# HOPE Follow-Up Algorithm: Unusual Cases

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MTN Virology Core
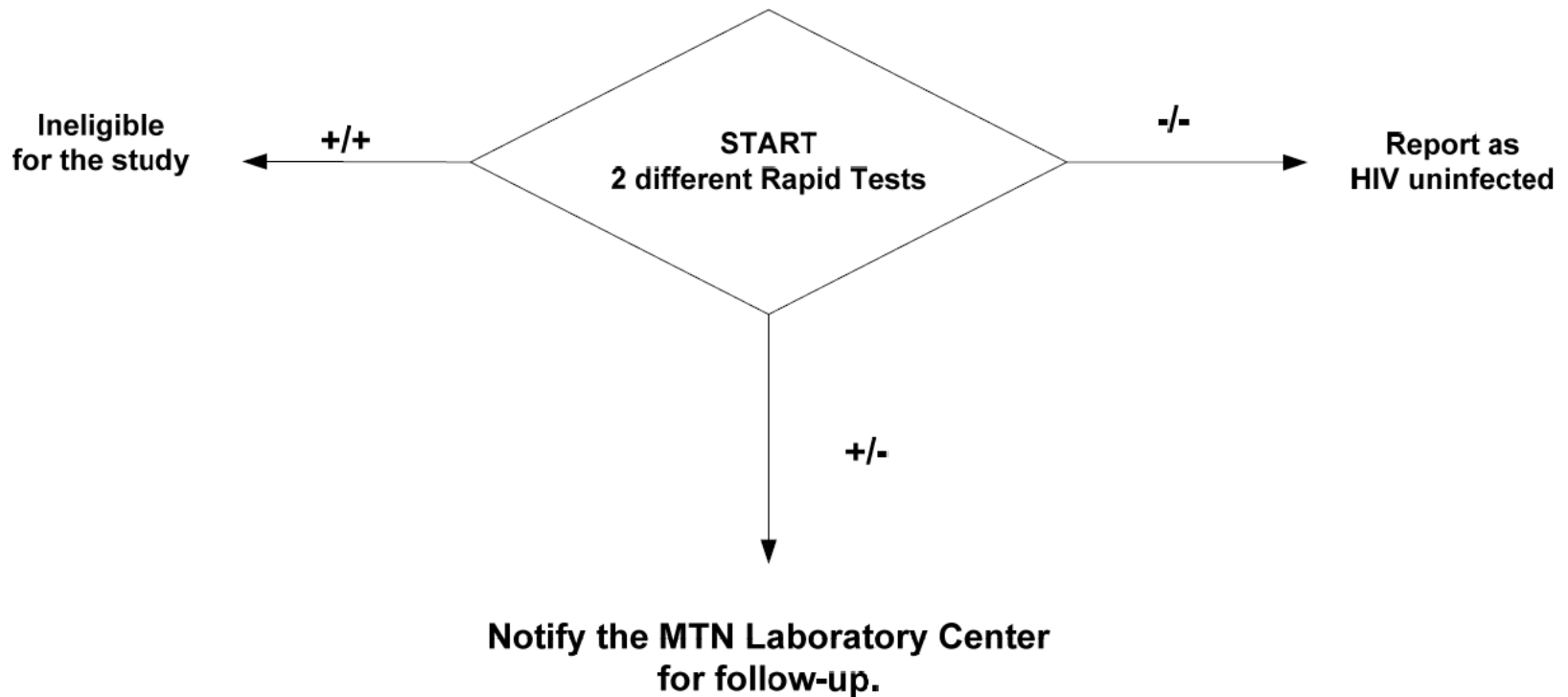
Regional Meeting Lab Breakout

Sept 27-28, 2016, Cape Town

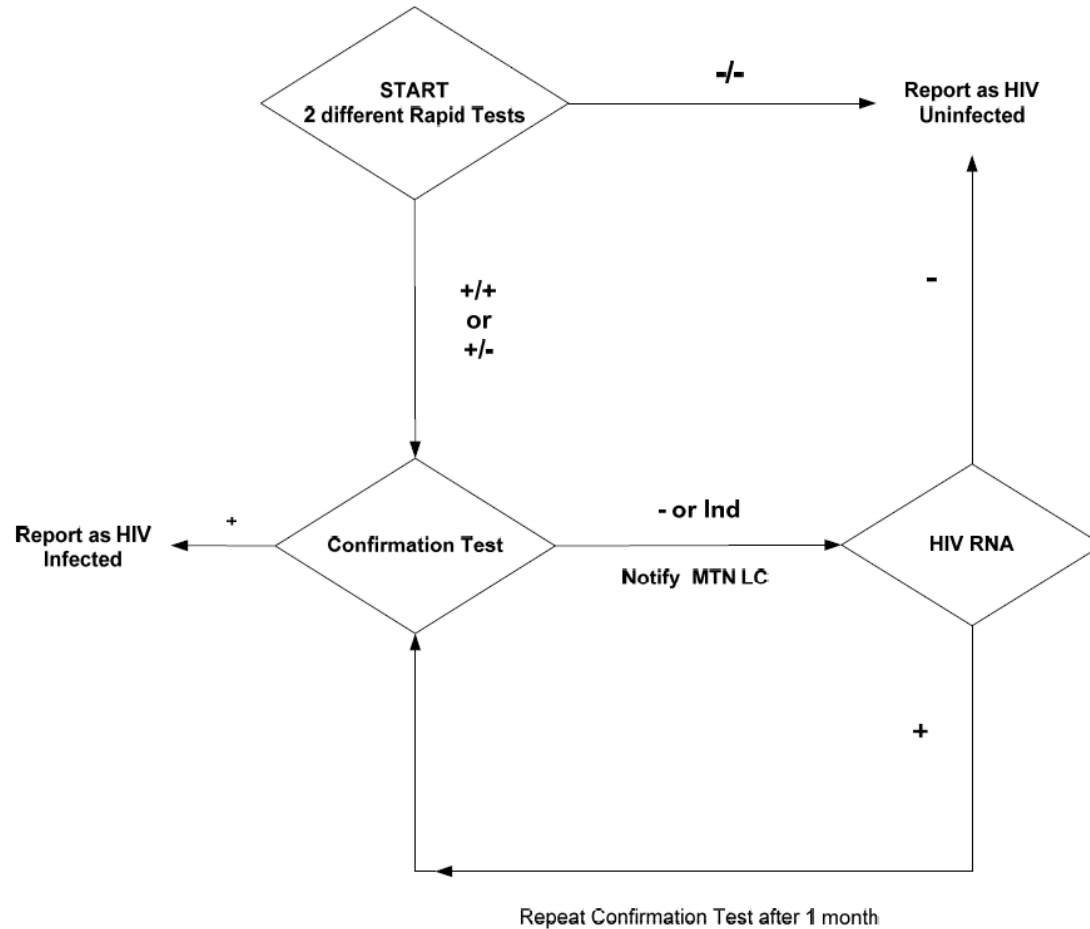# MTN-025 Testing Algorithm
## Screening/Enrollment

**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.

# MTN-025 Testing Algorithm
## Study Visits/Endpoint



APPENDIX III: ALGORITHM FOR HIV ANTIBODY TESTING FOR FOLLOW-UP

# 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**

Please notify LC using the Query Form
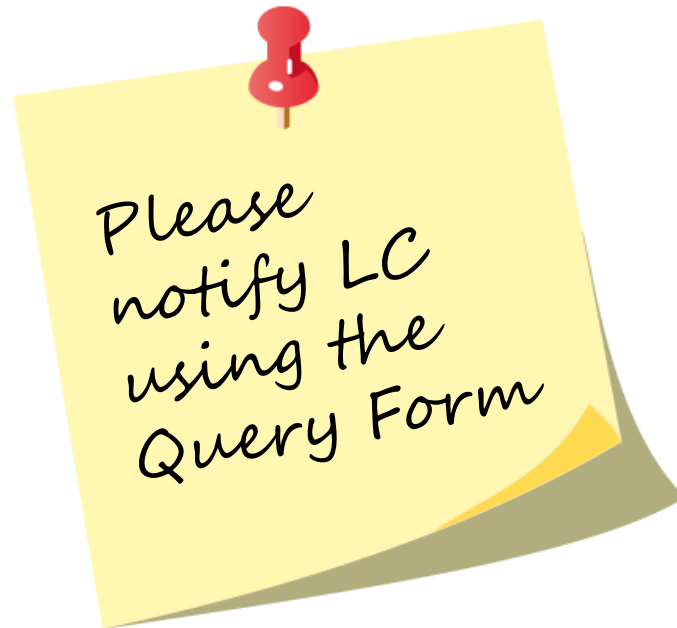
# Case 2:  Discordant Rapids

- 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$^{rd}$ and one 4$^{th}$ gen. rapid test:
- Why?
  - Participant is in the acute HIV infection phase (only HIV p24 <u>antigen</u> 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.



Image

1 2|3 4 5 6IC  G

HIV2 |  HIV1  I C

> 15D001200557

AHIV-ØZ

Interpretation

Interpretation type: Automatic

Band analysis:

| # | Name | Result |
|---|------|--------|
| 1 | gp36 | Absent |
| 2 | gp140 | Present |
| 3 | p31 | Absent |
| 4 | gp160 | Absent |
| 5 | p24 | Absent |
| 6 | gp41 | Absent |
| 7 | CTRL | Present |

# 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.

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

- 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

- <u>Action</u>: 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

| Viral Load Result | Final Status |
|---|---|
| ≥20 copies/mL (TaqMan) or ≥40 copies/mL (M2000) | HIV-infected |
| "Target not detected" | HIV-uninfected |
| "Detected, below the limit of detection" | **Further testing may be needed**<br>**Contact MTN LC** |

# 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](mailto: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

**Contacts at MTN LC and Virology Core**

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