

Section 6. Participant Follow-up

6.1 Study Follow-up Plan and Participant Retention Targets

Each enrolled pregnant woman will be followed through the completion of her pregnancy. Each enrolled infant will be followed until 12 months of age. To minimize bias and ensure accuracy of study results, each study site will target a minimum retention rate of 95% for all enrolled study participants. Further information on MTN-016 retention definitions and procedures is provided in Section 9.

6.2 Types of Follow-up Visits

Throughout the study follow-up period, two types of follow-up visits may be conducted:

- **Scheduled visits** are those visits required per protocol. MTN-016 specifies follow-up visits for pregnant participants quarterly. MTN-016 specifies follow-up visits for infants within 10 days of life, and at Months 1, 6, and 12. All scheduled follow-up visits are pre-assigned a visit code for purposes of data management as described in Section 13 of this SSP.
- **Interim visits** are those visits that take place between scheduled visits. Site staff may be required to assign visit codes to interim visits for purposes of data management as described in Section 13.

6.3 Follow-up Visit Scheduling

6.3.1 Target Visit Dates

Enrolled women and their infants will be scheduled to complete follow-up visits throughout their participation in the study. For each woman, all follow-up visits are targeted to take place based on her enrollment date. Target dates for infant visits are determined by the infant's date of birth.

Women enrolled while still pregnant will have follow-up visits scheduled on a quarterly basis up to and including the outcome of the pregnancy (pregnancy loss or labor and delivery).

Women enrolled after the outcome of their pregnancy will have no additional follow-up visits; if she enrolls her infant, the child will be followed up to 1 year of life.

Enrolled infants should be scheduled for follow up to conform as closely as possible to the target dates of within 10 days of birth and 1, 6, and 12 months of age.

6.3.2 Visit Windows

Acknowledging that it will not always be possible to complete follow-up visits on the targeted dates, there is an allowable visit window specifying on which study days (post-enrollment) the visit is allowed to be completed. For more information on visit windows see SSP Section 13.7.2.

Although the visit windows allow for some flexibility, the intent of the protocol-specified visit schedule is to conduct follow-up visits at specific intervals, and every effort should be

made to do so. The MTN SDMC will provide the Protocol Team with routine visit adherence reports for purposes of monitoring adherence to the visit schedule (see Section 15).

6.3.3 Missed Visits

For participants who do not complete any part of a scheduled visit within the allowable window, the visit will be considered “missed” and a Missed Visit case report form will be completed to document the missed visit (see Section 13).

6.4 Follow-up Visit Procedures

Required follow-up visit procedures are listed in Protocol Sections 7.1 through 7.9. Highlighted for reference below are the primary procedural requirements.

6.4.1 Woman Follow-up Procedures

- Administrative
 - Locator information
 - Reimbursement
- Clinical (see Section 10 for more details)
 - Update medical history
 - Update medication history
 - Update pregnancy course and/or outcome
 - Update genetic screening history
 - At least one ultrasound exam

6.4.2 Infant Follow-up Procedures

- Administrative
 - Locator information
 - Reimbursement
- Clinical (see Section 10 for more details)
 - Update medical history
 - Update medication history
 - Weight
 - Length
 - Head circumference
 - Physical exam (see Section 10.5.3)
 - **If consent to photograph infant has been obtained:** photographic documentation of suspected or confirmed anomalies
- Laboratories
 - Details about labs to be obtained as part of MTN-016 can be found in Section 12 (Laboratory Considerations). There are no protocol-required laboratory specimens for healthy women or their infants. Protocol-specific labs are HIV testing (PCR) of HIV-exposed infants and resistance testing of HIV-infected infants. Note: these tests may not be obtained without formal written consent.

6.5 Off-Site Visit Procedures

MTN-016 protocol Section 7 specifies that visit procedures may be conducted off-site with participant consent. Written informed consent should be obtained prior to conducting any visits off-site. Consenting to off-site visits is voluntary and women who choose not to consent may still enroll themselves and their infants in the study. Note that it is generally expected that regularly scheduled study visits will be conducted at the study clinic, and off-site visit procedures should occur infrequently. Off-site visit procedures are distinct from participant contacts made for the purposes of retention/tracing.

It is strongly suggested that sites include the option of off-site visits for a defined set of reasons and procedures based on site capacity thus ensuring advance preparation to respond to adherence and/or retention issues. Site-specific procedures for off-site visits should be described in site SOPs, which must be reviewed and approved by FHI 360 prior to implementation.

6.6 Participant Transfer Procedures

During the course of the study, participants may leave the area in which they enrolled in the study and re-locate to another area where the study is taking place. To maximize participant retention, participants who re-locate from one study location to another should be encouraged to continue their study participation at their new location. To accomplish this, study staff at both the original site (called the “transferring” site) and the new site (called the “receiving” site) will complete the process of a participant transfer.

Upon identifying the need for a participant transfer to another site, the transferring site will notify the receiving site as well as the MTN-016 study management team and the Network Lab. After the logistical details of the transfer have been discussed and agreed upon by the two sites, the following steps will be completed:

- The MTN SDMC will notify the transferring site of all outstanding data QC notes for the transferring participant; the transferring site will resolve these QCs.
- The transferring site will explain the transfer arrangements to the participant and obtain her written permission (Permission to Transfer form) to provide copies of her study records to the receiving site.
- The transferring site will deliver certified copies of all of the participant’s study records to the receiving site via courier or overnight mail service. The transferring site (clinic and lab, if indicated) will document all materials sent to the receiving site and inform the receiving site of the shipment date and expected arrival date. The receiving site (clinic and lab, if indicated) will confirm receipt of the shipment.
- The transferring site will complete and fax a Woman Participant Transfer/ Infant Participant Transfer, when indicated, case report form to the MTN SDMC (see Section 14 of this manual). Note that transfers must occur as woman-infant pairs, i.e., if an infant is being transferred for follow-up visits, the woman PTID materials must be certified copied and transferred along with the infant PTID materials.

- The receiving site will establish contact with the participant, obtain her written informed consent to continue in the study at the receiving site (using the receiving site's informed consent form), and complete and fax the Woman Participant Receipt and the Infant Participant Receipt case report forms to the MTN SDMC (see Section 14 of this manual).
- Upon receipt of the both Participant Transfer and Participant Receipt (for woman and infant) forms, the MTN SDMC will re-map the participants' PTIDs to reflect the change in site follow-up responsibility. The participant's original PTID and follow-up visit schedule will remain unchanged.
- The transferring site will retain responsibility for storage, and shipment to the MTN LC, if applicable, of all specimens collected from the infant participant prior to his or her transfer, unless otherwise instructed by the MTN LC.

6.7 Termination From MTN-016

If a participant's pregnancy outcome is known prior to her termination from the parent protocol, she should remain enrolled in MTN-016 until she has completed follow-up in the parent study. In other words, pregnancy outcome does not signify the end of study participation, just the end of follow-up for a given pregnancy. Once it has been determined that the mother will no longer be participating in MTN-016, she should be terminated from MTN-016. There is no special Study Exit Visit for MTN-016; however, sites should follow the guidance in SSP Section 13.3.5 to ensure proper documentation of study exit.

Infants will be terminated from MTN-016 at the end of their Month 12 study visit. Should there be any clinical follow-up required for ongoing conditions at study exit, sites may choose to refer infants to local pediatric providers or continue seeing the infant at the study visit as a courtesy. Any follow-up that occurs post-termination should be clearly chart noted, but no CRFs should be submitted to SCHARP after a participant's study exit.

6.7.1 Early Termination/Voluntary Withdrawal

As stated in Protocol Section 9.1, participants may be terminated early from MTN-016 if study sponsors, government or regulatory authorities, or site IRBs/ECs decide to end the study prior to its planned completion date.

Women may also voluntarily withdraw from the study for any reason at any time and/or withdraw their infants from the study. In the event that a woman or infant voluntarily withdraws from the study prior to the planned study exit date, she and/or her infant will be asked to complete one final study visit. For women, all procedures included as part of a regularly scheduled quarterly visit should be completed. If an ultrasound has not already been obtained, sites should attempt to conduct one at the time of early termination, or, if the site typically refers women to other facilities for ultrasound evaluation, see if the participant would be willing to complete the referral prior to exiting the study. Finally, if a records release is not already on file, site staff should ask the participant if she would be willing to sign a release allowing the study site to receive information from antenatal and/or delivery records post-termination from the study.

If any infants are withdrawn early from the study, the site should attempt to complete all procedures that are conducted during a regular study follow-up visit.

For both women and infants who terminate early from the study, sites should ensure that appropriate referrals have been made for participants who are HIV positive prior to exiting MTN-016.

If a participant who has voluntarily withdrawn early from the study wished to re-join MTN-016, she may resume study procedures and follow-up.