



New HIV Detection and Confirmation Testing Platforms

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Outline

1. The HIV window period and the advancement of HIV testing
2. HIV detection and confirmation methods: can we identify and verify infection earlier?
3. Comparing current and new testing platforms
4. Next steps for the MTN

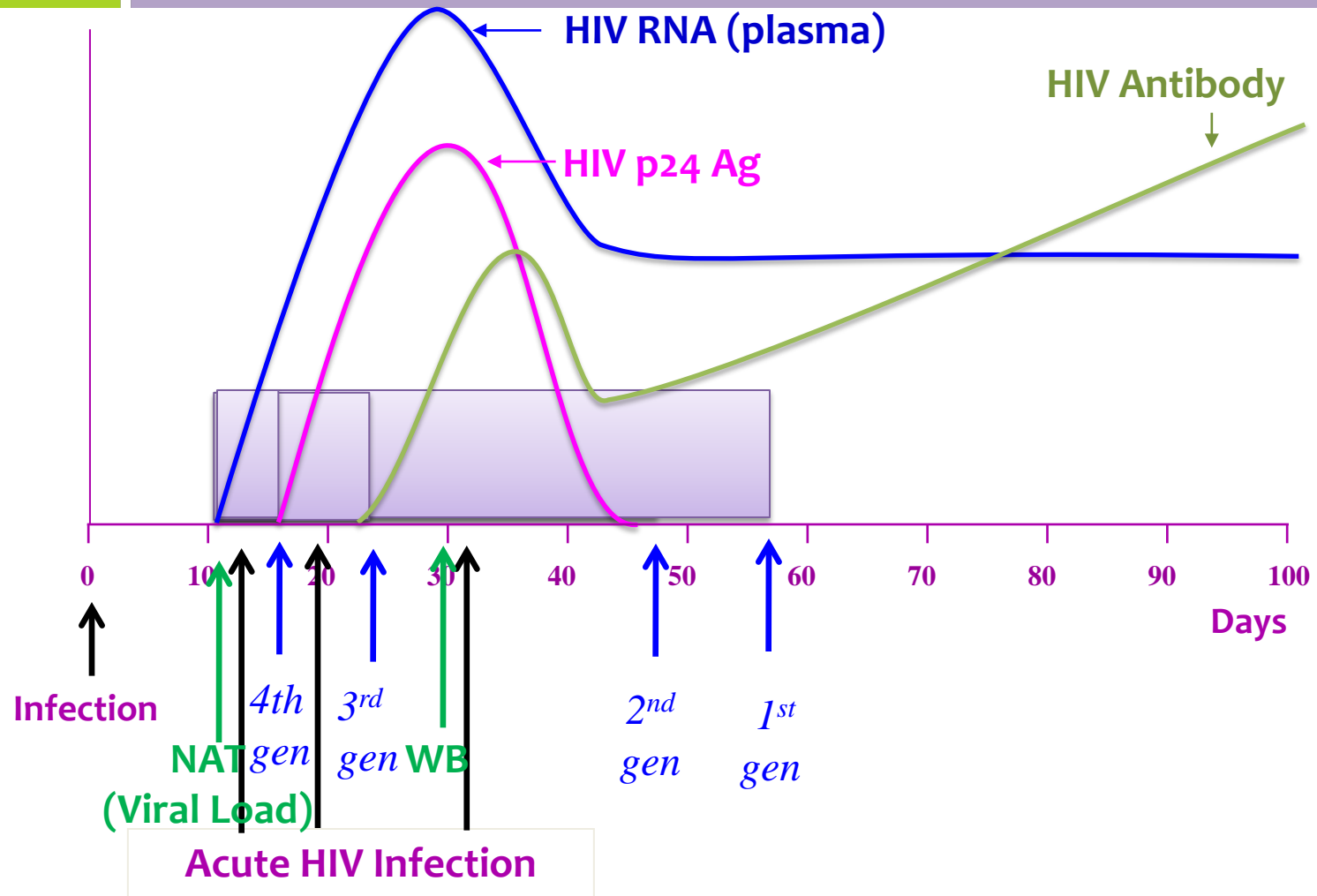
Closing the Window

- Early detection of HIV-1 benefits Phase III HIV prevention trials by:
 - Reducing the development of drug resistance by shortening time on study product during acute infection
 - Reducing HIV transmission to study participant partners during acute infection if participants are aware of their status earlier
 - Link to care/treatment earlier
 - More efficient determination of endpoints

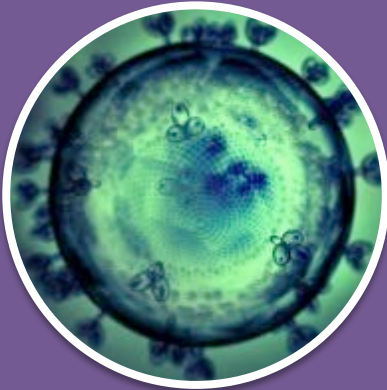
HIV Window Period

- **Window Period:** The time between initial HIV infection and when HIV can reliably be detected
- Advances in HIV testing have decreased the window period
 - Each new generation of test is more sensitive than its predecessor

HIV Infection and Laboratory Markers



Advancements in Detection and Confirmation



Viral lysate immunoassay

- GS HIV-1 Western Blot

1st Generation

<http://alerehiv.com/>



Antibody (IgG)

- MultiSpot

2nd Generation

<http://biorad.com/>



Antibody (IgG & IgM)

- Unigold Recombigen
- Oraquick Rapid Test
- Determine™ Rapid Test
- Bio Rad HIV 1/2 +O EIA

3rd Generation

<http://biorad.com/>



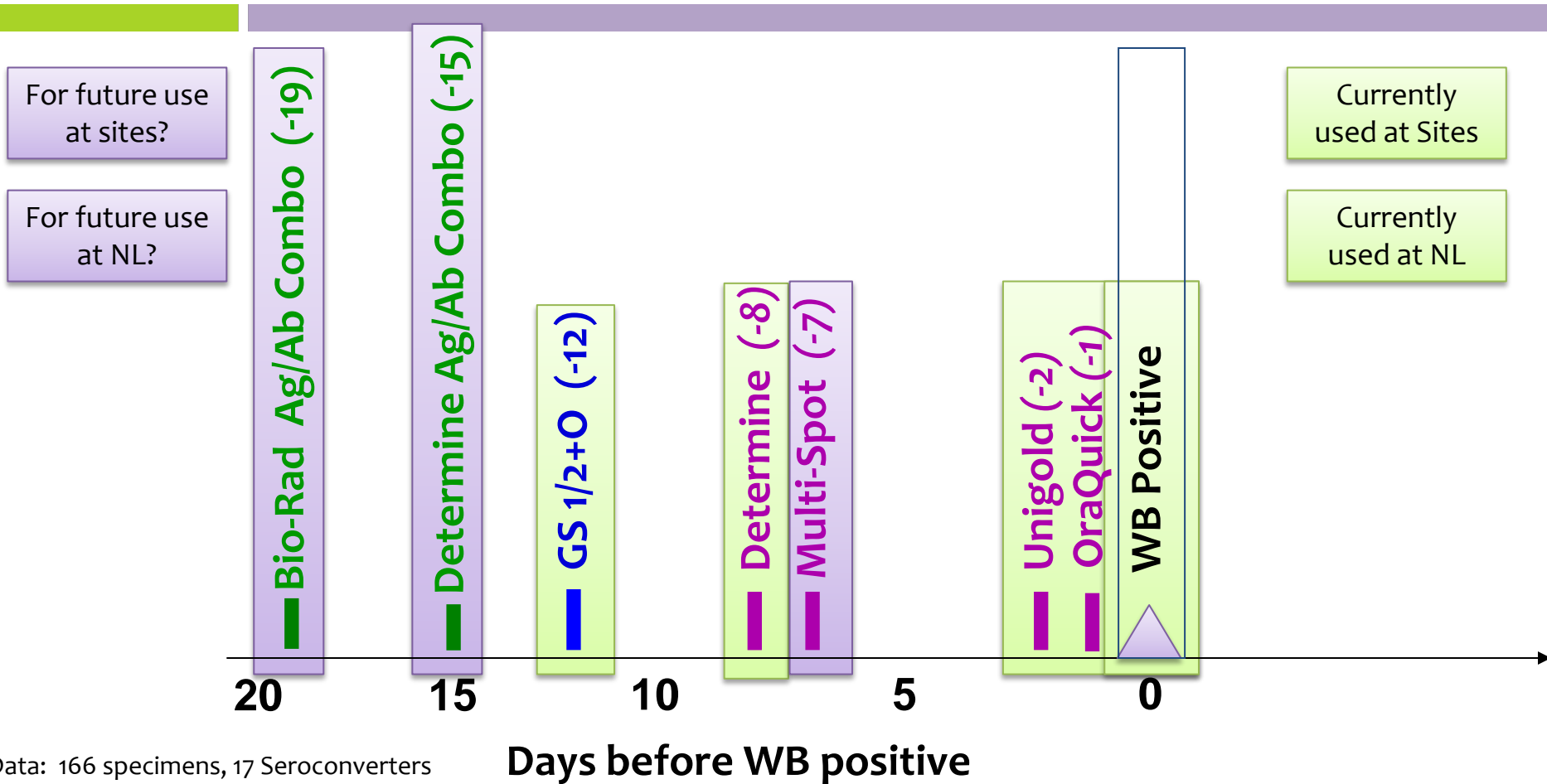
Antibody & Antigen (IgG, IgM & p24)

- Determine™ Combo Ag/Ab Rapid Test
- Bio Rad Combo Ab/Ag EIA

4th Generation

<http://alerehiv.com/>

A Timeline of Positive Test Results

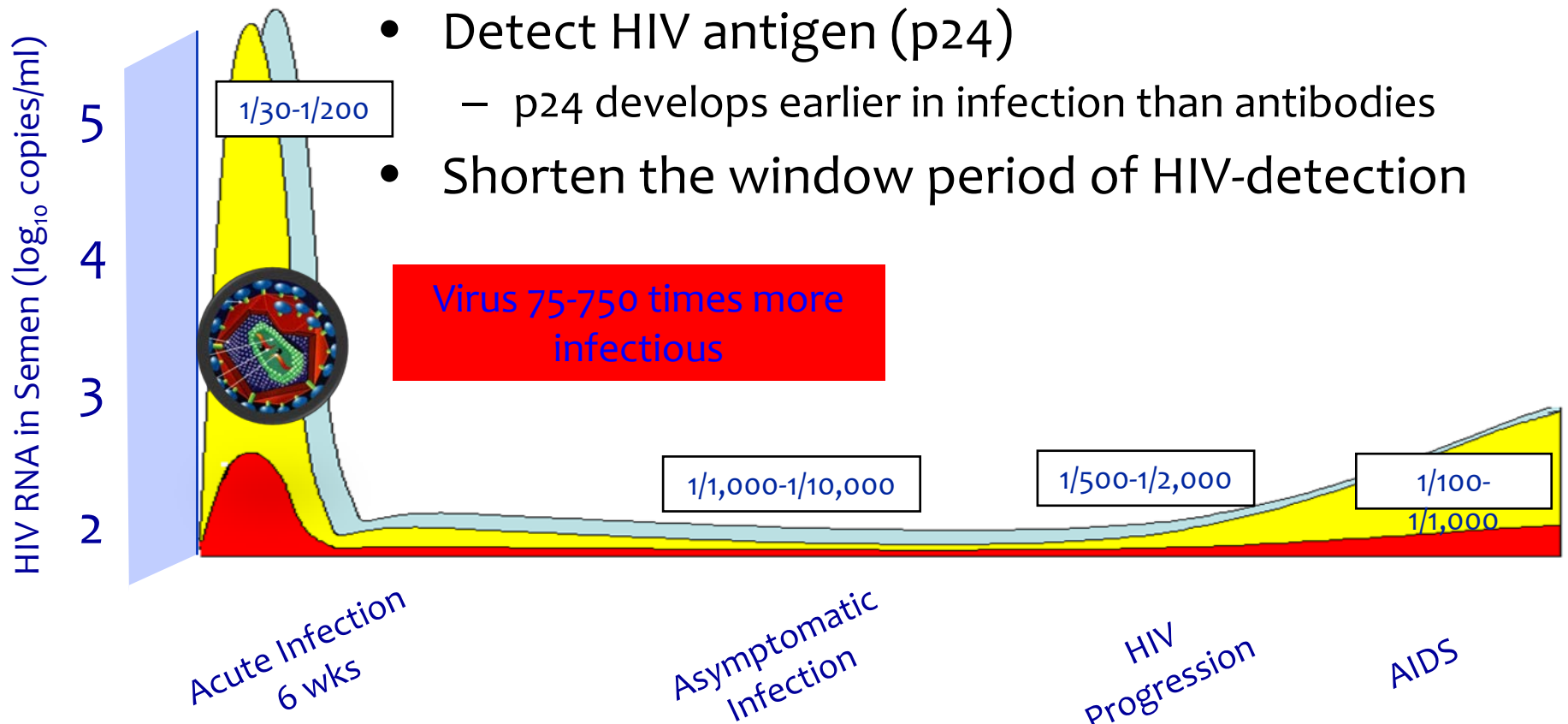


*Data: 166 specimens, 17 Seroconverters
 50 % Positive Cumulative Frequency
 (serum tested)

Modified from Masciotra et al, J Clin Virol 2011; Owen et al, J Clin Micro 2008; Keren et al, AIDS 2008 - XVII International AIDS Conference: Abstract no. THPE0052

4th Generation Tests

- Detect HIV antibodies (IgG & IgM)
- Detect HIV antigen (p24)
 - p24 develops earlier in infection than antibodies
- Shorten the window period of HIV-detection



Two New Tests for MTN?

- Alere Determine™ Combo Rapid Test
 - Screening test using Ab/Ag to detect HIV infection
- Bio-Rad HIV-1/2 Multi-Spot
 - Confirmatory test that differentiates between HIV-1 & HIV-2



<http://alerehiv.com>



<http://bio-rad.com>

Alere Determine™ Combo Rapid Test

- Would replace other rapid tests currently in use at sites

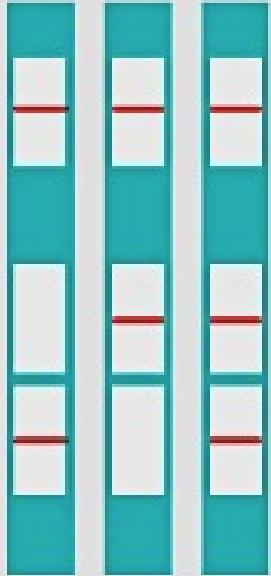

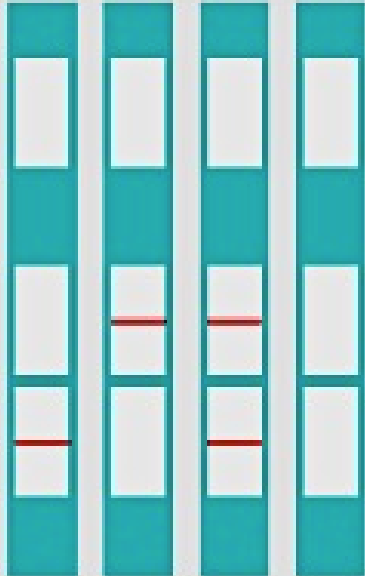
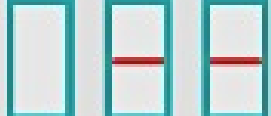


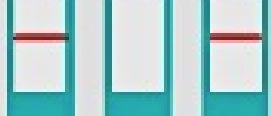

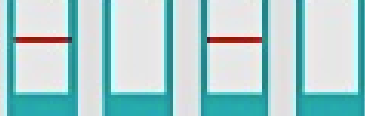


<http://alerehiv.com>

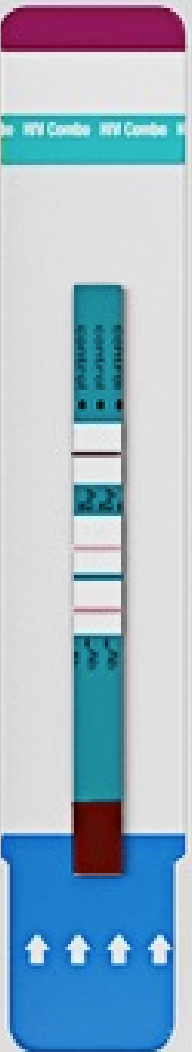
- Whole blood
- Results in 20 minutes
- Long shelf-life, easy to store

Alere Determine™ Combo Rapid Test

Read the results at 20mins to 30mins maximum.

Line	Positive	Negative	Invalid
Control			
Ag			
Ab			

The control line should appear for all results.
If it does not appear, the result is invalid.




Should we use this test?



CONS

- All labs need to be re-trained and certified
- This is the ONLY available Ab/Ag Rapid test
- Using two concurrent rapid tests could yield discordant results more often

- 
- Detect HIV 6-14 days earlier than current tests
 - Easy to use and store; long expiration dates
 - Fast results
 - High specificity (99.23% Ab, 99.66% Ag) and sensitivity (100%)



PROS

Think, Pair, Share!

Switching to the Determine Ab/Ag Combo test at my site would be EASY/HARD because...

I was wondering...

Being able to detect infection earlier IS/IS NOT important because...

I DO/DO NOT trust one rapid test to determine that a participant is negative because...

Multi-spot HIV-1/HIV-2 Test

- Would replace WB testing



- Can be done at site; fast results
- Differentiates between HIV-1 and HIV-2
- Nucleic acid testing (viral load) would still be used to resolve discordant or indeterminate results
- FDA-approved; can test with whole blood

Multi-spot HIV-1/HIV-2 Procedure



Step 1
Remove foil; press prefilter down. Label cartridge and specimen or control test tubes.



Step 2
Add 2 full droppers of Specimen Diluent to each test tube.



Step 3
Add one drop of each sample or control to each labeled tube using a transfer pipette. Mix well.



Step 4
Pour each sample into the prefilter of the labeled cartridge. Wait 2 minutes.



Step 5
Remove and discard prefilter.



Step 6
Fill the central well of each cartridge with Wash Solution.



Step 7
Once absorbed, add 3 drops of Conjugate. Wait 2 minutes.



Step 8
Fill well with Wash Solution and let absorb. Repeat.

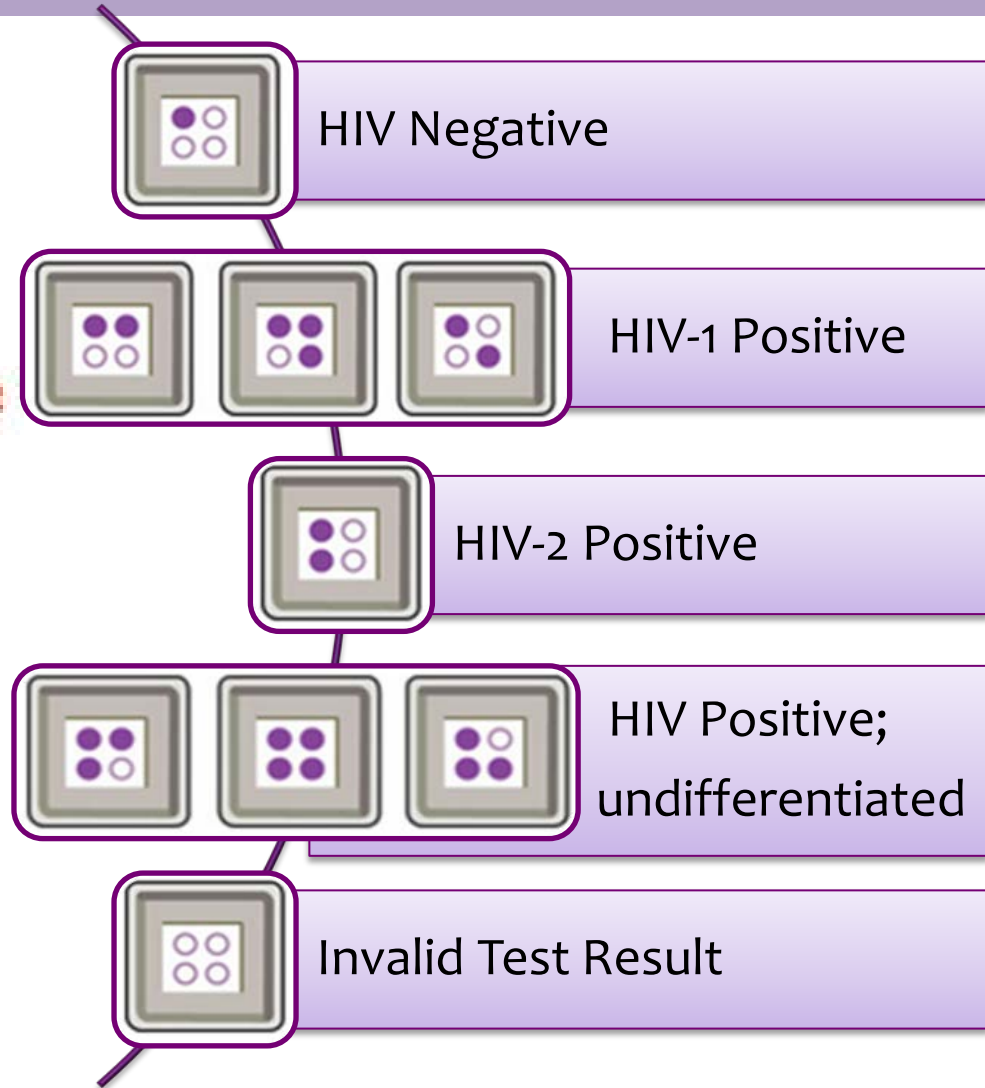
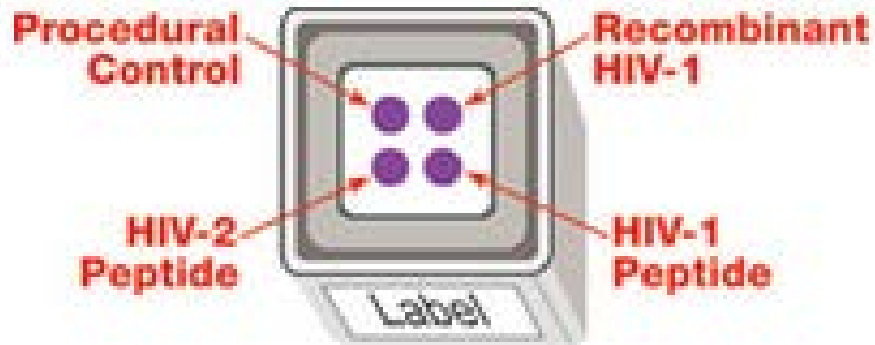


Step 9
Add 3 drops of Development Reagent. Wait 5 minutes.



Step 10
Fill well with Stop Solution. Allow to absorb and read results.

Multi-spot HIV-1/HIV-2 Results



Comparison of Multi-spot and WB


- 8,760 specimens tested positive by EIA and were tested by both WB and Multi-Spot
- Multi-spot was able to...
 - Detect an additional 14 HIV-1 infections
 - Differentiate 26 WB positives as HIV-2 infections
 - Detect an additional 12 HIV-2 infections

Should we use this test?



CONS

- Need to train and certify all testing personnel
- Doesn't provide all the information that WB does

- 
- Confirms HIV infection up to 7 days earlier than WB
 - Not subjective; easy to interpret
 - Point of care test; can be performed at site
 - High specificity and sensitivity (99.95%, 99.40%)
 - CDC Guidelines recommend Multi-Spot over WB



PROS

What would a new algorithm look like?

- If the MTN decides to use the Determine Ab/Ag Combo rapid test and the Multi-spot HIV-1/HIV-2 test, what would the new algorithm look like?
- Let's divide up by site and try to design an algorithm!

Parameters and things to think about...

- A screening test and a confirmation test are needed
- How many blood draws would be taken?
- Would the tests be performed side by side, or one after the other?
- Would Viral Load/DNA-PCR/WB be used? When would they be done?
- Is there a sample 1 and a sample 2?

Next Steps

If we decide to move forward and consider switching to these new tests:

- Virology CORE will compare all new assays to current tests
- the MTN algorithms will be adjusted for future studies

Acknowledgements

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