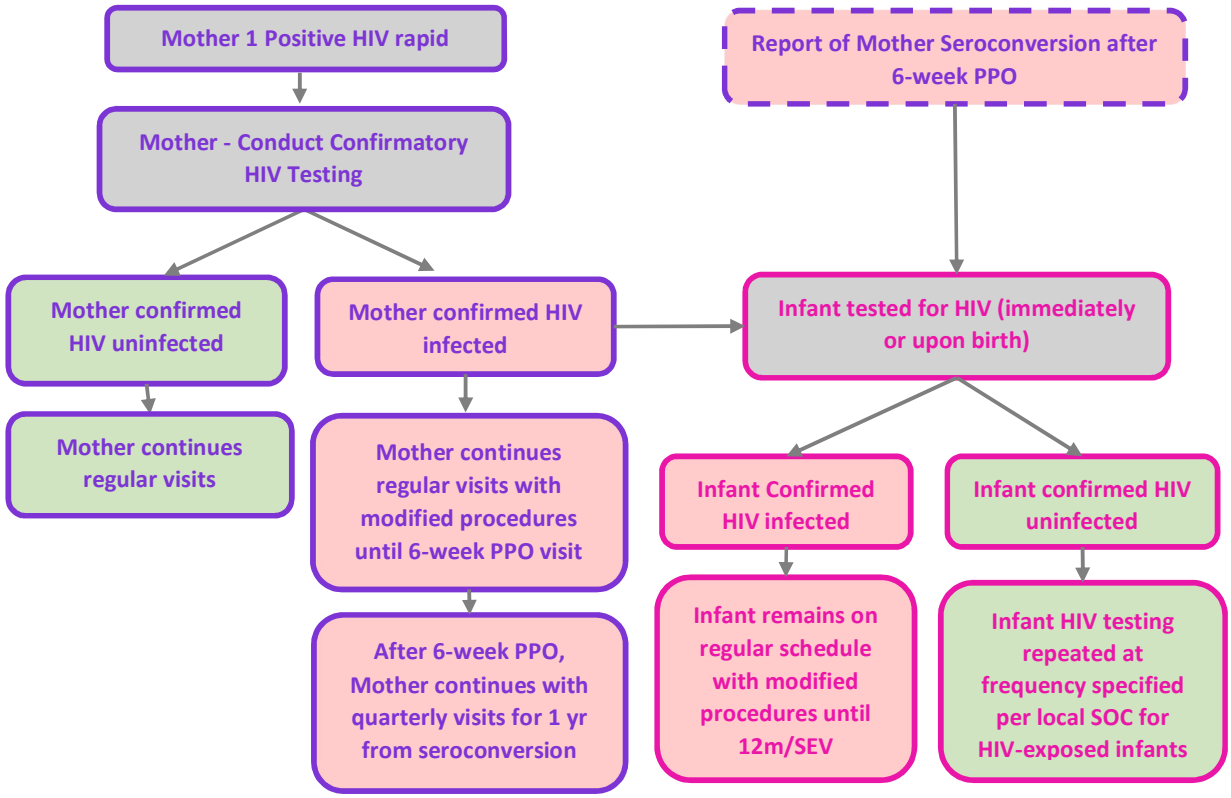
MTN-042/DELIVER Procedure Guide for HIV Confirmation and Seroconversion

Follow this guide immediately upon positive or discordant HIV Rapid tests for the mother during follow-up, or on report of HIV seroconversion of a mother who has exited the study but whose infant remains in follow-up. Refer to the MTN-042 SSP, Protocol, and site SOPs for additional details.

Follow-up Overview



I. Next steps when determining Mother HIV status: (complete at same visit as the HIV rapid tests)

1. Notify MTN LC using query form (do not wait for MTN response to proceed with testing). The form can be found on the MTN-042 Study Implementation Tools website.
2. Provide HIV post-test counseling for potential HIV infection using the **HIV Pre/Post Test and HIV/STI Risk Reduction Counseling Worksheet** and offer condoms. Explain the immediate procedures to be done.
3. Collect the following blood samples and send to lab for testing/storage:
    a. Second sample for HIV Confirmation - (See SSP 10.7.1 for collection instructions)
        i. Geenius HIV Confirmation (EDTA or plain tube 4 mL)
        ii. HIV-1 RNA PCR (per Local SOP)
        iii. CD4+ T cell Count (per Local SOP)
        iv. Plasma Storage for Algorithm Seroconversion (EDTA 10mL)
    b. DBS for Truvada user or plasma for DVR user (note: for DVR user, does not need to be separate sample from plasma collected for algorithm seroconversion).
    c. AST/ALT, CBC with platelets, and creatinine (and CrCl—*measure weight for CrCl calculation*)
4. Collect vaginal swabs for biomarkers
5. If pre-PO, collect used VR and send to lab, or any unused tablets/rings and send to pharmacy. Complete the following:
    a. **Participant-Specific Clinic Study Product Accountability Log**
    b. **Ring Insertion and Removal CRF** or **PrEP Provisions and Returns CRF**, as applicable.

c. **Study Product Request Slip** and **Product Hold Summary/Log CRF** for product HOLD

6 Document sample storage (including VR storage, if applicable) and laboratory test results, as applicable:
   a. **Specimen Storage CRF** and **LDMS Tracking Sheet**
   b. **HIV Test Result, HIV Confirmatory Results, Hematology** and **Chemistry Panel CRFs**

7 Complete all other procedures per the applicable visit checklist except for study product provision and associated study product counseling.

8 If confirmation tests can be done and provided to the participant in the same day, encourage the participant to remain at the clinic if her schedule permits.

II. Mother Confirmation Test Outcomes and Next Steps

→ Mother HIV uninfected

Second Sample Test Result	Geenius is Negative or Indeterminant → Notify MTN LC with updated query form If HIV RNA viral load below limit of detection, HIV uninfected

Immediately upon confirmation:

1 Provide and counsel on test results. (Can be done via phone contact if participant has left the clinic.)

2 RESUME study product by completing the **Study Product Request Slip** and updating **Product Hold Log CRF**

3 Continue study visits and procedures per original schedule.

→ Mother HIV infected/ Indeterminate

Sample 2 Test Result	Geenius is Positive (HIV infected)
	Geenius is Negative or Indeterminate → Notify MTN LC with updated query form If HIV RNA viral load is above limit of detection • Continue product HOLD. • Repeat Geenius one month later with a newly drawn Post HIV Seroconversion Confirmation sample (Geenius testing, CD4, RNA and plasma storage). Continue to repeat Geenius testing monthly or as specified by MTN LC until HIV status is confirmed. • Proceed with steps below **only after a positive confirmation**. If determined HIV-uninfected, original visit schedule can be resumed, including resumption of study product if Pre-PO. See HIV-uninfected instructions above.

Immediately upon HIV infection confirmation:

1 PERMANENTLY DISCONTINUE study product by completing **Study Product Request Slip** and the **Discontinuation of Study Product CRF.**

2 If pre-PO, retrieve dispensed VR or unused tablets within 24 hours (if not already done).

3 If participant has left clinic, bring her in for an interim visit as soon as possible for the following steps.
   a. Counsel on HIV infection status
   b. Provide referrals for HIV care and treatment including PMTCT as needed per site SOP
   c. Encourage participant to remain in study follow-up with a modified visit/procedure schedule for 1 year (See considerations in section III below)*

4 If Pre-PO, plan to test infant upon birth or, if post-PO, and mother permits, test infant at this visit (if present) or bring infant in for testing ASAP at an interim visit (See section IV for infant testing guidelines).

* For a participant who chooses NOT to remain in the study, request that she complete any Early Termination Visit procedures with modified study procedure for seroconverters (see III.B-C below). If needed, attempt to bring the participant back one month later for Post HIV Seroconverter Confirmation testing and plasma storage, and repeat Geenius test.

III. Further Study Visit Considerations for Mother Seroconverters

For mothers who choose to remain in DELIVER study follow-up:

A. Continue regular visit schedule with modified procedures (see III.C below) through scheduled 6-week PPO Visit but do not exit the participant. Refer to the **Seroconverter Schedule Tool** (within the Visit Calendar Tool) for the post-seroconversion testing schedule**.**

B. At the next clinic visit following HIV confirmation and every 3 months thereafter for the remainder of her regularly scheduled follow-up visits, complete the following:
- **a.** Collect blood samples and test for: HIV-1 RNA PCR, CD4+ T cell Count, Plasma Storage for Post HIV Seroconverter Confirmation.

C. All other protocol-specified procedures as scheduled at study visits should be performed except for:
- **a.** HIV-1 testing
- **b.** Provision/retrieval/collection of study VR(s) or study tablets, and provision of product use instructions
- **c.** Collection of drug level and vaginal swab for biomarker specimens
- **d.** Behavioral and product preference/acceptability assessments (cohorts 2-4 only)
- **e.** Provision of HIV pre- and post-test, protocol adherence, and product adherence counseling. *Note: modified HIV/STI Risk reduction counseling and contraceptive counseling should still be provided.*

D. After her 6-week PPO visit, transition to quarterly visits until 1 year from her seroconversion date. Complete procedures as outlined on the quarterly seroconverter visit checklist (See sample **MTN-042 Mother Seroconverter Quarterly Visit Checklist).** Reference the **Seroconverter Schedule Tool** (within the Visit Calendar Tool) for the post-seroconversion testing/quarterly visit schedule**.**

IV. Testing and Confirming HIV in Infants of Seroconverted Mothers

Infant testing will occur:

A. Upon delivery of a live infant by an HIV-infected mother at the PPO visit (or as soon as possible after birth)

B. Upon HIV seroconversion (either from study testing or report from external testing) of a mother between the birth of her infant and her infant's first birthday

Perform the following:

1 Confirm the mother agrees for HIV testing to be done on her infant. If she declines, provide referrals for local testing and contact PSRT for next steps.

2 Collect blood for infant HIV-1 testing per local standard of care.

3 Document test results on **Infant HIV Confirmatory Results CRF**

4 Notify MTN LC using query form

→ Infant HIV uninfected (per local SOP)

Immediately upon confirmation:

1 Provide and counsel on infant test results to mother. (Can be done via phone contact if participant has left the clinic.)

2 Infant continues study per original visit schedule

3 Repeat HIV-1 testing at a frequency specified per local SOC for HIV-exposed infants

→ Infant HIV infected/ Indeterminate (per local SOP)

Immediately upon confirmation:

4 Provide and counsel on infant test results to mother. (Can be done via phone contact if participant has left the clinic.)

5 Collect blood for Plasma Storage, CD4+ T cell count, and HIV-1 RNA PCR and document on **Seroconverter Results CRF** in infant casebook

a. Note: plasma sample will also be used for HIV-1 genotyping (no separate sample required); contact the MTN LC for guidance. May be performed at additional/alternate time points IOR or MTN LC discretion.

6 Facilitate rapid referral of the infant for appropriate further management including necessary blood tests, urgent ART initiation, and adherence counselling and follow up for the mother.

7 Encourage for infant to remain in study follow-up per his/her regular schedule (to exit at 12-month visit).

* For an infant who does NOT remain in the study, request the infant complete any Early Termination Visit procedures (12-month visit).

Starting at the infant's next scheduled clinic visit (thru 12-Month visit)

1 Include the following testing in the infant's visit procedures.

A. Plasma storage (4 mL purple top (EDTA) tube)

a. Note: As requested by site IoR or at the discretion of the LC, HIV-1 Genotypic Resistance Test may be conducted from the stored plasma sample.

B. HIV-1 RNA PCR (2 mL purple top (EDTA) tube or local equivalent)

C. CD4+ T cell count (2 mL purple top (EDTA) tube or local equivalent)

2 Document test results on **Seroconverter Results CRF**