Section 4. Participant Accrual

This section covers general guidelines for accrual and recruitment methods at each site. Additional information regarding participant accrual can be found in the MTN-016 Protocol Section 10.5.

4.1 Study Accrual Plan

MTN-016 study staff will recruit all women who become pregnant during participation in HIV prevention trials or who have or had planned exposures in pregnancy safety studies (provided pregnancy outcome was less than 1 year from the date of the enrollment/screening visit). All infants born to women enrolled in MTN-016 are to be enrolled as well.

Potential participants should be recruited into MTN-016 as soon as possible after confirmation of pregnancy and/or pregnancy outcome to maximize data collection for each participant. However, women may be enrolled in MTN-016 up to one year from the time of their pregnancy outcome and infants may be enrolled in MTN-016 provided they have not reached their 1 year birth date. Participants who initially decline enrollment into MTN-016 may be re-approached throughout the period of eligibility, per IoR discretion. All eligible participants should be offered enrollment into MTN-016 regardless of retention challenges in the parent protocol.

For microbicide trial participants who become pregnant prior to site-specific activation of MTN-016, study staff will retrospectively contact the participants for possible enrollment in MTN-016 (unless the participants have refused further contact with study staff). For microbicide trial participants who become pregnant after activation of MTN-016, study staff will prospectively contact the participants for possible enrollment in MTN-016.

MTN-016 recruitment efforts should include education about the MTN-016 study, including but not limited to the general study objectives, the schedule of study visits and types of visit procedures, expected duration of participation, and the risks and benefits of enrollment. To minimize visit burden, participants should be offered the opportunity to combine MTN-016 visits with ongoing parent protocol visits, if desirable to the participant. Sites should monitor reasons for declining MTN-016 enrollment, and periodically assess whether adjustments to recruitment strategies are needed. If participants initially decline or are undecided about MTN-016 and need more time to consider their decision to enroll, sites should have systems in place to check back in with participants periodically to see if their circumstances have changed. Sites may consider developing site-specific recruitment scripts or informational materials about MTN-016 to facilitate recruitment.

Per the reporting plan in Section 15 of this manual, the MTN Statistical and Data Management Center (SDMC) will routinely provide the MTN-016 Protocol Team with progress reports on the status of participant accrual at each study site.

4.2 Screening and Enrollment: Definitions and Procedures

The term “screening” refers to procedures performed to determine whether a potential participant is eligible to take part in MTN-016. The study eligibility criteria are defined in Protocol Section 5 and listed in Figure 4-1.

The study eligibility criteria for the woman are listed in Protocol Sections 5.2 and 5.3 and for the infant in Sections 5.4 and 5.5. Figure 4-1 (below) lists the eligibility criteria to be assessed at the screening and enrollment visit.

Figure 4-1
Eligibility Assessments for MTN-016

Inclusion and Exclusion Criteria Assessed at Screening and Enrollment Visit (Woman)
Be willing and able to provide written informed consent
History of participation in an HIV prevention agent trial OR planned exposure to an HIV prevention agent in a pregnancy safety trial
During participation in parent trial has or had known pregnancy confirmed by: A: Two consecutive monthly study visits, at least 14 days apart, with positive pregnancy tests, in the absence of signs/symptoms of miscarriage or participant report of pregnancy termination*.OR B: one or more of the following: • Auscultation of fetal heart tones • Positive pregnancy confirmed by clinic staff in the presence of a clinically confirmed enlarged uterus • Positive pregnancy test confirmed by clinic staff in the presence of missed menses (no menses occurring at least 60 days from the first day of the last menses) by participant report**Clinical assessment of fetal movement • Demonstration of pregnancy by ultrasound
Able and willing to provide adequate locator information
Has no condition that would complicate interpretation of study outcome data, make participation unsafe or would otherwise interfere with achieving study objectives
Pregnancy outcome was diagnosed 1 year ago or less
Inclusion and Exclusion Criteria Assessed at Initial Visit (Infant)
Informed consent for participation provided by parent(s)/guardians
Born to EMBRACE participant from pregnancy concurrent with participation in parent study
Has no condition that would complicate interpretation of study outcome data, make participation unsafe or would otherwise interfere with achieving study objectives
Is less than 1 year of age

*In other words, women who have known or suspected miscarriages or report pregnancy terminations should not be enrolled into MTN-016. For any women who are contemplating termination should have enrollment into MTN-016 deferred until a final decision has been made and only be enrolled if the decision is to carry the pregnancy to term.

**For amenorrheic or irregularly cycling women, two consecutive positive hCG tests (criterion A) or any of the other clinical signs of pregnancy included under the criteria B listing will be used to confirm MTN-016 eligibility.

For any participant who receives her first positive pregnancy test on her scheduled exit date from the parent protocol, every effort should be made to use one of the Criteria B options above to confirm the participant's pregnancy on the same day for the purposes of MTN-016 enrollment. In cases when this is not possible, the site

should contact the MTN-016 management team (mtn016mgmt@mtnstopshiv.org) as soon as possible for guidance. Site staff should refrain from completing termination CRFs until a response from the management team has been received.

If a participant reports recent TOP, a pregnancy test may still read positive for several weeks. In the event of a positive pregnancy test occurring less than 60 days from reported date of TOP, delay eligibility assessment until a new or ongoing pregnancy (failed TOP) is confirmed at the subsequent visit and contact mtn016mgmt@mtnstopshiv.org<mailto:mtn016mgmt@mtnstopshiv.org> for guidance.

Should a participant have a positive pregnancy test later than 60 days from date of TOP (per participant report), this will serve as the first positive pregnancy test for a new pregnancy, and eligibility should be assessed per eligibility criteria in Figure 4-1.

Should site staff identify that an ineligible participant has inadvertently been enrolled in the study, the Investigator of Record or designee should contact the MTN-016 management team (mtn016mgmt@mtnstopshiv.org) for guidance on the subsequent action to be taken.

The screening and enrollment procedures for the woman are described in protocol Section 7.1, for the infant in protocol Section 7.6, and are also listed below.

Woman screening and enrollment procedures include the following:

- Administrative
    - Obtain written informed consent for screening and enrollment of mother
    - Identification number assignment (PTID)
    - Locator information
    - Eligibility assessment
    - Reimbursement
    - Schedule next visit
- Clinical (see Section 10 for more details)
    - Obtain medical history
    - Obtain medication history
    - Obtain pregnancy history
    - Obtain genetic screening history

Newborn/Initial Visit procedures include the following (note that if the timing of the Newborn/Initial Visit corresponds to the visit window for a scheduled 1-, 6-, or 12-month follow-up visit, procedures need not be duplicated within that particular visit window):

- Administrative
    - Written informed consent for screening and enrollment of infant, or verbal confirmation of previous consent, if already obtained
    - Eligibility assessment
    - Identification number assignment (if not already assigned)

    - Locator information
    - Reimbursement
    - Schedule next visit
- Clinical (see Section 10 for more details)
    - Medical history
    - Medication history
    - Weight
    - Length
    - Head circumference
    - Abdominal circumference (preferably within 10 days, but no later than Month 1 Visit)
    - Physical exam
    - Photographic documentation of suspected or confirmed anomalies as clinically indicated
- Laboratory
    - If clinically indicated according to the IoR/designee, US Food and Drug Administration (FDA)-approved HIV test with confirmatory tests as indicated

4.2.3 Screening and Enrollment Timeframe

Screening and enrollment for the woman may be at any time during the pregnancy up to and/or within 1 year of the outcome of the pregnancy. Woman participants are considered enrolled in MTN-016 when they have been assigned an MTN-016 PTID.

Screening and enrollment of the infant may take place from the time of birth up to but excluding the first birthday. In addition to the eligibility criteria outlined in the protocol and in figure 4-1 above, an infant must be born alive and complete at least one study visit to be considered enrolled in the study.

If an infant presents for screening and enrollment at a time period that falls outside of one of the infant visit windows for MTN-016, the screening and enrollment procedures may be conducted as part of an interim visit. Sites are encouraged to take this approach, rather than to delay enrollment of the infant until the next visit window opens. Form completion guidance for infant enrollments during interim visits is available in Section 13 of this manual. The following procedures should be conducted as part of this visit:

- Informed consent for screening and enrollment of infant
- Eligibility assessment
- Assignment of PTID
- Locator information
- Medical history
- Medication history
- Physical exam
- Weight
- Length
- Head circumference
- Abdominal circumference (but not after Month 1)
- Photographic documentation of suspected or confirmed anomalies

- HIV testing, if needed

4.2.4 Screening and Enrollment Logs

The DAIDS SOP for Essential Documents requires study sites to document screening and enrollment activity on screening and enrollment logs. Screening and enrollment logs may be maintained separately or combined into one log. Appendices 4-1 and 4-2 present sample screening and enrollment logs suitable for use in MTN-016.

4.2.5 Assignment of Participant ID Numbers

Participant IDs will be assigned to each woman participant who provides informed consent. SCHARP will provide the study site with a listing of Woman Participant ID (PTID) numbers for use in MTN-016. Infant Participant IDs will correspond directly with the woman's PTID and will be assigned when the infant is enrolled in MTN-016. As shown in Figure 4-2, the listing will be formatted such that it may be used as the log linking PTIDs and participant names at each site.

Further information regarding the structure of PTIDs for MTN-016 can be found in Section 13. PTIDs will be assigned to all potential participants who provide written informed consent for the study, regardless of whether they enroll in the study. Only one PTID will be assigned to each potential participant; she will maintain this PTID for all subsequent pregnancies. Site staff are responsible for establishing SOPs and staff responsibilities for proper storage, handling, and maintenance of the PTID list such that participant confidentiality is maintained, individual PTIDs are assigned to only one participant, and individual participants are assigned only one PTID.

Figure 4-2
Sample Site-Specific PTID List for MTN-016

	Woman ID	Infant ID	Participant Name	Date*	Staff Initials
1	WWW-0001-Z-0				
		WWW-0001-Z-1			
		WWW-0001-Z-2			
2	WWW-0002-Z-0				
		WWW-0002-Z-1			
3	WWW-0003-Z-0				
		WWW-0003-Z-1			
4	WWW-0004-Z-0				
		WWW-0004-Z-1			
5	WWW-0005-Z-0				
		WWW-0005-Z-1			

*If name is unknown at the time that infant ID is assigned, please include here date of ID assignment
Note: For multiple gestations, increase ID suffix by one (see WWW-0001-Z-1 and -2).