

# LESSONS LEARNED FROM HPTN 035/HIV CONFIRMATORY TESTING

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# BACKGROUND

Laboratories validated the sensitivity and specificity of the HIV testing algorithm to be used in HPTN 035 prior to the start of the study by testing 100 known (confirmed) HIV positive and 100 known HIV negative samples.

The sensitivity and specificity for the test kits to be used (Abbott Determine, Trinity Biotech Unigold, and OraSure Oraquick) all met manufacturer recommendations.

## HPTN 035 -

- ◉ Review of log sheets and QA by lab for the in-clinic testing was implemented
  
- ◉ QA confirmatory testing by NL

# HPTN 035 PROBLEMS

- ◉ An increase in the number of discordant rapid results was noticed at two sites.
- ◉ Sample 2 not stored
- ◉ WB interpretation was not being performed in a standard fashion across the sites even with one test kit used. Interpretation was correct by techs, changed by reviewer.
- ◉ Incorrect kit used, inappropriate use of QC and kits

**Results:**

Country/Site	# Discordant/ # Tests	% discordant [95% CI]
Blantyre	10/2197	0.5 [0.2, 0.8]
Lilongwe	71/3827	1.9 [1.5, 2.3]
-Before Dec 2006		2.9 [2.1, 3.8]
-Since Dec 2006		1.2 [0.8, 1.7]
South Africa	34/6525	0.5 [0.4, 0.7]
Zambia	1/1357	0.1 [0.0, 0.4]
Zimbabwe	7/2169	0.3 [0.1, 0.7]

- ◉ 123 discordant results have occurred in 64 subjects. The discordancy rate was higher in Lilongwe (71/32, 2.2 cases/subject) than at other sites (52/32, 1.6 cases/subject). The rate dropped significantly after retraining (from 2.9% to 1.2%,  $p < 0.01$ ), but remained higher than the rate in South Africa using the same test kits (1.2% vs. 0.5%,  $p < 0.01$ ). Discordant results occurring after re-training have been verified by the study's central laboratory. In reviewing the data, no particular combination (Unigold +/Determine -, Unigold -/Determine +, Oraquick +/Determine-, or Oraquick -/Determine +) of rapid HIV test kits produced more discordant results.
- ◉ Further testing (including HIV-1 AMPLICOR RNA PCR, Roche Diagnostics, Branchburg NJ) confirmed that most of the 64 subjects with discordant results were HIV-uninfected.

# LESSONS LEARNED

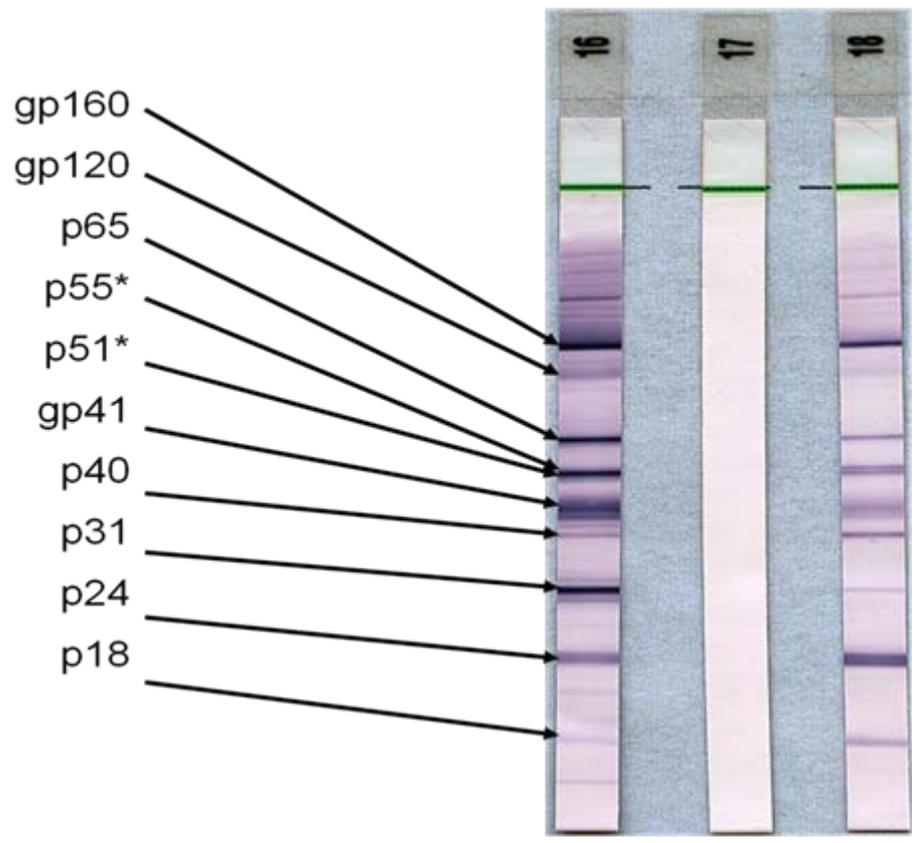
- Attention to increases in discordant rapid results - clinic needs to notify lab
- increase QA
- review competency
- review log sheets
- review lot numbers

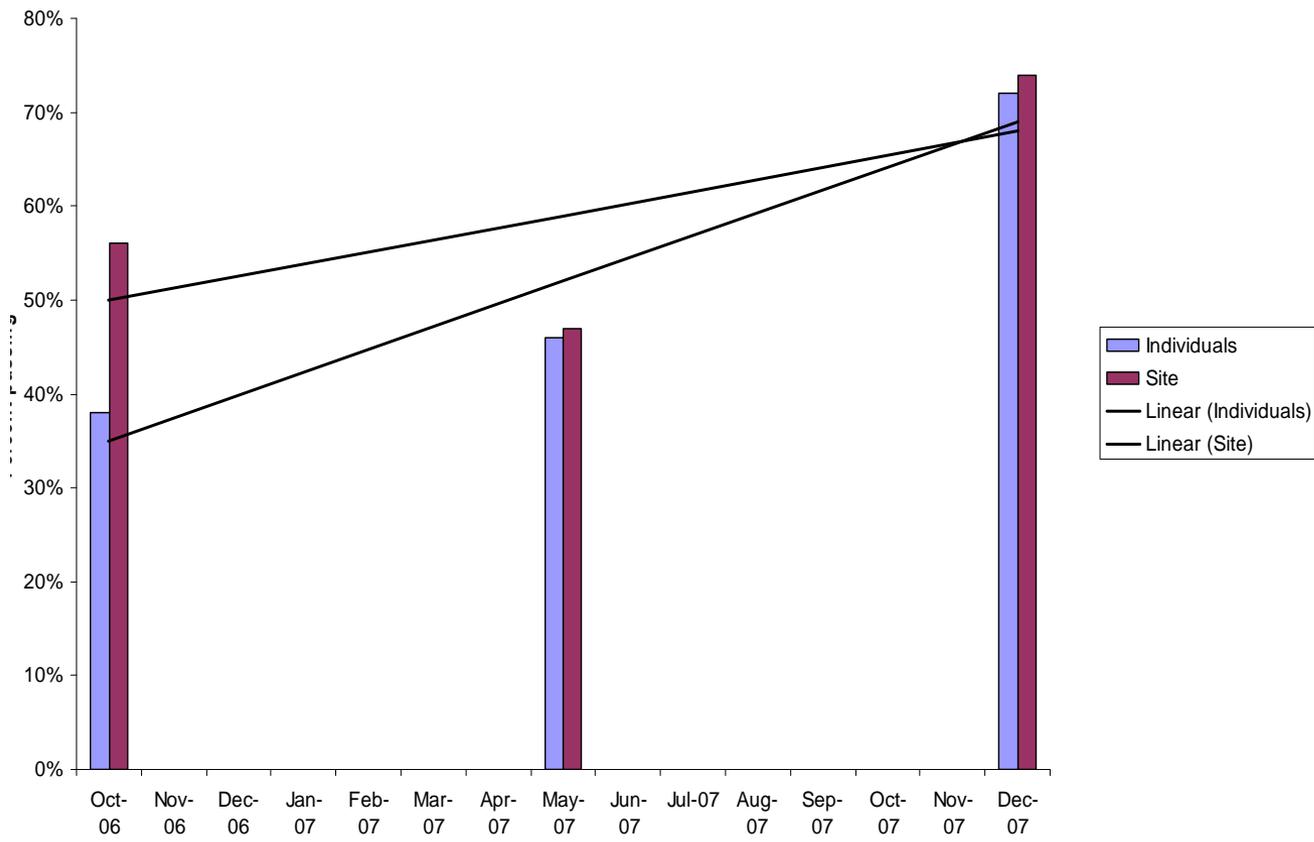
# LESSONS LEARNED

- Review of WB results showed
  - Problem with incorrect kit used
  - Problem with assay procedure (cross contamination, weak staining)
  - Incorrect band calling
  - Incorrect interpretation
  - Incorrect reviewer interpretation
  - Incorrect control blots interpretation

WB On line proficiency panel developed.







# NL QA

- ◉ To date a handful of HIV QA discrepancies between site testing and NL testing.
- ◉ Multiple discordant results on participants goes to the endpoint committee
- ◉ LDMS reconciliations - important in ensuring sample 2 collected and stored
- ◉ Inform NL of any testing problems / concern