant. This may be different than the language the participant provided informed consent in, as long as fluency is confirmed/documentated in both languages (e.g. on the IC coversheet). Any deviation from this should be documented in the participant's record (e.g. in chart notes or visit checklists).

3.6 Assignment of Participant ID and FGD Numbers

The site should assign one PTID to each potential participant after informed consent for the study has been obtained. PTIDs are assigned in sequential order within the range as potential participants complete informed consent. Staff should ensure that each PTID is assigned only once and should track this by using the MTN-041 PTID/ Name Link Log. Both FGD and IDI participants are assigned PTIDs using the same structure.

The Participant Status Forms (PSF) will capture the MTN-041 PTID of the participant, regardless of whether they enroll in the study. The MTN-041 PTID should be used for all subsequent MTN-041 documentation.

MTN-041 PTID boxes are located near the upper left corner of each CRF page. The PTIDs used for this study are six digits long and are formatted as "41-XXXX". To distinguish the FGD numbers from the PTIDs, FGD numbers are five digits long and include the letter 'F' to signify that it is a focus group.

Table 3-02: Range of PTIDs and FGD Numbers by Site

| Site | PTID Range | FGD # Range |
|----------|--------------------|------------------|
| WRHI | 41-2001 to 41-2099 | 41-F21 to 41-F29 |
| Zimbabwe | 41-4001 to 41-4099 | 41-F41 to 41-F49 |
| MUJHU | 41-6001 to 41-6099 | 41-F61 to 41-F69 |
| Blantyre | 41-8001 to 41-8099 | 41-F81 to 41-F89 |

Table 3-03: PTID Breakdown

| 1 st Digit | 2 nd - 4 th Digit |
|-----------------------|--|
| Site # | Sequential for individual identification |
| WRHI = 2 | 001-099 |
| Zimbabwe = 4 | |
| MUJHU = 6 | |
| Blantyre = 8 | |

All FGDs should be numbered in sequential order using the range of numbers assigned in Table 3-02. Note that each participant included within an FGD will still receive a unique PTID per the specified PTID ranges.

3.7 Eligibility Determination and SOP

It is the responsibility of the site Investigator of Record (IoR) and other designated staff to ensure that only participants who meet the study eligibility criteria are enrolled in the study. Each study site must describe how study staff will fulfill this responsibility within their SOP for Participant Accrual and Eligibility Determination. This SOP minimally should contain the following elements related to eligibility determination:

- Eligibility determination procedures, including:
 - Eligibility assessment procedures
 - Final confirmation and sign-off procedures prior to enrollment
 - Documentation of all eligibility criteria (met or not met)
- Ethical and human subject considerations
- Staff responsibilities for all of the above (direct and supervisory)
- QC/QA procedures (if not specified elsewhere)

Should study staff identify that an ineligible participant has inadvertently been enrolled in the study, the IoR or designee should contact the MTN-041 Management Team (mtn041mgmt@mtnstopshiv.org) immediately.

The MTN-041 Behavioral Eligibility Worksheet should be used to evaluate inclusion and exclusion criteria that rely on participant self-report. This worksheet is available on the MTN-041 website, and should be translated into local languages and administered in the preferred language of the participant. As per instructions on the form, only administer questions relevant to the applicable participant cohort (e.g. pregnant breastfeeding women, male partners, etc.).

The MTN-041 Eligibility Checklist will be completed following written informed consent and should be used to document and sign off on final participant eligibility. Only staff delegated the responsibility of eligibility determination on the study DoA log should sign off on this checklist. **The act of completing and signing the eligibility checklist is the act of enrollment into MTN-041.**

Inclusion criteria:

All participants

1. Able and willing to provide written informed consent in one of the study languages.
2. Able and willing to complete the required study procedures.

Currently or recently pregnant or breastfeeding women

3. Between the ages of 18 to 40 years old (inclusive) at Enrolment, verified per site standard operating procedures (SOPs).
4. Currently or recently (within two years) pregnant or breastfeeding (by self-report).

Male partners

5. Aged 18 years or older at Enrolment, verified per site SOPs.
6. Identifies as a primary sexual partner of a woman who is currently or was recently (within two years) pregnant or breastfeeding.

Grandmothers

7. Aged 18 years or older at Enrolment, verified per site SOPs.

8. Identifies as a maternal or paternal grandmother of whose daughter or daughter-in-law is currently or was recently (within two years) pregnant or breastfeeding.

Note: The term “daughter-in-law” includes women who are/were not married to their male partner during or after pregnancy.

Service provider KIs

9. Aged 18 years or older at Enrolment, verified per site SOPs.
10. Currently working as a clinician (e.g., obstetrician, nurse, pharmacist, etc.), traditional care provider (e.g., TBA, healer, midwife, etc.), social service provider (e.g., social worker, family planning counselor, etc.) or community health worker in one of the study countries, verified per site SOPs.
11. Experienced in providing services to pregnant and/or breastfeeding women.

For community leader KIs:

12. Aged 18 years or older at Enrolment, verified per site SOPs.
13. Currently acting in a community leadership role (e.g., local chief, religious leader, etc.).

Exclusion criteria:

1. Has any condition that, in the opinion of the Investigator of Record (IoR)/designee, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives.

Currently or recently pregnant or breastfeeding women:

2. Known HIV-positive status, verified per recent health record (e.g., health passport, ante-natal book, HIV test card, or similar document) or by self-report if health record(s) not available.

NOTE:

- *This exclusion criterion is standard across all MTN protocols and may be used to justify a range of reasons for participant exclusion from MTN-041. For example, if a participant is enrolled in another HIV prevention study at the time she is approached for MTN-041 participation, the IoR may decide to exclude her if s/he feels it might complicate interpretation of MTN-041 data.*
- *Though it is not explicitly identified within eligibility criteria, women who may have experienced an interruption of pregnancy or other adverse pregnancy outcome are still be eligible if “recently pregnant”. As with any other condition, the Investigator of Record (IoR)/designee should use her/his discretion in determining her eligibility to participate, in order to avoid harm for anyone who may still be grieving. This same discretion should be applied to male partners and grandmothers whose partners and daughters/daughters-in-law, respectively, have experienced an adverse pregnancy outcome.*

3.8 Screening and Enrollment Logs

The DAIDS policy on Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials requires study sites to document screening and enrollment activity on Screening and Enrollment Logs. Screening and Enrollment Logs will provide a comprehensive picture of all participants screened and enrolled in the study. In addition to the log, each participant that is screened for MTN-041 should have a completed Participant Status Form (PSF CRF), which will indicate enrollment into MTN-041 or reasons for non-enrollment. Each individual who provides informed consent is provided with the next chronological PTID. Participants that meet all eligibility criteria and have final sign-off of enrollment status documented on the MTN-041 Eligibility Checklist are considered enrolled in the study.

An example of a Screening and Enrollment Log can be found on the MTN-041 website. The site is encouraged to modify this as needed. This log at a minimum must include the MTN-041 PTID, screening date, study group, interview type, and enrollment date or reason for non-enrollment (if applicable), and staff initials and date.

3.9 Weekly MTN-041 Progress Reports

Once MTN-041 accrual is initiated, study staff will report the total number of participants screened and enrolled to RTI on a weekly basis, along with other key progress indicators, as necessary. RTI will send a Screening and Enrollment report to the MTN-041 Management Team prior to each scheduled management team call.

3.10 Visit Planning and Expected Participation Duration

Screening and enrollment procedures, completion of CRFs and the IDI/FGD may be conducted on the same day or over more than one day.

3.10.1 Visit Scheduling

Each site should determine its approach for scheduling IDIs/FGDs and outline plans in site-specific SOPs for MTN-041 Accrual and Eligibility Determination (review this SSP for accrual and eligibility considerations).

We encourage site staff to be flexible in scheduling IDIs/FGDs by allowing after-hours and weekend meeting times, and/or alternate venues to make the meetings convenient for the participants, provided the venue is suitable for the IDI/FGD (see Section 3.5: Visit Location above).

Site Staff should consider the availability of all necessary interview staff (e.g. qualitative interviewers, note takers) when scheduling participants for their IDI/FGD.

The total duration of study participation for each participant is not anticipated to exceed 6 hours, including administrative and data collection procedures. Each IDI is not anticipated to exceed 2 hours and each FGD is expected to take up to 4 hours. Sites should consider visit length and make efforts to minimize participant fatigue when scheduling participants for study visit procedures.

3.10.2 Visit Checklists

Visit checklists will be used to document completion of all required study procedures and data collection forms for each visit and each type of participant in MTN-041. There are three types of visit checklists for MTN-041 (templates are available on the MTN-041 website):

1. IDI Visit Checklist
2. Group FGD Visit Checklist
3. Individual FGD Visit Checklist

The IDI Visit Checklist is to be completed for all IDIs, including service provider key informants, community leader key informants, and individual IDIs of community members originally recruited for FGDs (This type of IDI should be rare and needs prior approval from management team. See Section 3:11.3 of this SSP regarding special considerations and approvals required to conduct this type of IDI)

The Group FGD Visit Checklist is to be used for all FGD types, including pregnant/breastfeeding women, male partners, and grandmothers. One group FGD visit checklist is completed per FGD.

The Individual FGD Visit Checklist is to be used for participants of all FGD types, including pregnant/breastfeeding women, male partners, and grandmothers. One individual FGD visit checklist is completed per FGD participant.

These checklists should be modified as needed to ensure they fit with systems at the site, then reviewed by the MTN LOC (FHI 360) for approval prior to implementation.

3.10.3 Preparing for the Study Visit

Before each study visit, please be sure to:

- Consult the Version Control Table for MTN-041 and ensure the correct versions (English and local language) of the following will be used during the visit:
 - Informed Consent Form
 - IDI/FGD guide
 - Visit checklists and Eligibility worksheet and checklist, Video and/or storyboard, and
 - CRFs
- Confirm which type of IDI/FGD will be done with the participant: pregnant/breastfeeding women, male partners, grandmothers, or key informants
 - **For Key Informant IDIs and IDIs of community members originally recruited for FGDs:** Ensure individuals selected for IDIs have been approved by the MTN-041 management team prior to conducting the interview.
 - **Note:** FGDs conducted with female participants (i.e. pregnant/breastfeeding women and grandmothers) should be conducted by female staff, and FGDs conducted with men (male partners) should be conducted by male staff. Key informant interviews may be conducted by either male or female interviewers.
- Ensure the applicable staff member has reminded the participant of her or his visit, per the site MTN-041 Accrual and Eligibility SOP.
- Confirm the availability of the interview venue/room.
- Confirm that the audio-recorder is charged and/or has batteries and is functioning correctly.
- Confirm the availability of the note-taker. If no note-taker is available, interviewer will ensure they have proper materials to take notes themselves during IDI/FGD.
- Confirm that technical needs for showing participant education video are met (and, that back-up systems—i.e. staff availability to read video script or storyboard—are in place).
- Confirm that placebo products are available to show participants as examples.

3.11 Conducting the Study Visit

Details about Study Procedure design can be found in the Study Protocol Section 7. For each study visit, completion of the following procedures for each participant is required and should be documented on applicable Study Visit Checklist:

1. **Conduct Screening and Enrollment Procedures:** Details outlined in Section 3.6 of this SSP.
2. **Conduct Focus Group Discussion (FGD) or in-depth interview (IDI):** Details outlined below.
3. **Provide reimbursement for study visit:** Participants should be reimbursed as specified in site-specific IRB-approved informed consent.

3.12 In-Depth Interview/Focus Group Discussion

The IDI or FGD will take place once the appropriate study visit procedures have been completed. To begin, greet the participant, introduce yourself and explain your role in the discussion (e.g. interviewer/facilitator, observer, note-taker) and help the participant(s) get settled and comfortable in the interview space. The interviewer will describe how the interview will work, including that it will be recorded and that a note-taker will be present.

The IDI/FGD will follow a discussion guide but will allow for iteration, probing, and digression on relevant themes. The interviewer may start the discussion with an ice-breaker to increase rapport as

well as understanding of the context of participants' backgrounds. IDIs/FGDs will be audio-recorded and later translated and transcribed. Ideally a note-taker will be present to take notes during the session, but if only an interviewer is available, the IDI/FGD may still proceed, and the interviewer will take brief notes as the interview occurs.

Split Visits: If an IDI participant is not able to complete the interview in one day, s/he may be rescheduled to come back and complete the rest of the interview on another day, ideally within one week of the initial visit. Any split visits must be documented in participant file notes. If an individual is unable to complete participation in an FGD (i.e. s/he leaves the FGD before it is complete), this should be documented in the debrief notes for the FGD as well as in the participant file notes. S/he will not rejoin another FGD unless deemed necessary by the Management Team.

Note that the informational video (or storyboard) is designed to be shown to all participants during the interview, immediately prior to asking questions about PrEP/vaginal ring use during pregnancy. The transition into the video (or storyboard) is indicated by the following text within the guides:

As explained before, we are interested in getting your opinion about two different products that women can use for HIV prevention, daily oral PrEP tablets and the monthly vaginal ring.
[Give information on products and/or show or provide samples of products to the group]

Ideally, sites will have all necessary IRB approvals for the MTN-041 informational video at the time of study activation. If approval of the video is delayed, IDIs/FGDs may proceed and staff should instead review the storyboard with participants (showing each picture and reading the text provided in the participants preferred language) or read the video script while displaying the PDF of the storyboard. This decision should be based on which materials are fully IRB approved at the time of the IDI/FGD.

3.12.1 After the IDI/FGD is Completed

There are a number of steps to follow after the IDI/FGD is complete. They are as follows:

1. Immediately following the IDI/FGD, the participant(s) will be thanked and reimbursed according to site specific IRB approved informed consent forms.
2. The interviewer will complete her or his notes and complete the PSFs.
3. A debriefing report (DR)* will be completed on the same day as the discussion. Once completed, the DR must undergo a QC process at the site prior to being circulated to the study team.

**Note: If an IDI is conducted with a community participant (i.e. recently pregnant or breastfeeding woman, male partner, grandmother) instead of an FGD, staff should use the FGD Debrief Report to document the overview of that interview.*

Further details on the management of the audio-files, transcription/ translation process, discussion notes, debriefing reports, CRFs, and transcripts is described in SSP Section 6 (Data Management).