HOPE Follow-Up Algorithm: Unusual Cases

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APPENDIX II: ALGORITHM FOR HIV ANTIBODY TESTING-
SCREENING/ENROLLMENT

Ineligible for the study

+/

START
2 different Rapid Tests

-/

Report as HIV uninfected

+/

Notify the MTN Laboratory Center for follow-up.
APPENDIX III: ALGORITHM FOR HIV ANTIBODY TESTING FOR FOLLOW-UP

START
2 different Rapid Tests
-/-
Report as HIV Uninfected

/+/+ or +/-

Report as HIV Infected

Confirmation Test

- or Ind
Notify MTN LC

HIV RNA

Repeat Confirmation Test after 1 month
Algorithm Scenarios

- Discordant Rapids (Cases 1-2)
- Faint bands on rapid test (Case 3)
- Acute Infection (Case 4)
- Geenius (Cases 5-7)
- Discrepant Results (Case 8)
- Viral load (Case 9)
Case 1: Discordant Rapids

• A former ASPIRE participant comes in to screen for HOPE.
• Her Alere Combo result is NEGATIVE.
• Her OraQuick result is POSITIVE.

What should you do?
Screening/Enrollment

If rapids are **discordant**…
(one positive and one negative)

- Inform the MTN LC by submitting a query form.
- The LC will respond in 24 hours, but do not wait for a response.
  - Immediately collect blood
  - Perform a Geenius confirmatory test
  - Perform or send for plasma viral load (HIV RNA PCR)

**IMPORTANT:** the participant has not completed enrollment procedures, so blood or plasma may not be stored for future testing at this time.
Special Circumstances

- Enrolling participants who have discordant rapid test results who confirm as HIV negative **is permitted**
Case 2: Discordant Rapids

- A participant comes in for her quarterly visit.
- Her rapid test results are:
  - Determine Combo: POSITIVE (Ag only)
  - Unigold: NEGATIVE

What should be done next?
Discordant Rapids

• Rapid test discordance may occur more frequently when using one 3\textsuperscript{rd} and one 4\textsuperscript{th} gen. rapid test:

• Why?
  – Participant is in the acute HIV infection phase (only HIV p24 antigen is detectable at this time)
  – One test may be more sensitive in its ability to detect antibodies to HIV than the other.

• What to do?
  – Follow testing algorithm and continue with the Geenius confirmatory test and HIV RNA
  – Familiarize yourself with counseling messages following discordant results
Case 3: Faint band on rapid test

- Unigold was performed and the result was a very faint band in the test window. There was no problem with the control band.
- The technician and checker could not decide whether to call it positive or negative.

What should be done?
Err on the side of calling it “POS”

- If a band of ANY INTENSITY (faint or strong) is seen in the test window, it should be reported as HIV POSITIVE
- All positive rapid results are confirmed by Geenius and HIV RNA, minimizing the chance of misdiagnosing a participant as HIV POS
- A false NEG result could lead to participant back on product for another 3 months during acute infection
Case 4: Acute Infection

- A participant comes in for her month 6 visit and gets a negative result on both rapid tests.
- She reports that she had unprotected sex with her boyfriend 3 weeks ago, and has since been feeling a flu-like illness.
- She knows that her boyfriend has other partners

*Should more testing be done?*
Acute Infection

During follow up, participants who request an HIV test at an interim visit or report a risk exposure should have HIV RNA PCR performed even if they have 2 negative rapid test results.
Case 5: Geenius Interpretation

• Geenius is performed for confirmatory testing. The machine reports a band as “present” that cannot be visually seen.
Geenius Reader Issues

• Make sure bands seen on cassette match interpretation by machine.
• Don’t accept run and re-read cassette or immediately re-perform Geenius test on a new cassette
• Report any inconsistencies to LC
Case 6: HIV-2 Positive (Geenius)

- You perform the Geenius assay and get a result of “HIV-2 Positive”

Should you accept this result?  
What testing should you do next?
HIV-2 Results

- HIV-2 is a different virus than HIV-1
- HIV-1 RNA PCR (Roche TaqMan or Abbott M2000) cannot be used to confirm HIV-2 infection.
- HIV-2 is uncommon in sub-Saharan Africa and there have been zero cases of HIV-2 infection to date in seroconverters from HPTN-035, VOICE and ASPIRE
HIV-2 Results

1. Repeat Geenius assay. Send LC a query form.

2. If the Geenius is again HIV-2 positive, the LC will request an expedited sample shipment to the LC in Pittsburgh.
   - This would be expensive but should be rare and may be justified for participant safety if HIV-2 cannot be confirmed locally.

3. The LC will send to a local lab in Pittsburgh that can confirm HIV-2 infection.
Case 7: HIV-2 Indeterminate (Geenius)

• You perform the Geenius assay and get a result of “HIV-2 Indeterminate”

Should you accept this result? What testing should you do next?
False Indeterminate Results

• According to the Geenius package insert:
  – HIV-1/2 false indeterminate rate: 4.33% for all sample types
  – HIV-2-specific false indeterminate rate is 1.7% for whole blood.

• In the combined MTN validation of Geenius at all HOPE sites (excluding Zimbabwe) 9/580 tests were HIV-2 false indeterminate (1.6%).

This means we will likely see cases of false HIV-2 indeterminate results in HOPE.
Next steps

- Immediately re-test the sample on Geenius.

<table>
<thead>
<tr>
<th>NEGATIVE</th>
<th>INDETERMINATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Accept the result</td>
<td>• Re-test participant in one month</td>
</tr>
<tr>
<td>• Re-test participant in 1 month (this will require an interim visit if past M3)</td>
<td>• No further action if re-test result is NEGATIVE</td>
</tr>
<tr>
<td>• This is consistent with package insert instructions in the FDA-approved version of the kit.</td>
<td>• Participant is HIV-2 uninfected</td>
</tr>
</tbody>
</table>

- LC will request an expedited sample shipment to confirm HIV-2 infection using a lab in Pittsburgh after 2 separate HIV-2 positive results.
Case 8: Discrepant Results

- Geenius does not confirm an HIV Combo Positive sample.
  - This is a likely scenario if the sample was originally only ANTIGEN positive.
HIV Combo and Geenius
Discrepant result

• **Action**: Follow testing algorithm ➔ Perform HIV RNA PCR and prepare an MTN HIV testing query form.
Case 9: Viral Load Ambiguity

• An HIV RNA test is run on the Abbott m2000 after discordant rapids and a negative Geenius.

• The result is “Detected, below the limit of detection”

Is the participant HIV positive?
## Confirmatory Testing

<table>
<thead>
<tr>
<th>Viral Load Result</th>
<th>Final Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥20 copies/mL (TaqMan) or ≥40 copies/mL (M2000)</td>
<td>HIV-infected</td>
</tr>
<tr>
<td>“Target not detected”</td>
<td>HIV-uninfected</td>
</tr>
<tr>
<td>“Detected, below the limit of detection”</td>
<td><strong>Further testing may be needed</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Contact MTN LC</strong></td>
</tr>
</tbody>
</table>
MTN HIV Testing Query Form

- Discordant rapids
- Neg or Ind Geenius
- HIV-2 result
- Unusual test pattern
- Acute infection
- Any HIV testing case that requires assistance from MTN LC
Send Query Form to MTN LC

• Email query form to: mtnvirology@mtnstopshiv.org

• MTN LC will respond and reply to query with comments directly on form

• Continue using same form for new information for same PTID

• When “Query Closed” box is ticked, form can be filed.
References

MTN Virology Core
mtnvirology@mtnstopshiv.org

MTN-025 SSP Section 13: Laboratory Considerations
http://www.mtnstopshiv.org/node/7334

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